Transcriptional regulation in *Salmonella enterica* by the LysR-type factor LeuO

TESIS DOCTORAL

ELENA ESPINOSA ALFARO

Departamento de Genética

Universidad de Sevilla

Transcriptional regulation in *Salmonella enterica* by the LysR-type factor LeuO

Memoria elaborada por Elena Espinosa Alfaro para optar al grado de Doctora en Biología

Tesis realizada bajo la dirección del Dr. Josep Casadesús Pursals, en el Departamento de Genética de la Facultad de Biología de la Universidad de Sevilla

Josep Casadesús Pursals Elena Espinosa Alfaro

CONTENTS

RESUMEN

En *Salmonella enterica* serovar Typhimurium, igual que en el resto de procariotas, el cromosoma se encuentra compactado en una región del citoplasma denominada nucleoide. Esta compactación es debida, en parte, a la presencia de proteínas asociadas al nucleoide (NAPs), entre las cuales destaca H-NS, que además de conferir estructura al cromosoma tiene un papel esencial en la regulación de genes situados en las zonas a las que se une. Dichas zonas poseen un bajo porcentaje de G+C, que es una característica habitual de regiones adquiridas por transferencia horizontal.

H-NS actúa habitualmente reprimiendo la expresión génica. Sin embargo, en determinadas circunstancias los genes reprimidos por H-NS deben ser expresados. Para ello, la célula posee mecanismos para evitar la represión por H-NS, y entre ellos se encuentra la proteína LeuO.

LeuO es una proteína reguladora perteneciente a la familia LysR. En un principio se describió como una proteína implicada en el superenrollamiento del cromosoma y posteriormente se estudió su función reguladora como antagonista de H-NS. En esta Tesis se han caracterizado los sitios de unión de LeuO en el cromosoma de *S*. Typhimurium usando coinmunoprecipitación de cromatina asociada a un chip. Se ha detectado un elevado número de dianas, la mayoría de las cuales son a su vez dianas de la ARN polimerasa. Hay que destacar que, a pesar de que muchos puntos de unión de LeuO coinciden con los de H-NS, corroborando su función como antagonista, se han encontrado numerosas dianas no relacionadas con H-NS, lo que sugiere una función reguladora independiente de H-NS en determinadas circunstancias.

Se detectaron dianas en genes adquiridos por transferencia horizontal. Entre ellos se encontraban genes relacionados con la virulencia, como es el caso de la isla de patogenicidad 1 (SPI-1).

La isla de patogenicidad 1 de *Salmonella* contiene los genes necesarios para invadir el epitelio intestinal. Esta región está sometida a una estricta regulación transcripcional y posttranscripcional. Debido a la presencia de genes de SPI-1 entre las dianas de LeuO, se estudió la implicación de LeuO en la expresión de dichos genes. Mediante aproximaciones genéticas, como análisis de epistasia o escrutinios genéticos, y moleculares, como retardo en gel o análisis de footprinting, se determinó que la represión de SPI1 se realizaba a través de dos vías independientes, siendo una de ellas la activación de la transcripción del represor HilE.

Además, se observó una drástica disminución en la capacidad invasiva de *S*. Typhimurium en condiciones de expresión de LeuO.

S. Typhimurium posee un plásmido de virulencia (pSLT). Este plásmido contiene genes implicados en virulencia (*spv*) necesarios para la infección sistémica en ratones, genes relacionados con la adhesión celular al epitelio intestinal (*pef*) y un operón *tra* que contiene todos los elementos necesarios para la transferencia conjugativa. Tras el análisis de los puntos de unión de LeuO en el cromosoma se realizó una búsqueda de las posibles dianas en pSLT, obteniéndose el mayor número dentro del operón *tra* y observándose una disminución en la frecuencia conjugativa en presencia de LeuO.

Entre las posibles dianas de LeuO se encontraba la región promotora de *finP*, a la que se comprobó que se unía mediante técnicas de retardo en gel. El sistema FinOP o sistema de inhibición de la fertilidad es clave en la regulación de la transferencia conjugativa. En presencia de LeuO aumentaba la expresión de *finP* causando una represión de la transcripción de *tra* y por tanto, inhibiendo la transferencia del plásmido de virulencia mediante conjugación.

INTRODUCTION

I.1. The genus Salmonella

The genus *Salmonella* includes facultative anaerobic, rod-shaped Gram-negative bacteria. Most Salmonellae are motile, express peritrichous flagella and are able to infect a variety of hosts including mammals, birds, reptiles, and amphibians. The genus *Salmonella* belongs to the family *Enterobaceriaceae*, which is classified in the γ-proteobacteria subdivision. *Salmonella* is a close relative of *Escherichia*, *Shigella* and *Citrobacter*.

The genus *Salmonella* includes two species: *S. enterica* and *S. bongori* (Tindall *et al.*, 2005). *S. enterica* is divided in six subspecies (Grimont., 2007): *enterica* (I), *salamae* (II), *arizonae* (IIIa), *diarizonae* (IIIb), *houtenae* (IV) and *indica* (VI). These subspecies are classified into serovars. *Salmonella* serovars are distinguished by antisera that recognize two highly variable surface antigens, the O antigen and the H antigen. Serological differences reflect variations in the exposed part of the lipopolysaccharide and in flagellin, respectively (McQuiston *et al.*, 2004)(Grimont, 2007). More than 2500 serovars have been described (Grimont, 2007).

Salmonella enterica subspecies I, which includes more than 1300 serovars and accounts for the 99% of human *Salmonella* infections, is commonly isolated form birds and mammals (McClelland *et al.*, 2001), whereas *Salmonella bongori* and *Salmonella enterica* subspecies II, IIIa, IIIb, IV and VI are usually associated with cold-blooded vertebrates (Baumler *et al.*, 1998).

Serovars belonging to subsp. *enterica* differ in their host specifity and in the type of disease that they promote. Some serovars are host-restricted (specialists), while others can infect a broad variety of animal hosts (generalists) (Baumler & Fang, 2013). The diseases caused by *Salmonella* vary from gastroenteritis to septicemia, and the outcome of the infection depends on the specific serovar-host combination. An example of specialist is *S*. Typhi, the causing agent of typhoid fever; in contrast, *S*. Typhimurium produces mild gastroenteritis in humans but causes a systemic disease similar to human typhoid fever when infecting mice.

Clinical relevance of Salmonella

S. Typhi causes more than 27 million of cases of typhoid fever worldwide, with 217,000 deaths approximately (Crump & Mintz), whereas *S.* Typhimurium and Enteriditis cause 94 million cases worldwide with 155,000 deaths per year (Majowicz *et al.*) and cause high rates of

bacteremia in immunocompromised patients and, In sub-Saharian Africa, *S.* Typhimurium and Enteriditis cause high rates of bacteremia in immunocompromised patients and in children (Feasey *et al.,* Graham).

I.1.1.Evolution of *Salmonella* pathogenicity

Salmonella and *E. coli* are close relatives but diverged 120-160 million years ago. The acquisition of virulence factors by horizontal gene transfer (HGT) has played a crucial role in *Salmonella* evolution (Ochman & Wilson, 1987, Groisman & Ochman, 1997). Horizontally-acquired genes include pathogenicity islands and prophages which have a low G+C content and are often integrated at tRNA genes (Groisman *et al.*, 1993, Schmidt & Hensel, 2004). Acquisition of plasmids has also contributed to *Salmonella* evolution.

Type III secretion systems (TTSS (acquired by HGT play major roles in *S. enterica* pathogenesis (Hueck, 1998, Pallen *et al.*, 2003). *Salmonella* pathogenicity island 1 (SPI-1) was acquired first, and allowed the pathogen to invade epithelial host cells and induce an inflammatory response (Fig I.1.) (Galan, 2001). The divergence between the two *Salmonella* species was marked by the acquisition of the second pathogenicity island (SPI-2), which promoted the intracellular survival and replication of *S.* Typhimurium (Hensel, 2000) and it is essential for systemic infection in the murine model of typhoid fever (Bispham *et al.*, 2001) (Fig I.1.1).

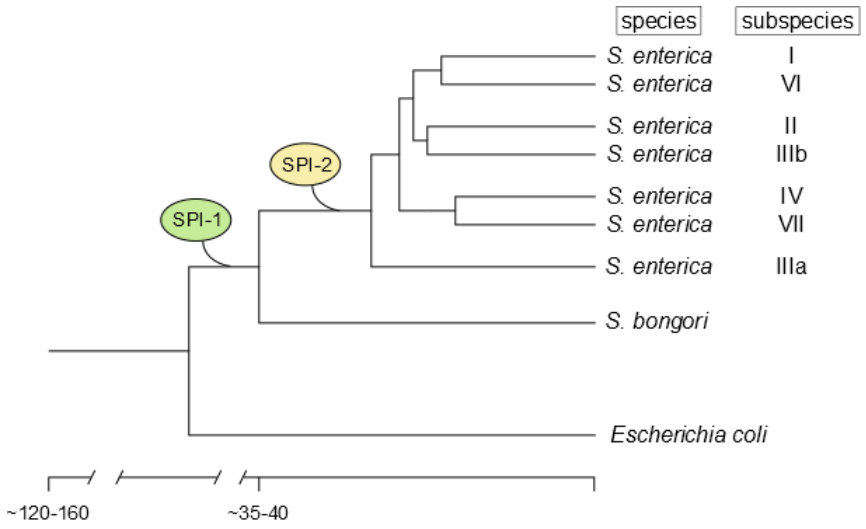


Fig I.1.1. Dendrogram showing phylogenetic relationships among *Salmonella* subspecies. Acquisition of *Salmonella* pathogenicity islands 1 and 2 (SPI-1 and SPI-2), which are highly conserved among all *S. enterica* strains, were key events in the evolution of *Salmonella* spp. The line below the dendrogram represents the time in millions of years. Adapted from Ehrbar and Hardt (Ehrbar & Hardt, 2005).

I.1.3. Virulence of *S.* Typhimurium

Infection by *S*. Typhimurium begins with the ingestion of contaminated food or water by the host. In a first step, *Salmonella* has to overcome the acid pH of the stomach which serves as a barrier to bacterial pathogens. Activation of the acid tolerance response (ATR), which maintains an intracellular pH higher than the extracellular pH, permits *Salmonella* survival in the stomach (Foster & Hall, 1991). In turn, acivation of bile resistance responses permits *Salmonella* survival in the duodenum (Ref.).

Salmonella interaction with the mammalian intestine occurs at the ileum. *Salmonella* adheres to the intestinal epithelium, and invades either M cells of the Peyer's patches or enterocytes (Jones *et al.*, 1994, Takeuchi, 1967) (Fig I.1.2). During invasion there is a profound rearrangement of the eukaryotic cytoskeleton, and these modifications disrupt the epithelial brush border inducing the formation of membrane ruffles that introduce the bacteria inside vesicles called *Salmonella*-containing vacuoles (SCVs) (Finlay *et al.*, 1991, Francis *et al.*, 1993) (Fig I.1.2).

SCVs are integrated in the endocytic pathway, but *Salmonella* induces changes in this pathway avoiding the fusion with the secondary lysosomes (Garcia-del Portillo & Finlay, 1995, Rathman *et al.*, 1997). A process called vacuole-actin polymerization is produced when an F-actin meshwork that is necessary for the maintenance of the integrity of the vacuole membrane is formed around the SVC (Meresse *et al.*, 2001). SVCs migrate to a perinuclear position in the cell, near the Golgi apparatus (Deiwick *et al.*, 2006, Salcedo & Holden, 2003). Furthermore, long filamentous membrane structures called *Salmonella*-induced filaments (SIFs) are formed. These structures are tubular aggregates along a scaffold of microtubules that are originated from the SVC and extend throughout the cell (Garcia-del Portillo *et al.*, 1993, Rajashekar *et al.*, 2008, Knodler *et al.*, 2003).

Some SVCs migrate to the basolateral membrane and transcytose to the intestinal epithelium where *Salmonella* is engulfed by three kinds of phagocytes (neutrophils, macrophages and dendritic cells) that transport bacterial cells to the mesenteric lymph nodes through the intestinal lymph (Fabrega & Vila) (Figure I.1.2). Dendritic cells can also open the tight junction of the epithelial cells, develop dendrites, send them to the lumen and take up bacteria directly from the intestinal lumen (Rescigno, 2006) (Figure I.1.2). Macrophages and neutrophils are recruited in response to inflammatory signals, and phagocytate bacteria integrating them within SVCs following a mechanism similar to that described above (Fabrega

& Vila) (Figure I.1.2). Migration of bacteria inside phagocytes favours the dissemination of *Salmonella* in the host and the development of a systemic infection.

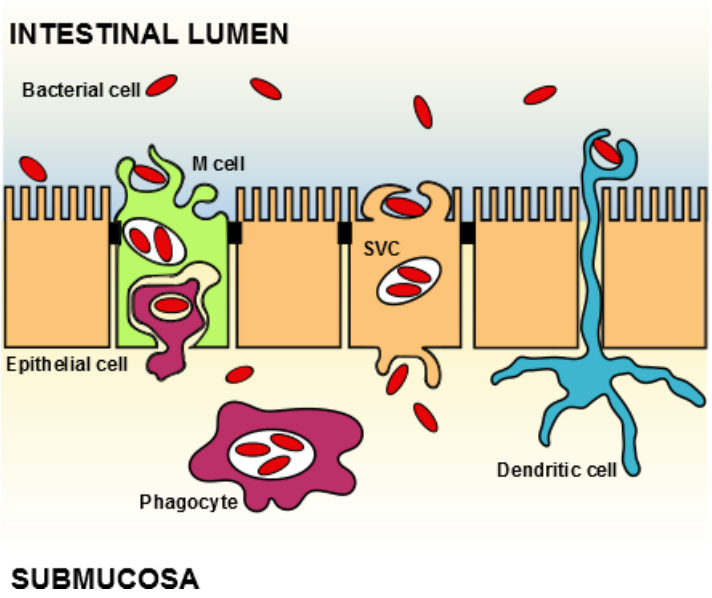


Figure I.1.2. Pathogenesis model of *S*. Typhimurium. Bacterial cells attach to the intestinal epithelium and the invasion process takes place. Alternatively, bacterial cells can be taken up directly by dendritic cells of the submucosa. Once in the cytoplasm, *Salmonella* localizes and replicates inside the SCV. The SCV transcytoses to the basolateral membrane and releases the bacterial cells to the submucosa. Bacteria are internalized within phagocytes and localized again in a SCV and these infected phagocytes can disseminate trough the lymph and the bloodstream. Figure adapted from Fabrega and Vila (Fabrega & Vila).

I.2. Salmonella pathogenicity island 1 (SPI-1)

As described above, the first step in *Salmonella* pathogenesis is the colonization of the intestine and the accession to lymph tissue. This process starts with the invasion of the epithelium, and is mediated by the type three secretion system (TTSS) encoded by *Salmonella* pathogenicity island 1 (SPI-1).

SPI-1 is a 40 kb island of *Salmonella*-specific DNA, localized at centisome 63 on the chromosome (Darwin & Miller, 1999b). SPI1 contains all the genes necessary to produce a functional TTSS apparatus, several secreted effectors and transcriptional regulators like *hilA*, *hilC*, *hilD* and *invF* (Figure I.2.1).

TTSS have been often described as nanosyringes, and are used to inject bacterial effectors into the host cells (Van Engelenburg & Palmer, Marlovits & Stebbins). The secreted effector proteins SipB-A, AvrA and SptP are encoded in SPI-1 (Lostroh & Lee, 2001). Other

effectors like SopB or SopE are encoded outside of SPI-1 on bacteriophages or pathogenicity islets (Wallis & Galyov, 2000).

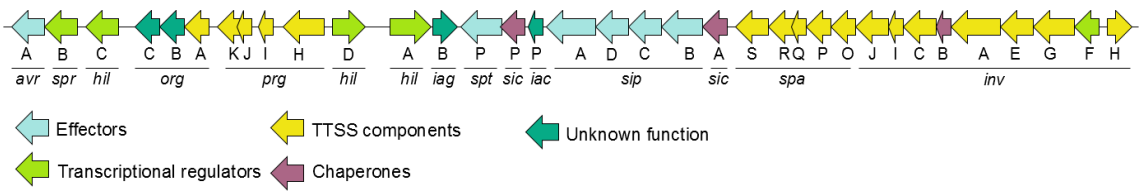


Figure I.2.1. Diagram of TTSS components encoded on SPI-1. The region encoding the operon *sitBCDA* is not shown in the figure. Adapted from Lostroh and Lee (Lostroh & Lee, 2001).

I.3.1. TTSS structure

TTSS is a macromolecular structure composed of a basal body (called inner rod), a needle, and a translocon (Moest & Meresse) (Figure I.3.2).

The basal body is composed by three different structures: an inner ring made of 24 subunits of PrgK and PrgH, a neck that spans the periplasmic space and an outer ring. The neck and outer ring are composed of 15 units of InvG (Moest & Meresse) (Figure I.3.2). Linked to the basal body there is a cytosolic complex necessary to make the structure functional.

The needle is composed of PrgI protein units that assemble spontaneously on the basal body and grow to the distal end as a flagellar filament. The needle is linked to the inner rod through PrgJ protein that, in turn, controls the length of the needle. The tip of the needle, formed by 5 molecules of SipD, interacts with PrgI (Moest & Meresse) (Figure I.3.2).

Translocation of effector proteins is a multistep process. Effectors are delivered form the bacterial cytosol through the TTSS to the eukaryotic host cell, and this secretion is promoted by an ATPase.

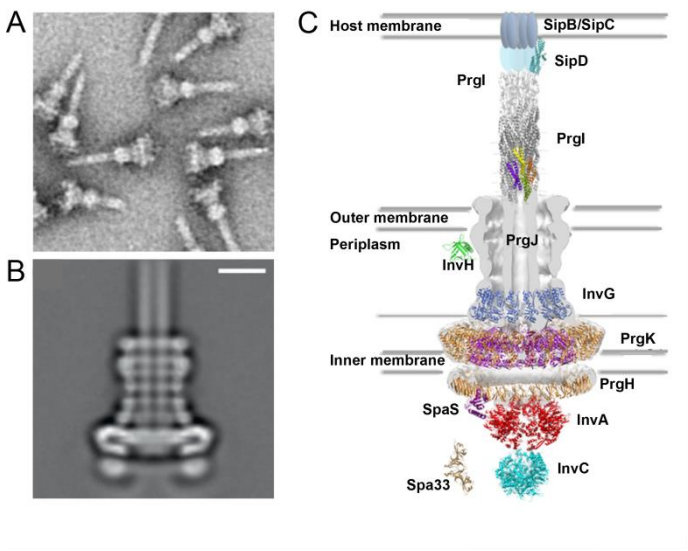


Fig I.3.2. TTSS-1 structure. A. Electron microscopy picture of the needle complex. B. Picture of a class-average from cyro-electron microscopy of a *Salmonella* TTSS-1. Scale bar: 10 nm Photo: Thomas C. Marlovits (Moest & Meresse) C. Diagram of a TTSS (Burkinshaw & Strynadka).

I.3.2 SPI-1 main regulators

Salmonella pathogenicity island 1 is essential to inject effector proteins inside the host cell by forming the needle-like structure described above. SPI-1 expression is tightly regulated by five main regulators that form a feed-forward regulatory loop, and by additional regulators encoded outside of SPI-1.

HilA

HilA is transcriptional regulator belonging to the OmpR/ToxR family (Bajaj *et al.*, 1995). It is encoded inside SPI-1 and activates directly or indirectly most SPI-1 genes. HilA binds *prgH* and *invF* promoters, and activates the transcription of these operons and the *sic/sip* operon as well (Figure I.3.4.).

HilA has a revelant role in SPI-1 expression, as indicated by the fact that mutations in *hilA* cause a drastic decrease in the invasion of M cells and in mouse virulence (Bajaj et al., 1995, Penheiter *et al.*, 1997). Due to this relevant role in infection, *hilA* is subjected to a strict regulation by many different regulators. It is positively activated by the SPI-1 regulators HilD, HilC and RtsA, and it is negatively regulated by H-NS, Hha, PhoPQ and Fnr (Queiroz *et al.,* Fahlen *et al.*, 2001, Bajaj *et al.*, 1996, Fink *et al.*, 2007) (Figure I.3.4.).

InvF

InvF is an AraC/XylS-like transcriptional activator that is required for efficient invasion of cultured epithelial cells (Kaniga *et al.*, 1994, Darwin & Miller, 1999a). InvF is the first???? open reading frame of SPI-1 gene cluster (Kaniga et al., 1994), and it is required, in conjunction with the chaperone SicA (Darwin & Miller, 1999a, Darwin & Miller, 2001), for the expression of *sic/sip* operons by directly binding to *sicA* promoter. InvF also activates the expression of effectors encoded outside of SPI-1 such as SopB, SopE and the effector SptP (Darwin & Miller, 1999a, Darwin & Miller, 2001, Eichelberg & Galan, 1999) (Figure I.3.4.). Expression of *invF* is activated by HilA (Lostroh *et al.*, 2000) and by HilD and HilC (Akbar *et al.*, 2003).

HilD

HilD is as an AraC/XylS-like protein, is encoded in SPI-1, and it has been described as one of the most important regulators of SPI-1. HilD positively regulates SPI-1 expression at different levels. HilD is able to regulate expression of the SPI- 1 regulators *hilA*, *hilC*, *invF* and *rtsA* by binding upstream their promoters (Schechter & Lee, 2001, Olekhnovich & Kadner, 2002, Akbar et al., 2003) (Figure I.3.4.) Synthesis of HilD is subjected to tight regulation at transcriptional and posttranscriptional levels. At the transcriptional level, *hilD* is regulated by the SPI-1 regulators RtsA and HilC- However, HilD is able to bind to its own promoter and to induce transcription independently of the presence of other regulators (Ellermeier *et al.*, 2005, Olekhnovich & Kadner, 2002) (Figure I.3.3).

At the postranscriptional level, the 3' UTR of *hilD* mRNA, which is unusually long, has a critical role in *hilD* mRNA stability. It has been proposed that the *hilD* 3' UTR is a target for the Hfq chaperone and the degradosome (Lopez-Garrido *et al.*). HilD translation is regulated by FliZ, SirA, StdEF and by an unknown mechanism under Dam methylation control (Lopez-Garrido & Casadesus, Lopez-Garrido & Casadesus, Chubiz *et al.,* Teplitski *et al.*, 2003). HilD activity is negatively regulated by HilE, a protein that interferes with HilD, and by the Lon protease that degrades HilD (Takaya *et al.*, 2005, Baxter *et al.*, 2003) (Figure I.3.4.).

HilD activity is not restricted to SPI-1 regulation; in addition, crosstalk between SPI-1 and SPI-2 connects both islands. HilD controls transcription of *ssrAB*, the two-regulatory component system of SPI-2 (Bustamante *et al.*, 2008). HilD activates also transcription *flhDC*, the flagellar master operon, which is essential for *Salmonella* motility (Singer *et al.*). Recently, novel HilD targets have been described, many of them outside SPI-1 (Petrone *et al.*).

HilC

HilC is an AraC/XylS-like transcriptional regulator encoded in SPI-1. HilC binds upstream the promoters of *hilD*, *hilA*, *invF* and its own promoter, activating SPI-1 expression. HilC and HilD may recognize the same DNA binding regions (Olekhnovich & Kadner, 2002). HilC is also positively regulated by HilD and RtsA (Ellermeier et al., 2005, Ellermeier & Slauch, 2003). At the protein level is known that Lon protease degrades HilC (Takaya et al., 2005) (Figure I.3.4.).

RtsA

RtsA belongs to the AraC/XylS family transcriptional regulators and is homologous to HilC and HilD. The *rtsA* gene forms part of an operon with two transcriptional regulators, *rtsAB*, localized in a 15 Kb island near the $tRNA^{PheU}$ (Ellermeier & Slauch, 2003). RtsA regulates SPI-1 by activating the *hilA* and *invF* promoters, whereas RtsB represses *flhDC* promoter expression (Ellermeier & Slauch, 2003) (Figure I.3.4.).

Like the other SPI-1 transcriptional regulators described above, RtsA is part of the SPI-1 feed-forward loop. RtsA activates its own transcription as well as transcription of *hilC* and *hilD*, and is regulated by HilC and HilD, sharing with these proteins the binding site in the *rtsA* promoter (Olekhnovich & Kadner, 2007).

I.3.3 Other regulators of SPI-1

Transcriptional regulators:

-H-NS and Hha

H-NS is a global regulator that binds A+T regions (Lucchini *et al.*, 2006, Dorman, 2007, Navarre *et al.*, 2006). HhA is a low molecular weight protein that plays a role in bacterial gene regulation acting together with H-NS in a protein complex (Madrid *et al.*, 2007). H-NS and Hha are negative regulators of SPI-1. H-NS and Hha downregulate SPI-1 expression by binding the *hilA* and *rtsA* promoters (Fahlen et al., 2001, Olekhnovich & Kadner, 2006, Olekhnovich & Kadner, 2007, Queiroz et al.) (Figure I.3.4.).

- Fur

The iron-responsive regulator Fur is required for systemic infection in mice (Troxell *et al.*). Fur binds to a divalent cation (mainly Fe^{2+}) and then binds to DNA to directly repress downstream genes (Kadner, 2005). In SPI-1, Fur-mediated regulation is carried out through H-NS. Fur binds the H-NS promoter, inhibiting its expression and thereby activating SPI-1 expression (Troxell et al.).

- Fis

Fis is a nucleoid-associated protein involved in DNA replication, recombination, and transcription. Fis modulates DNA topology in a growth phase-dependent manner (Finkel & Johnson, 1993). Fis activates SPI-1 expression, and a *fis* mutant is attenuated upon mouse infection (Wilson *et al.*, 2001) (Figure I.3.4.).

- PhoPQ

The PhoPQ two-component system regulates SPI-1 expression (Figure I.3.4.). Low extracellular cation concentrations and acid pH activates the sensor kinase PhoQ, which activates the regulator PhoP (Garcia Vescovi *et al.*, 1996). Activated PhoP represses SPI-1 through *hilA* (Golubeva *et al.*), and activates the transcription of *pag* genes which, in turn down-regulate *hilA* expression (Lucas & Lee, 2001, Boddicker *et al.*, 2003).

- Fnr

In *E. coli*, transition from aerobic to anaerobic environments and *vice versa* involve changes in the expression of a large number of genes. The global anaerobic regulator Fnr is a DNA-binding protein that senses O_2 concentrations and controls the expression of multiple genes (Fink et al., 2007). In *S*. Typhimurium, Fnr activates SPI-1 transcription, and is essential for invasion in the mouse model (Fink et al., 2007).

Post-transcriptional regulators:

- Dam and StdEF

Deoxyadenosil methyltransferases are common in bacteria (Cheng, 1995). DNA adenine methylase (Dam) methylates adenine at 5'-GATC-3' sites by postreplicative modification (Marinus & Morris, 1973). Dam provides signals to initiate chromosome replication (Messer *et al.*, 1985), to direct chromosome segregation (Ogden *et al.*, 1988) and to

target the daughter strand for mismatch repair (Glickman *et al.*, 1978). Due to its multiple roles, Dam methylation is an important factor in cellular welfare, and its loss causes pleiotropic defects (McGraw & Marinus, 1980, Peterson & Mount, 1987, Torreblanca & Casadesus, 1996, Pucciarelli *et al.*, 2002, Prieto *et al.*, 2004) and impairs virulence in mouse model (Heithoff *et al.*, 1999, Garcia-Del Portillo *et al.*, 1999). Dam is also involved in the regulation of gene expression (Balbontin *et al.*, 2006). Dam-regulated genes can be classified into two classes: genes whose expression is coupled to the cell cycle and genes whose expression is controlled by Dam methylation patterns (combinations of methylated and nonmethylated GATC sites).

Dam activates SPI-1 expression by upregulating *hilD* at the posttrancriptional level (Lopez-Garrido & Casadesus). Dam-mediated regulation of SPI-1 turns out to be indirect: Dam methylation represses the *std* fimbrial operon, and two products of this operon (StdE and StdF) repress SPI-1 (Lopez-Garrido & Casadesus) (Figure I.3.4.).

- FliZ

FliZ is a posttranscriptional regulator that positively regulates SPI-1 expression at the level of HilD protein. A *fliZ* mutant is attenuated in the mouse model of *Salmonella* infection (Chubiz et al.).

- SirA

SirA/BarA is a two-component system that activates SPI-1 expression by both direct and indirect mechanisms. SirA directly activates SPI-1 expression binding to *hilA* and *hilC* promoters and activating transcription of these genes (Altier *et al.*, 2000, Johnston *et al.*, 1996, Teplitski et al., 2003). Indirectly, SirA regulates SPI-1 through CsrA (Teplitski et al., 2003).

CsrA is a posttranscriptional regulator that alters the stability of its target mRNAs, and it has been described as a positive or a negative regulator depending upon its target (Liu & Romeo, 1997, Liu *et al.*, 1995, Baker *et al.*, 2002, Teplitski et al., 2003, Wei *et al.*, 2001, Romeo *et al.*, 1993). The Csr system comprises two additional untranslated regulatory RNA molecules, CsrB and CsrC. It has been proposed that CsrB and CsrC bind to CsrA titrating it from its targets (Liu *et al.*, 1997, Weilbacher *et al.*, 2003). Otherwise, it has been proposed that CsrA itself regulates *csrB* and *csrC* expression (Fortune *et al.*, 2006).

SirA can bind the *csrB* promoter, and SirA/BarA can activate *csrB* and *csrC* expression (Teplitski et al., 2003, Fortune et al., 2006). CsrB and CsrC bind and titrate CsrA (Fortune et al., 2006). The reduction in free CsrA leads to the induction of SPI-1 genes, although the direct

target, or targets, of CsrA in the invasion pathways are not known (Altier et al., 2000, Fortune et al., 2006) (Figure I.3.4.).

- Lon and DnaK

The ATP-protease Lon and the DnaK chaperone have been described to regulate SPI-1 expression. Lon protease reduces SPI-1 expression by degrading HilC and HilD, whereas DnaK negatively regulates *lon* expression increasing invasion (Takaya et al., 2005, Takaya *et al.*, 2004)(Fifure I.3.4.).

- HilE

HilE negatively regulates SPI-1 activity, and repression requires HilD. A *hilE* strain has invasion rates higher than the wild type (Boddicker et al., 2003, Fahlen *et al.*, 2000). The *hilE* gene maps at centisome 98, and the region has characteristics of a pathogenicity island: it is located near a $tRNA^{Leu}$ and has a low G+C content, 48.1% (Baxter et al., 2003).

HilE downregulates SPI-1 at the posttranscriptional level. Two-hybrid analysis indicates that HilE interacts with the HilD protein (Baxter et al., 2003) (Figure I.3.4.).

HilE is regulated at the transcriptional and posttranscriptional level. At the transcriptional level, *hilE* transcription is regulated by FimZ and MIc (Baxter & Jones, 2005, Lim *et al.*, 2007). FimZ is a transcriptional regulator encoded in the *fim* gene cluster that contains all the components of the type I fimbriae involved in invasion of intestinal epithelial cells (Tavendale *et al.*, 1983). MIc is a global regulator of carbohydrate metabolism that controls genes involved in sugar utilization (Lee *et al.*, 2000, Nam *et al.*, 2001). Expression of *hilE* is driven by three different promoters: P1, whose transcriptional start site is located at position -55; P2, located at -160 position; and P3, located at -335 position from the ATG. To activate *hilE* expression, FimZ binds the P2 promoter, whereas MIc binds the P3 promoter and represses transcription (Baxter & Jones, 2005, Lim et al., 2007) (Figure I.3.3).

At the posttranscriptional level, *hilE* is regulated by IsrM, a pathogenicity island-specific sRNA which binds to *hilE* mRNA and downregulates its expression (Gong *et al.*). An additional target of this sRNA is *sopA* mRNA (Gong et al.).

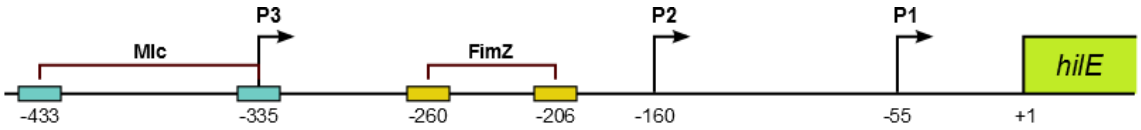


Fig I.3.3. Diagram of the locations of *hilE* promoters and binding sites of FimZ and MIc. The numbers are relative to *hilE* translational start site. The arrows indicate the transcriptional start sites of P1 (-55), P2 (-160) and P3 (-335). Binding sites for FimZ and MIc are shown by yellow and blue boxes, respectively. Numbers below boxes indicate the center of the binding sites. Modified from Lim *et al*. (Lim et al., 2007).

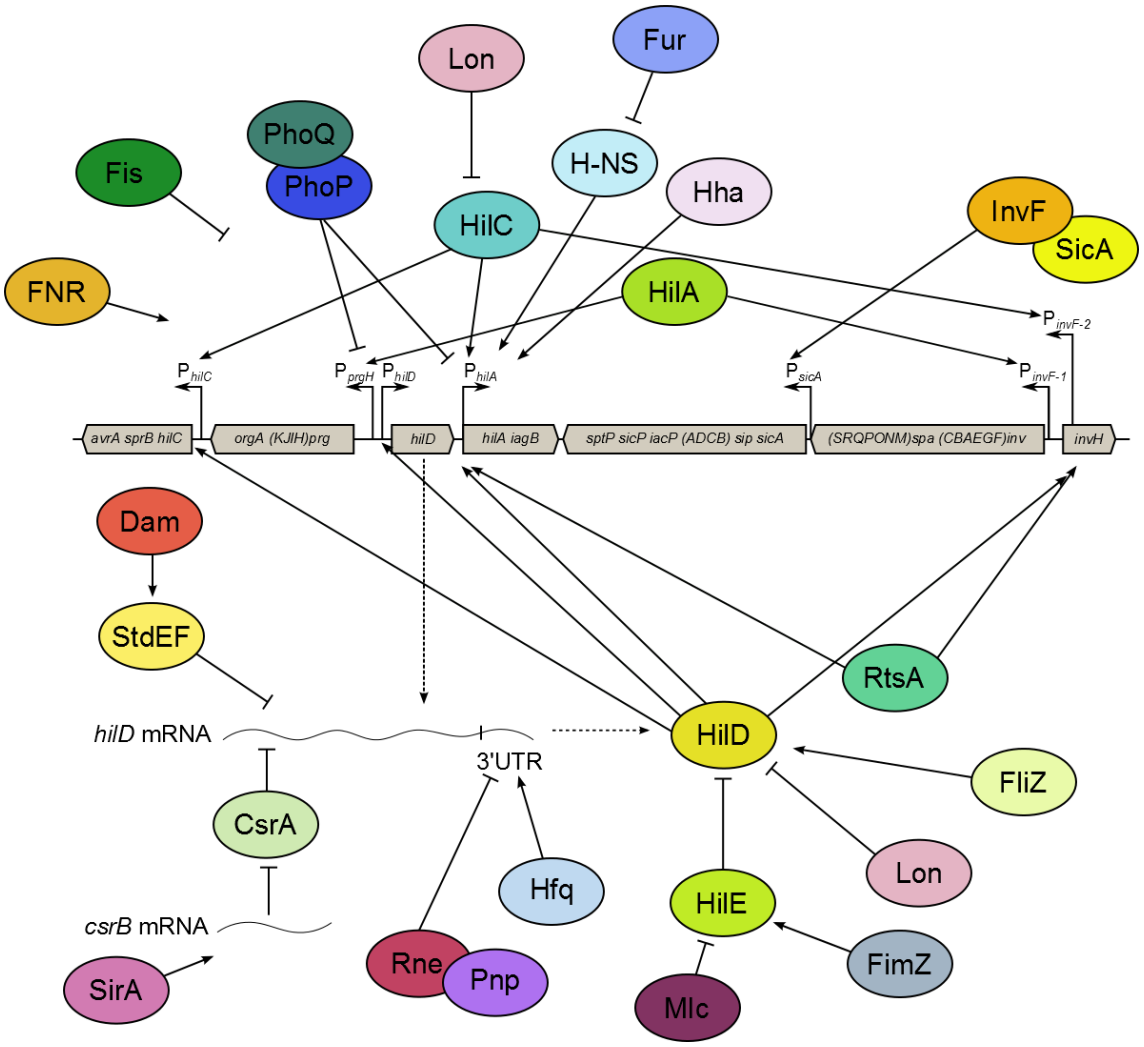


Figure I.3.4. Diagram of the regulatory network of SPI-1. Positive effects are indicated by lines ending in arrowheads, whereas blunt lines indicate negative regulatory effects.

I.4. The *Salmonella enterica* virulence plasmid

In *E. coli*, *Shigella*, *Yersinia* or *Salmonella*, certain virulence factors responsible for pathogenicity are encoded on plasmids. In *Salmonella,* plasmids have been found only in a few serovars belonging to the subspecies I. These serotypes are also among those most frequently associated with disease in homeothermic vertebrates. These plasmids are 50 to 90 Kb in size, and have been called "serovar-specific plasmids" (Rotger & Casadesus, 1999). These plasmids are usually very stable, and are present in the cell in a low copy number (1-2 copies per chromosome).

In *S*. Typhimurium LT2, virulence plasmid was described by Dowman y Meynell and was designated as pSLT by Jones et al. (Dowman & Meynell, 1970, Jones *et al.*, 1982). Although *S*. Typhimurium virulence plasmid had a complete *tra* operon it was previously described as a mobilizable but not self-transmissible plasmid (Jones et al., 1982, Ou *et al.*, 1990, Sanderson *et al.*, 1983), however, Ahmer et al. showed that pSLT of 14028 and LT2 were self-transmissible (Ahmer *et al.*, 1999), and Garcia-Quintanilla and Casadesus demonstrated it in SL1344 (Garcia-Quintanilla & Casadesus).

The virulence plasmid of *S. enterica* contains a 7.8 Kb region called *spv* (*Salmonella* plasmid virulence) required for the systemic phase of disease (Gulig *et al.*, 1993). The distribution of the *spv* operon in *S. enterica* subspecies I suggests that this operon was acquired by horizontal transfer (Boyd & Hartl, 1998). The presence of *tra* operons (complete or incomplete) in most virulence plasmids suggests that a *Salmonella* ancestor acquired the virulence plasmid by conjugation, and that divergence has occurred during the evolution of serovars (Rotger & Casadesus, 1999). For instance, the virulence plasmids of *S. enterica* serotypes Enteritidis and Choleraesuis can be considered variants of the virulence plasmid of *S*. Typhimurium, generated by deletion events upon divergence from a common ancestor (Baumler et al., 1998) (Figure I.4.1.). Even though virulence plasmids play a role in pathogenesis, plasmid-cured strains are able to colonize and persist in the spleen and the liver.

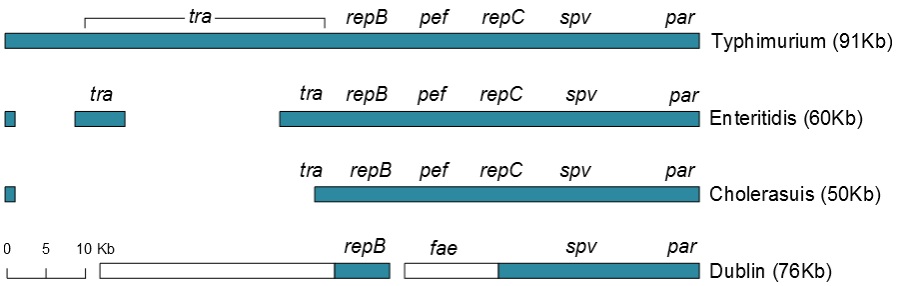


Figure I.4.1. Linear genetic maps of virulence plasmids of *S. enterica* subspecies I serotypes. Regions of homology are shown in blue. Areas of the plasmid of *S. enterica* serotype Dublin that are not present in *S. enterica* serotype Typhimurium are shown as open bars. Adapted from Baumler *et al*. (Baumler et al., 1998).

Other pSLT loci involved in virulence include the *pef* (plasmid-encoded fimbriae) locus, which is involved in bacterial adhesion to intestinal epithelial cells (Baumler *et al.*, 1996), and the *srg* region which includes the *rck* (resistance to complement killing) gene. The Rck product confers high level-serum resistance.

I.4.1. The transfer region of the *Salmonella enterica* virulence plasmid

Conjugation is a process in which a donor cell elaborates a conjugative pilus that identifies a recipient cell, retracts, and brings the two cells in close contact. Plasmid DNA is then transferred to the recipient cell through the mating pore, converted to double-strand DNA, recircularized, and established in the recipient cell. Genes encoded in the transfer region (*tra*) are involved in pilus biogenesis, mating pair stabilization, DNA transfer, and surface exclusion.

The *Salmonella* virulence plasmid is conjugative in many strains (Ahmer et al., 1999). In mice, pSLT is transferred at high frequencies, and mating occurs in the ileum, the distal portion of the small intestine (Garcia-Quintanilla *et al.*, 2008). Virulence plasmid transfer in the ileum may compensate for plasmid loss during intestinal passage. This view is consistent with the fact that bile salts, which have plasmid curing capacity (Garcia-Quintanilla *et al.*, 2006), are found at high concentrations in the mammalian intestine, especially in the duodenum (Hofmann, 1998).

The *tra* region of pSLT contains several transcriptional unitis. The P_{traM} and P_{traJ} promoters are located near the origin of transfer (*oriT*) and regulate transcription of *traM* and *traJ,* respectively. P_{traY} is located upstream *traY,* and regulates the expression of a multicistronic operon of approximately 30 Kb. Additional promoters P_{trbF}, P_{traS}, P_{traT} and P_{traD} are located within this operon. In the opposite direction there are two promoters, P_{finP} and P_{artA} (Zatyka, 1998) (Figure I.4.2).

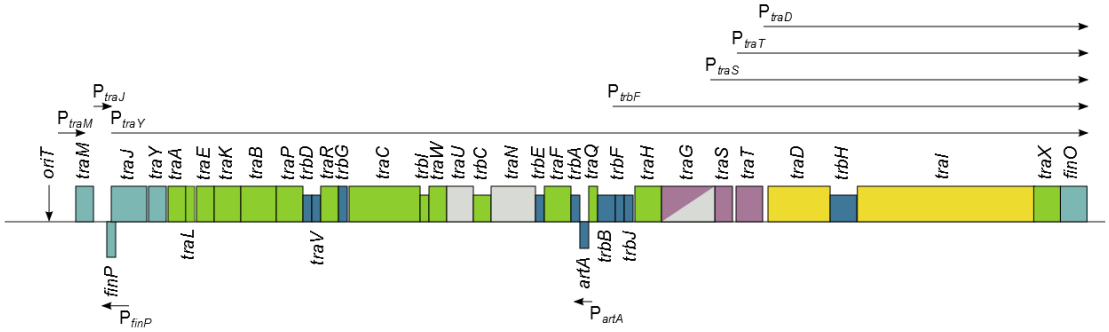


Figure I.4.2. Diagram of the F-plasmid transfer region. Arrows denote transcripts initiated at the indicated promoters. The functional class associated with a particular gene is indicated by the color: green, pilus biogenesis; violet, surface or entry exclusion; grey, mating-aggregate stabilization; blue, regulation; yellow, nicking and initiation of the DNA transfer; dark blue, unknown function.

The pSLT-encoded pilus is a thick flexible structure involved in mating pair formation (Mpf), pilus retraction and mating pair stabilization (Mps). Conjugative pili are composed of one repeating subunit, pilin, encoded by the *traA* gene, arranged in a helical filament. Pili are assembled in the inner membrane, and assembly is dependent on the TraC ATPase. Pilin is encoded as propilin (*traA*) and is processed in the inner membrane by the leader peptidase I (LepB). The pilin N-terminus is then acetylated by TraX.

I.4.2. Regulation of the *tra* operon

Regulation of *tra* operon expression is complex, and involves regulatory proteins encoded on both the plasmid and the host chromosome. Many features of *tra* regulation in pSLT are also found in the F sex factor and in other F-like plasmids.

TraJ

TraJ is a transcriptional activator of the *tra* operon, and acts at the main promoter, P_{traY} (Finnegan & Willetts, 1972, Frost *et al.*, 1994). TraJ contains a helix-turn-helix (HTH) DNA-binding site and a PAS (Per ARNT Sim) domain. This kind of domain, first identified in Drosophila proteins PER and ARNT, is found in many eukaryotic and prokaryotic proteins, and usually plays a sensor role. The HTH domain seems to be essential for TraJ binding to DNA cognate sites (Rodriguez-Maillard *et al.*). The PAS domain may be involved in binding transient metals (Arutyunov *et al.*). TraJ acts as a homodimer and the PAS domain plays a role in protein stability (Arutyunov et al., Rodriguez-Maillard et al.).

The FinOP system

In F-like plasmids, the FinOP fertility inhibition system controls conjugation at post-transcriptional level. In F, *finP* encodes a 79 nt antisense RNA that is complementary to the 5' untranslated region of *traJ* mRNA (Mullineaux & Willetts, 1985, Dempsey, 1987, Finlay *et al.*, 1986). The FinP structure consists of two stem loops (SLI and SLII), separated by a short, four base single-stranded region (van Biesen *et al.*, 1993). In turn, *traJ* mRNA contains a sequence of 105 nucleotides that forms three stem-loops, called SLIc, SLIIc and SLIII (van Biesen et al., 1993) (Figure I.4.3.B).

The ribosome binding site (RBS) of *traJ* is located in SLIc. FinP binds to *traJ* mRNA SLIc region sequestering its RBS and preventing its translation (Koraimann *et al.*, 1996), the duplex FinP/*traJ* mRNA formed is then rapidly degraded by the RNase III (Jerome *et al.*, 1999)(Figure I.4.3.B).

FinO is a chaperone that contributes to repression of conjugal transfer by FinP (Arthur *et al.*, 2003), in F, the *finO* gene is interrupted by an IS3 element, causing constitutive transfer (Cheah & Skurray, 1986, Yoshioka *et al.*, 1987). FinO binds FinP and *traJ* mRNA, stabilizing FinP against degradation (Lee *et al.*, 1992, Jerome et al., 1999) and promoting duplex formation between the complementary RNA molecules (van Biesen & Frost, 1994).

FinO binds FinP preventing its degradation by RNase E (Jerome et al., 1999) and allowing the FinP concentration to increase to sufficient levels to mediate *traJ* repression- The requirement of FinO can be alleviated by providing FinP at elevated concentrations in the cell (Lee et al., 1992, Frost *et al.*, 1989, Koraimann *et al.*, 1991, Koraimann et al., 1996) Figure I.4.3.A).

Eight different alleles of *finP* have been described among F plasmids, and the highest variability is found in the loops (Frost et al., 1994, Finlay et al., 1986, Jerome & Frost, 1999). The loop sequences of FinP and *traJ* mRNA are thought to be the responsible of the plasmid specificity (Koraimann et al., 1991, Koraimann et al., 1996) and could be the initial site of interaction between the sense and antisense RNAs. Despite the variations in the FinP loop sequences of different F-like plasmids, a common motif has been described, 5'-YUNR-3', where Y is a pyrimide, N is any base and R is a purine (Frost et al., 1994). This short RNA motif is a key structural element in the loops of many antisense RNA molecules (Franch *et al.*, 1999).

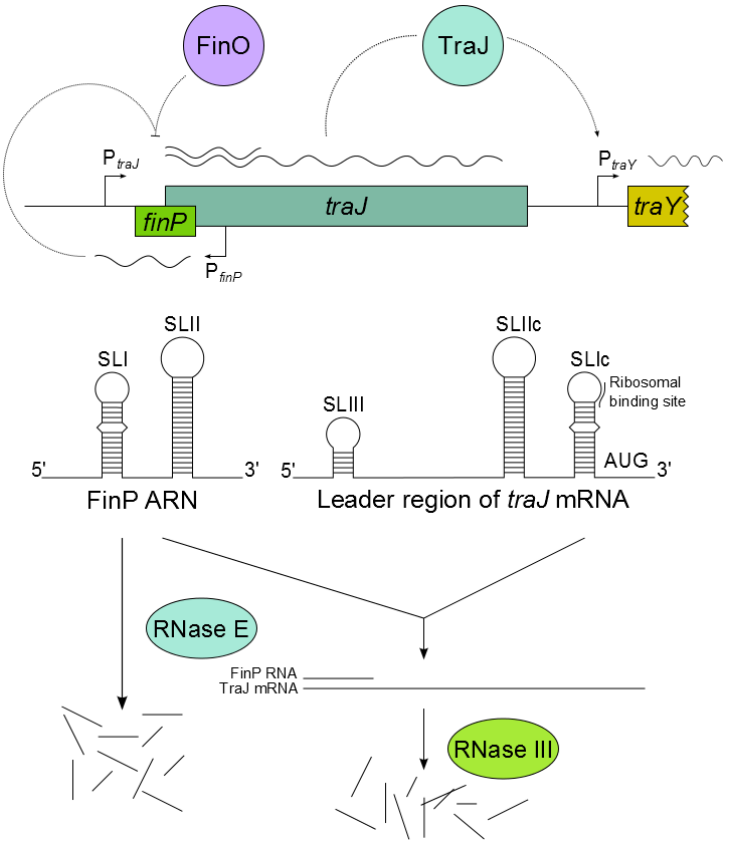


Figure I.4.3 Regulation by the fertility-inhibition system. A. Diagram of the system. Wave-shaped lines represent RNA molecules. Promoter positions and transcription are indicated by straight arrows. Arrows denote activation and blunt lines denote inhibition. B. Secondary structure diagram of FinP RNA and the leader region of *traJ* mRNA. Endonuclease E (RNase E) cleaves FinP, whereas endoribonuclease III (RNase III) degrades the duplex FinP-*traJ* mRNA.

TraY

TraY is encoded by the promoter-proximal gene protein of the *tra* operon. TraY is a DNA-binding protein that regulates transcription from the P_{traM} and P_{traY} promoters, by binding oriT and P_{traY} regions (Penfold *et al.*, 1996, Silverman & Sholl, 1996, Stockwell *et al.*, 2000) (Figure I.4.4). In F, TraY binds to its own promoter activating transcription (Penfold *et al.*, 1996, Silverman & Sholl, 1996), whereas in R100 the binding of TraY to P_{traY} represses it (Inamoto & Ohtsubo, 1990, Nelson *et al.*, 1993, Penfold et al., 1996, Silverman & Sholl, 1996, Stockwell et al., 2000). On the other hand, TraY acts as a positive regulator of *traM* transcription in F, R1 and R100 (Penfold et al., 1996, Stockwell et al., 2000).

TraM

TraM has two different roles in conjugal transfer of F-like plasmids. During conjugation, TraM is essential for nicking and unwinding the plasmid DNA. In addition, TraM binds its own promoter and undergoes autogenous repression of transcription (Figure I.4.4).

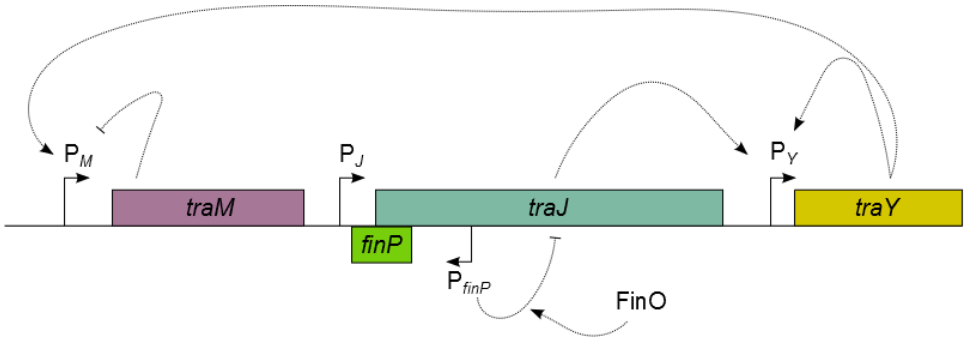


Figure I.4.4. Diagram of the regulatory circuit of the F-like tra region. Positive effects are indicated by lines ending in arrowheads, whereas blunt lines indicate negative regulatory effects. P_{traM}, P_{traJ}, P_{traY} and P_{finP} indicate the *traM*, *traJ*, *tray* and *finP* promoters respectively. Adapted from Gubbins *et al* (Gubbins *et al.*, 2002).

Host-encoded regulators

Host-encoded factors involved in mating and pili synthesis include the global regulators ArcA, IHF, H-NS, Crp, Lrp, GroEL and Hfq, the metabolism-related factors Cpx, FlhDC, FruR, GcvA or Sdh, and DNA modification (Dam methylation).

- ArcA

ArcA is the response regulator of a system involved in sensing the redox state of a bacterial cell and allows adaptation to changes in O_2 concentration. The sensor kinase of this two-component system is AcrB, which phosphorylates AcrA in response to microaerobiosis (Lynch & Lin, 1996). Approximately 120 operons are regulated directly or indirectly by AcrAB (Liu & De Wulf, 2004). AcrA was previously described as a gene required for expression of F-like plasmids (Beutin & Achtman, 1979). In the F sex factor, ArcA and TraJ are required for P_{traY} activation (Silverman *et al.*, 1991) (Figure I.4.5.). In pSLT, ArcA regulates conjugation by two different mechanisms. In aerobiosis, ArcA seems to activate P_{traY} expression in an AcrB independent manner, whereas in microaerobiosis the sensor kinase AcrB is necessary for activation (Serna *et al.*). ArcA binds upstream the P_{traY} promoter, and the binding site is conserved among F-like plasmids (Serna et al., Strohmaier *et al.*, 1998, Silverman et al., 1991).

- IHF

Integration host factor (IHF) is a nucleoid-associated protein (NAP) that binds multiple DNA targets, acting as a transcription factor for many genes in *E. coli* (Grainger *et al.*, 2006). IHF bends DNA sharply, and often regulates transcription in conjunction with other NAPs and transcription factors (Browning *et al.*).

In F, IHF forms part of the relaxosome with the TraY and TraI proteins (Howard *et al.*, 1995) and these three components of the relaxosome are required for the nicking reaction *in vitro* (Nelson *et al.*, 1995). IHF binds to two different sites in F *oriT* (Tsai *et al.*, 1990) and enhances the cleaving activity of TraI in vitro (Inamoto *et al.*, 1994, Nelson et al., 1995)(Figure I.4.5.).

- H-NS

Regulation of conjugation carried by H-NS was first described in the F-like plasmid pRK100 in which H-NS acts as an activator of *traJ* expression (Starcic-Erjavec *et al.*, 2003). However, H-NS acts as a strong repressor of *traJ* and *traM* expression in F (Will *et al.*, 2004) by binding to P_{traJ} and P_{traM} promoters (Will et al., 2004). H-NS also binds to intrinsically curved DNA at P_{traY} downregulating transcription from this promoter (Will & Frost, 2006a, Will & Frost, 2006b, Wagner *et al.*)(Figure I.4.5.). In pSLT, it has been reported that H-NS represses transcription of both *traJ* and *finP* (Camacho *et al.*, 2005, Will & Frost, 2006a).

- Lrp

The leucine-responsive regulatory protein (LRP) is a bacterial global regulator that can act as an activator and as a repressor. In pSLT, Lrp positively regulates conjugation by activating *traJ* transcription (Camacho & Casadesus, 2002). The *traJ* upstream activating sequence (UAS) contains two Lrp binding sites, LRP-1 and LRP-2, and Lrp binding two both sites is necessary for *traJ* transcription. LRP-2 contains a GATC site whose methylation state influences Lrp binding (Camacho & Casadesus, 2002, Torreblanca *et al.*, 1999). If the GATC is methylated in both strands, Lrp is unable to bind to LRP-2 with an appropriate pattern, and *traJ* expression is prevented. When the plasmid replicates and the *traJ* UAS becomes hemimethylated, Lrp can bind to both LRP-1 and LPR-2, and activates *traJ* expression (Camacho & Casadesus, 2005)(Figure I.4.5.). Activation may occur in one of the plasmid daughter molecules only (Camacho & Casadesus, 2005).

- Hfq

Hfq (host factor required for phage Qβ RNA replication) is a chaperone that has a role in stability, translation, and RNA bacteriophage replication, often by interacting with small RNAs (Valentin-Hansen *et al.*, 2004, Gottesman, 2004). Hfq preferentially binds regions of AU-rich RNA, flanked by structured regions (Moller *et al.*, 2002, Zhang *et al.*, 2002). In F, Hfq binds to the intergenic UTR, 3' to *traM* and 5' to *traJ,* decreasing the stability of transcripts containing this region (Will & Frost, 2006b)(Figure I.4.5.). However, Hfq does not appear to be involved in fertility inhibition and has no role in FinOP-mediated repression. Hfq appears to act as a repressor of TraJ and TraM synthesis by desestabilizing the corresponding transcripts (Will & Frost, 2006b).

- Cpx

The CpxAR two-component system senses envelope stress and responds to this signal via a phosphotransfer reaction. The stress signal is transferred from the CpxA sensor kinase to CpxR. Once phosphorylated, CpxR binds to its target promoters at a consensus sequence (Pogliano *et al.*, 1997, Weber & Silverman, 1988, De Wulf *et al.*, 1999)(Hoch 1995).

The *cpx* (conjugative plasmid expression) regulon was firstly identified by the effects of *cpx* mutations on conjugation. Namely, *cpxA** gain-of-function mutations caused a decrease in conjugation due to the absence of pili in the cell surface (McEwen & Silverman, 1980b, McEwen & Silverman, 1980a). Regulation is indirect: Under stress conditions, the CpxAR

system promote degradation of the transcriptional activator TraJ via the HslVU protease (Lau-Wong *et al.*, 2008)(Figure I.4.5.).

- Sdh

Succinate dehydrogenase catalyses the oxidation of succinate to fumarate in the tricarboxylic acid cycle (Hederstedt & Rutberg, 1981) (ackrell 1992). Expression of *sdhCDAB* is regulated in response to oxygen availability and by the composition of the growth medium (Iuchi *et al.*, 1994, Park & Gunsalus, 1995). ArcA binds to the *sdhCDAB* promoter and represses its expression especially under anaerobic conditions (Shen & Gunsalus, 1997). In rich medium *sdhCDAB* inhibits pSLT conjugation, probably by an indirect manner. It has been proposed that ArcAB may regulate conjugation by activating *tra* operon expression and by repressing *sdhCDBA* (Serna et al.)(Figure I.4.5.).

- Dam methylation

Dam methylation represses the pSLT *tra* operon (Torreblanca et al., 1999), a phenomenon also observed in other F-like plasmids such as F and R100 (Torreblanca et al., 1999, Camacho & Casadesus, 2005). As described above, Dam regulation downregulates traJ expression by inhibiting Lrp binding to the UAS in the absence of plasmid replication. In addition, Dam methylation relieves H-NS-mediated repression of the *finP* promoter by an unknown mechanism (Camacho et al., 2005).

- GroEL and CRP

Other host-components that have been described as regulators of F-like plasmids conjugation are the cAMP receptor protein, which positively regulates *traJ* expression (Starcic *et al.*, 2003)m and the heat shock chaperone GroEL, which downregulates R1 conjugation by degrading TraJ upon heat shock (Zahrl *et al.*, 2007)(Figure I.4.5.).

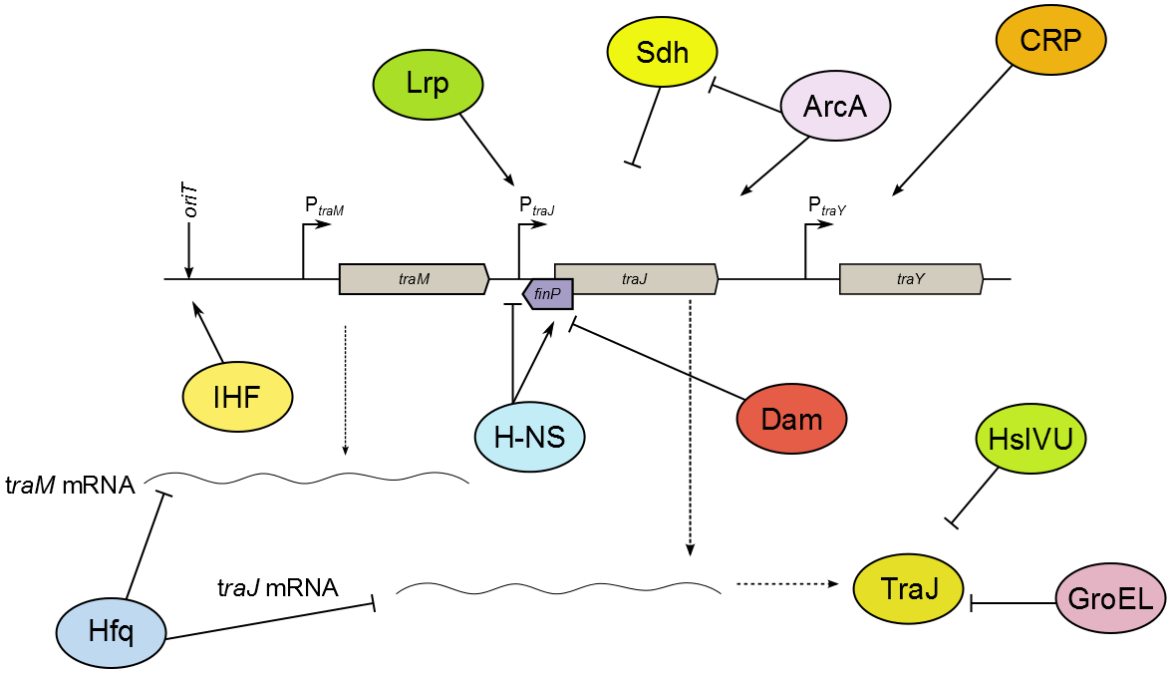


Figure I.4.5. Schematic representation of the plasmid regulatory circuit of F *tra* region. Positive effects are indicated by lines ending in arrowheads, whereas blunt lines indicate negative regulatory effects.

Appendix 1

Transcriptional silencing and anti-silencing in *Salmonella* by nucleoid-associated proteins and LysR-type transcriptional regulators

A.1. Nucleoid-associated proteins

In prokaryotes, the genome is not surrounded by a nuclear membrane; it is located in the cytoplasm in a region called nucleoid. In the nucleoid, the bacterial chromosome is subjected to compaction by a combination of factors including molecular crowding, DNA polymer dynamics, supercoiling and interaction of the DNA with other molecules such as nucleoid-associated protein (NAPs) (Pelletier *et al.,* Dillon & Dorman, de Vries). In addition to participate in conferring structure to the DNA, supercoiling and NAPs regulate gene expression.

NAPs are proteins with low-molecular mass whose monomeric subunits can dimerize or oligomerize. NAPs bind to the DNA, altering the DNA structure by bending, wrapping or bridging it, helping to maintain the appropriate level of chromosome supercoiling depending on the different environmental conditions (Tupper *et al.*, 1994, Zhang *et al.*, 1996, Dame, 2005, Travers & Muskhelishvili, 2005). NAPs have also an important role regulating transcription in a positive and negative manner (Dillon & Dorman).

A.2. H-NS

H-NS is a protein of 15 KDa that is present in approximately 20,000 copies per genome equivalent, is widely represented in Gram-negative bacteria (Dorman, 2007) and has a key role in bacterial gene regulation due to ability to bind DNA and RNA (Brescia *et al.*, 2004). H-NS silences the expression of target genes and plays also a role in DNA compaction. H-NS is highly expressed and is detectable at a constant level throughout the growth cycle.

Horizontal gene transfer is a mechanism that increases bacterial genetic variability. In enteric bacteria, regions that have been acquired recently in evolution have the common characteristic of a low G+C content, and H-NS represses preferentially these regions (Lucchini et al., 2006, Dorman, 2007, Navarre *et al.*, 2007). In *S*. Typhimurium, H-NS binds preferentially to A+T rich regions preventing gene expression (Lucchini et al., 2006, Navarre et al., 2006). In *E.*

coli, H-NS regulates almost the 5% of the genome, repressing more than 80% of horizontally-acquired genes (Hommais *et al.*, 2001).

The mechanisms by which H-NS represses transcription have been extensively studied. First, H-NS binds to intrinsically curved DNA at the promoter to be regulated (Dame *et al.*, 2001, Rimsky *et al.*, 2001). Second, repression is carried out by the formation of a loop closed by two patches of H-NS, inside which RNA polymerase is trapped, or by blocking binding of RNA polymerase to the promoter inhibiting transcription elongation (Schroder & Wagner, 2000, Dame *et al.*, 2002, Prosseda *et al.*, 2004).

A nucleic acid-binding domain in the H-NS carboxyl-terminal region is responsible for the recognition of intrinsically curved DNA. In turn, the N-terminal domain is a dimerization domain that has the capacity to form oligomers, possibly through the flexible linker domain that connects the DNA binding domain with the dimerization domain (Dorman, 2004, Rimsky, 2004). At low concentrations, H-NS exists as a dimer, but at higher concentrations or when bound at promoters, H-NS can multimerize into tetramers or oligomers, and this multimerization seems to be a requisite for its silencing function (Navarre et al., 2007). H-NS binds forming bridges between adjacents helices of DNA and also can polymerize along the DNA (Dame, 2005, Dame et al., 2001, Dame *et al.*, 2000, Dame et al., 2002, Dame & Wuite, 2003) (Figure I.2.1).

H-NS-like proteins share a domain structure organization and are able to form heterodimers and oligomers (Dorman *et al.*, 1999). A relevant H-NS homologue of enteric bacteria that can interact with H-NS is HhA (Paytubi *et al.*, 2004, Nieto *et al.*, 2002, Johansson & Uhlin, 1999). Hha is generally belived to modulate the DNA-binding and nucleoid-organizing properties of H-NS by forming heteromeric complexes H-NS-Hha-DNA (Madrid et al., 2007, Madrid *et al.*, 2002, Nieto *et al.*, 2000). StpA is an H-NS paralogue that partially compensates *hns* inactivation and is able to form heterodimeric complexes with H-NS (Deighan *et al.*, 2000, Shi & Bennett, 1994, Williams *et al.*, 1996, Leonard *et al.*, 2009).

Although the silencing of horizontally-acquired genes by H-NS may have selective value by avoiding inappropriate expression thereby reducing concomitant fitness costs, H-NS-repressed genes are expressed under specific conditions. Hence, the bacterial cell must possess mechanisms to counteract transcriptional silencing by H-NS. One such mechanism involves the LysR-like protein LeuO (Navarre et al., 2007, Stoebel *et al.*, 2008, Stratmann *et al.*, 2008, De la Cruz *et al.*, 2007, Shimada *et al.*).

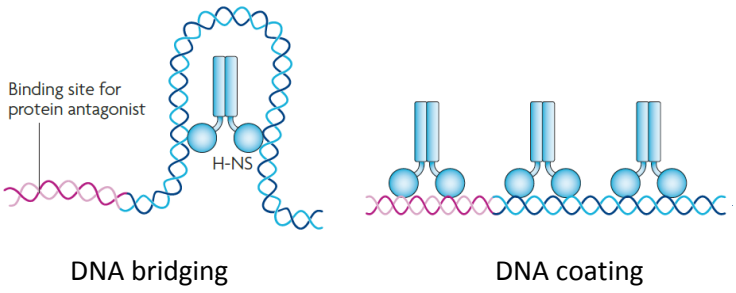


Fig I.2.1. DNA binding modes of nucleoid-associated proteins. H-NS binds to DNA and influences its structure. This binding can result in DNA bridging (left), in which protein binds to two sites that are further apart and causes the DNA between them to form a loop or in DNA coating (right), in which the protein binds to two sites that are close together or the same strand. Picture adapted from Dillon and Dorman (Dillon & Dorman).

A.3. LTTR transcriptional regulators

LysR-type transcriptional regulators (LTTRs) are the most abundant family protein in the prokaryotic kingdom. LTTRs are highly conserved and ubiquitous among bacteria. Genes that encode LTTRs have a characteristically high G+C content due to a distinct Lys/Arg ratio (Maddocks & Oyston, 2008).

Members of this family have been described as global transcriptional regulators acting either as activators or as repressors. The presence of a co-inducer is often necessary to carry out their function; the co-inducer can be a product or an intermediate of a metabolic/synthesis pathway (Heroven & Dersch, 2006, Hernandez-Lucas *et al.*, 2008).

A typical LTTR is made of approximately 330 aminoacids. The C-terminus domain is a co-factor binding domain and the N-terminus is a helix-turn-helix motif that binds DNA. LTTRs proteins are usually tetramers (dimers of dimers). Each dimer comprises two subunits a DNA-binding domain and a regulatory domain joined by a linker region each one (Maddocks & Oyston, 2008).

The LTTR-binding DNA sequence, called LTTR box, is a palindromic sequence, and often forms part of an imperfect, dyadic region. The sequence presents the consensus T-N_{11}-A, but can vary in both base pair composition and length. LTTRs can cause DNA bending between 50° to 100°, and this bending is often determined by the presence of the co-inducer (Maddocks & Oyston, 2008). LTTR expression is often subjected to autoregulation, and the regulatory

binding site of the genes contains an LTTR-box, suggesting that this is the recognition sequence for autoregulation.

A.4. LeuO

LeuO is a LysR-type transcriptional regulator. The *leuO* gene is located at the intergenic region between the *ilvIH* and *leuABCD* operons, and is divergently transcribed with respect to the *leuABDC* operon (Figure I.2.2). This region is highly conserved among *Enterobacteriaceae* and it has been studied in *E. coli*, *Salmonella*, *Yersinia enterocolitica* and *Vibrio cholerae.* LeuO was firstly described as a regulator implicated in DNA supercoiling, and later as an H-NS antagonist (Fang & Wu, 1998a, Hernandez-Lucas et al., 2008, Shimada et al., Stratmann *et al.*).

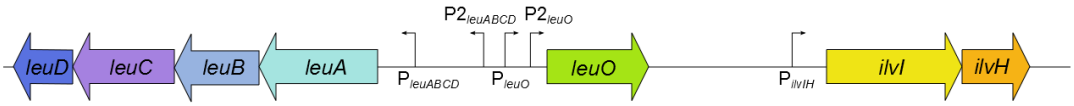


Figure I.2.2. Chromosomal location of *leuO* gene. Diagram adapted from Stratmann *et al*.(Stratmann et al.).

LeuO expression

Natural conditions that permit *leuO* expression remain unclear. In *E. coli* it was proposed to be expressed under stress conditions in stationary phase, and this expression was supposed to be guanosine 3',5'-bispyrophosphate (ppGpp) dependent (Fang *et al.*, 2000). Activation of *leuO* expression has been also described under phosphorous restriction in *E. coli* (VanBogelen *et al.*, 1996). In turn, Shimada *et al*., reported that *leuO* expression in *E. coli* increases after one week of incubation at 37° C, whereas *hns* expression decreases as days pass by (Shimada et al.). *In vivo*, evidence exists that *Salmonella* may express *leuO* during infection of *C. elegans* and of mice (Tenor *et al.*, 2004, Lawley *et al.*, 2006).

LeuO self-regulation

The gene cluster *ilvIH-leuO-leuABCD* has a complex regulation, in which H-NS and LeuO pkay an important role (Fang & Wu, 1998a, Chen *et al.*, 2003, Chen & Wu, 2005, Stratmann et al.). The interest of the scientific community in this gene cluster is mainly due to the role carried out by supercoiling in transcription of the promoters in the region. Initially, it was

found that in *S*. Typhimurium a point mutation in the *leu* promoter (*leu-500*) rendered the promoter inactive, but this effect was suppressed in a *topA* (topoisomerase I) mutant, suggesting that the *leu-500* promoter was supercoiling sensitive (Margolin *et al.*, 1985, Pruss & Drlica, 1985, Richardson *et al.*, 1988, Lilley & Higgins, 1991, Chen *et al.*, 1992, Chen *et al.*, 1994, Tan *et al.*, 1994). Later, it was shown that *leu-500* promoter activation depends on transcription of the *ilvIH* operon and of the *leuO* gene, suggesting that topoisomerase acts over the 1.9 kb region in the chromosome, and that a supercoiling relay mechanism that activates *ilvIH* results in an activation of *leuO* and finally of *leuABCD* (Wu *et al.*, 1995, Fang & Wu, 1998a, Fang & Wu, 1998b, Wu & Fang, 2003). Two additional models of regulation have been proposed, one based in H-NS repression and LeuO derepression and another based in H-NS silencing and RcsB-BglJ activation (Chen *et al.*, 2005, Chen et al., 2003, Chen & Wu, 2005, Stratmann et al.).

The model proposed by Chen *et al*., is based in H-NS silencing and LeuO derepression, in which regulation by LeuO and H-NS is dependent on the presence of two regions called locus control regions (LCRs) with a high A+T content. LCR-I is located between the *leuABCD* and *leuO* promoters, and comprises three different regions called AT3, AT8 and AT7 (Figure I.2.3). The AT3 and AT7 regions contain a LeuO binding site, whereas AT8 is called a silencer and is a target for H-NS protein. LCR-II is located upstream the *ilvIH* promoter and harbours a weak LeuO binding site (Figure I.2.3). In this model of regulation, AT8 is a silencer region to which H-NS binds forming a filament avoiding gene transcription. Under de-repressing conditions, LeuO binds to AT7 and to the LeuO binding site in LCR-II forming a DNA loop which blocks H-NS filament spreading and permits *leuO* transcription (Figure I.2.3.A.). This model also proposes that LeuO binds with lower affinity to AT3 forming a DNA small loop, avoiding H-NS binding to the silencer region and leading to *leuO* transcription (Figure I.2.3.C.). On the other hand, if LeuO binds the AT3 and LCR-II regions, H-NS can bind to the AT8 spread along *leuO* promoter avoiding *leuO* transcription (Chen & Wu, 2005) (Figure I.2.3.B.).

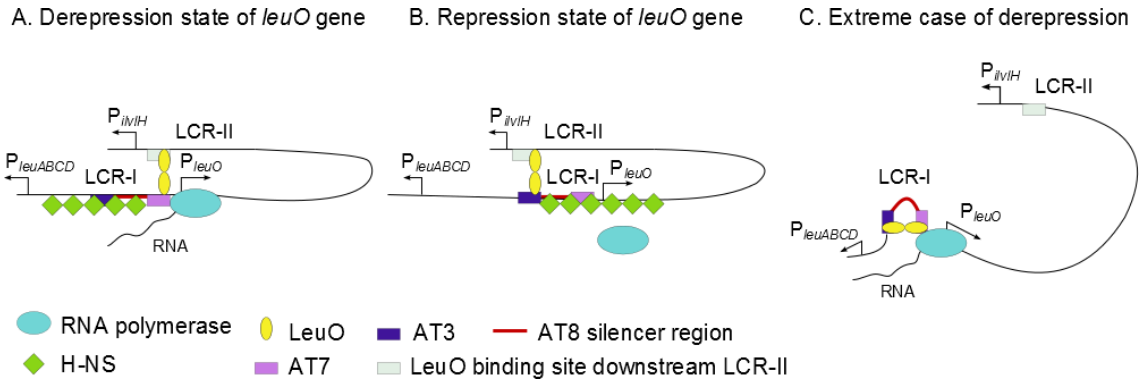


Figure I.2.3 Model of Chen *et al*. of *leuO* regulation by DNA looping-mediated LeuO-LeuO interaction. A. LeuO interacts with AT7 and LCR-II avoiding H-NS spreading and leading *leuO* transcription. B. LeuO interacts with AT3 and LCR-II leading H-NS spreading and avoiding *leuO* transcription. C. LeuO interacts with AT3 and AT7 avoiding H-NS binding to the silencer region and its repression, leading *leuO* transcription. Adapted from Chen and Wu (Chen & Wu, 2005).

The model proposed by Stratmann *et al*., is based upon H-NS silencing of the *ilvIH-leuO-leuABCD* gene cluster in conjuction with StpA, activation by the RcsB-BglJ heterodimer, and autorepression by LeuO. RcsB is a transcription factor that is the response regulator of the Rcs two-component phosphorelay system that senses perturbations of the outer membrane and the peptidoglycan layer (Majdalani & Gottesman, 2005). BglJ is a transcription factor that activates *bgl* operon expression (Venkatesh *et al.*). Stratmann *et al*., have described in *E. coli* the presence of two new promoters in the intergenic region between *leuABCD* and *leuO*. One of them, $P2_{leuO}$, is located 149 bp downstream P_{leuO}, previously described by Fang and Wu (Fang & Wu, 1998a). $P2_{leu}$ is located 289 bp upstream P_{leu} (Wessler & Calvo, 1981) (Figure I.2.4). In this model, it is proposed that H-NS or StpA act as silencers by binding at the intergenic region between $P2_{leuO}$ and P_{leuO}. Transcription can be activated by binding of BcsB-BglJ upstream P_{leuO} avoiding H-NS spreading. Under these conditions, LeuO can act as a weak activator. However, when the LeuO concentration is very high, it can act as a strong repressor of its own transcription (Stratmann et al.) (Figure I.2.4).

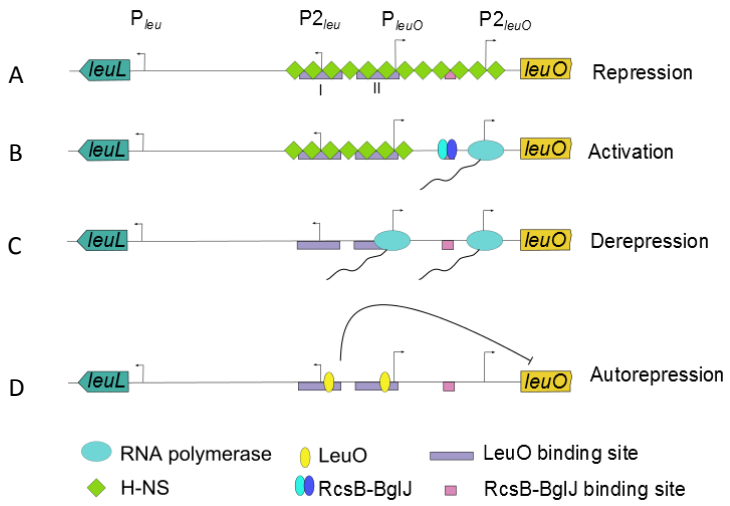


Figure I.2.4. Model of Stramann *et al*, of *leuO* regulation. A. Under standard laboratory conditions transcription is repressed by H-NS and/or StpA. B. Transcription can be activated by binding of RscB-BglJ upstream $P2_{leuO}$ promoter and avoiding H-NS/StpA spreading. C. Derepression of *leuO* expression in absence of H-NS, StpA and RcsB-BglJ, in this case RNAP can access both P_{leuO} and $P2_{leuO}$. C. In case of high concentration of LeuO, it may bind to the two central LeuO binding sites causing repression of the $P2_{leu}$ and P_{leuO} promoters and in addition of $P2_{leuO}$ promoter, acting in this case as an autorepressor. Modified from Stratmann *et al*. (Stratmann et al.).

Physiological roles of LeuO

LeuO was originally identified in *Salmonella* as an activator of the *leuABCD* leucine biosynthesis operon (Hertzberg *et al.*, 1980). LeuO also activates the *bglGFB* operon, implicated in β-glucoside utilization (Ueguchi *et al.*, 1998), and the LuxR-type transcriptional factors *yjjQ-bglJ* that regulate the *bgl* operon (Stratmann et al., 2008). LeuO also activates the expression of the outer membrane quiescent porins OmpS1 and OmpS2, which are implicated in *Salmonella* virulence in the mouse model (Fernandez-Mora *et al.*, 2004, De la Cruz et al., 2007, Hernandez-Lucas et al., 2008, Lawley et al., 2006, Rodriguez-Morales *et al.*, 2006). On the other hand, LeuO represses thr *cadCBA* operon, implicated in lysine decarboxylation (Shi & Bennett, 1995) and the *dsrA* gene that encodes an sRNA involved in translational control of *rpoS* and *hns* (Klauck *et al.*, 1997, Repoila & Gottesman, 2003).

LeuO also regulates the expression of CRISPR regions (Clustered Regularly Interspaced Short Palindromic Repeats) and *cas* genes (CRISPR associated genes). CRISPR form an immune system that uses sRNA to target mobile genetic elements. These regions are repeated sequences of approximately 30 nucleotides that are separated by unique sequences of similar

size, called spacers, that are commonly derived from phages and plasmids (Mojica *et al.*, 2000, Bolotin *et al.*, 2005, Mojica *et al.*, 2005, Pourcel *et al.*, 2005). The presence of a spacer that matches to a viral or plasmid sequence confers resistance to invasion by these elements (Barrangou *et al.*, 2007, Brouns *et al.*, 2008, Marraffini & Sontheimer, 2008). CRISPR are transcribed as a large mRNA which is cleaved by a Cas endonuclease at the repeat sequences generating small transcripts (crRNA) that are used by the Cas proteins to target exogenous genetic material, leading to their degradation (Brouns et al., 2008, Carte *et al.*, 2008, Haurwitz *et al.,* Garneau *et al.,* Marraffini & Sontheimer, Hale *et al.*, 2009). H-NS binds with high affinity upstream *cas* promoter and represses its expression (Pul *et al.*), LeuO acts as an antagonist binding to the same region, avoiding H-NS spreading and permitting RNA polymerase binding and operon transcription (Westra *et al.,* Medina-Aparicio *et al.*).

In *E. coli* it has been described that LeuO binds upstream genes with a wide variety of functions (Shimada *et al.*, 2009, Shimada et al.). The list includes transcriptional regulators like *envR*, membrane proteins like *fepE* implicated in the chain length of lipopolysaccharide O antigen, and the *acrEF* operon that encodes a multidrug efflux pump (Shimada et al., 2009). Ishimada *et al*. found 140 LeuO-binding sites in *E. coli* genome, of which 133 (95%) overlapped with H-NS binding sites, supporting the view that LeuO may be an antagonist of H-NS mediated silencing (De la Cruz et al., 2007, Navarre et al., 2007, Hernandez-Lucas et al., 2008, Stoebel et al., 2008, Stratmann et al., 2008).

Other examples of the antagonist role of LeuO over H-NS, are the activation of *ompS1* transcription by LeuO binding in H-NS nucleation site or the activation of the expression of the operons *assT-dsbL-dsbI* and *bgl* (De la Cruz et al., 2007, Gallego-Hernandez *et al.,* Madhusudan *et al.*, 2005).

LeuO has been studied in other genera. For example, in *V. cholerae* LeuO regulates biofilm formation (Moorthy & Watnick, 2005). In *Y. enterocolitica,* LeuO regulates invasion by activating the *rovA* gene which encodes a MarR-type transcriptional regulator of the invasion gene *inv* (Lawrenz & Miller, 2007).

OBJECTIVES

A previous study from our laboratory had shown that the nucleoid-associated protein H-NS is a repressor of *finP,* a gene located in the *Salmonella enterica* virulence plasmid (Camacho 2005). A search for T-POP insertions that suppressed H-NS-mediated repression of *finP* yielded a T-POP insertion located upstream of the *leuO* gene. Suppression was observed only in the presence of tetracycline, suggesting that the phenotype was not caused by loss-of-function but by activation of *leuO* transcription. These observations, which remain unpublished, drew our attention towards LeuO, a LysR-type transcriptional regulator poorly known in *Salmonella enterica* expect for a few studies in serovar Typhi. Among the interesting features of LeuO discussed at the literature was its potential role as an antagonist of H-NS and the fact that LeuO seemed to be a quiescent cell function expressed under unknown conditions. On these grounds, we addressed the study of LeuO in *Salmonella enterica* serovar Typhimurium by undertaking the following objectives:

1. Characterization of LeuO binding sites in the genome of *Salmonella enterica* by chromatin immunoprecipitation on chip.

2. Analysis of the distribution of LeuO, H-NS, and RNA polymerase binding sites in the *Salmonella* genome by chromatin immunoprecipitation on chip.

3. Transcriptomic analyis of *S. enterica* gene expression in the presence and in the absence of LeuO, in an attempt to identify genes under LeuO control.

4. Genetic and molecular analysis of LeuO-mediated control of gene expression in two horizontally-acquired elements of the *Salmonella* genome: the pathogenicity island 1 (SPI-1) and the virulence plasmid, pSLT.

Objectives 1-3 are the subject of the first chapter of this Thesis (LeuO is a global regulator of gene expression in *Salmonella enterica* serovar Tyhimurium). Objective 4 is divided between Chapter 2 (Regulation of *Salmonella enterica* pathogenicity island 1 (SPI-1) by the LysR type regulator LeuO) and Chapter 3 (Regulation of conjugal transfer of pSLT by LeuO).

MATERIALS AND METHODS

M.1. Bacterial strains

Salmonella enterica serovar Typhimurium and *Escherichia coli* strains used in this Thesis are listed in Table M1. *Salmonella enterica* strains are derivatives of ATCC 14028 or SL1344.

Table M1. Table of strains used in this work.

Strain	Genotype	Reference
E. coli		
DH5α	*supE44* Δ*lacU169* (Φ80 *lacZΔM15*) *hsdR17 recA1 endA1 gyrA96 thi-1 reA1*	(Hanahan, 1983)
BL-21	F⁻ *dcm ompT hsdS* (rB- mB-) *gal* (malB+) K-12 (λS)	Stratagene
S. enterica		
14028	Wild type strain	ATCC
SL1344	*his*	Hoiseth & Stocker, 1981
CJD1034scd	SL1344 *his leuO*::3xFLAG	This work
CJD1028scd	SL1344 *his hns*::3xFLAG	S. Dillon
-	SL1344 *his hns*::Km	-
SV5282	14028 *hilA::lacZ*	J.López-Garrido
SV5295	14028 *invF::lacZ*	J.López-Garrido
SV5301	14028 *invH::lacZ*	J.López-Garrido
SV5384	14028 *hilC::lacZ*	J.López-Garrido
SV5386	14028 *hilD hilC::lacZ*	J.López-Garrido
SV5534	14028 –pSLT *trg::MudQ*	M.García-Quintanilla
SV5546	14028 *hilD rtsA::lacZ*	This work
SV5556	14028 *spvA::tn5dkm*	Hensel *et al.*, 1995
SV5584	14028 *rtsA::lacZ*	J.López-Garrido
SV5586	14028 *hilE::Km*	This work
SV6055	14028 *SPI1::Km*	Baison-Olmo *et al.*, 2012
SV6141	14028 T-POP *leuO*	This work
SV6142	14028 T-POP *ΔleuO*	This work
SV6413	14028 *hilD930::lacZ*	Lopez-Garrido & Casadesus, 2012
SV6841	14028 T-POP *leuO hilA::lacZ*	This work
SV6842	14028 T-POP *ΔleuO hilA::lacZ*	This work
SV6844	14028 T-POP *leuO hilC::lacZ*	This work
SV6845	14028 T-POP *ΔleuO hilC::lacZ*	This work
SV6847	14028 T-POP *leuO invF::lacZ*	This work
SV6848	14028 T-POP *ΔleuO invF::lacZ*	This work
SV6850	14028 T-POP *leuO hilD930::lacZ*	This work
SV6851	14028 T-POP *ΔleuO 930::lacZ*	This work
SV6853	14028 T-POP *leuO rtsA::lacZ*	This work
SV6854	14028 T-POP *ΔleuO rtsA::lacZ*	This work
SV7034	14028 T-POP *leuO invH::lacZ*	This work
SV7035	14028 T-POP *ΔleuO invH::lacZ*	This work
SV7036	14028 T-POP *leuO hilE::Tn10dCm hilC::lacZ*	This work
SV7037	14028 T-POP *leuO hilE::Km*	This work

SV7038	14028 T-POP *ΔleuO hilE::Km*	This work
SV7044	14028 T-POP *leuO hilD hilC::lacZ*	This work
SV7045	14028 T-POP *ΔleuO hilD hilC::lacZ*	This work
SV7048	14028 T-POP *leuO hilD rtsA::lacZ*	This work
SV7049	14028 T-POP *ΔleuO hilD rtsA::lacZ*	This work
SV7312	14028 T-POP *leuO hilD*::HA	This work
SV7313	14028 T-POP *ΔleuO hilD*::HA	This work
SV7315	14028 T-POP *leuO hilE hilD*::HA	This work
SV7316	14028 T-POP *ΔleuO hilD*::HA	This work
SV7317	14028 *hilD hilE rtsA::lacZ*	This work
SV7318	14028 T-POP *leuO hilD hilE rtsA::lacZ*	This work
SV7319	14028 T-POP *ΔleuO hilD hilE rtsA::lacZ*	This work
SV7320	14028 *hilD hilE hilC::lacZ*	This work
SV7321	14028 T-POP *leuO hilD hilE hilC::lacZ*	This work
SV7322	14028 T-POP *ΔleuO hilD hilE hilC::lacZ*	This work
SV7323	SL1344 *his dam* T-POP *ΔleuO pefA::GFP*	This work
SV7327	14028 T-POP *leuO hilE::lacZ*	This work
SV7328	14028 T-POP *ΔleuO hilE::lacZ*	This work
SV7424	SL1344 *his* T-POP *leuO*	This work
SV7425	SL1344 *his* T-POP *ΔleuO*	This work
SV7741	14028 T-POP *leuO*/pIC552	This work
SV7742	14028 T-POP *ΔleuO*/pIC552	This work
SV7743	14028 T-POP *leuO*/pIZ1997	This work
SV7744	14028 T-POP *ΔleuO*/pIZ1997	This work
SV7745	14028 T-POP *leuO*/pIZ1998	This work
SV7746	14028 T-POP *ΔleuO*/pIZ1998	This work
SV7747	14028 T-POP *leuO*/pIZ1999	This work
SV7748	14028 T-POP *ΔleuO*/pIZ1999	This work
SV7749	14028 T-POP *leuO*/pIZ2000	This work
SV7750	14028 T-POP *ΔleuO*/pIZ2000	This work
SV7783	14028 T-POP *leuO spvA::tn5dKm*	This work
SV7784	14028 T-POP *ΔleuO spvA:.tn5dKm*	This work
SV7892	14028 *traN::3xflag*	M. García-Quintanilla
SV7952	14028 T-POP *leuO traN::3xflag*	This work
SV7953	14028 T-POP *ΔleuO traN::3xflag*	This work
SV7975	14028 *sipB*::GFP	I. Cota & S.B. Hernández
SV7976	14028 *hilE sipB*::GFP	This work
SV7977	14028 T-POP *leuO sipB*::GFP	This work
SV7978	14028 T-POP *ΔleuO sipB*::GFP	This work
SV7979	14028 T-POP *leuO hilE sipB*::GFP	This work
SV7980	14028 T-POP *ΔleuO hilE sipB*::GFP	This work

SV strains belong to Professors J. Casadesús and F. Ramos-Morales laboratory collection. CJD strains belong to Professor C. Dorman laboratory collection.

M.2. Bacteriophages

P22 HT105/1 *int201* (Schmieger, 1972) was used as transducing bacteriophage. For P22 sensitivity assays, the clear-plaque H5 derivative, which harbors a mutation in *c2* gene, was used. The P22 *c2* gene is an equivalent of *cI* gene in phage λ.

M.3. Culture media, solutions and growth conditions

M.3.1. Bacterial media and growth conditions

Culture media

- LB: Luria-Bertani medium. Rich medium used for the normal growth of *Salmonella* and *E. coli*.

Tryptone	10 g/l
Yeast extract	5 g/l
NaCl	10 g/l

- LB + 0.3M: Rich media used to obtain the highest rates of invasiveness; in this case LB was supplemented with NaCl at final concentration of 0.3 M.

- Low phosphate medium (LPM): Minimal medium that mimics the growth conditions inside the SVC of *S. enterica*.

KCl	5 mM
$(NH_4)_2SO_4$	7.5 mM
K_2SO_4	0.5 mM
Casamino acids	0.1%
Glycerol	38 mM
MES	80 mM
K_2HPO_4/KH_2PO_4	337.5 µM
$MgCl_2$	10 mM
pH 7adjusted with KOH	

- EBU: Rich medium used to discard the presence of lysogenic isolates after transduction. EBU is LB medium supplemented with the following components:

  K_2HPO_4 25% 10 ml/l

  Glucose 50% 5 ml/l

  Fluorescein 1% 2.5 ml/l

  Evans Blue 1% 1.25 ml/l

- SOB: Rich medium used to grow competent cells:

  Tryptone 20 g/l

  Yeast extract 5 g/l

  NaCl 0.5 g/l

  KCl 0.19 g/l

  pH 7 adjusted with NaOH

  After autoclaving, 5 ml of $MgCl_2$ 2 M was added.

For solid media, agar was added as a final concentration of 15 g/l. When necessary, antibiotics or other chemicals were added to the medium to the final concentrations shown in Table M2.

Table M2. Final concentration of antibiotics and other chemicals used in this Thesis.

Chemical	Final concentration
Antibiotics	
Ampicilin (Ap)	100 μg/ml
Chloramphenicol (Cm)	20 μg/ml
Kanamycin (Km)	50 μg/ml
Tetracycline (Tet)	5 μg/ml
Chlortetracycline*	5 μg/ml
Other chemicals	
EGTA	0.004 μg/ml
X-Gal	40 μg/ml

Chlortetracycline* was added to LB medium. Autoclaving eliminates the antibiotic activity of chlortetracycline but does not affect the capacity of the antibiotic to induce the tetracycline efflux system of Tn10 (Rappleye & Roth, 1997).

Growth conditions:

E. coli and *S. enterica* were routinely grown at 37°C, and exceptionally at 30°C. Cultures were shaken at 200 rpm. For microaerophilic conditions, 5 ml of bacteria were incubated at 37° C without shaking in plastic tubes of 10 ml of capacity.

M.3.2. Epithelial cells

For invasion assays, HeLa human epithelial cells (ATCC CCL2) were used. The medium used was DMEM ("Dulbecco's modified Eagle's medium", PAA) supplemented with 10% of inactivated bovine fetal serum (to inactivate it, serum was incubated at 56° C for 30 minutes, to avoid the lysis of tumorigenic cells), L-glutamine 2 mM, penicillin 100 U/ml and streptomycin 100 µg/ml. In *Salmonella* invasion experiments, antibiotics were not added to the medium. Cells were grown in plates of 10 cm of diameter (with 10 ml of culture medium) or 24 multiwell plates (with 1 ml of culture medium per well) at 37° with 5% CO_2 in a Biotech Galaxy incubator (New Brunswick Scientific, Eppendorf, Enfield, USA). Cells were sub-cultured twice per week as follows: DMEM was removed, HeLa cells were washed twice with PBS 1x and 1 ml of trypsin 1x (diluted in PBS 1x) was added. Cells were incubated for 10 minutes at 37° C and 5% CO_2 and were collected in fresh medium.

M.3.3. Solutions

- PBS 10x:

NaCl	1.37 M
KCl	27 mM
$Na_2HPO_4 \cdot 7H_2O$	43 mM
KH_2PO4	14 mM
pH 7.3	

M.4. Bacterial transduction

M.4.1. P22 lysates

To prepare P22 lysates, 4 ml of P22 stock was mixed with 1 ml of the donor strain. The mixture was incubated at 37° C and 200 rpm for 8-16 h (8 h is the optimal time to obtain the highest rates of cellular lysis). Bacterial debris was removed by centrifugation for 20 min at 4,500 rpm. The supernatant was recovered in a glass fresh tube, and 800 µl of chloroform were added and vortexed. The lysates were maintained at room temperature for a few hours and then stored at 4° C; under these conditions the lysates are stable for months or years.

- P22 stock:

NB	100 ml
E50x	2 ml
Glucose 20%	1 ml
P22 phage	0.1 ml

- NB: Nutrient broth

Meat extract	3 g/l
Peptone	5 g/l

- E50x:

$H_3C_6H5O_7 \cdot H_2O$	300 g/l
$MgSO_4$	14 g/l
$K_2HPO_4 \cdot 3H_2O$	1965 g/l
$NaNH_4HPO_4 \cdot H_2O$	525 g/l

The chemicals were added to 1 l of warm H_2O following the order indicates in the table. Water was added until the total volume reached 3 l. The medium was cooled and sterilized with chloroform.

M.4.2. Transduction in liquid medium

To carry out transduction in liquid medium, an aliquot of the recipient strain and an aliquot of an appropriate dilution of the lysate of the donor strain were mixed in a sterile 1.5 ml tube. This mixture was incubated at 37° C and 200 rpm for 30-45 min (depending on the marker of transduction). The mixture was spread on selective plates that were incubated at 37° C until colonies appeared.

This method does not yield independent transductants, but incubations shorter than 30 minutes do not permit transductants to divide, so the proportion of twins is minimal. On the other hand, it has the advantages of being fast and repetitive. Using dilutions of the transduction mixture, a number of multiplicities of infection can be tested for the same transduction.

M.4.3. Detection of lysogenic transductants

Transductans harboring a selective marker could have been infected by P22 phage and become pseudolysogenic (the *int* mutation avoids integration, and delays the formation of true lysogens). As time goes on, pseudolysogens become resistant or immune to new P22 infections and cannot be lysed or transduced again. Pseudolysogeny should thus be avoided. For this purpose, transductant colonies were isolated in EBU plates (with antibiotics if necessary). In these plates, pseudolysogens are dark colored and P22-free colonies are light colored. This color difference is due to cell lysis in the pseudolysogenic colony, which causes acidification of the medium and turning of the pH indicator, darkening the agar. A transductant was considered P22-free when streaking did not give rise to any dark colony.

M.4.4. P22 sensitivity assay

In EBU plates, isolates that forms light colour colonies could be lysogens that do not undergo visible lysis. These isolates are P22-resistant and can be mistaken by real P22-free isolates. To avoid this situation, an assay to detect P22-sensitive strains is advisable. A streak with a P22 H5 lysate is done on an LB or EBU plate, and air-dried. The test strain is then streaked in a perpendicular way to the H5 streak. P22-sensitive strains grow until they reach the H5 streak, while P22-resistant strains grow over the streak.

M.5. Conjugation

To perform assays of conjugative transfer of the pSLT plasmid, cultures of donor and recipient strains were grown overnight in LB with chlortetracycline. An aliquot of 1 ml was recovered, centrifuged at 13,000 rpm for 3 minutes and washed with 1 ml of LB with chlortetracycline. Cells were harvested by centrifugation and the pellet was re-suspended in 20 µl of LB with chlortetracycline. The donor and the recipient were then sucked onto a Millipore filter of 0.45 µm pore size. The filters were placed on LB plates with chlortetracycline and incubated at 37^{o} C for 4 h in a GasPak microaerophilic jar (Camacho & Casadesus, 2002). Microaerophilic conditions were obtained by a GENbox Anaer bag, supplied by BioMériex (Marcy l'Etoile, France). An anaerobic indicator was used to show to monitor microaerophilic conditions.

M.6. DNA manipulation and transfer

M.6.1. Plasmids

Plasmids used in this Thesis are listed in Table M3.

Table M3. List of plasmids used in this thesis.

Plasmid	Description	Reference
pCE36	FRT *lacZY* oriR6K, Km^{r}	Ellermeier *et al.*, 2002
pCE37	FRT *lacZY* oriR6K, Km^{r}	Ellermeier *et al.*, 2002
pCE40	*aph* FRT '*lacZ lacY*$^{+}$ t_{his} oriR6K, Km^{r}	Ellermeier *et al.*, 2002
pCP20	*bla cat cI*857 λP_R *flp* pSC101 oriTS, Ap^{r}, Cm^{r}	Cherepanov & Wackernagel, 1995
pIC552	*galK' lac*$^{+}$, Ap^{r}	Macian *et al.*, 1994
pKD3	*bla* FRT *cat* FRT PS1 PS2 oriR6K, Ap^{r}, Cm^{r}	Datsenko & Wanner, 2000
pKD4	*bla* FRT *aph* FRT PS1 PS2 oriR6K, Ap^{r}, Km^{r}	Datsenko & Wanner, 2000
pKD13	*bla* FRT *aph* FRT PS1 PS4 oriR6K, Ap^{r}, Km^{r}	Datsenko & Wanner, 2000
pKD46	*bla* P_{BAD} *gam bet exo* pSC101 oriTS, Ap^{r}	Datsenko & Wanner, 2000
pNK2880	*Ptac-tnpA ats-1 ats-2*, Ap^{r}	Kleckner *et al.*, 1991
pSUB11	Km^{r}, 3xFLAG	Uzzau *et al.*, 2001
pET21a	vector used to construct 6His fusions ,Ap^{r}	Novagen
pIZ1871	pET21a-*leuO*-6His	This work

pIZ1997	pIC552-*hilE*(-505/-56)Ap^r	This work
pIZ1998	pIC552-*hilE*(-159/-56)Ap^r	This work
pIZ1999	pIC552-*hilE*(-334/-161)Ap^r	This work
pIZ2000	pIC552-*hilE*(-505/-336)Ap^r	This work

M.6.2. Extraction of plasmid DNA

For the extraction of plasmid DNA was used the commercial system GenElute^{TM} Plasmid Miniprep Kit provided by Sigma-Aldrich Co (St. Louis, Missouri, USA).

M.6.3. Extraction of genomic DNA

For the extraction of genomic DNA, 5 ml of cells grown in exponential phase were collected and re-suspended in 0.4 ml of buffer lysis, 4 µl of RNAse (10 mg/ml) were added and the mixture was incubated at 37^o C for 30 minutes. After that, 20 µl of proteinase K (20 mg/ml) was added and it was incubated for 2 h at 65^o C. Finally, were performed 3 or 4 extractions with phenol: chloroform-isoamyl alcohol in a 2: 1 proportion. Optionally, one extraction with chloroform: isoamyl alcohol (24:1) can be performed. DNA was precipitated al -20^o C by adding 1/10 volume of sodium acetate 3 M and 2.5 volumes of ethanol. After precipitation, genomic DNA was washed with 70 % ethanol and re-suspended in 20 µl of TER buffer.

- Buffer lysis

Tris-HCl	50 mM pH 8
EDTA	10 mM
NaCl	100 mM
SDS	0.2 %

- TER:

Tris-HCl	10 mM pH 7.5
EDTA	1 mM pH 8
RNAse	20 µg/ml

M.6.4. Digestion, modification and ligation of DNA fragments

Restriction endonucleases were supplied by Roche Diagnotics GmbH (Indianapolis, Indiana, USA), New England Biolabs (Beverly, Massachusetts, USA) and Promega Biotech (Madison, Wisconsin, USA). In each case, enzymes were used following the manufacturer's instructions.

For ligation of DNA fragments, 1 U of T4 DNA ligase (1U/µl, Roche Diagnostics) was used in the buffer supplied by the manufacturer. Routinely, the mixture was incubated at 16^{o} C for 12 hours at least.

M.6.5. Agarose DNA gel electrophoresis

Electrophoresis in an agarose gel was used to test the quality of DNA extraction, to determine DNA fragments after plasmid restriction, to estimate the efficiency of endonuclease restriction, etc. The agarose gel was submerged in TAE 1x buffer.

Low Electro Endosmosis agarose (Pronadisa, Conda, España) was employed. Its concentration varied between 0.8 and 1.5 % depending on the size of the fragments to be separated. The loading buffer used was a solution of bromophenol blue (0.125%) and Ficoll 400 (12.5%).

The 1 Kb ladder (GIBCO BRL, Life Technologies, New York, USA) was used as molecular weight marker. Samples were mixed with 1/10 of loading buffer. Ethidium bromide (0.5 µg/ml final concentration) was added to the gels to make bands visible. Gels were illuminated with a UV transilluminator; pictures were taken with a Polaroid ISO3000/36 snapshot film.

- TAE:

Tris-acetate	40 mM
EDTA	10 mM
pH 7.7	

M.6.6. Acrylamide DNA gel electrophoresis

Electrophoresis in acrylamide gels was performed for electrophoretic mobility shift assays. Acrylamide:bisacrylamide (29:1) was used at a final concentration of 6 % in TBE 0.5x.

Electrophoresis was carried out in a Hoefer SE400 (Hoefer Scientific Instruments, San Francisco, California) or in a Mini Protean® III (Bio-Rad, Hercules, California, USA) vertical system. Gels were prepared with lengths of 18 cm and 6 cm, respectively.

- TBE 5x

Trizma base	445 mM
Boric Acid	445 mM
EDTA pH8	10 mM

M.6.7. Isolation of DNA fragments from agarose gels

For the isolation of DNA fragments from agarose gels was used the commercial system Wizard^{R} SV Gel and PCR Clean-Up System supplied by Promega Co.

M.7. Bacterial transformation

M.7.1. High efficiency *E. coli* transformation

Competent cells were prepared using a variation of the Inoue method (Inoue *et al.*, 1990), which guarantees high transformation efficiency (between $5x10^7$ and $5x10^8$ transformants per µg of plasmid DNA). An overnight culture of *E. coli* DH5α was diluted 100-1000 times in 200 ml of SOB, and incubated at 22^{o} C and 200 rpm until the OD_{600} reached 0.5. The culture was chilled quickly on ice and kept on ice for 10 minutes. Cells were harvested by centrifugation at 2,500 g and 4^{o} C for 10 min. The pellet was re-suspended in 20 ml of cold TB, and 1.5 ml of DMSO was added. After 10 min incubation on ice, aliquots of 0.2 ml or 0.5 ml were prepared, freezed in liquid nitrogen, and stored at -80^{o} C.

For transformation, an aliquot of competent cells was slowly thawed on ice and was mixed with the plasmid. The mixture was incubated on ice for 30 minutes, subjected to heat shock (42^{o} C, 45 s), and cooled on ice for 1 min. One ml of LB was then added. The mixture was incubated at 37^{o} C for 1 h; finally, the cells were concentrated in 100 µl and spread on selective media.

- TB:

  PIPES 10 mM

  $CaCl_2$ 15 mM

  KCl 250 mM

  pH 6.7 with KOH

  $MnCl_2$ 55 mM

  This solution was sterilized by filtration

M.7.2. *E. coli* and *Salmonella* electroporation

An overnight culture, was diluted 1/100 in LB and, depending on the strain, was grown at 37° C or 30° C until a OD_{600} 0.6-0.8 was reached. The cultured was chilled on ice and kept on ice for 5 minutes. Twenty five ml were transferred to a tube, and cells were harvested by centrifugation at 4000 rpm for 5 min at 4° C. The supernatant was discarded and the bacterial pellet was softly re-suspended in 1 ml of cold ddH_2O. Once cells were re-suspended, 24 ml of cold water were added, and cells were washed again. Finally, cells were harvested and re-suspended in 250 µl of water.

Electroporation was performed by mixing 1 µl of plasmid DNA or 10 µl of PCR product with 40 µl of competent cells. The mixture was transferred to a previously cooled cuvette that has 2 mm of distance between the plates. The cuvette was subjected to an electric discharge in the electroporator (2.5 KV, 200 Ω and 25 µF). The electroporator employed was a BTX Electrocell Manipulator 600 (Harvard Apparatus, Holliston, Massachusetts, USA). After the discharge, 1 ml of LB was added to the cells, and the mixture was transferred to a 10 ml tube which was incubated at 37° C with shaking (200 rpm) for 1 h. Finally, cells were concentrated in 100 µl and spread on selective media.

M.8. Preparation of a pool of Tn10d::Cm insertions

A lysate of a strain carring a Tn10d::Cm insertion in an F' plasmid was prepared. This lysate was used to transduce a strain carrying plasmid pNK2880 (Kleckner *et al*., 1991). This plasmid produces ATS Tn10 transposase, allowing Tn10d::Cm complementation in *trans*. ATS transposase is less specific than the wild type transposase of Tn10. During transduction, the transposon enters the receptor strain inserted in a F' fragment, and cannot recombine with the host chromosome because there is no homology.

To obtain an independent collection of insertions of the Tn10d::Cm transposon, the following steps were followed: (i) 10 µl of a Tn10d::Cm lysate were transduced to 100 µl of the strain harboring pNK2880; (ii) transductions were incubated at 37° C for 30 minutes; (iii) transducions were spread in LB plates and incubated for 4 hours; (iv) replicates were made in LB with Cm and EGTA 10 mM (compound that chelates Ca^{2+} ions and avoids the P22 capsid assembly, by this way, reinfections are avoided and the probability of appeareance of pseudolysogenics decreases) and incubated at 37° C overnight; (v) transductant colonies were recovered with 1 ml of LB with EGTA. Colonies of various plates can be mixed; usually, collections are made with 2000-5000 colonies; (vi) 1 ml of cells were frozen with 75 µl of DMSO at -20° C; (vii) collection tubes were thawed in ice and diluted 1:25 in 5 ml of LB with Cm and EGTA; (viii) cells were incubated for 1.5 hours at 37° C, and centrifuged at 13000 rpm for 3 minutes. The pellets were washed 3-4 times with LB to eliminate EGTA; (ix) cells were re-suspended in 1 ml of LB; and (x) a lysate was prepared as described previously.

- EGTA 1M:

  EGTA 378.75 g/l

  NaOH 80 g/l

  pH 7 adjusted with HCl

  dH_2O was added until the volume reached 1 l.

M.9. Construction of bacterial strains

M.9.1. Oligonucleotides

Oligonucleotides used in amplification and sequencing were provided by Invitrogen Life Technologies and are listed in Table M4.

Table M4. Oligonucleotides used in this Thesis

Oligonucleotide	Sequence 5'-3'
pIZ1871 construction	
pET21-leuO-BamH1	TTTTGGATCCTATGCCAGAGGTCAAAACC
pET21-leuO-SalI	AAAAGTCGACTCGCTTACAAACAGAGACTAATAA

pIC552 derivatives	
Dir-P1-BlgII-pIC552	TTTTAGATCTGGCTATGGTTATTCAGGAAACG
Rev-P1-XhoI-pIC552	AAAACTCGAGTTGCTAAATACCTTCTGCCATC
Dir-P2-BlgII-pIC552	TTTTAGATCTAGTAAATATGTTCTATTGGAATGGTTG
Rev-P2-XhoI-pIC552	AAAACTCGAGTATAAGAACCATATCAAAAAAGAAATATC
Dir-P3-BlgII-pIC552	TTTTAGATCTGTCCGGGCATAAAGTCATATC
Rev-P3-XhoI-pIC552	AAAACTCGAGTGTGAATATATTTAATGTTTTTATCGCG
***leuO* deletion**	
leuO-P1	GGAGTTAAGCGTGACAGTGGAGTTAAATATGCCAGAGGTCCATATGAATATCCTCCTTAG
leuO-P2	CTGCCCGGTTTTATCGCTTACAAACAGAGACTAATAAATCTGTGTAGGCTGGAGCTGCTTC
***leuO*::3xFLAG**	
Dir-leuO-3xFLAG	TCAATGGATGGAAGATTTATTAGTCTCTGTTTGTAAGCGAGACTACAAAGACCATGACGG
Rev-leuO-3xFLAG	GAATAAACCAGAATTTGTTTCTGATTTATTCTGCCCGGTTCATATGAATATCCTCCTTAG
leuO-E1	AATGGTGTGACTCAGGACAC
leuO-E2	TCACAGCGACGAAAAGCATC
***hilE* deletion**	
hilE-PS1	TAGCGGGTGACGCTCAGGCGTTCGAACAAAACAGGAGTAGGTGTAGGCTGGAGCTGCTTC
hilE-PS4	GATGGACGCCATCTATTTAAAACTGGACGGTATTGAAGGCATTCCGGGGATCCGTCGACC
hilE-E1	ACGATGCTTGAATGCCTGGC
hilE-E2	TACTCGCGAGTAGTCGGAAG
ST-PCR	
ST1	GCCTTCTTATTCGGCCTTGAATTGATCATATGCGG
STGATAT	GGCCACGCGTCGACTAGTACNNNNNNNNNNGATAT
STACGCC	GGCCACGCGTCGACTAGTACNNNNNNNNNNACGCC
ST-PCR-Cm-2-EXT	GAAATGCCTCAAAATGTTCTTTACGATGCCATTGG
ST-PCR-Cm-2-INT	CAACGGTGGTATATCCAGTG
qRT-PCR	
leuO-RT-Dir	GTTTCGCAGACGCATTTGG
leuO-RT-Rev	AGCGATTCCGCAAACTCTTC

gmK-RT-Dir	TTGGCAGGGAGGCGTTT
gmK-RT-Rev	GCGCGAAGTGCCGTAGTAAT
envR-RT-For	CTATTGCGCAGTTCGCTTTG
envR-RT-Rev	CAGCGGCATCAGCGATATC
pipA-RT-For	ATTCCCGAACATGCACCAA
pipA-RT-Rev	GTTTATGGCAAGGCTGTCATGA
sopA-RT-For	CGAGTGGTCCGACCGTTT
sopA-RT-Rev	GCCACAACGCTGGTACAGGTA
sifA-RT-For	TCCCAGCACCAGCCAAAG
sifA-RT-Rev	TGGCGTGAAAAACCTGATCA
rfaH-RT-For	TCAGCCATTTTGTGCGCTT
rfaH-RT-Rev	TTCAGGATCGACAACGCCTT
ompA-RT-Dir	TGTAAGCGTCAGAACCGATACG
ompA-RT-Rev	GAGCAACCTGGATCCGAAAG
finP-RT-Dir	GGACACATAGGAACCTCCTCAA
finP-RT-Rev	TGTCACTCCCTGCATCGACT
EMSA	
pipA-EMSA-Dir	*FAM*-ATATTCGACAACAGGGCCTC
pipA-EMSA-Rev	TAGCGTTACCTGTATGTGGC
SL3361-EMSA-Dir	*FAM*-TCCTGGGTATTACTCTGCTG
SL3361-EMSA-Rev	TTCGTTTTTTCCGTCCAGCG
envR-EMSA-Dir	*FAM*-CCGAAAGCTCGTTATTCACC
envR-EMSA-Rev	TGCATTAATGCCTGCTGACG
hilE-Dir-EMSA	GTCCGGGCATAAAGTCATATC
hilE-Rev-EMSA6xFAM	*FAM*-TTGCTAAATACCTTCTGCCATC
hilE-Dir-EMSA-6xFAM	*FAM*-GTCCGGGCATAAAGTCATATC
hilE-Dir-EMSA-P1	GGCTATGGTTATTCAGGAAACG
hilE-Dir-EMSA-P2-6xFAM	*FAM*-AGTAAATATGTTCTATTGGAATGGTTG
hilE-Rev-EMSA-P2	TATAAGAACCATATCAAAAAAGAAATATC

hilE-Rev-EMSA-P3	TGTGAATATATTTAATGTTTTTATCGCG
STM4318-Dir-EMSA-6xFAM	*FAM*-AACACCTTCACCTAATGCCG
STM4318-Rev-EMSA	AACATCATCGGATCCATCG
finP2-Dir-EMSA-6xFAM	*FAM*-CCTCCTCACAAATTCACCTC
finP-Rev-EMSA	TATTGAACTCTTCTCTAAAG
Footprinting	
envR-For-Dnase	ATCATTCAACGTCGTGTTGG
envR-Rev-Dnase	TTATTTTGGGATGGGGTTCA

M.9.2. Polymerase chain reaction (PCR)

For PCR reactions, a Perkin Elmer Gene-Amp PCR system 2400 thermocycler (Perkin Elmer Cetus, Waltham, Massachusetts, USA) was used. PCR reactions were carried out with 1 ng of DNA, 100 µM of dNTPs (final concentration each), 1 µM of oligonucleotides, 1mM of $MgCl_2$, and 1 U of Taq polymerase per reaction in a final volume of 100 µl. The polymerase used in these reactions was Taq Expand^{TM} High Fidelity PCR System supplied by Roche Diagnostics GmbH.

To confirm clones and mutations, colony PCR was performed using Go Taq® Flexi DNA Polymerase (Promega Co.), in these cases, a mixture with 100 µM of dNTPs each one, 0.2 µM of oligonucleotides, 1 mM of $MgCl_2$ as final concentration and 1 U of *Taq* polymerase per reaction in a final volume of 25 µl was prepared. A colony was re-suspended in this mixture and was used as DNA template.

Before use PCR products, enzyme, oligonucleotides and dNPTs were cleaned using the commercial Wizard® SV Gel and PCR Clean-Up System, which was supplied by Promega Co.

M.10. Semi-random, two-step PCR (ST-PCR)

The ST-PCR protocol was used to amplify genomic regions adjacent to a Tn10d::Cm insertion (Fig M1). In a first step, a PCR reaction was carried out over candidates using oligonucleotides ST-PCR-Cm2-EXT and STGATAT or STACGCC (Table M4) in a final volume of 25 µl, following the next protocol: (i) first denaturation, 2 min at 94^{o} C; (ii) 6 cycles of

denaturation (94° C, 30 s), annealing (42° C, 30 s, -1° C per cycle), and extension (72° C, 3 minutes); (iii) 25 cycles of denaturing (94° C, 30 s), annealing (65° C, 30 s), and extension (72° C, 3 minutes); and (iv) a final incubation at 72° C for 7 min to finish the extension. The second reaction was carried out with the oligonucleotides ST1 and ST-PCR-Cm2-INT. The DNA product of the previous PCR was diluted 1:5 and 1 µl was used as DNA template. The second PCR protocol was: (i) first denaturation, 30 s at 94° C; (ii) 30 cycles of denaturation (94° C, 30 s), annealing (56° C, 30 s), and extension (72° C, 2 min); and (iii) a final extension at 72° C for 7 minutes to finish the extension. Final products were sequenced using the oligonucleotides ST1 and ST-PCR-Cm2-INT.

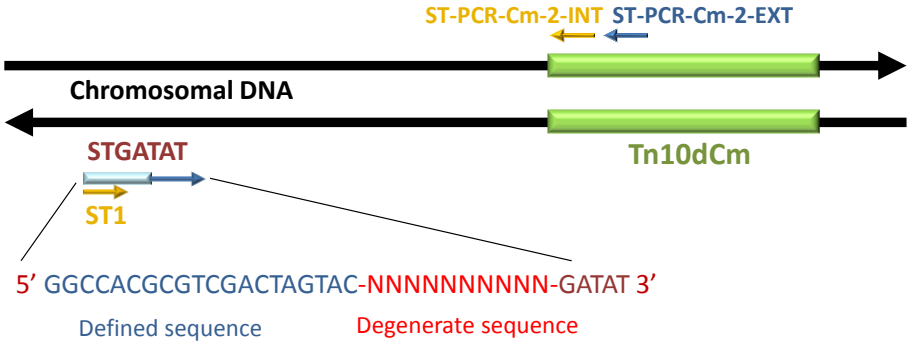


Fig. M1. Representative scheme of the PCR reactions. The last five nucleotides of the oligonucleotides STGATAT allows the hybridization of the oligonucleotides along the genome of *Salmonella* at a certain number of base pairs. There were used two different kinds of these oligonucleotides, one finished in GATAT and the other, in ACGCC. Because the *Salmonella* genome has a G+C content of 52%, oligonucleotides STGATAT will bind every 1159 bp [1/(0,26 x 0,24 x 0,24 x 0,24 x 0,24)], and oligonucleotides STACGCC will bind every 912 bp [1/(0,24 x 0,26 x 0,26 x 0,26 x 0,26)]. The drawing has been adapted from Chun *et al*. 1997 (Chun *et al.*, 1997).

M.11. Chromosomal gene disruption using PCR products

To obtain knockout mutants of chromosomal genes, the method described by Datsenko and Wanner was used (Datsenko & Wanner, 2000). This method is based in the λ Red recombination system. One of the reasons why *E. coli* and *Salmonella* are not transformable with linear DNA is due to the presence of intracellular exonuceases that degrade it. The λ Red system harbors *α*, *β* and *exo* genes that codify for the proteins Gam, Bet and Exo, respectively. Gam inhibits host exonuclease V, allowing the Bet and Exo proteins to carry out recombination of the DNA. The strategy consists in replacing the chromosomal sequence (for example gene B in Fig. M2) by an antibiotic resistance marker that is generated by PCR using oligonucleotides that harbor 40 nucleotides of homology with the sequence to be

replaced (H1 and H2 in Fig. M2). λ Red recombination gene expression is carried out under an inducible promoter inside a termosensitive low copy number plasmid (pKD46). After selection, gene resistant marker can be removed using a different plasmid (pCP20) that harbors the FLP recombinase of the 2 µ plasmid of *Saccharomyces cerevisiae*. FLP system acts over FRT repetitions ("FLP recognition target") that flank the sequence (Fig M2). Plasmids that harbors Red and FLP system are termosensitives and can by cured easily growing the cells at 37° C.

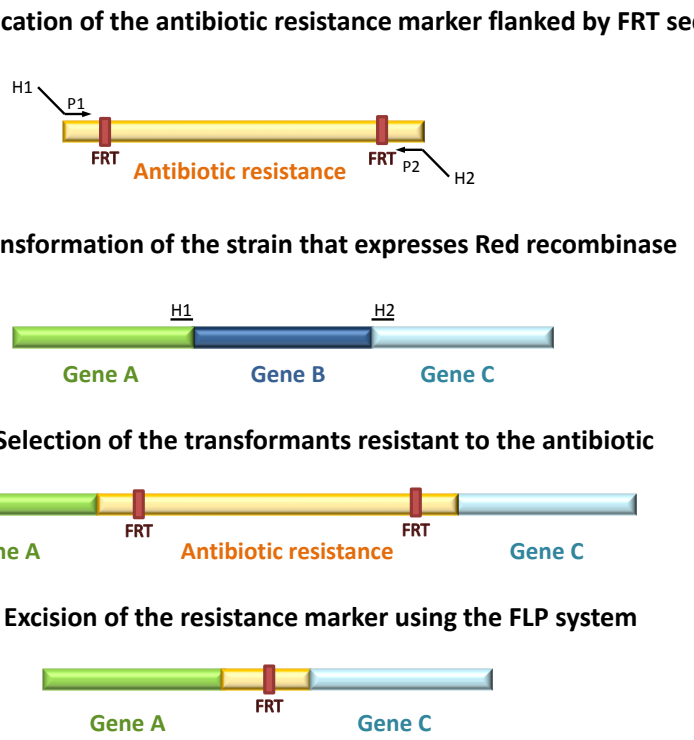


Fig. M2: Scheme of the inactivation system by PCR. H1 and H2 are related to the homology regions with the disrupting sequence. P1 and P2 are the homology sequences that flank the antibiotic gene sequence. Figure adapted from Datsenko and Wanner (Datsenko & Wanner, 2000).

M.11.1. Preparation of DNA for substitution

Plasmids used as templates in PCR reactions were pKD3 (Cm^R), pKD4 (Km^R) and pKD13 (Km^R). Oligonucleotides had 40 nucleotides that were homologous to the genomic DNA and 20 nucleotides that were homologous with pKD3, pKD4 and pKD13. PCR reactions were carried out at 55° C of annealing temperature and 2 minutes of extension, the enzyme employed was "Taq Expand^{TM} High Fidelity PCR System" supplied by Roche Diagnostics GmbH. PCR product was subjected to an electrophoresis in agarose gel and the amplification band was purified

using the commercial system "Wizard® SV Gel and PCR Clean-Up System", which was supplied by Promega Co.

M.11.2. Cell transformation

Competent cells of wild type strain that harbored pKD46 plasmid were prepared. This plasmid expresses λ Red system under the *araB* promoter, which is inducible by arabinose. Cultures grown in LB with ampicillin at 30° C were diluted 1:100 into LB with ampicillin and arabinose (1 mM) and they were incubated in a shaker at 30° C until they reached an OD_{600} 0.5. The competent cells were prepared and electroporation was done as described previously.

M.11.3. Excision of the resistance marker

After the substitution of the genomic genes, mutations were transferred to different genomic backgrounds by transduction with P22 and selecting in the appropriate selective media. When it was necessary the resistance marker of the host was excised by transducing the plasmid pCP20 with P22. This transduction was incubated at 30° C for 1 h and was spread in LB with ampicillin. To eliminate the plasmid, EBU plates were prepared without antibiotic and incubated at 37° C. To confirm the excision of the marker, the strains were streaked in plates of LB ampicillin and plates of LB with chloramphenicol or kanamycin. The excision of the antibiotic marker was checked by colony PCR with external oligonucleotides.

M.11.4. Strain construction by transductional transfer of genetic markers

Genetic markers were transferred from one strain to another by transduction. The recipient strain was transduced using a P22 lysate from a strain with the desirable genetic marker. All the markers used in this thesis were selected directly by spreading the transduction mixture on selective media. If necessary, acquisition of the marker by the transductant was confirmed by PCR or phenotypic analysis.

M.12. Construction of *lac* fusions

M.12.1 Chromosomal fusions

The method described by Ellermeier *et al.* was used to construct transcriptional and translational fusions (Ellermeier *et al.*, 2002). This method allows the construction of *lac* fusions using the FLP/FRT recombination system. As described previously in the method developed by Datsenko and Wanner (Datsenko & Wanner, 2000), a selectable marker (e. g., conferring antibiotic resistance) can be inserted at any place in the bacterial chromosome. The insertion is flanked by two FRT sites, and the marker can be removed using the plasmid pCP20, that harbors the FLP system. As a result of the excision there is one FRT site only at the insertion place (Fig M3). This FRT site can be used to insert a plasmid that harbors a FRT site upstream of the *lacZY* genes, yielding a transcriptional or translational fusion depending on the plasmid chosen. Ellermeier *et al*. constructed three different plasmids: pCE36 and pCE37 for transcriptional fusions, and pCE40 for translational fusions. Plasmid pCE40 lacks the ribosomal binding site of *lacZ* and has STOP codons in all the frames, except one. These plasmids harbor a Km resistant gene and the replication origin of R6K (which is active when the protein π is present). Choice of plasmid depended on the orientation of the FRT in the original mutation (Fig M3).

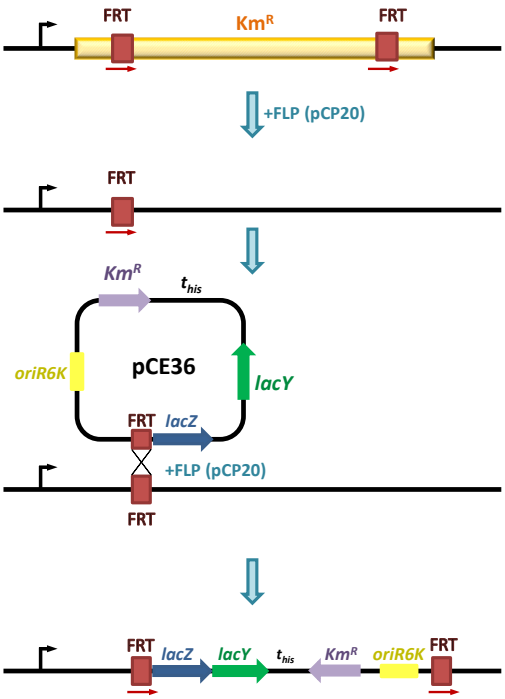


Fig. M3: Scheme of construction of a *lac* fusion in the chromosome. As an example, the construction of a transcriptional fusion using the plasmid pCE36 is shown (Ellermeier *et al.*, 2002).

M.12.2. Plasmid fusions

Plasmid pIC552 was used to construct transcriptional *lacZ* fusions *in vitro*; in this plasmid, the *lacZ* ORF is preceded by the translational start site of *galK* (Macian *et al.*, 1994). The *galK* ribosomal binding site and its adjacent region guarantee a high efficiency of the *lacZ* translation, so that the β-galactosidase activity is directly proportional to the transcriptional activity *in vivo* of the fragment cloned. Cloning of *hilE* promoters on pIC522 plasmid was performed using oligonucleotides listed in Table M4.

M.13. Construction of 3xFLAG fusions

The method described by Uzzau *et al.* (Uzzau et al., 2001) was used for tagging proteins with the 3xFLAG epitope. This method is an adaptation of the Datsenko and Wanner recombineering procedure (Datsenko & Wanner, 2000). The objective is to manipulate the chromosomal sequence, adding a DNA fragment that contains the sequence of the 3xFLAG epitope and a selectable marker (Km^R). The construction is made by PCR and transformation (Fig. M4). As a rule, one of the oligonucleotides used in the amplification has a sequence of roughly 40 nucleotides P1 in Fig M4) that corresponds to the downstream nucleotides of the gene to be tagged without its STOP codon. The other oligonucleotide (P2 in Fig M4) contains a sequence of 40 nucleotides homologous to the sequence next to the STOP codon (but in the complementary DNA strand). The plasmid used as template is pSUB11 (Table M3) which harbors three copies of the FLAG epitope next to a Km resistance gene. The PCR product is used to transform a strain that contains the pKD46 plasmid, which expresses the λ Red system. Correct insertion of the epitope can be proven by PCR using external oligonucleotides, and by Western blot using anti-FLAG monoclonal antibodies. If necessary, the Km marker can be excised by FLP recombinase.

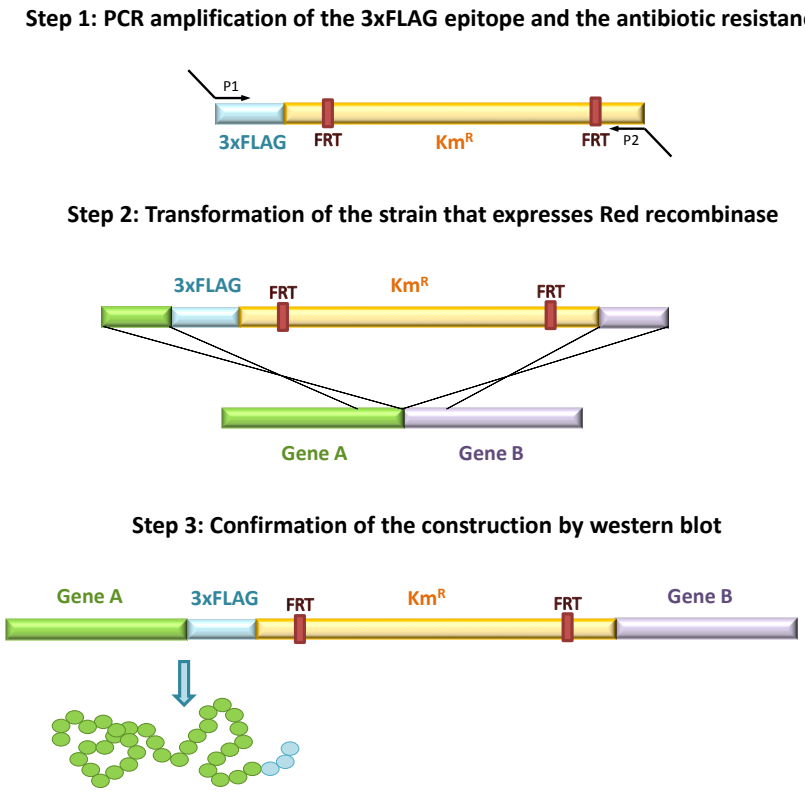


Fig M4: Construction of fusion proteins with the 3xFLAG epitope.

M.15. DNA sequencing

Plasmid DNA and chromosomal DNA obtained by PCR were sequenced in the sequencing service of Sistemas Genómicos S.L. (Parque Tecnológico de Paterna, Valencia) or by Stab Vida (Oeiras, Portugal).

M.16. DNA sequence analysis

Bioinformatic analysis of DNA sequences was performed using the algorithms of molecular biology of the National Center for Biotechnology Information (NCBI) at www.ncbi.nlm.nih.gov.

M.17. ChIP-on-CHIP

M.17.1. Chromatin immunoprecipitation

For chromatin immunoprecipitation, 25 ml of SL1344 cells were harvested for each ChIP procedure following the protocol described in Dillon *et al.,* (Dillon *et al.,*2010).

Fixation

Cells were collected by centrifugation at 4,000 rpm for 8 min at room temperature and re-suspended in 50 ml of pre-warmed PBS 1x at 37^{o} C in a glass flask. DNA-protein and protein-protein interactions were cross-linked by adding formaldehyde (37%). Addition of 1355 µl formaldehyde was performed drop-wise to a final concentration of 1%. The cross-linking was carried out at room temperature with constant but gentle stirring for 30 min. Addition of 3.425 ml of ice-cold 2M glycine to a final concentration of 0.125 M was performed by constant but gentle stirring for 5 min at room temperature to stop the cross-linking reaction. Cells were transferred to 50 ml falcon tubes and kept on ice whenever possible. The cells were pelleted by centrifuging at 4000 rpm for 8 min at 4^{o} C.

Cell lysis

After removing the supernatant, the cells were re-suspended in 1.2 ml of lysis buffer (LB) and incubated on ice for 10 minutes.

Sonication

1.8 ml of IP dilution buffer (IPDB) was added, and the samples were transferred to 5 ml glass falcon tubes (Falcon 2058). The chromatin was sonicated to reduce the DNA length to an average size of approximately 550 bp using the Sanyo/MSE Soniprep sonicator (London, UK). The tip of the probe was dipped to reach approximately halfway down the total level of the liquid sample and the tube was kept constantly on ice. The settings used for the sonicator were: amplitude, 10 microns; number of bursts, 8; length of bursts, 30 seconds. The samples were allowed to cool on ice for 1 min each pulse (5 µl of the sheared chromatin was run on an

agarose gel to check sonication). The sonicated chromatin was transferred to 2 ml microfuge tubes and spun down at 13000 for 10 minutes at 4^{o} C.

Immunoprecipitation

The supernatant was transferred to a 15 ml falcon tube and 3 ml of IPBD was added (LB:IPBD ratio was 1:4), the sheared chromatin can be snap frozen in liquid nitrogen at this stage and the frozen samples should be stored at -70^{o} C. When needed, the samples should be thawed on ice and the experiment carried on as per protocol.

The chromatin was pre-cleared by adding 50 µl of normal rabbit IgG (Upstate Biotechnology, New YorK, USA). The samples were incubated for 1 hour at 4^{o} C on rotating wheel. 100 µl of homogeneous protein G-agarose (Roche) was added to the pre-cleared chromatin and the samples were incubated for 3-5 hours at 4^{o} C on a rotating wheel. The samples were centrifuged at 7500 rpm for 2 minutes at 4^{o} C to pellet the protein G-agarose beads and the supernatant was used to set up various immunoprecipitation (IP) conditions in 2 ml microfuge tubes. An aliquot of 200 µl of chromatin was stored at -20^{o} C to be used as input sample for array hybridizations. Experimental and control ChIP conditions were set up as follows:

- Normal species specific IgG control (matching the species from which antibody used in ChIP conditions(s) was derived) – 1350 ml of chromatin + 10 µg species specific IgG.
- ChIP conditions – 1350 of chromatin + 5-10 µg of antibody (3 µl for FLAG-tag antibody and 10 µl of RNAP).

The samples were incubated at 4^{o} C overnight on a rotating wheel, centrifuged at 13000 for 5 minutes at 4^{o} C and transferred to fresh 2 ml microfuge tubes. 50 µl of homogeneous protein G-agarose suspension was added to each sample and the samples were incubated at 4^{o} C for at least 3 hours on a rotating wheel. The samples were centrifuged at 7500 rpm for 2 minutes at 4^{o} C to pellet the protein G-agarose beads. The supernatant was removed and the protein G-agarose beads were carefully washed. For each wash, buffer was added, the samples were vortexed briefly, were centrifuged at 7500 rpm for 2 minutes at 4^{o} C and left to stand on ice for 1 minute before removing the supernatant. These washes were carried out in the following sequence:

a) The beads were washed twice with 750 µl of cold IP wash buffer 1. The beads were transferred to a 1.5 microfuge tube after the first wash.

b) The beads were washed once with 750 µl of cold IP wash buffer 2.

c) The beads were washed twice with 750 µl of cold TE pH 8.0.

Elution

DNA-protein-antibody complexes were eluted from the protein G-agarose beads by adding 225 IP elution buffer (IPEB). The bead pellets were re-suspended in IPEB, briefly vortexed and centrifuged at 7500 rpm for 2 minutes at room temperature. The supernatant was collected in fresh 1.5 ml microfuges tubes. The bead pellets in the original tubes were re-suspended in 225 µl of IPEB again, briefly vortexed and centrifuged at 7500 rpm for 2 minutes. Both elutions were combined in the same tube.

Reversal of cross-link

The reversal of cross-link step was carried out on the Input sample which was stored at -20^{o} C previously. 0.1 µl of RNase A (10 mg/ml, 50 Kuntiz units/mg, ICN Biochemicals, Santa Ana, California, USA) and 16 µl of 5M NaCl (to the final concentration of 0.3 M) was added to the Input DNA sample. Similarly, 0.2 µl of RNase A (10 mg/ml, 50 Kunitz units/mg) and 27 µl of 5 M NaCl (to a final concentration of 0.3 M) was added to each of the IP test samples. All the samples including the Input DNA sample were incubated at 65^{o} C for 6 hours to reverse the cross-links. 9 µl of Proteinase K (10 mg/ml, 20 U/mg, Gibco BRL) was added to each sample and incubated at 45^{o} C overnight, the samples can be stored after this step. When needed the samples can be thawed at room temperature and the DNA extracted as per the protocol.

Extraction of DNA

Two µl yeast tRNA (5 mg/ml, Invitrogen, Life Technologies) was added to each sample just before adding 250 µl of phenol (Sigma) and 250 µl of chloroform. The samples were vortexed and centrifuged at 13000 rpm for 5 min at room temperature. The aqueous layer (top layer) was collected in fresh 1.5 ml microfuge tubes and 500 µl of chloroform was added to each sample. The samples were vortexed and centrifuged at 13000 rpm for 5 min at room temperature. The aqueous layer was transferred to a fresh 2 ml microfuge tube. 5 µg of glycogen (5 mg/ml, Roche), 1 µl of yeast tRNA (5 mg/ml, Invitrogen) and 50 µl of 3 M NaAc (pH 5.2) was added to each sample and mixed well. The DNA was precipitated with 1375 µl of

100% ethanol and incubated at -70° C for 30 min (or -20° C overnight). The samples were centrifuged at 13000 rpm for 20 min at 4° C. The DNA pellets were washed with 500 µl of ice-cold 70% ethanol and air-dried for 10-15 minutes. The DNA pellets of the IP were re-suspended in 50 µl of sterile filtered HPLC water and 100 µl for the Input DNA samples. 5 µl of each sample was run on a 1% agarose TBE 1x gel and visualized with ethidium bromide to check DNA size. Samples were stored at -20° C.

M.17.2. Labelling for array hybridization

The DNA was labeled using BioPrime Random Labeling Kit (Invitrogen). The following reagents were mixed on ice in a 1.5 ml microfuge: 60 µl 2.5x random oligonucleotide solution, x µl DNA and (70.5-x) µl sterile H_2O (x was the DNA amount labeled and it was different for input and ChIP samples). The amount of DNA labeled was 20 µl of unamplified ChIP DNA and approximately 300 ng of Input DNA. This mixture was heated at 100° C for 10 minutes to denature the DNA and then snap-chilled on ice, from this point samples were kept in the dark. The following reagents were added to the tubes on ice: 15 µl of 10x dNTPs mix; 1.5 µl Cy3/Cy5 labeled dCTP 1 mM (1 mM Cy3-dCTP, 1 mM Cy5-dCTP, GE Healthcare, Wilmington, MA, USA), Input samples were labeled with Cy5 dCTP and ChIP samples were labeled with Cy3 dCTP and 3 µl Klenow fragment (40 U/µl). The final volume per labeling reaction was 150 µl. The reagents were mixed gently but thoroughly and incubated at 37° C overnight. 15 µl of stop buffer was added to the reaction mix to terminate the reaction.

- Lysis buffer (LB)

Tris-HCl	50 mM pH 8.1
EDTA	10 mM
SDS	1%
Sigma protease inhibitor tablet	

- IP dilution buffer (IPDB)

Tris-HCl	20 mM pH 8.1
NaCl	150 mM
EDTA	2 mM
Triton X-100	1%
SDS	0.01%

Sigma protein inhibitor tablet

- IP wash buffer 1 (IPWB1)

Tris-HCl	20 mM pH 8.1
NaCl	50 mM
EDTA	2 mM
Triton X-100	1%
SDS	0.01%

- IP wash buffer 2 (IPWB2)

Tris-HCl	10 mM pH 8.1
LiCl	250 mM
EDTA	1 mM
NP-40	1%
Deoxycholic acid	1%

- IP elution buffer (IPEB)

NaHCO3	100 mM
SDS	1%

- TE (pH 8)

Tris base	10 mM pH 8
EDTA	1 mM

M.17.3. Purification of labeled DNA samples

Micro-spin G50 columns (Ge Helthcare) were used to remove unlabeled nucleotides from the labeled DNA samples. Three columns were used for each of the 150 µl labelling reactions. The resin was re-suspended in the columns by vortexing gently. The caps were loosened and the bottoms of the tubes were snapped off. The columns were placed in 2 ml microfuge tubes and centrifuged at 1700 g for 1 min. 50 µl of sterile filtered HPLC water was applied to the resin-bed and the columns were centrifuged at 1700 g for 1 min. The columns were placed in fresh 1.5 ml microfuge tubes and the labelled DNA samples were carefully applied to the resin-bed. The columns were then centrifuged at 1700 g for 2 min. The purified

DNA samples were collected in the 1.5 ml microfuge tubes and the samples from the same labelled reaction were pooled together. The final volume of the labelled DNA samples was approximately 180 µl. Five µl of each labelled DNA was analyzed on a 1% agarose TBE 1x gel and stained with ethidium bromide for visualization. The samples were used for hybridization and stored in the dark at -20^{o}C.

M.17.4. Microarray hybridization

The microarrays used in this study were designed and produced by Oxford Gene Technology (Oxfordshire, UK). The microarrays consisted of 43,453 60-mer oligonucleotides tiled throughout the *S.* Typhimurium SL1344 chromosome and pSLT plasmid. Microarrays were hybridized for 24 hours in a hybridization oven (Agilent Technologies, Santa Clara, California, USA) and washed according to instructions provided by Oxford Gene Technology.

M.17.5. Microarray data acquisition, analysis and data access

The microarray slides were scanned using an Agilent G2505C scanner. Cy3 and Cy5 images were acquired at 3-micron resolution. Scanned images were analyzed using Agilent Feature extraction software. This software package was used to quantify the fluorescent intensities of each spot representing an array element. Background subtracted fluorescence values were reported for each spot in the Cy3 and Cy5 channels and used to calculate a background subtracted Cy3/Cy5 ratios. The baseline levels of each dataset were normalized to a value of one, allowing all the experiments to be directly compared form this baseline value. The data centring was performed by calculating the median ratio for each experiment and dividing all the Cy3/Cy5 ratios (obtained in that experiment) by this number. The ChIPOTle algorithm (Buck *et al.*, 2005) was used to define regions of enrichment in ChIP-on-chip datasets by using a sliding window approach. ChIPOTle calculates the average $\log_2$ ratio within each window and the fold cut-off chosen was $\log_{21}$. A window size of 500 bp and a step size of 125 bp were used for analyzing the datasets, the rationale being that the ChIP procedure produces DNA fragments of approximately 500 bp in size. The raw ChIP-on-chip datasets have been submitted to the Geo database (accession number GSE35826).

M.18. RNA manipulation

M.18.1. RNA extraction

RNA extraction using the commercial system "SV total RNA isolation system"

RNA was extracted from *S.* Typhimurium using the SV total RNA isolation system (Promega) following the protocol described at htpp://www.ifr.ac.uk/safety/microarray/protocols.html. The quantity and quality of the extracted RNA were determined using a ND-1000 spectrophotometer (Nanodrop Technologies, Wilmington, Delaware). To diminish genomic DNA contamination, the preparation was treated with DNase I (Turbo DNA free, Applied Biosystems/Ambion, Austin, Texas, USA).

RNA extraction based in TRIzol® method

The RNA was extracted following the TRIzol® method with minor modifications. Trisure, a commercial similar reagent, was used instead of TRIzol. Bacterial cultures were diluted 1:100 into LB with chlortetracycline, and were incubated at 37^{o} C at 200 rpm until they reached an OD_{600} 2. Two ml of cells were harvested by centrifugation and were re-suspended in 100 µl of TE (Tris-HCl 10 mM pH 7.5 and EDTA 1 mM pH 8) with lysozyme 3 mg/ml. Samples were frozen and thawed at -20^{o} C to favor the lysis. At this point, with the samples frozen, the protocol can be stopped and can be continued at any time. Subsequently, 1 ml of Trisure (Bioline, Taunton, Massachusetts, USA) was added, and the preparation was incubated for 5 min at room temperature. Samples were centrifuged at 4^{o} C at 13,000 rpm for 10 min. The supernatants were recovered and poured out in clean tubes (eliminating the genomic DNA in this step). Two hundred µl of chloroform were added, and the samples were vortexed for 15 s and centrifuged for 15 min at 4^{o} C and 13,000 rpm. The supernatants were carefully recovered, avoiding recovering the interphase, and transferred to clean tubes. Five hundred µl of isopropanol were added. Samples were mixed by inversion 2-3 times and they were incubated at room temperature for 10 min. Samples were then centrifuged for 10 min. The supernatants were discarded and the pellets were washed with cold ethanol at 70%. The samples were centrifuged at 4^{o} C and 13,000 rpm for 5 min. The supernatants were discarded and pellets were air-dried. The pellets were kept at -20^{o} C until use. The pellets were re-suspended in 30 µl

of RNAse-free H_2O (autoclaved ddH_2O is enough). To obtain a homogeneous mixture, the samples were incubated for a few minutes at 65° C.

- RNA phenol extraction

Whenever RNA samples were not clean enough, they were subjected to phenol treatment. First, ddH_2O was added until a final volume of 150 µl. The same volume of phenol was then added and the preparation was mixed by vortexing. The samples were centrifuged at 4° C and 13,000 rpm for 5 min. The aqueous layer was recovered in a clean tube. The same volume of chloroform: isoamyl acid (24:1) was then added. The samples were mixed by vortexing and centrifuged at 4° C at 13,000 rpm for 5 min. The aqueous layer was recovered and 2.5 volumes of ethanol and 1:10 volumes of sodium acetate 3 M pH 5.2 were added. The samples were precipitated at -20° C for at least 30 min. After precipitation, the samples were centrifuged at 4° C and 13,000 rpm for 30 min, and washed with ethanol 70 %.

M.19. Quantitative RT-PCR (qRT-PCR)

Retrotranscription was performed using "High Capacity cDNA Archive Kit" (Applied Biosystems, Foster City, California, USA) or "Quantiscript" system (Qiagen, Venlo, The Netherlands) for the ARN samples extracted with "SV total RNA isolation" system or "TRIzol®" method, respectively. ARN retrotranscription was carried out following manufacturer's protocol. Quantitative RT-PCR reactions were performed in "LightCycler 480 II" (Roche). Each reaction was carried out in a total volume of 10 µl on a 480-well optical reaction plate (Roche) containing 5 µl SYBR, 0.5 µl DYE II (Takara, Japan), 4.6 µl cDNA (1/10 dilution) and two gene-specific primers at a final concentration of 0.2 mM. Real-time cycling conditions were: (i) 95° C, 10 s; (ii) 45 cycles at 95° C, 5 s and 60° C, 20 s; (iii) 95° C 1 s, 65° C 0 s and 95° C, 1 s. A non-template control was included for each primer set. The expression of the target genes were normalized to the expression of a constitutive gene used as internal control. Oligonucleotides used in qRT-PCR are listed in table M4 (oligonucleotides were designed with PRIMER3 software).

M.19.1. Quantification of qRT-PCR results

Quantitative RT-PCR data were analyzed using the "$2^{-\Delta\Delta Ct}$" method, in which the amount of mRNA of a target gene in an experimental sample is normalized to a reference gene and relative to a control sample. This method is based in the comparison of the threshold cycle of amplification (Ct) of a target gene against a reference gene, obtaining the ΔCt value ($Ct_{target\ gene} - Ct_{reference\ gene}$). ΔCt experimental sample value is compared to the ΔCt control sample, obtaining the ΔΔCt value ($\Delta Ct_{experimental\ sample} - \Delta Ct_{control\ sample}$). The $2^{-\Delta\Delta Ct}$ represents the fold-change of the target gene in the experimental sample respect to the control sample.

Previously to the qRT-PCR, a study of the efficiency of amplification of the oligonucleotides was carried out. Serial dilutions of cDNA were used as templates of the PCR. A standard curve was graphically represented as a semi-log regression line plot of Ct values against log of input nucleic acid. Efficiency of the qRT-PCR was calculated using the slope of the regression line following the next equation:

$$Efficiency\ (\%) = \left[10^{\left(\frac{1}{slope}\right)} - 1\right] x\ 100$$

M.20. Protein analysis

M.20.1. Preparation of protein extracts for polyacrylamide gels analysis.

Bacterial cultures were diluted 1:100 in LB with chlortetracycline and were grown at 37° C and 200 rpm until they reached OD_{600} 2. One ml was centrifuged at 13,000 rpm for 5 min. The supernatant was discarded and the pellet was re-suspended in Laemmli buffer (SB4x: Bromophenol blue 0.000125%, Tris-HCl pH 6.8 200 mM, β-mercaptoethanol 20%, glycerol 40% and SDS 8%). The samples were boiled at 95° C for 10 min and centrifuged at 13,000 rpm for a few seconds and were loaded in an electrophoresis gel.

M.20.2 Polyacrylamide gel electrophoresis

Proteins were separated by their molecular weight by the SDS-PAGE system (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) described by Laemmli (Laemmli, 1970). In

a Mini Protean® III (Bio-Rad) vertical system, proteins were packed in a stacking gel 1 cm long, to be separated afterwards in a resolving gel 5 cm long. The acrylamide percentage varied between 10% and 12% depending on the size of the proteins to be separated, and the stacking gel contained 4% acrylamide. Electrophoresis was performed in running buffer 1x, subjected to an electric field of 175 V for 45-60 min.

- Stacking gel:

Tris-HCl	125 mM pH 6.8
SDS	0.1 % (w/v)
Acrylamide: bisacrylamide 40% (Solu Gel 29:1 Ultra Pure, Pronadisa)	4%
TEMED	0.1% (v/v)
Ammonium persulfate	0.05% (w/v)

- Resolving gel:

Tris-HCl	375 mM pH 8.8
SDS	0.1 % (w/v)
Acrylamide: bisacrylamide 40%	10-12%
TEMED	0.05% (v/v)
Ammonium persulfate	0.05% (w/v)

- Running buffer (10x):

Glycine	144.1 g/l
SDS	10 g/l
Trizma base	30.3 g/l
pH 8.8	

M.20.3. Molecular weight markers

As molecular weight ladders, two different commercial markers were used: SDS-PAGE Molecular Weight Standards Low Range and Prestained SDS-PAGE Standards Broad Range (Bio-Rad).

M.20.4. Coomasie blue staining

Coomassie Brilliant Blue R-250 (Sigma-Aldrich) was used to stain SDS-PAGE gels. For staining, gels were submerged into a staining solution for 30 min. The staining solution was then removed, the gel was washed with dH_2O, and submerged into destaining solution. The gel was covered with destaining solution until protein bands were visible.

- Staining solution:

Coomassie Brilliant Blue R-250	0.25% (w/v)
Acetic acid	10% (v/v)
Ethanol	10% (v/v)

- Destaining solution:

Acetic acid	10% (v/v)
Ethanol	40% (v/v)

M.21. Immunodetection of proteins by Western blot

M.21.1. Nitrocellulose membrane transfer

Proteins subjected to SDS-PAGE were transferred to a nitrocellulose filter (Amersham Hybond-ECL, GE Healthcare) using a wet transfer system (Trans-Blot cell, Bio-Rad). The gel in contact with the nitrocellulose filter was enclosed with Whatman 3MM paper, and everything was soaked in transfer buffer 1x. Upon introduction into the electrophoretic tank, the sample was subjected to an electric field of 80 V for 120 min. To avoid increasing the temperature of the tank, an ice container was introduced inside it.

- Transfer buffer 4x:

Trizma base	12.1 g/l
Glycine	57.6 g/l

Transfer buffer 1x contains 20% ethanol and 0.04% SDS.

M.21.2. Ponceau staining

After transfer, the membrane was washed twice with dH_2O and was stained with Red Ponceau Solution for 3 minutes. The membrane was washed again with dH_2O until bands were visible. This provided a loading control if necessary.

- Red Ponceau Solution

Red Ponceau	0.5% (w/v)
Acetic acid	1%

M.21.3. Nitrocellulose membrane blocking

Previously to the incubation with antibodies, a nitrocellulose membrane was saturated with blocking buffer for at least 30 min at room temperature with soft shaking or at 4°C overnight.

- Blocking buffer:

Skimmed milk (Difco, BD, Massachusets, USA)	5% (w/v)
Sodium azide	0.02%

  This buffer was prepared in TBS-Tween 1x.

- TBS-Tween 10x:

Trizma base	24.2 g/l
NaCl	80 g/l
Tween-20	10 ml
pH 7.6	

M.21.4. Incubation with primary antibody

After membrane blocking, the primary antibody, which was appropriately diluted in blocking buffer, was added. The preparation was incubated two hours at room temperature or at 4° C overnight. Primary antibodies used in this Thesis are listed in table M5.

M.21.5. Incubation with secondary antibody

After the incubation with primary antibody, membranes were washed three times with TBS-Tween 1x buffer for 10 minutes each one, then, membranes were incubated with secondary antibody (Table M5) in an appropriate dilution in TBS-Tween 1x for 1 h at room temperature. Secondary antibodies have the peroxidase enzyme conjugated (HRP). After this step, membranes were washed six times with TBS-Tween 1x for 5 min.

Table M5. List of antibodies used in this work.

Antibody	Type	Source	Company	Dilution
Anti-FLAG M2	Primary, monoclonal	Mouse	Sigma	1:5000
Anti-HA	Primary, monoclonal	Mouse	Covance	1:1000
Anti-RNA polymerase β' subunit	Primary, monoclonal	Mouse	Neoclone	-
Anti-GroEL	Primary, polyclonal	Rabbit	Sigma	1:20000
Anti-DnaK (8E2/2)	Primary, monoclonal	Mouse	Assay Designs	1:5000
Anti-mouse HRP conjugated	Secondary, polyclonal	Goat	Bio-Rad	1:5000
Anti-rabbit HRP conjugated	Secondary, polyclonal	Goat	Ge Healthcare	1:7500

M.21.6. Signal detection

Finally, signal detection was performed using SuperSignal® West Pico Chemiluminescent Substrate" (Thermo Scientific, Waltham, Massachusetts, USA). This substrate is very sensitive to the reaction carried out by HPR. Pictures were taken using the Fujifilm LAS 3000 mini system.

M.22. $LeuO_{6His}$ protein purification

M. 22.1. Cloning of *leuO* gene in pET21a

In first step, a 6His C-terminal fusion of *leuO* was carried out by cloning the gene in the protein expression vector pET21a. Cloning was carried out by a PCR of *leuO* gene using the oligonucleotides pET21-leuO-BamHI and pE21-leuO-SalI (Table M4). The PCR fragment was

purified using the commercial kit Wizard® SV Gel and PCR Clean-Up System, supplied by Promega Co. This fragment was excised with the restriction enzymes BamHI and SalI, and was cloned in frame in the vector pET21a. The ligation mixture was transformed into *E. coli* DH5α. Clones were confirmed by purification of the plasmid, enzyme restriction and DNA sequencing of the candidates.

M.22.2. Expression of $LeuO_{6His}$ protein

In a first step, pIZ1871 (pET21a-$leuO_{6His}$) was transformed into the protease-free strain *E. coli* BL21. An LB with Ap overnight culture grown at 30° C was diluted 1:100 in 200 ml of LB with Ap and incubated in a shaker at 30° C until cells reached OD_{600} 0.4. IPTG 1 mM was then added to the culture and it was incubated at 30° C for 4 h. Cells were harvested by centrifugation at 4° C and 4,500 rpm for 15 minutes. Supernatant was discarded and pellets were kept at -20° C. Pellets were thawed and re-suspended in lysis buffer (5 ml per 0.5 g of pellet) with a protease inhibitor cocktail (Sigma Aldrich). The mixture was sonicated in a 50 ml tube for 1 minute 4 times using a Branson Sonifier 250 sonicator supplied by Biogen Científica S.A. (Madrid, Spain). Samples were centrifuged at 4° C for 30 min at 10,000 rpm.

M.22.3. Purification of $LeuO_{6His}$ protein

The next step was the isolation of the $LeuO_{6His}$ protein from the rest of the proteins, after the centrifugation the supernatant was recovered and filtrated with a 0.22 µm filter. $LeuO_{6His}$ was purified by chromatography affinity at 4° C using a column that contains an agarose matrix bound to nickel ions (Ge Healthcare). Column was washed with 5 ml of washing buffer 1 and 5 ml of washing buffer 2. In this way, unspecific proteins bound to the Ni^{2+} column were removed. $LeuO_{6His}$ protein was eluted with 5 ml of elution buffer and was analyzed in a polyacrylamide gel. During the elution the protein was recovered in 5 fractions of 1 ml each one. The fractions that contained the protein were mixed and dialyzed against the dialysis buffer in dialysis tubes (Dialysis tubing cellulose membranes, Sigma-Aldrich). The dialyzed fraction was analyzed by SDS-PAGE. When it was necessary the protein was concentrated using an Amicon® Ultra Centrifugal Filters (Milliopore, Darmstadt, Germany). Protein was frozen in liquid N_2 and kept at -80° C.

- Lysis buffer:

Tris-HCl	20 mM
NaCl	300 mM
Imidazole	10 mM

- Wash buffer 1:

Tris-HCl	20 mM
NaCl	300 mM
Imidazole	50 mM

- Wash buffer 2:

Tris-HCl	20 mM
NaCl	300 mM
Imidazole	100 mM

- Elution buffer:

Tris-HCl	20 mM
NaCl	300 mM
Imidazole	300 mM

- Dialysis buffer:

Tris-HCl	20 mM
NaCl	300 mM
Glycerol	10 %

M.22.4. Protein quantification

Protein concentration was quantified in polyacrylamide gel. Increasing concentrations of bovine serum albumin (BSA) and $LeuO_{6His}$ were loaded in a polyacrylamide gel and stained with Coomasie. Gel was scanned and intensity of each BSA band sample was measured using Image J software. A linear regression was performed representing the BSA concentration versus its band intensity obtained with Image J. $LeuO_{6His}$ amount was extrapolated from this linear regression.

M.23. Interaction DNA-protein

DNA fragments used for DNA-protein interactions were amplified by PCR using the oligonucleotides listed in table M4. *Salmonella* 14028 or *Salmonella* SL1344 were used as DNA templates. Oligonucleotides (Table M4) were labeled with 6-carboxifluorescein (6xFAM)

M.23.1. Electrophoretic mobility shift assays (EMSA)

To carry out binding assays, DNA fragments and increasing concentrations of $LeuO_{6His}$ protein were mixed as described by De la Cruz *et al*., (De la Cruz *et al.*, 2007). DNA fragments and protein were mixed in LeuO binding buffer in a final volume of 15 µl and were incubated at room temperature for 30 minutes, loading buffer was added to the samples and were loaded into a TBE 0.5x gel (6% acrylamide:bisacrylamide 29:1, TBE 0.5x) and subjected to an electric field of 25 mA per gel for 30-90 minutes. DNA fragments were visualized with a FLA-5100 Imaging system (Fujifilm, Tokyo, Japan).

- LeuO binding buffer 10x:

HEPES	20 mM
KCl	100 mM
$MgCl_2$	2 mM
EDTA	0.1 mM
Glycerol	20 %

- Loading buffer:

TBE	0.5x
Glycerol	20%
Bromophenol blue	
Xylene cyanol	

M.23.2. Slot blot assays

To carry out slot blot assays, DNA-protein binding was performed as previously described. After binding, 500 µl of PBS 1x were added to the sample and were blotted to a

nitrocellulose filter, using a PR 600 Slot Blot Manifold (Hoefer Scientific Instruments, San Francisco, California, USA). Slot blot was connected to a portable vacuum/pressure pump (Millipore). Wells were washed five times with PBS 1x, and membranes were air-dried. DNA fragments were visualized as described above.

M.23.3. Footprinting

DNase footprinting was performed as described by Cameron and Dorman (Cameron & Dorman, 2012) with minor modifications. DNase footprinting reactions were performed in 15 µl containing 1x LeuO binding buffer, 0.01 mM DDT, 100 ng μl^{-1} BSA, 50 nM of bait DNA and 4 µM of $LeuO_{6His}$ protein. LeuO-DNA binding was allowed to equilibrate at room temperature for 30 minutes. One µl (0.05 units) of DNase I (Roche) was then added, mixed gently, and incubated at room temperature for 5 minutes. Reactions were stopped by addition of 2 µl of EDTA (100 mM) following by vigorous vortexing and heat denaturation at 95^{o} C for 10 minutes. Digestion products were desalted using microspin G-25 columns (GE, Healthcare), and were analyzed on an "ABI 3730 DNA Analyzer" along with GeneScan 500-LIZ size standards (Applied Biosystems, Alcobendas, Spain).

M.24. β-galactosidase assays

B-galactosidase assays were performed following the method described by Miller (Miller, 1972), modified by Maloy (Maloy, 1990). $CHCH_3$-SDS was used to make cells permeable. One hundred µl of a culture were mixed with 700 µl of Z buffer, 30 µl of chloroform and 15 µl of SDS 0.1%. Samples were mixed by vortexing and were incubated for 5 minutes at 30^{o} C. Two hundred µl of a solution of orto-nitrophenyl-β-galactoside (ONPG) at 4 mg/ml concentration were added. The mixture was vortexed and incubated at 30^{o} C until the samples turned yellow. Five hundred µl of Na_2CO_3 1 M were then added to stop the reaction. The samples were centrifuged for 15 minutes at 13,000 rpm. The absorbance (Abs) was measured at 420 and 550 nm. B-galactosidase activity was calculated using the following equation:

$$Activity\ (MU) = \frac{OD_{420} - 1.7 \times OD_{550}}{V \times OD_{600} \times t} \times 1000$$

In which V is the volume of the culture in the reaction (ml), OD_{600} is the absorbance of the culture at 600 nm, and t is the time of the reaction (minutes).

- Z buffer:

$Na_2HPO_4 \cdot 7H_2O$	16.1 g/l
$NaH_2PO_4 \cdot H_2O$	5.5 g/l
KCl	0.75 g/l
$MgSO_4 \cdot 7H_2O$	0.246 g/l

  dH_2O was added until 1 l was reached. Before use, 2.7 ml of β-mercaptoethanol were added per liter of buffer.

M.25. Flow cytometry

Cells were grown in LB with chlortetracycline at 37° C until stationary phase (OD_{600}~2). Cells were washed and re-suspended in PBS to a final concentration $5x10^6$ cells ml^{-1}. Data acquisition and analysis were performed using a "Cytomics FC500-MPL cytometer" (Beckman Coulter, Brea, California, USA). Approximately, $5x10^6$ cells were analyzed for GFP expression. Data were collected for 40000 events per sample, and were analyzed with CPX and Flow Jo 8.7 Software.

M.27. Infection of HeLa cells

Epithelial cells were seeded in 24 well plates at a concentration $1.5x10^6$ cells/well. And they were incubated for 24 h at 37° C with 5% CO_2 in DMEM media without antibiotics. For these kind of infections, bacteria were grown under invasive conditions (LB 0.3 M NaCl with chlortetracycline in a sealed tube without shaking overnight) and were added as a multiplicity of infection (MOI) of 50 bacteria per cell. Cells were incubated at 37° C for 30 minutes and 5% CO_2, cells were washed twice with PBS 1x, covered with 500 µl of DMEM with Gm 100 µg/ml (Gm_{100}) and incubated again at 37° C for 90 minutes. Cells were washed again twice with PBS 1x and incubated for 10 minutes at 37° C with Triton X-100 1% to lysate the cells, 150 µl of PBS 1x were added to the cells and recovered. The invasion rate was calculated using the following equation:

$$Invasion\ rate\ (\%) = \frac{30\ \text{minutes}\ cfu}{culture\ cfu} \times 100$$

Where cfu (colony forming unit) are the colonies obtained in the seeded plates, multiplied by the dilution factor of the plate and the volume.

M.28. DNA sequence analysis

To test for the presence of over-represented motifs in DNA sequences bound by LeuO in *E. coli* and *S.* Typhimurium, the SELEX screening (Shimada *et al.*, 2011) and ChIPOTle datasets were manually curated to define short binding regions that could be analyzed by the Meme motif-finding program. For the SELEX data this involved extracting 500 bp of DNA sequence centred on the genomic co-ordinate presented for each LeuO binding site in Shimada *et al.,* (Shimada *et al*., 2011). For *S.* Typhimurium this involved selecting the highestscoring probes from the broader binding regions identified by ChIPOTle and the corresponding DNA sequences were extracted using the Artemis genome viewer (Rutherford *et al.*, 2000). The unbiased motif-finding program Meme (Bailey *et al.*, 2009) was used to search the curated datasets. Meme parameters were sets as follows: motifs could range in size from 10 to 50 bp, each DNA sequence could contain multiple or not motif sites, and both palindromic and non-palindromic motif could be found. The MAST program (Bailey *et al.*, 2009) was used to generate PSSM from the *E. coli* and *S.* Typhimurium LeuO motifs. The PSSMs were used to scan the *E. coli* K-12 MG1655 and *S.* Typhimurium SL1344 genome sequences for matches with an E-value < 0.1 and a position P-value < 0.0001.

M.29. Statistical analysis

To calculate averages and standard deviations, the programs used were “Prism 5.0” and “Microsoft Excel”.

RESULTS

Chapter 1

LeuO is a global regulator of gene expression in *Salmonella enterica* serovar Tyhimurium

C.1.1. Identification of LeuO target genes in *Salmonella enterica* using a ChIP approach.

Our strategy to unravel physiological roles of LeuO in *S.* Typhimurium was based on the identification of the network of LeuO target genes using a combination of chromatin immunoprecipitation (ChIP) and transcriptome analyses.

For chromatin immunoprecipitation we employed LeuO protein tagged with the FLAG epitope. LeuO-3xFLAG was cross-linked with DNA and immunoprecipitated using an anti-FLAG antibody. The DNA targets bound by LeuO were then identified by hybridization to a DNA microarray.

Bacterial cultures to be used in the ChIP assay were grown under conditions known to promote maximal LeuO protein expression: growth in a minimal low phosphate medium (LPM) to stationary phase (equivalent to an OD_{600} value of 1.4) (Figure C.1.1) (VanBogelen, Olson et al. 1996; Fang, Majumder et al. 2000).

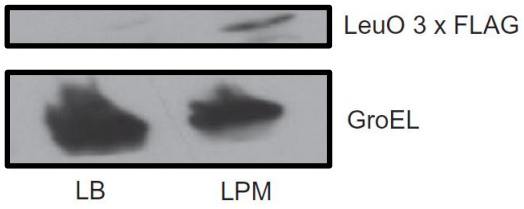


Figure C.1.1. Western blot analysis of LeuO protein levels in *S. enterica* SL 1344 grown to stationary phase in LB or LPM are shown in the top panel, GroEL loading controls are indicated in the bottom panel.

The LeuO-bound ChIP DNA fragments were fluorescently labelled with Cy3 dCPT while the genomic DNA control was labelled with Cy5 dCTP. The DNA samples were co-hybridized to a DNA tiling microarray and the intensity of fluorescence of each of the DNA probes was calculated (Figure C.1.2). The ChIPOTle peak finding programme (Buck, et al. 2005) was used to identified LeuO binding sites using a two-fold cut off. This procedure identified 261 binding regions common to two biological replicate experiments. However as the ChIP-chip procedure often results in the identification of false positive binding events (Waldminghaus and Skarstad) a control "mock" ChIP-chip experiment was also performed, in which normal mouse IgG antibodies were used during a ChIP reaction, to identify any DNA sequences that were non-specifically immunoprecipitated. The ChIPTOle programme identified 83 peaks in the control dataset that were also present in the LeuO dataset; consequently, these targets were

eliminated from the final analysis. Altogether, 178 LeuO binding sites were identified (Figure C.1.3). Previously characterized LeuO target genes from other bacterial species that were found in our dataset include the CRISPR/Cas operon (Figure C.1.2), *sdiA, ompN/ompS2, dnaE, cyoABCDE, tesB, fimD, sdhA, add, cpsG, nuoH, tdcD, treF* and *phoU* (Shimada, Bridier et al.; Turnbull, Kim et al.; Westra, Pul et al.). The presence of these targets validated our approach. A large number of new LeuO target genes were also identified in this study.

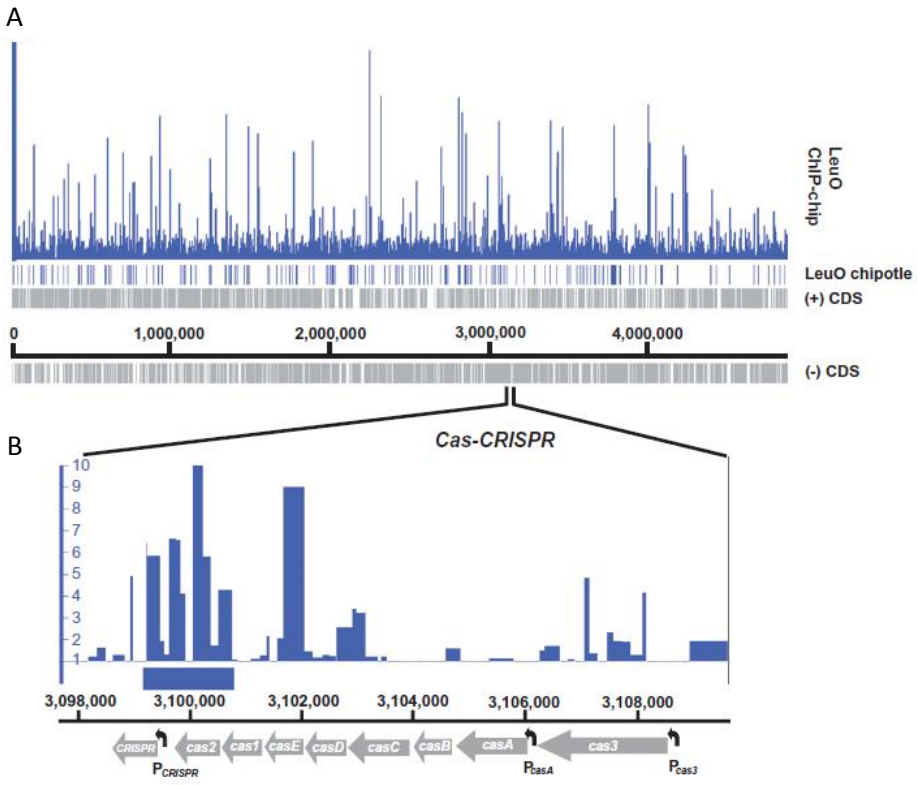


Figure C.1.2. A. Visualization of LeuO ChIP-chip data using the Integrated Genome Browser (IGB) for *S.* Typhimrium SL1344. The locations of LeuO binding sites, as defined by ChIPOTle algorithm, are indicated by horizontal bars in the LeuO ChIPOTle track. The locations of known coding sequences (CDS) on the plus (+) and minus (-) DNA strands and SL1344 chromosome co-ordinates are also shown. B. Detailed view of the *S.* Typhimurium CRISPR/Cas locus. LeuO ChIP-chip data are presented quantitatively, with enrichment ratios on the y-axis. The binding site identified by ChIPOTle is depicted by the blue rectangle and known promoter locations are indicated by bent arrows. The *cas3* transcription start site was determined by Kröger et al. (Kroger, et al.2012)

The evidence that LTTRs can exert their regulatory influence through binding to a wide variety of locations prompted us to examine the location of *S.* Typhimurium LeuO binding sites in detail. LeuO binding sites were classified based on their location, i.e. intergenic or within an ORF. Intergenic and intra-ORF sites were further subcategorized into Intergenic (I, located

upstream of an individual gene), Intergenic Convergent (IC, located between two convergently transcribed genes), Intergenic Divergent (ID, located between two divergently transcribed genes), ORF 3' (located within the 3' promoter-distal half of an ORF) and ORF 5' (located within the 5' promoter-proximal half of the ORF) (Figure C.1.3).

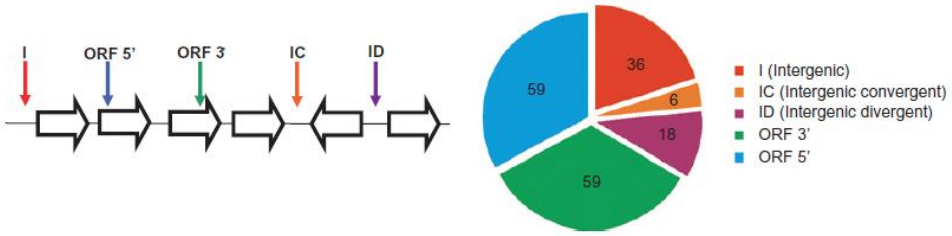


Figure C.1.3. Schematic representation of LeuO binding site classification as outlined in the text. The pie chart shows the relative distribution of LeuO binding sites among the location classes summarized in the genetic diagram on the left, with horizontal arrows used to represent ORFs and their relative orientations. The colours of the vertical arrows correspond to the colours in the pie chart segments.

Surprisingly, we found that only about 33% of binding sites were located in intergenic regions with the remaining ~ 66% of binding sites being located within ORFs (Figure C.1.3). Thirty-six of the 60 intergenic binding events were located upstream of an individual gene, 18 were located between divergently transcribed genes and six binding events were located between convergently transcribed genes, making target gene predictions based on binding site location difficult. The same number (59) of ORF binding events were distributed equally between the 5' and 3' regions of ORFs. It is possible that a proportion of these intra-ORF binding events have been incorrectly classified in the case of adjacent genes that share short intergenic regions. This is because the resolution capacity of the ChIP-chip method is limited by the average size of the sonicated DNA fragments (~ 500 bp). However, most represent intra-ORF LeuO binding sites of the type that have been documented previously for LeuO and other LysR-like regulators (Wilson *et al*., 1995; Viswanathan *et al*., 2007; Shimada *et al*., 2011).

C.1.2. Extension of the LeuO regulon.

Our ChIP-chip analysis greatly extended the number of known LeuO target genes in *S.* Typhimurium. LeuO binding has been mapped previously to the CRISPR-associated *casA* and

cas3 promoters in *S.* Typhi (Medina-Aparicio *et al*., 2011); here, we observed high levels of LeuO binding at the promoter for the CRISPR repeats with little or no binding at the *casA* and *cas3* promoters in *S.* Typhimurium (Figure C.1.2.). Other notable LeuO target genes are *sopA*, encoding an effector protein that is translocated by the *Salmonella* pathogenicity island (SPI) 1 type III secretion system, and *sifA,* the SPI-2 translocated effector gene. These are important virulence determinants of *S.* Typhimurium and their detection is consistent with the previous characterization of LeuO as a *Salmonella* virulence factor required for host-pathogen interactions (Tenor *et al*., 2004). The *rcsA* gene was also identified as a LeuO target. Its product, RcsA, is an auxiliary regulator for the Rcs (regulation of capsular polysaccharide biosynthesis) two-component phosphophorelay system that senses alterations in the outer membrane and the peptidoglycan layer of the cell envelope (Majdalani and Gottesman, 2005). The *rssB* gene, which encodes a response-regulatorlike adaptor protein (RssB) for ClpXP proteolytic degradation of the RpoS stress and stationary phase sigma factor (Klauck *et al*., 2001), was found to be a LeuO target. The observed binding of LeuO to its known target *ompS2*/*ompN* but not to *ompS1*/*ompS* provided an important insight. LeuO is known to induce *ompS2* expression at a lower concentration than required for the induction of *ompS1* (De la Cruz *et al*., 2007), consistent with LeuO having a higher affinity for the regulatory region of *ompS2*. The low intracellular concentration of LeuO when cultured in LPM may not allow LeuO to occupy lower affinity sites such as the regulatory region of *ompS1*. To investigate if the genome-wide binding pattern of LeuO was altered upon an increase in the intracellular concentration of LeuO, we used the inducible pBAD system to express 3xFLAG tagged LeuO and monitored its binding pattern using the ChIP-chip technique. This analysis revealed that LeuO bound to 331 chromosomal locations (after removal of any false positives also present in a mouse IgG control ChIP-chip) (Table S.1). We observed LeuO binding to other known targets including *ompS1* and *cas3*, which we did not detect previously. This is consistent with LeuO having a lower affinity for these sites so that a higher intracellular concentration of LeuO is required before full binding is achieved.

C.1.3. LeuO binding in close proximity to H-NS

LeuO has recently emerged as an important antagonist of H-NS (Hernandez-Lucas *et al*., 2008; Shimada *et al*., 2009; 2011) and it may exert this function by simply competing with H-NS for binding to DNA(Shimada *et al*., 2011) or acting as a barrier to H-NS polymerization (Chen *et al*., 2003; 2005; Chen and Wu, 2005). While LeuO is known to antagonize H-NS, its

own gene is repressed by H-NS (Klauck *et al*., 1997; Chen *et al*., 2001; Stratmann *et al*., 2012). Deletion of *hns* in *Salmonella* Typhimurium strain SL1344 resulted in a dramatic increase in LeuO protein levels (Figure C.1.4), confirming the repressive action of H-NS at the *leuO* gene in SL1344.

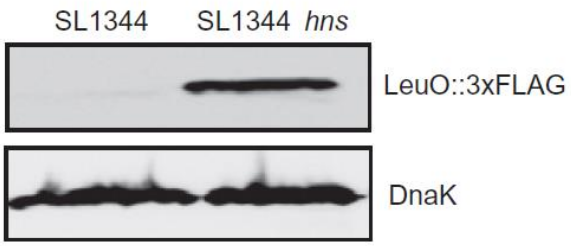


Figure C.1.4. Western immunoblot analysis of LeuO protein levels in wild-type SL1344 and SL1344 *hns* are shown in the top panel. DnaK loading controls are indicated in the bottom panel.

LeuO binding was observed in close proximity to a previously mapped H-NS binding site at *leuO* (Dillon *et al*., 2010), consistent with LeuO functioning as an H-NS antagonist in *S*. Typhimurium. It was important to determine which of the 178 *S.* Typhimurium LeuO binding events were associated with H-NS and to ascertain whether LeuO mediated its function by displacing H-NS or by another mechanism. To address these questions, H-NS binding to the SL1344 chromosome was examined by ChIP-chip analysis under the same growth conditions that are known to promote *leuO* expression (i.e. grown to stationary phase in LPM) (Figure C.1.5). In addition, previously published data (Dillon *et al*., 2010) on H-NS binding under standard laboratory growth conditions in which LeuO is undetectable [i.e. grown to exponential phase in Luria–Bertani (LB)] were analysed and the findings were integrated with those from the present investigation.

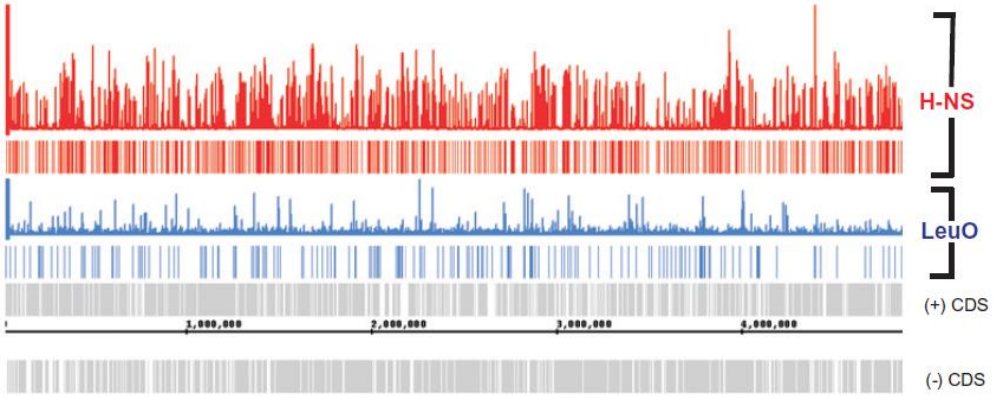


Figure C.1.5. Visualization of H-NS (red) and LeuO (blue) ChIP-chip data in the IGB with ChIPOTle identified binding sites depicted below each lane as horizontal bars. The locations of known CDS on the plus (+) and minus (-) DNA strands and SL1344 chromosome co-ordinates are also shown.

The ChIPOTle algorithm identified 496 H-NS binding regions in SL1344 grown in LPM (Table S.2) (456 binding regions were identified in LB, Dillon *et al.*, 2010). The locations of these H-NS binding regions were compared with the LeuO binding sites and those LeuO binding sites that overlapped with, or were located within 200 bp of, an H-NS binding region were classified as LeuO + H-NS sites; the remaining sites were classified as LeuO sites (Figure C.1.6 and Table S.1). We identified 68 LeuO sites that met our criteria for classification as LeuO + H-NS sites; the remaining 110 LeuO sites were not associated with H-NS colocalization and so were designated as LeuO sites. LeuO colocalization with H-NS at 68 locations is consistent with a global H-NS antagonism function. However, it is important to consider that LeuO may also repress some of its target genes, perhaps in conjunction with H-NS.

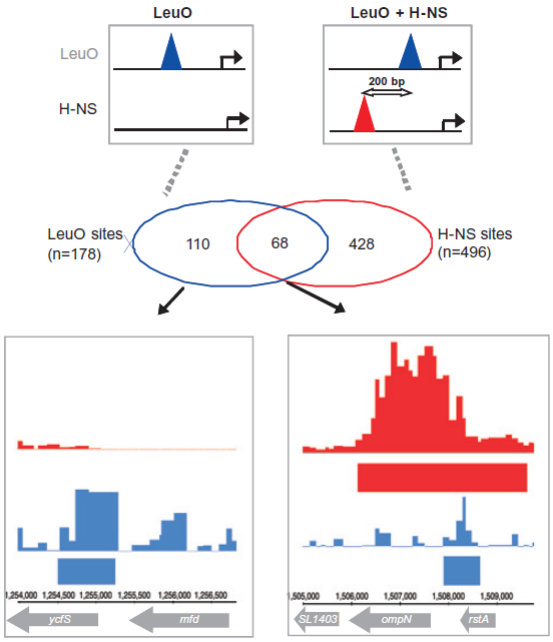


Figure C.1.6. Schematic representation of LeuO and H-NS overlap analysis. The Venn diagram illustrates the number of LeuO sites that did (LeuO + H-NS) and did not (LeuO) overlap with an H-NS binding site. Quantitative LeuO (blue) and H-NS (red) ChIP-chip data are shown for representative examples of LeuO and LeuO + H-NS binding sites.

This possibility is supported by the observation that LeuO and H-NS are both known to repress the *fimAICDFGH* operon in *E. coli* (Shimada *et al*., 2011). The 68 LeuO + H-NS sites represent only 38% of the total number of LeuO binding events; in contrast, Shimada *et al*. (2011) found that 95% of LeuO sites in *E. coli* overlapped with H-NS sites. We then examined average LeuO and H-NS occupancy at the two classes of LeuO binding sites. Average H-NS and LeuO ChIP occupancies were calculated +/-500 bp with respect to the centre of the LeuO binding sites. These surveys showed that the peak of LeuO binding was offset by 100 bp from the ChIPOTle peak centre (Figure C.1.7). However, an interesting pattern emerged: close analysis of regions of LeuO and H-NS co-occupancy revealed that the LeuO binding peak coincided consistently with a trough in the H-NS binding landscape (Figure C.1.7). The significance of this is not clear but may indicate that LeuO functions as an H-NS barrier or antagonist, taking up a position interposed between two consecutive H-NS binding peaks. It is also possible that the intracellular concentrations of LeuO might not be high enough to displace H-NS completely.

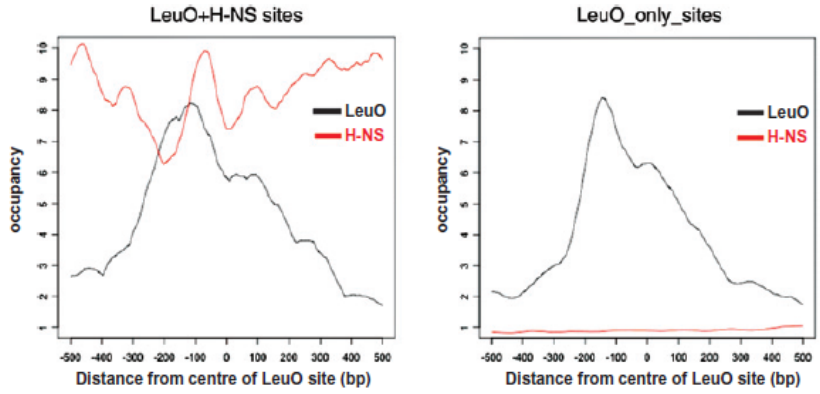


Figure C.1.7. Average plots of LeuO and H-NS occupancy (ChIP-chip enrichment ratios) at LeuO + H-NS and LeuO only sites. Averaged LeuO and H-NS data were plotted in 100 bp windows respect to the centre of ChIPOTle-defined LeuO binding sites.

We wished to know if LeuO could antagonize H-NS binding by competing with and displacing this protein from DNA. We examined H-NS binding at the 110 LeuO-only sites in LB-grown SL1344 and found that none of these 110 locations was occupied by H-NS (Table S.1). Therefore, the presence of LeuO had not simply resulted in the complete displacement of H-NS in LPM since these locations lacked H-NS binding in the absence of detectable levels of LeuO. Next we examined H-NS occupancy at the 68 LeuO + H-NS sites in LB-grown cultures and found

that fewer LeuO target genes were bound by H-NS in LB when compared with LPM (41 of the 68 genes were bound by H-NS in LB) (Table C.1.1).

LeuO LPM target genes (n=178)

	H-NS only	H-NS + RNAP	RNAP only	None
LPM	5	63	105	5
LB	30	11	50	46

Table C.1.1. The number of H-NS, RNA polymerase (RNAP) and LeuO colocalization events in LeuO-inducing conditions (LPM) is indicated in the first row of the table. The second row indicates the number of H-NS and RNAP binding events at the LPM defined LeuO sites in non-inducing conditions (LB).

Therefore, the presence of LeuO appeared to correlate with H-NS binding to more LeuO target genes, which would not be expected if LeuO simply displaced H-NS from its cognate binding sites. However, these results did not rule out the possibility that LeuO influenced the pattern of H-NS occupancy without completely displacing H-NS. Therefore, we calculated the average H-NS binding levels at LeuO binding sites in both LPM and LB (Figure C.1.8). This analysis revealed much higher levels of H-NS binding at LeuO target genes in LeuO-inducing (i.e. LPM) conditions compared with repressive (LB) conditions

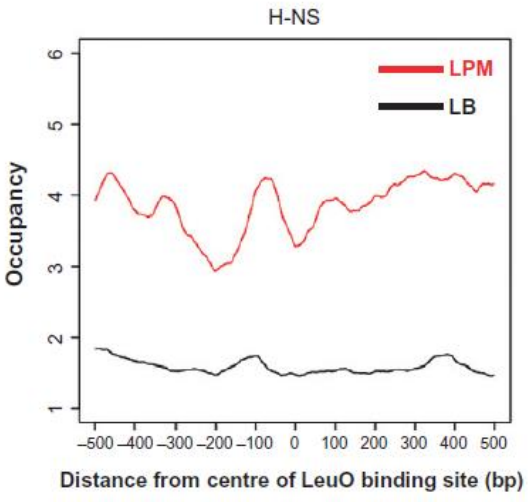


Figure C.1.8. An average plot of H-NS occupancy with respect to LeuO binding site location in LeuO inducing conditions (LPM) and non-inducing conditions (LB).

C.1.4. RNA polymerase recruitment to LeuO target genes.

To determine whether LeuO might recruit RNA polymerase, we examined RNA polymerase binding at LeuO target genes under LeuO-inducing growth conditions (LPM) and non-inducing growth conditions (LB). ChIPOTle analysis of both datasets and comparison with the location of LeuO binding sites revealed that 173 of the 178 LeuO binding sites were also associated with RNA polymerase binding in LPM (co-occupancy was defined as a LeuO binding region located within 200 bp of an RNA polymerase binding region), whereas only 61 of the LeuO binding sites were occupied by RNA polymerase upon growth in LB (Table C.1.1. and Table S.1). Next we plotted the mean RNA polymerase occupancy in both growth conditions with respect to the location of the LeuO binding sites (Figure C.1.9). RNA polymerase occupancy was plotted for a distance of +/-500 bp from the centre of the LeuO binding sites and was found to peak with respect to the centre of LeuO binding sites in both growth media. However, the average RNA polymerase occupancy in LeuO-inducing conditions (LPM) was much higher than in non-inducing conditions (LB) and the peak of binding was also broader. This is consistent with LeuO promoting the recruitment of RNA polymerase to target genes, and the broader peaks of binding are consistent with the detection of elongating RNA polymerase.

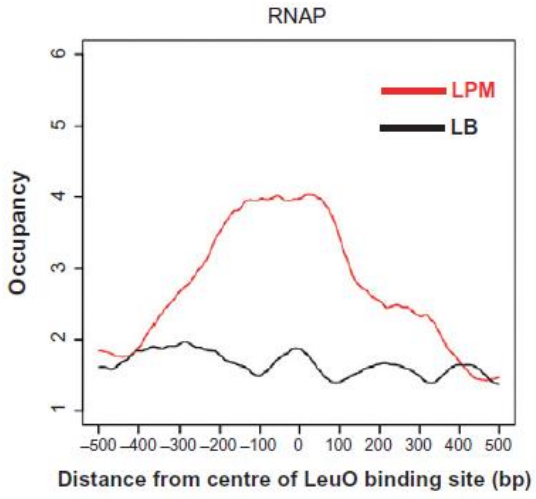


Figure C.1.9. An average plot of RNAP occupancy with respect to LeuO binding site location in LeuO inducing conditions (LPM) and non-inducing conditions (LB).

C.1.5. Identification of an A-T rich LeuO binding motif

We wanted to determine if LeuO binding was associated with a specific DNA motif in our ChIP-chip binding sites. The recent SELEX study of LeuO binding in *E. coli* (Shimada *et al*., 2011) also gave us information on the location of LeuO binding sites in a related species and we were able to incorporate this information into our analysis.

First, the *S*. Typhimurium LeuO + H-NS binding regions described above in which LeuO binding overlapped with or was close to an H-NS binding location were selected for DNA sequence motif analysis. We also created a list of DNA sequences bound by LeuO in *E. coli* by extracting 500 bp DNA sequences that centred on the genomic co-ordinate provided for each LeuO binding site by Shimada *et al*. (2011). Recall that almost all of the *E. coli* sites were of the LeuO + H-NS type. The details of these datasets are provided in Table C.1.2 and in the *Material and methods*.

Species	Dataset	Number of sequences	Average size (bp)	Total size (bp)	%A+T	Source
***Salmonella* Typhimurium**	LeuO+H-NS	64	653	41825	50.5	This study
Escherichia coli	E. coli LeuO	119	501	59619	59.9	Shimada et al. (2011)

Table C.1.2. Details of the manually curated *S*. Typhimurium and *E. coli* LeuO datasets used to derive the LeuO binding motifs.

Next we used the unbiased motif-finding algorithm Meme to search the two datasets for significantly over-represented sequence motifs (Bailey *et al*., 2009). Meme identified a 28 bp motif in both datasets (Figure C.1.10). Two striking features of the LeuO motifs are their imperfect dyad symmetry and their A + T richness. While some dyad symmetry is discernable in the *E. coli* logo, it is much harder to detect in its *S.* Typhimurium counterpart. Furthermore both motifs contain a central region matching the T-N_{11}-A LTTR box motif and alignment of the central T-N_{11}-A motifs of the sequence logos shows significant overlap between the two motifs (Figure C.1.10). However, the *E. coli* LTTR box displays a much stronger nucleotide preference at most positions, a sequence divergence that may explain why only 15 of the *E. coli* LeuO target genes were common to *S*. Typhimurium (Table S.1).

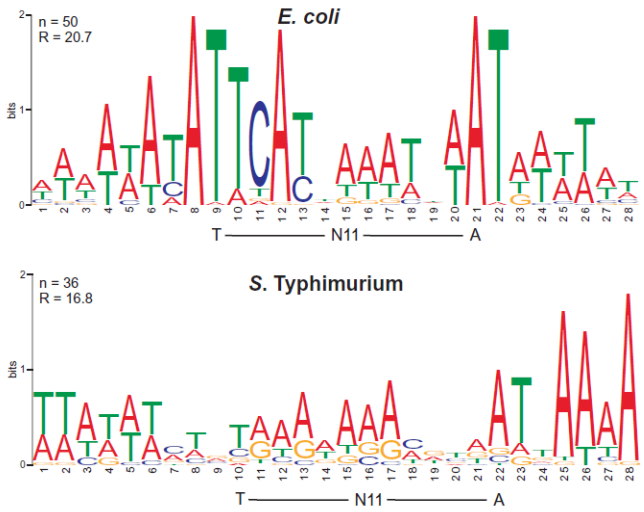


Figure C.1.10. Aligment of sequence logos illustrating the *E. coli* and *S.* Typhimurium motifs identified by Meme. The location of the LLTTR T-$_{N11}$-A box is indicated below each Logo.

C.1.6. Genome-wide prediction and validation of LeuO binding sites.

The identification of the 28 bp LeuO DNA binding motifs suggested that accurate prediction of LeuO binding sites in *E. coli* and *S.* Typhimurium genome sequences would be possible. We used the Motif Alignment and Search Tool (MAST), which is part of the MEME suite of tools used for motif discovery and searching (Bailey *et al*., 2009), to generate a position-specific scoring matrix (PSSM) from the LeuO sequence logos. This PSSM was used to search for sequence matches in the *S*. Typhimurium SL1344 and *E. coli* K-12 MG1655 genome sequences as described in the *Material and methods* section. This analysis resulted in the identification of 1263 and 1094 matches in the *S.* Typhimurium and *E. coli* genome sequences respectively (Figure C.1.11A and B; Table S.3). These predicted sites were often located in intrinsically curved A + T rich regions and are also associated with H-NS binding (Figure C.1.11A and Table S.4). Eight hundred and eighty-nine of the 1263 predicted LeuO binding sites in *S*. Typhimurium were associated with H-NS binding *in vivo*, suggesting that LeuO may function as a more global antagonist of H-NS than previously thought. In order to validate our genome-wide prediction of LeuO binding sites we searched for sites in other known LeuO regulated genes that were not identified in our ChIP-chip study. We correctly predicted sites in the 5' regulatory region of *leuO* itself (Chen and Wu, 2005), in the *yjjQ-bglJ* operon (Stratmann *et al*., 2008), in *ompS1*, *assT* (*stm3192*), and in the CRISPR-associated *casA* and *cas3* genes (Westra *et al*., 2010; Medina-Aparicio *et al*., 2011; Gallego-Hernandez *et al*., 2012). Furthermore LeuO binding sites

have been precisely mapped in the regulatory regions of *Salmonella* Typhi *casA* (Medina-Aparicio *et al*., 2011) and *ompS1* (De la Cruz *et al*., 2007) and our predicted binding sites map to these locations.

To further validate our genome-wide prediction of LeuO binding sites, three *S.* Typhimurium regions were tested for *in vitro* binding of purified LeuO protein by electrophoretic mobility shift assays (EMSA). The *pipA* and *envR* genes each contain one and two predicted LeuO sites respectively, while *SL3361,* which is located beside *envR* and does not contain a predicted LeuO binding site motif, was used as a negative control (Figure C.1.12A). Both *pipA* and *envR* DNA probes showed a clear pattern of retarded migration after incubation with increasing concentrations of purified LeuO while LeuO did not bind to the *SL3361* DNAprobe (Figure C.1.12A). The *envR* 5' regulatory region (P_{envR}) contains two predicted LeuO binding sites located in close proximity to each other (81 bp spacing) and displayed a higher affinity for LeuO binding than the *pipA* region.

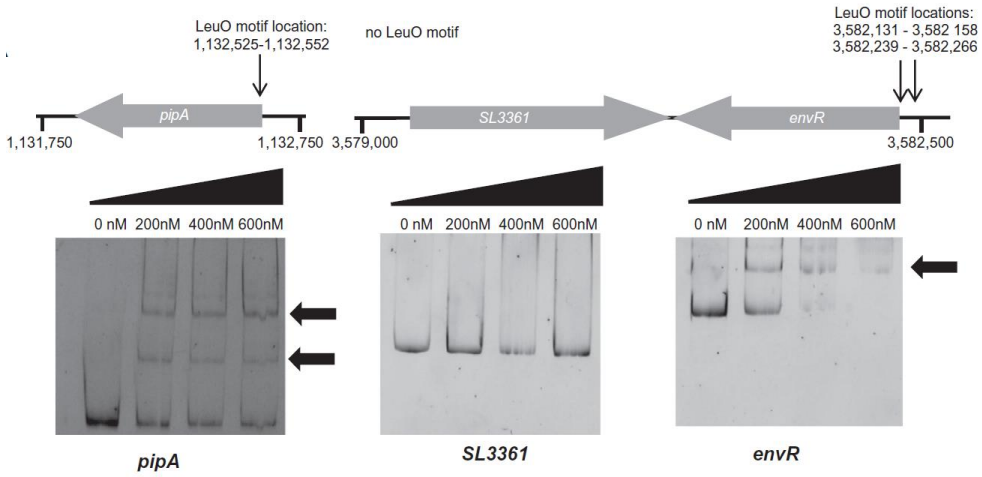
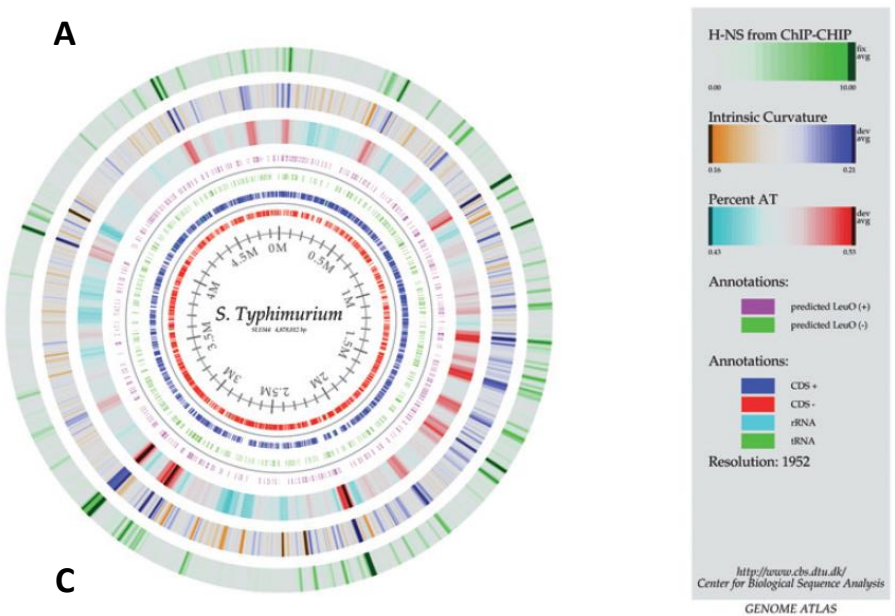
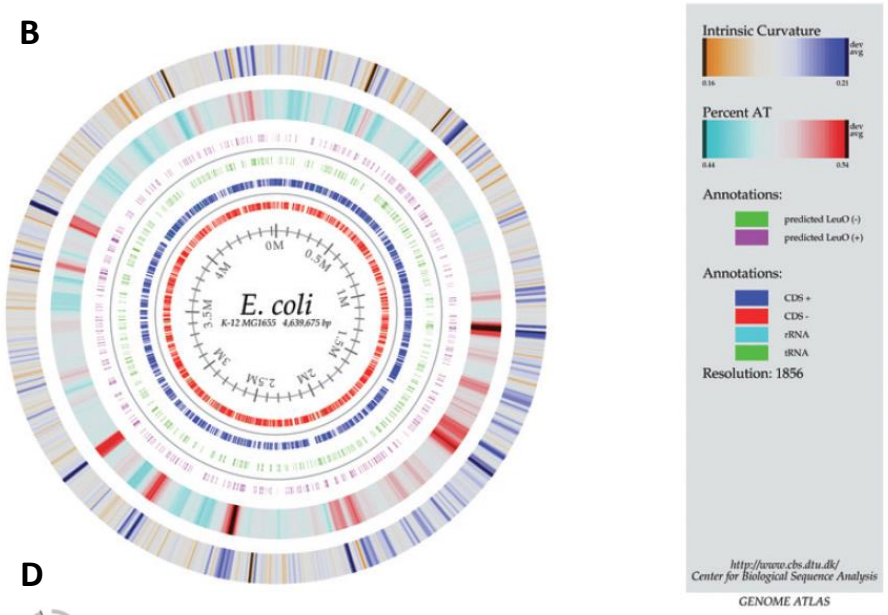
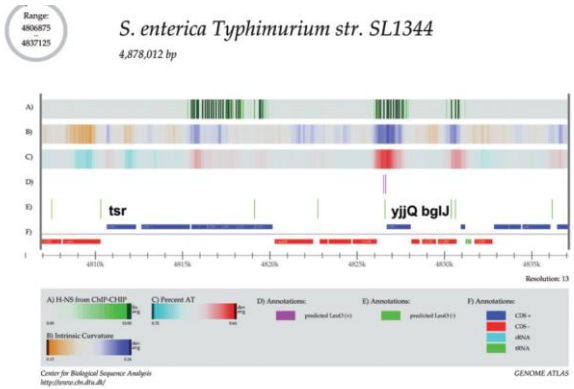
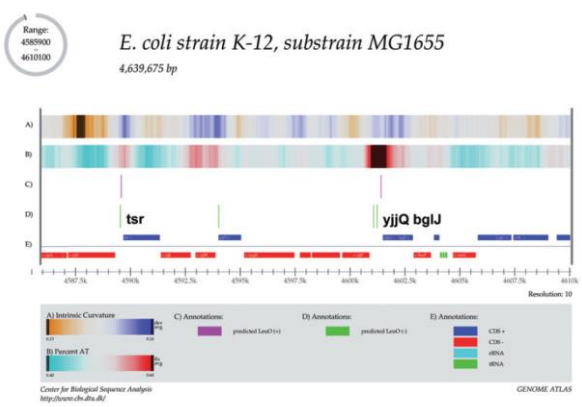


Figure C.1.12. EMSA analysis was used to validate predicted LeuO binding sites. pipA and envR were associated with one and two predicted binding sites respectively (indicated by thin black arrows) while SL3361 was not associated with a predicted site. DNA probes were incubated with increasing amounts of LeuO and complex formation is indicated by thick black arrows.


A
S. Typhimurium
H-NS from ChIP-CHIP
Intrinsic Curvature
Percent AT
Annotations:
predicted LeuO (+)
predicted LeuO (-)
Annotations:
CDS +
CDS -
rRNA
tRNA
Resolution: 1952
http://www.cbs.dtu.dk/
Center for Biological Sequence Analysis
GENOME ATLAS


B
E. coli
K-12 MG1655 4,639,675 bp
Intrinsic Curvature
Percent AT
Annotations:
predicted LeuO (-)
predicted LeuO (+)
Annotations:
CDS +
CDS -
rRNA
tRNA
Resolution: 1856
http://www.cbs.dtu.dk/
Center for Biological Sequence Analysis
GENOME ATLAS


C
S. enterica Typhimurium str. SL1344
4,878,012 bp
tsr
yjjQ bglJ
Resolution: 13
Center for Biological Sequence Analysis
GENOME ATLAS


D
E. coli strain K-12, substrain MG1655
4,639,675 bp
tsr
yjjQ bglJ
Resolution: 10
Center for Biological Sequence Analysis
GENOME ATLAS

The presence of two LeuO binding sites in close proximity and in helical register along the DNA may lead to LeuO oligomerization and DNA bending (Hryniewicz and Kredich, 1994), which may account for the apparently higher affinity observed for this DNA probe. Next we used primer extension to resolve DNase I footprints on PCR amplified DNA templates (Cameron and Dorman, 2012). This approach can be used to more accurately map LeuO binding sites and validate the location of predicted LeuO binding sites. A 400 bp DNA probe encompassing two predicted sites in P_{envR} was used as the target in our experiments. We identified five regions that were protected from DNase I digestion by LeuO, two of which overlapped with the location of the predicted binding sites (Figure C.1.13). Three other protected sites were identified further upstream of the *leuO* ORF which did not contain a predicted site but were located in a 60 bp region of high A + T content (66%), consistent with LeuO binding to A + T rich sequences.

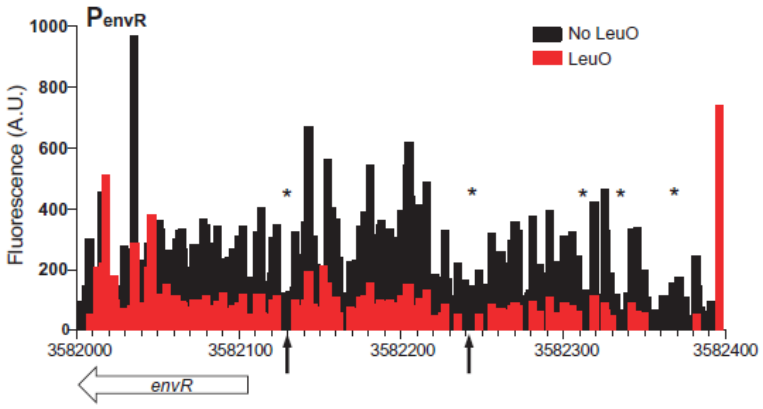


Figure C1.13. DNase I footprinting of LeuO binding to PenvR using end-labelled DNA fragments. The size and quantity of 6-FAM-labelled DNase I digestion products were measured by fluorescent DNA sequencing with capillary electrophoresis. The locations of predicted LeuO binding sites are indicated by arrows and protected regions are indicated by asterisks. SL1344 chromosome co-ordinates are indicated on the x-axis.

Finally we used quantitative RT-PCR to examine the effect of deleting *leuO* on the transcript levels of four predicted LeuO target genes which are also bound by H-NS (Table A4) *envR*, *pipA*, *sifA* and *sopA*. We examined transcript levels for these genes in (i) a strain that harbors a T-POP transposon (Lee *et al*., 2007) upstream of *leuO* in its native chromosomal location, so that *leuO* is overexpressed when tetracycline is added to the culture (SL1344 Tpop-*leuO*) and (ii) a strain that harbours a T-POP transposon upstream of *leuO* but the *leuO* gene is

deleted (SL1344 Tpop-Δ*leuO*). Deletion of *leuO* dramatically decreased the level of *envR* transcript (Figure C.1.14) and increased the levels of *sifA*, *sopA* and *pipA* transcripts (Figure C.1.14.).

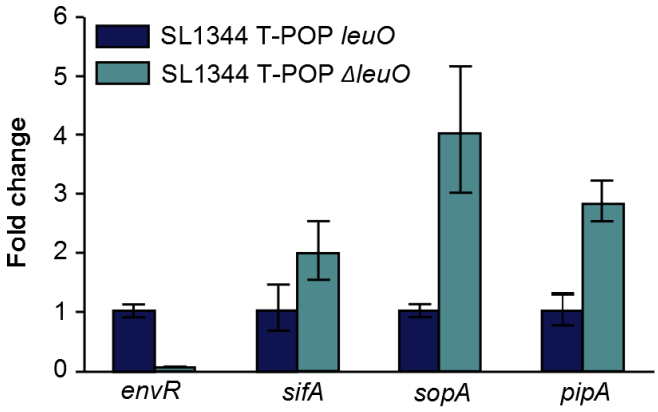


Figure C.1.14. qRT-PCR was used to monitor transcript levels for *envR*, *sifA*, *sopA* and *pipA* following *leuO* expression under T-POP promoter (SL1344 T-POP *leuO*) and deletion of leuO (SL1344 T-POP *ΔleuO*). Fold changes in transcript levels are expressed relative to strain SL1344 T-POP *leuO* which is normalized to 1.

The results of this analysis suggest that LeuO activates transcription of *envR*, perhaps by antagonizing H-NS, but appears to function as a repressor at the other target genes. It is possible that LeuO and H-NS function together to repress transcription of these genes. The location of the LeuO binding sites may be important as the predicted binding sites near *envR* are located upstream of the *envR* start codon, consistent with LeuO functioning as a transcriptional activator of this promoter. Conversely the predicted LeuO binding sites for *sifA*, *sopA* and *pipA* are all located downstream of the start codons, where LeuO binding is likely to have a repressive effect on transcription. Thus it appears that LeuO has a dual role as activator and repressor of transcription.

Chapter 2

Regulation of *Salmonella enterica* pathogenicity island 1 (SPI-1) by the LysR type regulator LeuO

C.2.1. Activation of LeuO transcription represses SPI-1

To confirm previous evidence indicating that SPI-1 might be repressed by LeuO (Dillon *et al*., 2012), we compared the expression of selected SPI-1 genes in the presence and in the absence of LeuO. Activation of *leuO* transcription was achieved by insertion of a T-POP element upstream of the *leuO* coding sequence (Figure C2.1).

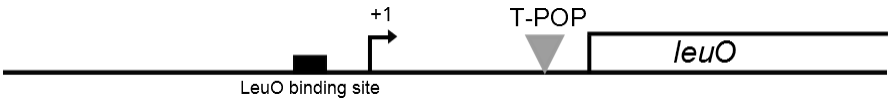


Figure C.2.1.Diagram of the *T-POP leuO* construct of strain SV6141. The T-POP element is inserted at a 5' untranslated region between the *leuO* promoter and the *leuO* coding sequence. Insertion of the 3 kb long T-POP element (Rappleye & Roth, 1997) renders the native *leuO* promoter unable to drive *leuO* transcription.

Transcription of *leuO* was activated by addition of autoclaved chlortetracycline (Rappleye and Roth, 1997; Lee *et al*., 2007; Dillon *et al*., 2012). This experimental design was chosen for the following reasons: (i) In *E. coli*, *leuO* expression increases in stationary cultures; in *S. enterica*, however, increase of *leuO* expression under such conditions is small (Figure C.2.2); (ii) We discarded the use of an Hns− mutant because *hns* mutations are detrimental in *S. enterica* ser. Typhimurium, unless accompanied by an *rpoS* mutation as in strain LT2 (Wilmes-Riesenberg *et al*., 1997); (iii) The combination of *hns* and *leuO* mutations strongly impairs *S. enterica* viability, and normal growth may require the acquisition of suppressor mutations of unknown nature (data not shown).

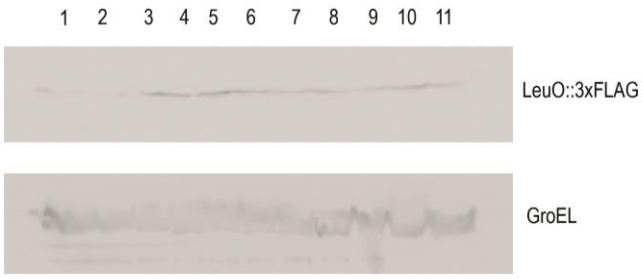


Figure C.2.2. Levels of LeuO::3xFLAG produced by strain SV6829 of *S. enterica* ser. Typhimurium upon cultivation in LB during 11 days under the conditions described elsewhere (Shimada *et al.*, 2011). GroEL was used as loading control.

Use of T-POP to drive *leuO* transcription does not cause viability problems, and has two additional advantages: (i) the transcription rate can be controlled by using different concentrations of tetracycline or chlortetracycline (Lee *et al*., 2007); (ii) in the strain engineered for this study (SV6141), T-POP prevents transcription from the native *leuO* promoter, thus avoiding a feedback loop of autogenous activation (Fang and Wu, 1998a,b) that might yield undesirably high levels of LeuO. Under the conditions employed in this study, the level of *leuO* expression was similar to that of an Hns− mutant (Figure C.2.3).

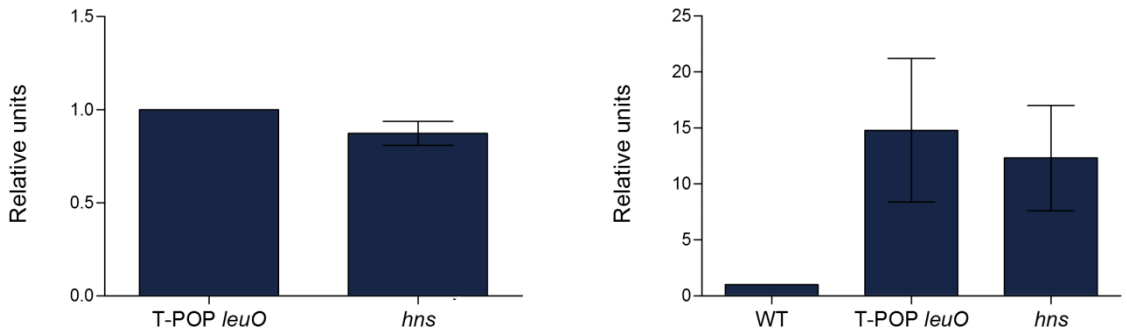


Figure C.2.3. A. Levels of *leuO* mRNA in strains SV6141 (T-POP *leuO*) and SV7853 (Δ*hns*), monitored by quantitative reverse transcriptase PCR. The RNA level found in SV6141 has been normalized to 1. B. Levels of *leuO* mRNA in strains ATCC 14028, SV6141, and SV7853, monitored by quantitative reverse transcriptase PCR. The RNA level found in ATCC 14028 has been normalized to 1. The primers used for RT-PCR are included in Table M.4 (leuO-RT-Dir and leuO-RTRev, and gmk-RT-Dir and gmk-RT-Rev as a control).

Expression of SPI-1 was monitored by measuring the β-galactosidase activity of *lac* fusions in six genes: *hilA*, *hilC*, *hilD* and *invF*, which encode transcriptional regulators of SPI-1 (Altier, 2005; Jones, 2005; Ellermeier and Slauch, 2007); *invH*, which encodes a component of the SPI-1 secretion apparatus (Ellermeier and Slauch, 2007); and *rtsA*, a transcriptional regulator of SPI-1 encoded outside SPI-1 (Ellermeier and Slauch, 2003; 2007; Jones, 2005). Activation of *leuO* transcription reduced the expression of all *lac* fusions (Figure C.2.4).

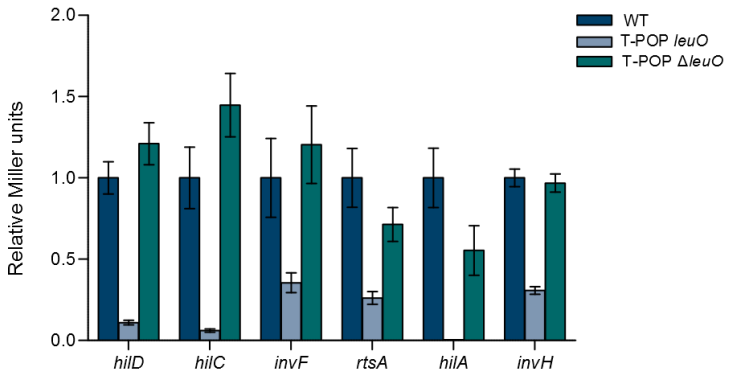


Figure C.2.4. Regulation of SPI-1 expression by LeuO. β-Galactosidase activity of *hilD::lac*, *hilC::lac*, *invF::lac*, *rtsA::lac*, *hilA::lac and invH::lac* fusions in the presence and in the absence of LeuO. Data are averages and standard deviations from > 3 independent experiments.

As controls, strains carrying the same *lac* fusions and a T-POP insertion unlinked to *leuO* (*zzz:T-POP*) were used. In four control strains, the β-galactosidase activities were similar to that of the wild type, in one strain was slightly higher, and in another strain was lower (Figure C.2.5). This experiment ruled out the possibility of an artefact caused by either T-POP or chlortetracycline. We thus concluded that LeuO does repress SPI-1.

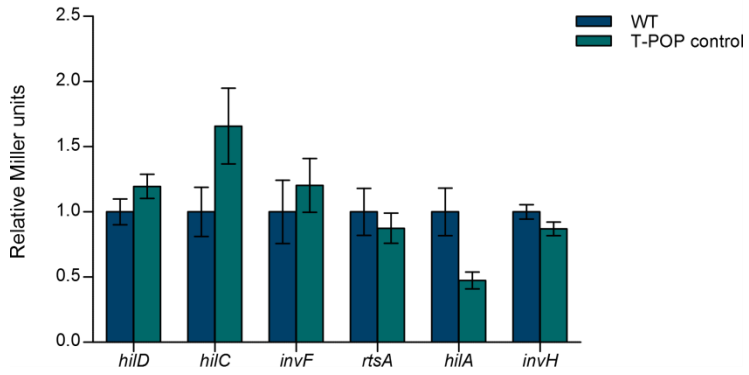


Figure C.2.5. Control experiment to confirm regulation of SPI-1 expression by LeuO. The strains used as controls contained a T-POP element unlinked to *leuO*: SV6849 (*zzz::T-POP hilD930::lacZ*), SV6843 (*zzz::TPOP hilC::lacZ*), SV6846 (*zzz::T-POP invF::lacZ*), SV6852 (*zzz::T-POP rtsA::lacZ*), SV6840 (*zzz::T-POP hilA::lacZ*), and SV7033 (*zzz::T-POP invH::lacZ*). Histograms represent ß-galactosidase activities of *hilD::lac, hilC::lac, invF::lac, rtsA::lac, hilA::lac, and invH::lac* fusions in the presence and in the absence of the T-POP element. Data are averages and standard deviations from >3 independent experiments. The activity of the *hilA::lac* fusion decreased moderately in the presence of the T-POP element and the activity of *hilC::lac* increased, but the others remained unaltered. This experiment confirmed that T-POP does not regulate SPI-1.

C.2.2. LeuO downregulates SPI-1 expression via HilE and HilD

Because SPI-1 expression is responsive to multiple regulators (Ellermeier and Slauch, 2007), we devised a genetic screen to ascertain whether a single cell function might transmit LeuO-mediated regulation to SPI-1. For this purpose, Tn10dCm mutagenesis was performed in a strain that carried the T-POP *leuO* construct and a *hilC::lac* translational fusion (SV6844).

When *leuO* transcription is activated, strain SV6844 is Lac− and forms white colonies on plates containing Xgal. In the screen, Lac+ (blue) colonies were sought among the Cmr isolates generated by Tn10dCm insertion. One such isolate was purified and re-constructed by P22 HT transduction to confirm that the Tn10dCm insertion suppressed *hilC::lac* downregulation by LeuO. The isolate was propagated as strain SV7036.

Amplification by semi-random PCR and sequencing of the Tn10dCm boundaries indicated that the Tn10dCm element of SV7036 had disrupted the *hilE* gene. Use of a HilE− null mutant constructed *ad hoc* (strain SV5586) provided independent evidence that lack of HilE suppressed *hilC::lac* downregulation by LeuO. Single cell analysis of gene expression by flow cytometry (Figure C.2.6.) confirmed that HilE plays a role in LeuO-mediated repression of SPI-1: (i) activation of *leuO* expression decreased the activity of a *sipB*::GFP fusion, abolishing bistable SPI-1 expression; (ii) lack of LeuO restored the wild type pattern of *sipB*::GFP expression, indicating that SPI-1 downregulation was caused by LeuO indeed; (iii) a *hilE* null mutation increased *sipB*::GFP expression and reduced the size of the SPI-1 (OFF) subpopulation, in agreement with the role of HilE as a SPI-1 repressor (Baxter *et al*., 2003); (iv) activation of *leuO* expression in a HilE− background yielded a small subpopulation of *sipB*-::GFP (OFF) cells; and (v) absence of both LeuO and HilE restored the wild type pattern of *sipB*::GFP expression. Altogether, these observations suggest that activation of LeuO expression downregulates SPI-1 by both HilE-dependent and HilE-independent mechanisms. However, activation of *leuO* transcription in a HilE+ background yields a homogeneous population of (SPI-1) OFF cells while activation of *leuO* transcription in the absence of HilE yields a small subpopulation of SPI-1 (OFF) cells. Hence, HilE-dependent downregulation seems to be the major 'pathway' of SPI-1 repression by LeuO.

Because HilE is a negative regulator of *hilD* (Baxter *et al*., 2003), a tentative interpretation for the occurrence of HilE-dependent SPI-1 repression was that LeuO might increase the HilE level, which in turn might inhibit HilD activity. Western blot analysis revealed that activation of *leuO* transcription decreased the HilD level, and the decrease was suppressed in a Δ*leuO* background (Figure C.2.7). We also observed that a *hilE* null mutation increased the HilD levels in the presence and in the absence of LeuO (Figure C.2.7), in accordance with two well known facts: the inhibition of HilD activity by HilE (Baxter *et al*., 2003) and the occurrence of autogenous activation of *hilD* transcription (Ellermeier *et al*., 2005). These experiments support the view that downregulation of SPI-1 by LeuO may involve HilE-mediated inhibition of HilD activity.

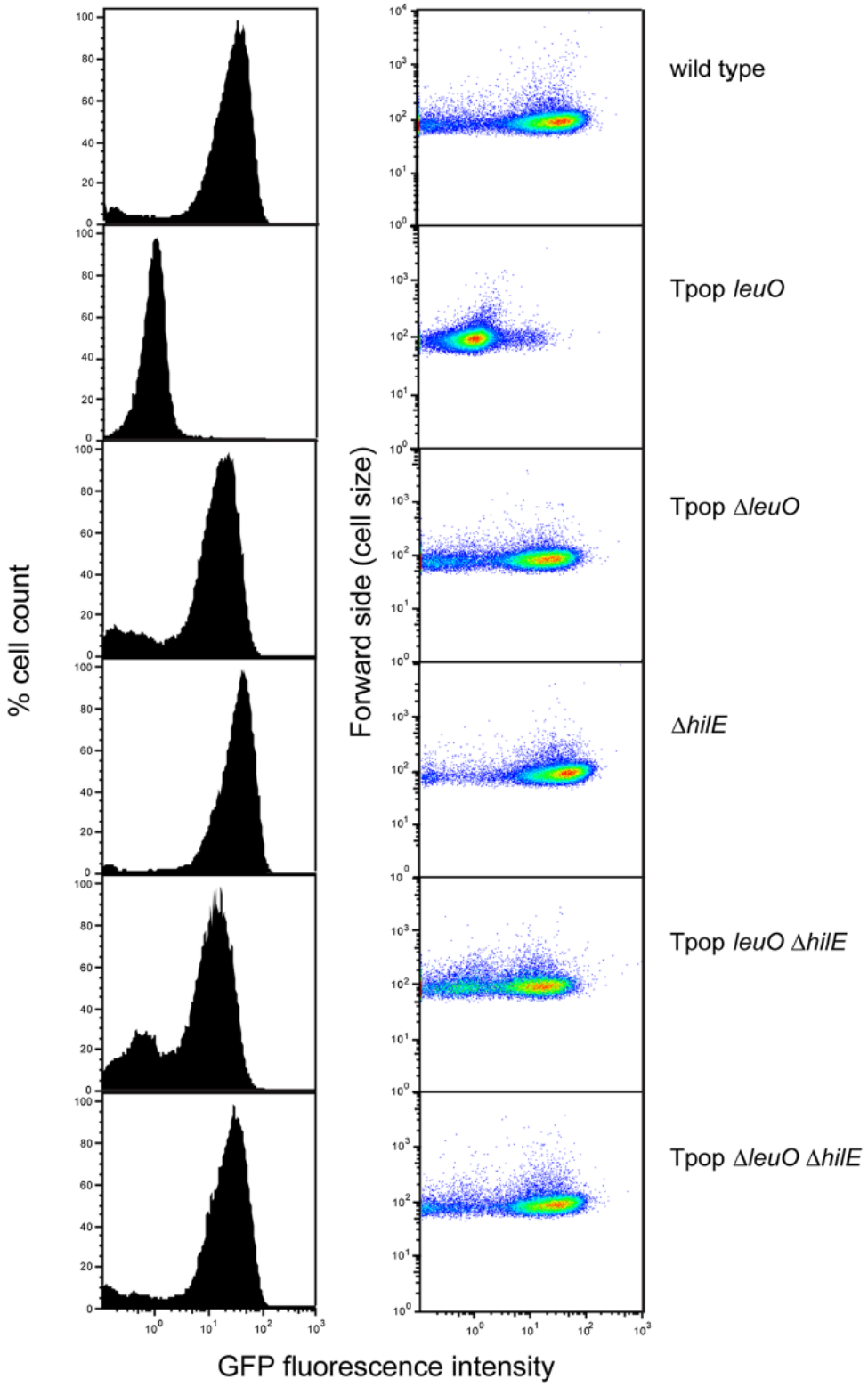


Figure C.2.6. Flow cytometry analysis of SPI-1 expression. Effect of a *hilE* null mutation on *sipB::GFP* expression in the presence and in the absence of LeuO (left column). Data were collected for 40 000 events per sample. In the histograms presented, the cell numbers have been normalized to 100. Data are also represented by a dot plot (right column).

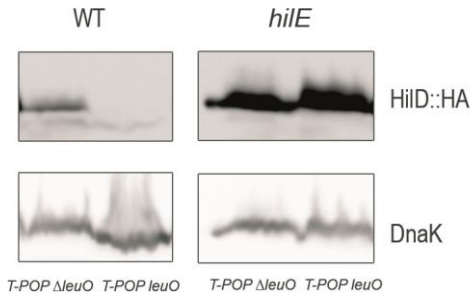


Figure C.2.7. Effect of a hilE mutation on the levels of HilD protein in the presence and in the absence of LeuO. DnaK was used as loading control in Western blots.

The involvement of HilD in LeuO-mediated SPI-1 repression was further investigated by epistasis analysis. This kind of analysis takes advantage of two well known traits of SPI-1 expression. One is redundancy of certain transcription factors involved in SPI-1 control (Altier, 2005; Jones, 2005; Ellermeier and Slauch, 2007). Another is that lack of a single transcription factor does not completely abolish expression of certain SPI-1 transcriptional units (Ellermeier *et al*., 2005). We thus designed experiments to test the effect of a *hilD* null mutation on the expression of *rtsA::lac* and *hilC::lac* fusions in the presence and in the absence of LeuO. If HilD was required for SPI-1 repression by LeuO, we reasoned, downregulation of SPI-1 by LeuO should not be observed in the absence of HilD. Results shown in Figure C.2.8 did not completely fulfil this prediction: moderate downregulation of SPI-1 by LeuO was observed in a HilD−background. Furthermore, even though a *hilD* mutation was epistatic over *hilE*, moderate repression of SPI-1 by LeuO was still observed in a HilD− HilE− background (Figure C.2.8). Hence, LeuO seems to repress SPI-1 by a major 'pathway' involving HilD and HilE, and also by minor, HilD and HilE-independent mechanisms. This conclusion is coherent with the detection of a subpopulation of SPI-1 (OFF) cells when LeuO expression was activated in a HilE− background (Figure C.2.6).

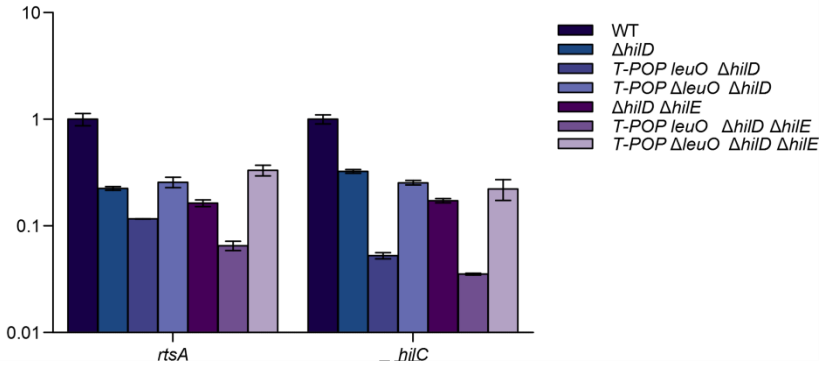


Figure C.2.8. Epistasis analysis of SPI-1 expression. Effect of LeuO expression on the β-galactosidase activity of *rtsA::lac* and *hilC::lac* translational fusions in HilD− and HilD− HilE− backgrounds. Data are averages and standard deviations from > 3 independent experiments.

C.2.3. LeuO activates *hilE* transcription

A tentative model for LeuO-mediated downregulation of SPI-1 via HilE and HilD is that LeuO may activate *hilE* expression, and that HilE-mediated inhibition of HilD activity (Baxter *et al*., 2003) may contribute to SPI-1 downregulation. To test whether LeuO is an activator of *hilE* expression, a *hilE::lacZ* translational fusion was constructed on the *Salmonella* chromosome. Comparison of β-galactosidase activities in the presence and in the absence of LeuO (strains SV7327 and SV7328) indicated that *hilE* expression is activated by LeuO (Figure C.2.9).

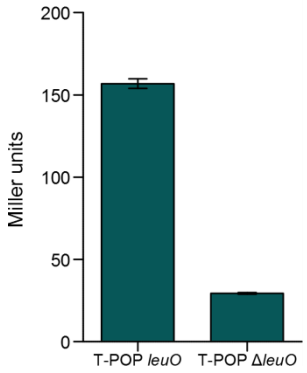


Figure C.2.9. β-Galactosidase activity of an *hilE::lac* translational fusion in the presence and in the absence of LeuO.

Transcription of *hilE* is known to be driven by three promoters (Lim *et al*., 2007). To identify the *hilE* promoter(s) under LeuO control, the P1, P2 and P3 promoters were cloned on the promoter-probe vector pIC552 (Macian *et al*., 1994) to generate transcriptional *lac* fusions. A construct contained the three promoters (pIZ1997), and the others contained individual promoters P1 (pIZ1998), P2 (pIZ1999) and P3 (pIZ2000). Diagrams of the constructs are shown in Figure C.2.10A. Measurements of β-galactosidase activities of the plasmid-borne *lac* fusions showed that LeuO regulates expression of the P1, P2 and P3 *hilE* promoters in an independent manner (Figure C.2.10B). However, LeuO-dependent regulation was found to be stronger when the three promoters were present (Figure C.2.10B).

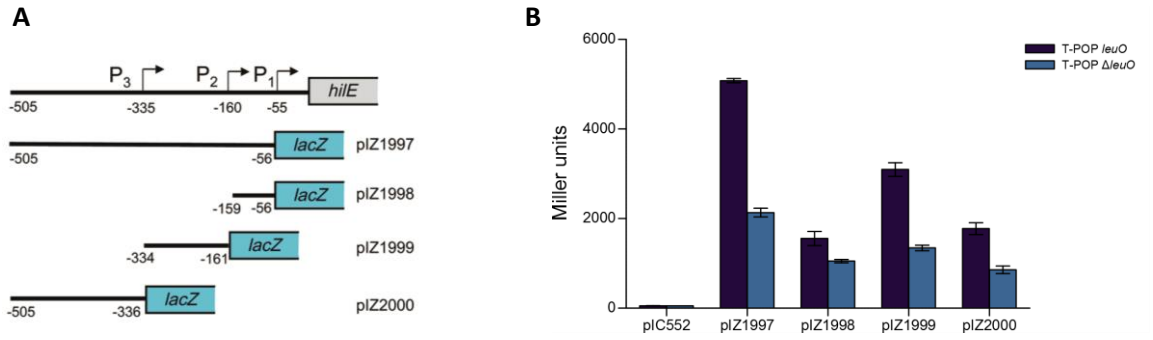


Figure C.2.10. A. Diagram of the *hilE* promoter region, drawn using information from (Lim *et al*., 2007). The DNA fragments cloned on pIC552 are represented below. The −505 to −56 fragment contains the three *hilE* promoters (plasmid pIZ1997). The −159 to −56 fragment contains the P1 promoter (pIZ1998). The −334 to −161 fragment contains the P2 promoter (pIZ1999). The −505 to −336 fragment contains the P3 promoter (pIZ2000). B. β-Galactosidase activities of pIZ1997, pIZ1998, pIZ1999 and pIZ2000 in the presence and in the absence of LeuO. The pIC552 vector was included as control. Data are averages and standard deviations from > 3 independent experiments.

C.2.4. Binding of LeuO to the *hilE* promoter

To test whether LeuO is able to bind the *hilE* promoter region, a slot blot binding assay was performed. A 449 bp DNA fragment containing the P1, P2 and P3 *hilE* promoters was incubated with increasing concentrations of LeuO protein. Binding was unambiguously detected (Figure C.2.11A). Quantitative analysis of binding (Figure C.2.11.B) indicated that, under the conditions of the assay, LeuO bound the *hilE* DNA fragment with an approximate *K*d of 0.37 µM. As a negative control, a binding assay with the *rtsA* promoter was performed, and LeuO was unable to bind the DNA fragment (data not shown).

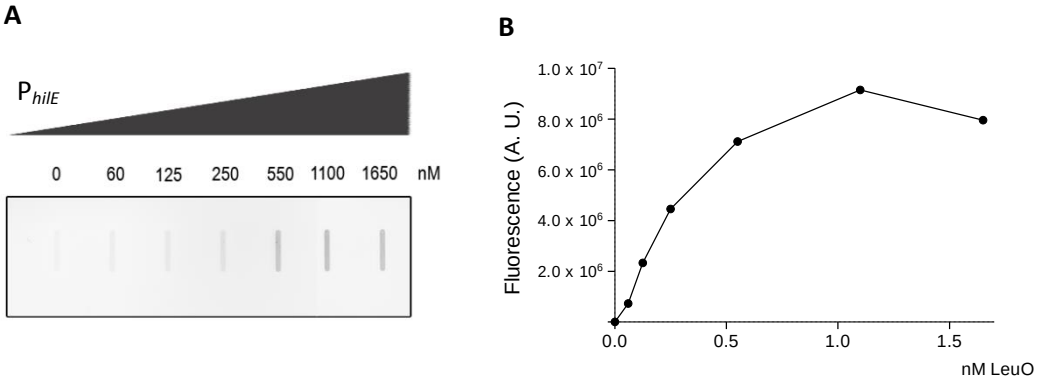


Figure C.2.11. Slot blot binding assay. A 449 bp DNA fragment containing the P1, P2 and P3 *hilE* promoters was incubated with increasing concentrations of LeuO-His6x. B. Quantification of the binding assay. The fluorescence of the DNA bound to the membrane was represented versus the concentration of LeuO-His6x protein.

Binding of LeuO to the *hilE* promoter region was also tested by electrophoretic mobility shift assays. DNA fragments that contained the entire promoter region or the individual P1, P2 and P3 promoters were used. LeuO binding was observed upstream of P2 and P3 but not upstream of P1 (Figure C.2.12A). This observation is consistent with two facts: (i) the weak level of P1-driven *hilE* transcription detected with the promoter-probe plasmid (Figure C.2.10B); (ii) the existence of putative LeuO binding sites upstream of P2 and P3 but not upstream of P1 (Figure C.2.13). Further evidence of LeuO binding to the *hilE* promoter region was obtained by DNA footprinting using the customary 449 bp DNA fragment as target. Protection from DNase I digestion was observed in the presence of LeuO (Figure C.2.12B). Protection was stronger at a region that overlaps the P3 promoter. Because LTTRs can act at a distance (Maddocks and Oyston, 2008; Momany and Neidle, 2012), LeuO binding at the P3 region may be sufficient to permit regulation of the downstream promoter P2 (and perhaps P1). It is also possible that lower affinity binding to P2 may boost transcription.

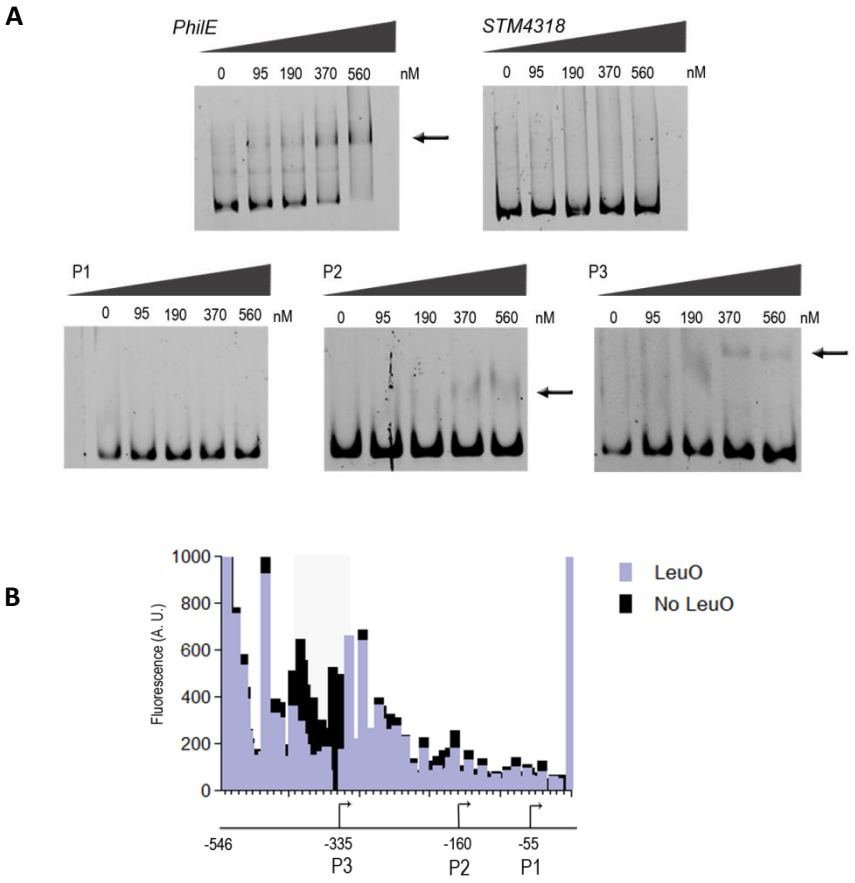


Figure C.2.12. A. Electrophoretic mobility shift assays of LeuOxHis6x binding to the *hilE* promoter region. P_{hilE} designates a DNA fragment containing the entire *hilE* promoter region, while P1, P2 and P3 designate DNA fragments containing individual *hilE* promoters. A DNA fragment containing the *S. enterica* gene *STM4318* was used as control. The concentrations of LeuO-His6x are indicated above each lane. B. DNase I footprinting of LeuOxHis6x binding to the *hilE* promoter region using end-labelled linear

DNA fragments. The size and quantity of 6-FAM-labelled digestion products were measured using a capillary electrophoresis DNA sequencing instrument.

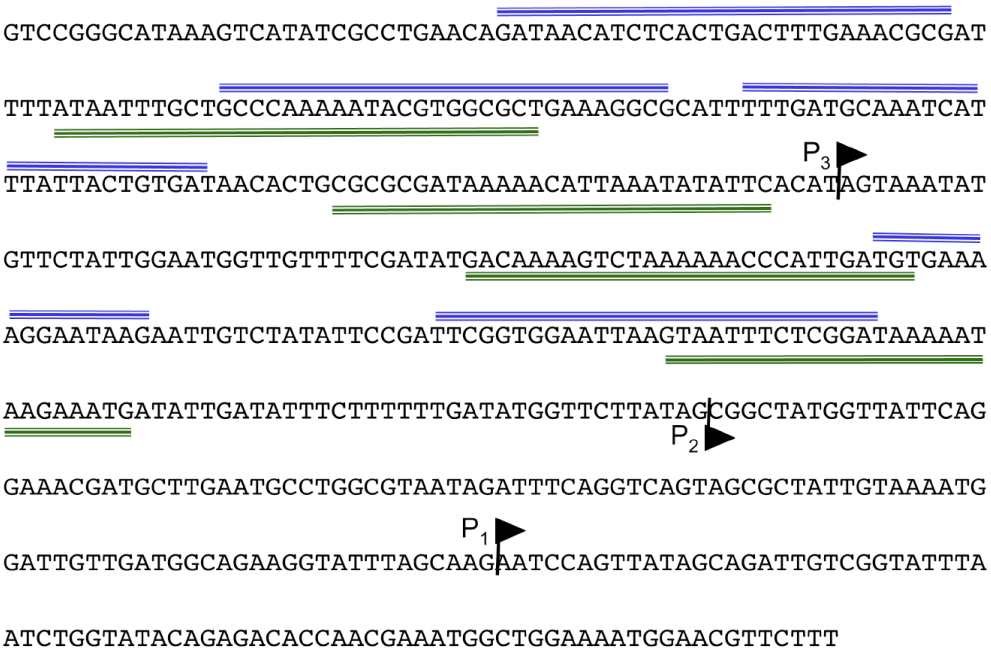


Figure C.2.13. Putative LeuO binding sites found in the *hilE* promoter region, identified with Clustal software (green) and with MEME (Bailey *et al.*, 2009) (http://meme.nbcr.net/meme/cgi-bin/meme.cgi) (blue). The transcription start sites are according to (Lim *et al.*, 2007).

C.2.5. Activation of *leuO* transcription inhibits epithelial cell invasion.

During infection of animals, *Salmonella* Typhimurium invades epithelial cells using the SPI-1 type 3 secretion system. The observation that LeuO downregulates SPI expression thus raised the question of whether activation of *hilE* transcription by LeuO might inhibit epithelial cell invasion. To test this possibility, assays of epithelial cell invasion were performed *in vitro*, and the invasion rates of T-POP *leuO* and T-POP Δ*leuO* strains were compared. As a control, a SPI-1 deletion mutant was included in the assays. Activation of *leuO* transcription decreased invasion > 100-fold, and lack of LeuO restored the wild type invasion rate (Figure C.2.14A). A HilE− mutant was more invasive than the wild type (Figure C.2.14B), an observation coherent with the role of HilE as a negative regulator of SPI-1 (Fahlen *et al*., 2000; Baxter *et al*., 2003). In the absence of HilE, activation of *leuO* transcription reduced epithelial cell invasion three- to fourfold (Figure C.2.14B), thereby providing further evidence for HilE-independent downregulation of SPI-1 by LeuO. We thus conclude that LeuO inhibits invasion of epithelial

cells by *Salmonella enterica* serovar Typhimurium, and that the main inhibition 'pathway' requires HilE. These conclusions are in agreement with the ability of LeuO to activate *hilE* transcription (Figure C.2.9, Figure C.2.10).

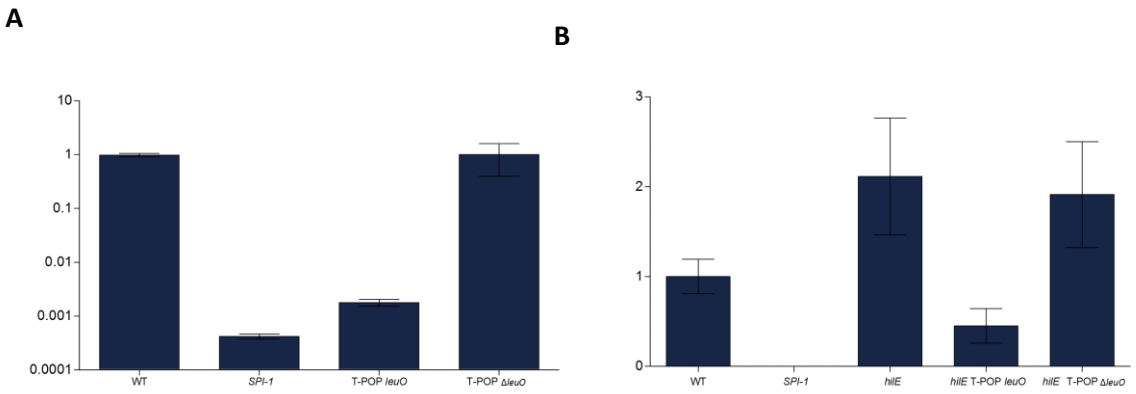


Figure C.2.14. Inhibition of S. enterica invasion by LeuO. A. Invasion of HeLa cells by the wild type (WT), a strain carrying a SPI-1 deletion (ΔSPI-1), a strain with leuO transcription driven by T-POP (T-POP *leuO*), and a leuO deletion mutant (T-POP Δ*leuO*). B. Invasion of HeLa cells by the wild type (WT), a strain carrying a SPI-1 deletion (ΔSPI-1), a HilE− null mutant, (Δ*hilE*), a HilE− null mutant with leuO transcription driven by T-POP (T-POP *leuO* Δ*hilE*), and a strain lacking both LeuO and HilE (T-POP Δ*leuO* Δ*hilE*). The invasion rate of the wild type was 0.1–0.3%, and was normalized to 1. Data are averages and standard deviations from > 6 independent experiments. Because of the disparate invasion rates of the strains under study, different scales are used in each graph.

Chapter 3

Regulation of conjugal transfer of pSLT by LeuO

C.3.1. Identification of LeuO targets in the *Salmonella* virulence plasmid using a ChIP-CHIP approach.

The novel roles for LeuO unveiled by the identification of cognate binding sites in the *Salmonella* chromosome raised the question of whether LeuO might also regulate loci located in the virulence plasmid. To identify LeuO targets in pSLT we performed a chromatin immunoprecipitation (ChIP) assay. LeuO targets were identified by hybridization to a DNA microarray. Bacterial cultures were grown in minimal low-phosphate (LPM) medium until stationary phase to obtain high levels of LeuO protein. ChIP-CHIP assays and analysis of LeuO targets were performed as described in Chapter 1. Twenty eight binding sites (Table C.3.1). Many of these sites are located in *tra* operon, which confers conjugal transfer capacity (Ahmer *et al.*, 1999); the *spv* operon, implicated in virulence (Baumler *et al.*, 1998) and the *pef* operon, implicated in adhesion to the intestinal lumen (Baumler *et al.*, 1996) (Table C.3.1).

Table C.3.1. LeuO targets in pSLT.

Gene	p-value	Strand	Mach start coordinate	Mach end coordinate
TraD	**6.0e-06**	**Forward**	**9599**	**9626**
TraS	**2.6e-05**	**Forward**	**11008**	**11035**
TraL	**1.3e-05**	**Forward**	**30648**	**30675**
TraY	**4.8e-05**	**Forward**	**31288**	**31315**
TraY	**6.6e-05**	**Reverse**	**31526**	**31553**
TraJ	**4.5e-05**	**Forward**	**31618**	**31645**
TraJ	**8.5e-05**	**Forward**	**31686**	**31713**
TraJ	**4.8e-05**	**Forward**	**31856**	**31883**
TraM	**9.0e-05**	**Forward**	**32465**	**32492**
TraM	**8.4e-06**	**Forward**	**32616**	**32643**
IR	**1.7e-05**	**Reverse**	**33074**	**33101**
IR	**6.2e-05**	**Reverse**	**34870**	**34897**
ParA	**4.8e-05**	**Reverse**	**49313**	**49340**
SamB2	**9.0e-05**	**Reverse**	**51308**	**51335**
TlpA	**8.0e-05**	**Reverse**	**54202**	**54229**
IR	**1.1e-05**	**Reverse**	**55547**	**55574**
SpvR	**5.5e-05**	**Reverse**	**61544**	**61571**
SpvR	**3.9e-05**	**Forward**	**62179**	**62206**
SpvB	**5.8e-05**	**Reverse**	**65168**	**65195**
SpvD	**1.7e-05**	**Reverse**	**66949**	**66976**
IR	**4.5e-05**	**Forward**	**73886**	**73913**
IR	**2.3e-06**	**Reverse**	**74322**	**74349**
SL1344_P1_0085	**1.1e-05**	**Reverse**	**78475**	**78502**

PefB	**1.2e-05**	**Forward**	**78876**	**78903**
PefB	**5.1e-05**	**Reverse**	**79710**	**79737**
SL1344_P1_0091	**2.8e-06**	**Forward**	**84142**	**84169**
PefI	**4.5e-05**	**Forward**	**85682**	**85709**
SrgC	**6.2e-05**	**Forward**	**89320**	**89347**

C.3.2. Regulation of the *tra* operon by LeuO

Most LeuO targets in the virulence plasmid pSLT localized in the *tra* operon, suggesting the possibility that LeuO might control conjugal transfer. This possibility is supported by the ocurrence of LeuO targets in the regulatory gene *traJ* and/or in the overlapping (also regulatory) *finP* gene. Even though the identification of LeuO targets had been carried out in strain SL1344, further work on pSLT was performed in ATCC 14028. The reason is that the virulence plasmid of SL1344 carries mutations that reduce the conjugation frequency (Garcia-Quintanilla & Casadesus). In fact, the virulence plasmid of SL1344 had been initially considered nonconjugative (Ahmer et al., 1999).

C.3.3. LeuO binds upstream the *finP* promoter

To validate the ChIP results, we performed an electrophoretic mobility shift assay (EMSA) with a DNA fragment that contained the three LeuO binding sites in *traJ*. This fragment was incubated with increasing concetrations of LeuO protein. As is shown in Figure C.3.1, LeuO binds the *traJ* DNA fragment, which contains the *finP* promoter. DNA fragments of *envR* and *SL3361* were incubated with increasing concentrations of LeuO and were used as positive and negative controls respectively, as previously described in Chapter 1.

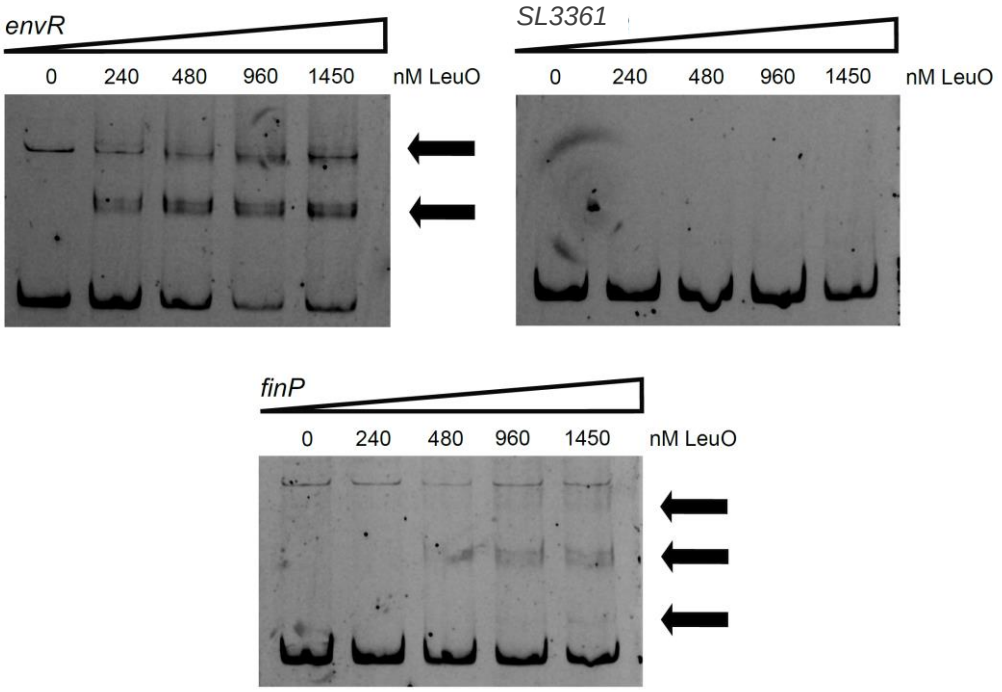


Figure C.3.1. Electrophoretic mobility shift assay of the *traJ/finP* region of pSLT. DNA fragments were incubated with increasing concentrations of LeuO. DNA fragments of *envR* and *SL3361* were used as positive and negative controls. The concentrations of LeuO-His6x are indicated above each lane.

C.3.4. LeuO positively regulates *finP* expression.

Binding of LeuO upstream the *finP* promoter raised the possibility that LeuO might regulate *finP* expression. To test this possibility, we performed a qRT-PCR to compare *finP* expression in a wild type strain, in a strain that expressed *leuO* under the control of a heterologous promoter (T-POP *leuO*), and in a strain in which *leuO* was deleted (T-POP *ΔleuO*). Expression of *leuO* increased *finP* expression approximately 3 fold (Figure C.3.2).

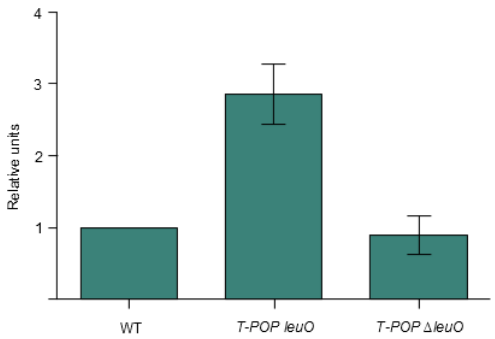


Figure C.3.2. Levels of FinP RNA in strains ATCC 14028, T-POP *leuO* (SV6141) and T-POP Δ*leuO* (SV6142), monitored by quantitative reverse transcriptase PCR. The RNA level found in ATCC 14028 has been

normalized to 1. The primers used for RT-PCR are included in Table M.4 (leuO-RT-Dir and leuO-RTRev, and gmk-RT-Dir and gmk-RT-Rev as a control).

C.3.5. LeuO downregulates *tra* expression.

FinP is an antisense RNA that binds *traJ* mRNA and triggers its degradation by RNase III (Jerome *et al.*, 1999). If LeuO activates *finP* expression, we reasoned, a consequence of this activation might be downregulation of *tra* expression. To test if LeuO represses *tra* expression we performed a western blot. The levels of TraN, a product of the *tra* operon, were monitored in the wild type (ATCC 14028 bacgkround), in a strain expressing *leuO* (T-POP *leuO*), and in a strain in which *leuO* had been deleted (T-POP *ΔleuO*). As shown in figure C.3.3. when *leuO* is expressed (T-POP *leuO*) the level of TraN protein decreases with respect to both the wild type and the strain in which *leuO* had been deleted.

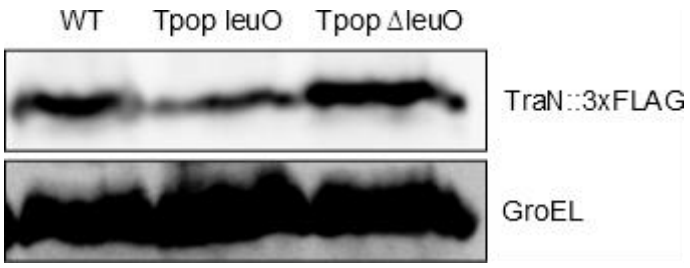


Figure C.3.3. Levels of TraN protein in extracts from strains SV7892, SV7952 (T-POP *leuO*) and SV7953 (T-POP Δ*leuO*). GroEL was used as loading control.

C.3.6. LeuO represses conjugal transfer of pSLT.

To test whether LeuO-mediated activation of *finP* transcription altered the frequency of conjugation, we performed mating assays using the following donor strains: an appropriate ATCC 14208 derivative (SV5556, called "wild type" in Figure C.3.4), a strain with *leuO* under T-POP control (SV7783, T-POP *leuO*), and a strain in which *leuO* had been deleted (SV7784, T-POP *ΔleuO*). Expression of *leuO* causes a decrease approximately of 10 fold in the frequency of conjugation (Figure C.3.4).

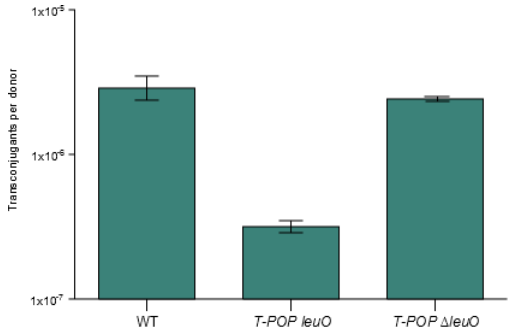


Figure C.3.4. Effect of *leuO* expression on conjugal transfer. SV5556, SV7783 and SV7784 were used as donors and SV5534 was used as recipient. SV7783 expresses *leuO* under the control of a heterologous promoter (T-POP *leuO*). In SV7784, the *leuO* gene has been deleted (T-POP *ΔleuO*). Data are averages and standard deviations from >3 independent matings.

Altogether, the above observations support the idea that LeuO acts as a negative regulator of conjugation by binding upstream the *finP* promoter, and activating its transcription. An increased FinP RNA level must enhance traJ mRNA turnover, resulting in lowered expression of the *tra* operon.

DISCUSSION

D.1. LeuO acts as a global regulator in *S.* Typhimurium

LeuO is a LTTR highly conserved among members of the family *Enterobacteriaceae*. The *leuO* gene is located at the intergenic region between the *ilvIH* and *leuABCD* operons {Fang, 1998 #42}. LeuO was initially described as a regulator involved in DNA supercoiling, and later as an H-NS antagonist {Fang, 1998 #42}{Hernandez-Lucas, 2008 #73}{Shimada, #70}{Stratmann, #44}. Genetic and biochemical analyses of LeuO have been mostly performed in *E. coli* (Shimada *et al.,* Shimada *et al.*, 2009). In *Salmonella*, roles for LeuO in virulence gene regulation have been described in serovar Typhi (Gallego-Hernandez *et al.,* Hernandez-Lucas *et al.*, 2008) but not in *S*. Typhimurium.

We identified the LeuO targets in the genome of serovar Typhimurium (strain SL1344) by chromatin immunoprecipitation. A large number of LeuO targets (178) were found in a wide variety of chromosome locations. In previous genome-wide studies, the majority of bacterial transcription factors have been found to bind predominantly to non-coding DNA sequences (Grainger *et al.*, 2007, Grainger *et al.*, 2006, Grainger *et al.*, 2005, Grainger *et al.*, 2004, Cho *et al.*, 2008, Shimada et al., Wei *et al.*). Because most transcription factors regulate transcription by binding to DNA sites located upstream of promoters, it is not surprising that LTTRs bind intergenic regions upstream of the genes they regulate (Maddocks & Oyston, 2008). Some such binding sites are close to the promoters (-55 to +20) wilhe others are located more than 200 bp upstream of the promoter. However, binding sites within ORFs are also found (Wilson *et al.*, 1995, Viswanathan *et al.*, 2007). In our experiments, the majority of LeuO binding sites were located within ORFs.

The significance of intra-ORF binding is unclear. Because in in some instances LeuO has been shown to act as a negative regulator (Hernandez-Lucas et al., 2008, Shimada et al., 2009), LeuO binding to intragenic regions might contribute to repress transcription. In other coding regions bound by H-NS forming transcriptionally repressive nucleoprotein complexes (Nagarajavel *et al.*, 2007), binding of LeuO to internal regions might antagonize H-NS activity.. It is also possible that LeuO binding across ORFs may reflect an architectural role for the LeuO protein in determining the structure of the nucleoid (Chen & Wu, 2005).

Before this study, knowledge of LeuO targets in the *Salmonella* genome was limited to to relatively few loci in *S.* Typhi rather than *S.* Typhimurium (De la Cruz *et al*., 2007; Hernandez-Lucas *et al*., 2008; Medina-Aparicio *et al*., 2011; Turnbull *et al*., 2012). The 164 new *S.* Typhimurium LeuO binding sites identified here are located in genes involved in a variety of

cellular processes. The list includes inner/outer membrane proteins, transport proteins, motility factors, cell division proteins, oxidative stress response proteins and also other LTTRs (Table S1). Despite the large number of targets found, the list may be incomplete: it is not inconceivable that under appropriate growth conditions *Salmonella* might synthesize larger amounts of LeuO that might in turn occupy even more binding sites than documented here. The fact that we are only starting to understand the growth conditions under which LeuO plays a regulatory role justifies this caveat (Gallego-Hernandez *et al*., 2012).

The nucleoid protein H-NS protein acts as a global repressor of ~ 20% of genes in *S.* Typhimurium (Dorman, 2004; Dillon and Dorman, 2010). H-NS represses transcription by binding to curved AT-rich DNA sequences, and mediates its repressive function by preventing RNA polymerase binding or by trapping RNA polymerase at promoters (Dame *et al*., 2006; Lucchini *et al*., 2006; Navarre *et al*., 2006; Walthers *et al*., 2011). Counteracting the repressive function of H-NS may be important if the cell needs to express H-NS regulated genes; not surprisingly, a number of H-NS antagonism mechanisms have been described (Stoebel *et al*., 2008). LeuO has recently emerged as an antagonist of H-NS (Hernandez-Lucas *et al*., 2008; Shimada *et al*., 2009; 2011), and and may exert this function by competing with H-NS for binding to DNA (Shimada *et al*., 2011) or by acting as a barrier to H-NS polymerization (Chen *et al*., 2003; 2005; Chen and Wu, 2005).

We identified 68 LeuO sites that colocalized with H-NS, a number lower than that reported in the *E. coli* genome (Shimada et al.). After the analysis of the average LeuO and H-NS occupancy in those targets, it was observed that LeuO peak coincided with the H-NS binding landscape. This may indicate that LeuO functions as an H-NS barrier or antagonist, taking up a position interposed between two consecutive H-NS binding peaks.

Analysis of target occupancy by LeuO and H-NS under conditions that induce *leuO* expression (LPM) and under non-inducing conditions (LB) supports a model in which LeuO may induce remodeling of the nucleoprotein complex, overcoming H-NS-mediated repression without stripping H-NS from the DNA. A mechanism of this kind has been proposed for other H-NS antagonists in *S.* Typhimurium, such as the SlyA protein and OmpR (Perez *et al*., 2008; Cameron and Dorman, 2012). The ability of LeuO to form DNA-protein-DNA bridges, analogous to those created by LacI, might also allow LeuO to interfere with H-NS activity without removing the protein from the DNA. Significantly, the LacI protein can replace LeuO as an H-NS antagonist at *leuO* (Chen and Wu, 2005), a finding that is consistent with the two proteins operating through a common mechanism. Here, the LeuO/LacI proteins erect a DNA–protein–

DNA bridge between two binding sites that contains H-NS behind a LeuO/LacI barrier. This barrier may protect a nearby promoter from encroachment by H-NS polymerization without the need to displace H-NS from the DNA.

LTTRs are known to bind sites overlapping or adjacent to the target promoter to repress or activate transcription (Maddocks and Oyston, 2008). It has been suggested that LTTRs activate transcription by interacting with the C-terminal domain of the alpha subunit of RNA polymerase (aCTD). For example, the LTTR family member OxyR increases RNA polymerase binding to OxyR-dependent promoters, suggesting that OxyR activates transcription partly by recruiting RNA polymerase (Kullik *et al*., 1995).

LeuO appears to be associated with active transcription, as the vast majority of LeuO target genes are associated with RNA polymerase binding in LPM. However, it cannot be excluded that some of these co-localization events represent transcriptionally repressive events as LeuO may prevent promoter clearance by trapping RNA polymerase at promoters, a property already described for H-NS (Dame *et al*., 2002). The presence of RNA polymerase at 105 LeuO target genes in inducing conditions (and its absence in non-inducing conditions) suggests that LeuO recruits RNA polymerase, but the observation that 63 of the 68 LeuO + H-NS co-occupancy sites are also associated with RNA polymerase binding is intriguing as binding of H-NS and RNA polymerase are believed to be mutually exclusive in *Salmonella* (Lucchini *et al*., 2006). However, as discussed above, this may indicate trapping of RNA polymerase by LeuO and H-NS. Alternatively, LeuO may remodel H-NS oligomers and allow RNA polymerase to bind to promoters without the need to displace H-NS. We cannot discount the other possibility: that all three factors do not in fact colocalize in all individual cells as ChIP quantifies protein occupancy across a population of cells.

The ability of proteins to recognize specific DNA sequences is a key feature of many biological processes. Recognition of a specific DNA sequence by a protein often involves the formation of specific hydrogen bonds between amino acids and nucleotides (Garvie and Wolberger, 2001). For LysR-like proteins, a DNA sequence known as the LTTR box has been identified (Maddocks and Oyston, 2008). The consensus sequence of the LTTR box is T-N_{11}-A and often displays imperfect dyad symmetry (Parsek *et al*., 1994). However, this motif is highly degenerate and does not give an accurate understanding of the DNA sequences with which LeuO interacts. In the *S*. Typhimurium and *E. coli* genomes, we identified a 28 bp LeuO binding motif with a central region that matched to the regions described previously to LTTR binding motifs. There is a clear divergence between the motifs in both species, and this divergence

may explain why only 15 of the *E. coli* LeuO target genes are shared with *S*. Typhimurium (Table S1).

Regulon divergence is not uncommon even in closely related species, and this is reflected in differences in the presence and nature of regulatory protein binding sites (Perez and Groisman, 2009). While the *E. coli* and *S*. Typhimurium LeuO proteins are highly related (87% amino acid identity) there are a number of amino acid differences in the N-terminal DNA binding domain which may have altered DNA binding site specificity. Furthermore, selective pressure associated with the acquisition and regulatory integration of horizontally acquired SPIs that contain a large number of predicted LeuO binding sites may have also altered DNA binding site preference.

We know that the LTTR box motif is often associated with dyad symmetry (Schell, 1993; Grob *et al*., 1997; Sheehan and Dorman, 1998) and this property appears to be a general feature of the extended 28 bp motifs identified here, albeit weakly in *S.* Typhimurium. The presence of dyad symmetry is consistent with individual LeuO subunits binding to half-sites to form a dimer. However, LTTRs are known to be functionally active as tetramers that protect large regions of DNA (50–60 bp) (Maddocks and Oyston, 2008). Tetramer formation by LeuO would lend itself to DNA–protein–DNA bridging, as it is the case with tetrameric LacI (Chen and Wu, 2005). This would allow LeuO to participate in both short-range and long-range protein–DNA interactions, facilitated by DNA looping.

The extremely high A+T content of both logos (Fig. C1.10) is consistent with the proposed role of LeuO as an H-NS antagonist as H-NS binds to A + T rich sequences (Lucchini *et al*., 2006; Navarre *et al*., 2006; Dillon *et al*., 2010). Furthermore both logos contain a central A-tract at nucleotide positions 15–17. These A-tracts are intriguing because DNA structural studies have determined that A-tracts are associated with narrowing of the DNA minor groove (Beveridge *et al*., 2004; Rohs *et al*., 2009). Variation in DNA shape, in particular DNA minor groove width and DNA twist, is emerging as an important 'indirect' mechanism used by proteins to achieve DNA binding specificity in the absence of base-specific contacts (Rohs *et al*., 2009; Cameron and Dorman, 2012). In this mechanism the bases are not necessarily involved in contacting the protein but in allowing the DNA to assume a conformation that facilitates protein binding (Rohs *et al*., 2009). These flexible bases are often located in linker sequences that connect two half-sites that are directly bound by protein subunits (Hizver *et al*., 2001; Rohs *et al*., 2009). The quasi-palindromic nature and presence of A-tracts in the LeuO

motifs suggests that a combination of direct amino-acid-base-pair interactions and DNA shape may be important features in determining LeuO binding specificity.

After the identification of the LeuO DNA binding motif, we validated our genome-wide prediction, and observed that LeuO seems to have indeed a dual role as transcriptional activator and repressor (Figure C1.14.). Transcriptional activation by LeuO is well documented. In addition, LeuO has been shown to repress the acid stress regulator *cadC*, the gene encoding the small RNA *dsrA*, and the *fimAICDFGH* operon in *E. coli* (Shi and Bennett, 1995; Repoila and Gottesman, 2001; Shimada *et al*., 2011). Furthermore, LeuO has a complex relationship with its own gene, antagonizing H-NS-mediated *leuO* repression and antagonizing RcsB-BglJ-mediated *leuO* activation (Chen and Wu, 2005; Stratmann *et al*., 2012). Many of the genes on the A + T-rich SPIs 1 and 2 are repressed by H-NS (Dillon *et al*., 2010) and our analysis identified 25 predicted LeuO sites in SPI1 and 11 in SPI2. This may explain why LeuO was identified as a virulence factor in a *S.* Typhimurium host-pathogen model system (Tenor *et al*., 2004) and in a long-term systemic infection mouse model system (Lawley *et al*., 2006). It is also important to point out that 24 of 44 genes encoding *S.* Typhimurium LTTRs (Lahiri *et al*., 2009) contain one or more predicted LeuO binding site(s) in their regulatory region. These include the gene encoding TdcA, which is involved in the metabolism of L-serine and L-threonine (Kim *et al*., 2009), and the gene encoding NhaR, which regulates a sodium proton antiporter (Rahav-Manor *et al*., 1992). These LTTRs and their neighbouring regulatory targets are also repressed by H-NS (Table S2), suggesting a complex regulatory interplay between LeuO, other LTTRs and H-NS. As LTTRs often auto-regulate their own expression (Maddocks and Oyston, 2008), it is possible that LeuO establishes a heterotypic interaction with the corresponding LTTR family member to facilitate this auto-regulation (Knapp and Hu, 2010). The presence of LeuO binding sites at so many LTTR genes shows that LeuO also has the potential to co-ordinate their expression within a LeuO dependent regulatory network.

D.2. Regulation of SPI-1 by LeuO

In serovars Typhi and Typhimurium of *Salmonella enterica* LeuO has been shown to regulate virulence-related genes (Fernandez-Mora *et al*., 2004; Tenor *et al*., 2004; Rodriguez-Morales *et al*., 2006; Hernandez-Lucas *et al*., 2008). Given these antecedents, the identification of LeuO binding sites in *Salmonella* pathogenicity island 1 (Chapter 1), combined with the observation that deletion of *leuO* increased expression of the SPI-1 gene *sopA* (Chapter 1), suggested that LeuO might regulate SPI-1, a major determinant of *Salmonella* virulence (Galan and Curtiss, 1989). Multiple controls adjust SPI-1 expression to conditions that permit invasion

of epithelial cells (Altier, 2005; Jones, 2005; Ellermeier and Slauch, 2007). Because activation of SPI-1 expression requires relief from H-NS-mediated silencing (Lucchini *et al*., 2006; Navarre *et al*., 2006) and LeuO acts often as an H-NS antagonist (Hernandez-Lucas *et al*., 2008; Shimada *et al*., 2009; 2011; Stratmann *et al*., 2012), the possibility that LeuO might repress SPI-1 was intriguing.

LeuO is a quiescent LTTR under standard laboratory conditions because *leuO* transcription is repressed by H-NS (Klauck *et al*., 1997). To study LeuO-dependent regulation of SPI-1 in *S. enterica* serovar Typhimurium, transcription of the *leuO* gene was freed from H-NS repression by introducing a T-POP element upstream of *leuO* (Figure C.2.2.). Activation of *leuO* transcription was found to downregulate genes belonging to independent transcriptional units within SPI-1, as well as the SPI-1- controlled *rtsA* gene located outside SPI-1 (Figure C.2.4.). These experiments confirmed that LeuO represses SPI-1 expression. A consequence of SPI-1 repression by LeuO is reduced invasion of epithelial cells *in vitro* (Figure C.2.14.).

A genetic screen for loss-of-function mutations that restored SPI-1 expression in the presence of LeuO provided evidence that the *hilE* gene is necessary for LeuO mediated repression of SPI-1, an hypothesis confirmed upon directed construction of a HilE− mutant. The *hilE* gene is located outside SPI-1, and encodes a repressor of SPI-1 expression (Baxter *et al*., 2003). HilE inactivates the transcriptional activator HilD (Baxter *et al*., 2003). HilD inactivation disrupts a positive feedback loop for *hilD* autogenous activation and causes SPI-1 repression (Ellermeier *et al*., 2005). We thus considered that LeuO might activate *hilE* transcription, and that HilE might repress SPI-1 via HilD inactivation (Figure D.1).

The existence of a LeuO-HilE-HilD 'pathway' of SPI-1 repression in *S. enterica* serovar Typhimurium is supported by several lines of evidence: (i) lack of HilE relieves LeuO-mediated repression of SPI-1 (Figure C.2.6.); (ii) activation of *leuO* transcription decreases the level of HilD protein (Figure C.2.7); (iii) the HilD protein decrease caused by LeuO is suppressed by a *hilE* mutation (Figure C.2.7); and (iv) LeuO activates transcription of *hilE* (Figure C.2.10.).

In the absence of HilE, however, LeuO remains able to downregulate expression of SPI-1 (Figure C.2.8) and to reduce epithelial cell invasion (Figure C.2.14.). HilD is likewise dispensable for HilE-independent downregulation of SPI-1 by LeuO (Figure C.2.8). However, HilE-independent SPI-1 repression appears to be weak in comparison with the HilE-dependent 'pathway' (Figures C.2.6, C.2.8 and D.1). This conclusion is in agreement with the observation

that activation of *leuO* transcription decreases epithelial cell invasion > 100-fold in the presence of HilE and only three- to fourfold in the absence of HilE (Figure C.2.14.).

Our ignorance of natural conditions that permit *leuO* expression advises against interpretation of the physiological significance of SPI-1 regulation by LeuO. However, a conceivable scenario is that LeuO might either backup or relieve H-NS repression of certain loci, in a fashion reminiscent of the HN-S-repressed VirT-VirB regulatory cascade in *Shigella* (Tobe *et al*., 1993). Because HilE is a SPI-1 repressor, a tentative model is that activation of *hilE* transcription by LeuO might boost SPI-1 repression, perhaps under conditions in which H-NS fails to do so. Such hypothetical conditions can be expected to activate *leuO* expression because *leuO* transcription is also repressed by H-NS (Klauck *et al*., 1997). The existence of a subordinate machinery to secure SPI-1 silencing might have selective value because SPI-1 expression causes growth retardation (Sturm *et al*., 2010). Tight repression of SPI-1 might have also selective value in environments different from the animal intestine. For instance, colonization of plants by *Salmonella* is more efficient in the absence of SPI-1 components, perhaps because the presence of the SPI-1 secretion apparatus in the *Salmonella* envelope triggers a defence response by the plant (Iniguez *et al*., 2005).

The view that LeuO may back up or replace H-NS to silence SPI-1 is consistent with the existence of overlapping controls that contribute to silencing of horizontally acquired genes. For instance, the *E. coli* nucleoid associated proteins Hha and YdgT enhance silencing of foreign genes by H-NS (Vivero *et al*., 2008; Banos *et al*., 2009). Interestingly, YdgT and Hha appear to be redundant, and YdgT has been proposed to act as a backup molecule (Paytubi *et al*., 2004). The intricacy of accommodating horizontally acquired genes in the host regulatory network (Ochman *et al*., 2000; Lercher and Pal, 2008; Price *et al*., 2008) may confer adaptive value to redundant control.

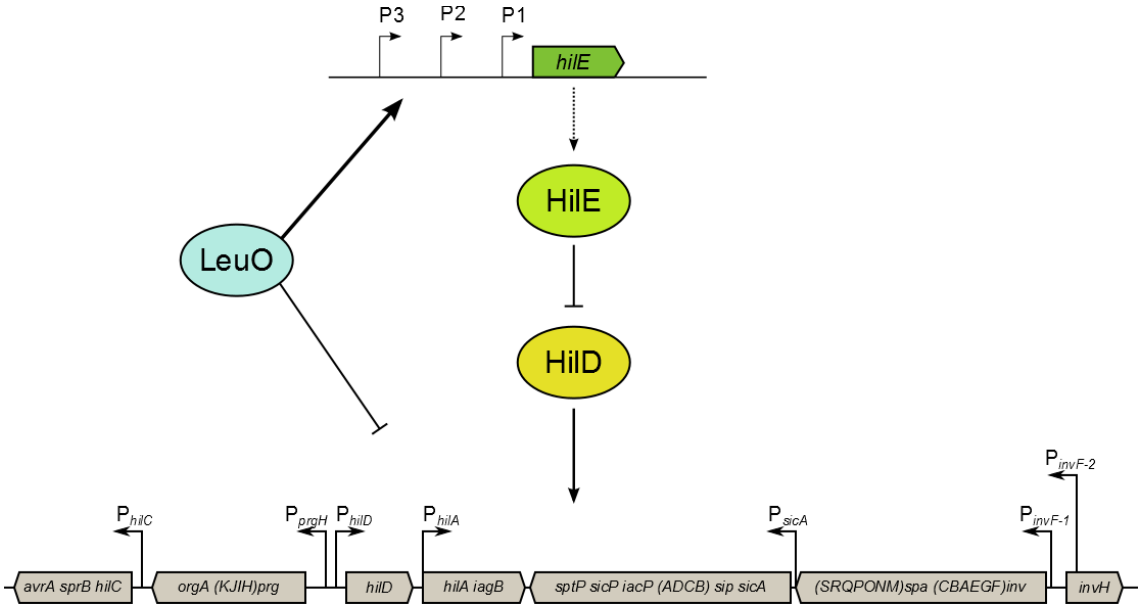


Figure D.1.: Scheme of LeuO regulation of SPI-1. LeuO mainly represses SPI-1 through a HilE-dependent pathway by the direct activation of HilE (arrow) and through a HilE-independent pathway (blunt line).

D.3. Regulation of pSLT transfer by LeuO

When ChIP-CHIP analysis was extended to the *S*. Typhimurium virulence plasmid (pSLT), 28 LeuO targets were identified under LeuO expression conditions (LPM) (VanBogelen *et al.*, 1996). Most LeuO targets were located in loci involved either in *Salmonella* virulence or in pSLT conjugative transfer. For instance, LeuO was found to bind to the *spv* operon, required for systemic infection (Gulig *et al.*, 1993), and to the *pef* operon, involved in bacterial adhesion to intestinal epithelial cells (Baumler *et al.*, 1996). Further work was centered on genes involved in conjugative transfer of plasmid pSLT. As shown in Table C.3.1, LeuO binds to multiple loci in the *tra* operon and to 3 sites within the *traJ/finP* region (Table C.3.1 and Figure C.3.1).

The finding that LeuO is able to bins *traJ/finP* is consistent with previous, unpublished observations from our laboratory suggesting that LeuO is a positive activator of *finP* transcription. For instance, a screen for T-POP insertions that relieved *finP* transcriptional repression in a *dam* background (Camacho et al. 2005) yielded a T-POP insertion upstream of the *leuO* promoter. In the presence of either tetracycline or autoclaved tetracycline, activation of *leuO* transcription from an outward T-POP promoter increased *finP* transcription (unpublished data).

In this study, we show that LeuO binds upstream of the *finP* promoter, thus providing an explanation for the phenomenon described above. LeuO binding relieves H-NS-mediated inhibition, which is exerted both on *finP* and on the overlapping *traJ* gene (Camacho et al. 2005). Activation of *finP* transcription results in inhibition of conjugal transfer (Fig. X). This regulatory pattern may illustrate the complexity of the interactions between LeuO and H-NS. At the *finP* gene, LeuO acts as an H-NS antagonist. However, because FinP RNA is an inhibitor of conjugation (Ref.), activation of *finP* transcription is synergistic with H-NS-mediated repression of *tra* operon expression. This regulatory pattern suggests that LeuO may act as a backup mechanism for inhibition of conjugal transfer under special conditions (e. g., perhaps under conditions in which H-NS-mediated control is inefficient). Because synthesis of the conjugation apparatus represents a burden for the host cell (REF. Zatyka & Thomas), redundant mechanisms for control of *tra* operon expression may have selective value.

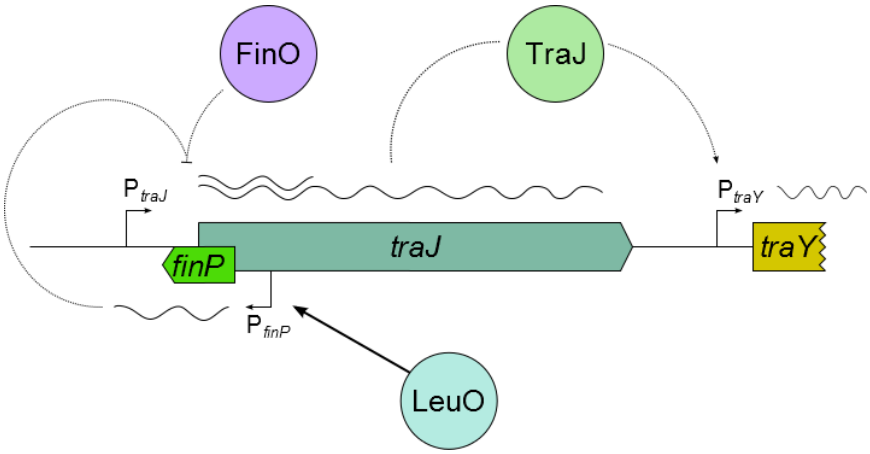


Figure D.2: Model of regulation of conjugation by LeuO. Activation and repression are represented by arrows and blunt lines, respectively.

CONCLUSIONS

1. Chromatin-immunoprecipitation-on-chip identified 178 LeuO binding sites on the chromosome of *Salmonella enterica* serovar Typhimurium strain SL1344. These sites were located both at the core and at the horizontally acquired genome, and included housekeeping genes and genes known to contribute to virulence.

2. RNA polymerase bound 173 of the 178 LeuO targets, consistent with LeuO being a transcriptional regulator.

3. Sixty-eight LeuO targets were co-bound by the global repressor protein, H-NS. Thus, LeuO targets two classes of genes, some bound by H-NS and others that are not bound by H-NS.

4. Analysis of LeuO binding sites revealed a consensus conforming to the TN(11)A motif common to LysR-type transcription factors.

5. Activation of *leuO* transcription downregulates pathogenicity island 1 (SPI-1) and inhibits invasion of epithelial cells by *Salmonella enterica* serovar Typhimurium.

6. Dowregulation of SPI-1 by LeuO involves activation of *hilE* transcription. In turn, increased synthesis of HilE reduces the level of HilD protein, presumably by reducing HilD activity. In addition, LeuO downregulates SPI-1 by minor and uncharacterized HilE-independent pathway.

7. LeuO binds to 28 sites in the *Salmonella* virulence plasmid. Most such sites are located in the plasmid region that contains genes involved in conjugal transfer.

8. LeuO activates transcription of the *finP* gene in the *Salmonella* virulence plasmid. As a consequence, LeuO inhibits conjugal transfer.

REFERENCES

Achtman, M., N. Kennedy & R. Skurray, (1977) Cell-cell interactions in conjugating *Escherichia coli*: role of TraT protein in surface exclusion. Proc Natl Acad Sci USA 74: 5104-5108.

Ackrell, B. A., M. K. Johnson, R. P. Gunsalus, & G, Ceccini, (1992). Structure and function of succinate dehydrogenase and fumarete reductase. Chemistry and biochemistry of flavoenzymes, vol. 3. Muller, f. (ed.) boca raton: crc press, pp. 229-297.

Ahmer, B. M., M. Tran & F. Heffron, (1999) The virulence plasmid of *Salmonella typhimurium* is self-transmissible. J Bacteriol 181: 1364-1368.

Akbar, S., L. M. Schechter, C. P. Lostroh & C. A. Lee, (2003) AraC/XylS family members, HilD and HilC, directly activate virulence gene expression independently of HilA in *Salmonella typhimurium*. Mol Microbiol 47: 715-728.

Altier, C., (2005) Genetic and environmental control of *Salmonella* invasion. J Microbiol 43 Spec No: 85-92.

Altier, C., M. Suyemoto, A. I. Ruiz, K. D. Burnham & R. Maurer, (2000) Characterization of two novel regulatory genes affecting *Salmonella* invasion gene expression. Mol Microbiol 35: 635-646.

Arthur, D. C., A. F. Ghetu, M. J. Gubbins, R. A. Edwards, L. S. Frost & J. N. Glover, (2003) FinO is an RNA chaperone that facilitates sense-antisense RNA interactions. EMBO J 22: 6346-6355.

Arutyunov, D., B. Arenson, J. Manchak & L. S. Frost, (2010) F plasmid TraF and TraH are components of an outer membrane complex involved in conjugation. J Bacteriol 192: 1730-1734.

Arutyunov, D. & L. S. Frost, F conjugation: back to the beginning. Plasmid 70: 18-32.

Arutyunov, D., J. M. Rodriguez-Maillard & L. S. Frost, A PAS domain within F plasmid TraJ is critical for its function as a transcriptional activator. Biochem Cell Biol 89: 396-404.

Bailey, T. L., M. Boden, F. A. Buske, M. Frith, C. E. Grant, L. Clementi, J. Ren, W. W. Li & W. S. Noble, (2009) MEME SUITE: tools for motif discovery and searching. Nucleic Acids Res 37: W202-208.

Baison-Olmo, F., E. Cardenal-Munoz & F. Ramos-Morales, PipB2 is a substrate of the *Salmonella* pathogenicity island 1-encoded type III secretion system. Biochem Biophys Res Commun 423: 240-246.

Bajaj, V., C. Hwang & C. A. Lee, (1995) HilA is a novel ompR/toxR family member that activates the expression of *Salmonella typhimurium* invasion genes. Mol Microbiol 18: 715-727.

Bajaj, V., R. L. Lucas, C. Hwang & C. A. Lee, (1996) Co-ordinate regulation of *Salmonella typhimurium* invasion genes by environmental and regulatory factors is mediated by control of *hilA* expression. Mol Microbiol 22: 703-714.

Baker, C. S., I. Morozov, K. Suzuki, T. Romeo & P. Babitzke, (2002) CsrA regulates glycogen biosynthesis by preventing translation of *glgC* in *Escherichia coli*. Mol Microbiol 44: 1599-1610.

Balbontin, R., G. Rowley, M. G. Pucciarelli, J. Lopez-Garrido, Y. Wormstone, S. Lucchini, F. Garcia-Del Portillo, J. C. Hinton & J. Casadesus, (2006) DNA adenine methylation regulates virulence gene expression in *Salmonella enterica* serovar Typhimurium. J Bacteriol 188: 8160-8168.

Barrangou, R., C. Fremaux, H. Deveau, M. Richards, P. Boyaval, S. Moineau, D. A. Romero & P. Horvath, (2007) CRISPR provides acquired resistance against viruses in prokaryotes. Science 315: 1709-1712.

Baumler, A. J., R. M. Tsolis, F. A. Bowe, J. G. Kusters, S. Hoffmann & F. Heffron, (1996) The *pef* fimbrial operon of *Salmonella typhimurium* mediates adhesion to murine small intestine and is necessary for fluid accumulation in the infant mouse. Infect Immun 64: 61-68.

Baumler, A. J., R. M. Tsolis, T. A. Ficht & L. G. Adams, (1998) Evolution of host adaptation in *Salmonella enterica*. Infect Immun 66: 4579-4587.

Baxter, M. A., T. F. Fahlen, R. L. Wilson & B. D. Jones, (2003) HilE interacts with HilD and negatively regulates *hilA* transcription and expression of the *Salmonella enterica* serovar Typhimurium invasive phenotype. Infect Immun 71: 1295-1305.

Baxter, M. A. & B. D. Jones, (2005) The *fimYZ* genes regulate *Salmonella enterica* serovar Typhimurium invasion in addition to type 1 fimbrial expression and bacterial motility. Infect Immun 73: 1377-1385.

Behlau, I. & S. I. Miller, (1993) A PhoP-repressed gene promotes *Salmonella typhimurium* invasion of epithelial cells. J Bacteriol 175: 4475-4484.

Belden, W. J. & S. I. Miller, (1994) Further characterization of the PhoP regulon: identification of new PhoP-activated virulence loci. Infect Immun 62: 5095-5101.

Beutin, L. & M. Achtman, (1979) Two *Escherichia coli* chromosomal cistrons, *sfrA* and *sfrB*, which are needed for expression of F factor *tra* functions. J Bacteriol 139: 730-737.

Beveridge, D. L., S. B. Dixit, G. Barreiro & K. M. Thayer, (2004) Molecular dynamics simulations of DNA curvature and flexibility: helix phasing and premelting. Biopolymers 73: 380-403.

Bispham, J., B. N. Tripathi, P. R. Watson & T. S. Wallis, (2001) *Salmonella* pathogenicity island 2 influences both systemic salmonellosis and *Salmonella*-induced enteritis in calves. Infect Immun 69: 367-377.

Boddicker, J. D., B. M. Knosp & B. D. Jones, (2003) Transcription of the *Salmonella* invasion gene activator, *hilA*, requires HilD activation in the absence of negative regulators. J Bacteriol 185: 525-533.

Bolotin, A., B. Quinquis, A. Sorokin & S. D. Ehrlich, (2005) Clustered regularly interspaced short palindrome repeats (CRISPRs) have spacers of extrachromosomal origin. Microbiology 151: 2551-2561.

Boyd, E. F. & D. L. Hartl, (1998) *Salmonella* virulence plasmid. Modular acquisition of the *spv* virulence region by an F-plasmid in *Salmonella enterica* subspecies I and insertion into the chromosome of subspecies II, IIIa, IV and VII isolates. Genetics 149: 1183-1190.

Brescia, C. C., M. K. Kaw & D. D. Sledjeski, (2004) The DNA binding protein H-NS binds to and alters the stability of RNA in vitro and in vivo. J Mol Biol 339: 505-514.

Brouns, S. J., M. M. Jore, M. Lundgren, E. R. Westra, R. J. Slijkhuis, A. P. Snijders, M. J. Dickman, K. S. Makarova, E. V. Koonin & J. van der Oost, (2008) Small CRISPR RNAs guide antiviral defense in prokaryotes. Science 321: 960-964.

Browning, D. F., D. C. Grainger & S. J. Busby, Effects of nucleoid-associated proteins on bacterial chromosome structure and gene expression. Curr Opin Microbiol 13: 773-780.

Buck, M. J., A. B. Nobel & J. D. Lieb, (2005) ChIPOTle: a user-friendly tool for the analysis of ChIP-chip data. Genome Biol 6: R97.

Burkinshaw, B. J. & N. C. Strynadka, Assembly and structure of the T3SS. Biochim Biophys Acta.

Bustamante, V. H., L. C. Martinez, F. J. Santana, L. A. Knodler, O. Steele-Mortimer & J. L. Puente, (2008) HilD-mediated transcriptional cross-talk between SPI-1 and SPI-2. Proc Natl Acad Sci USA 105: 14591-14596.

Byrd, D. R. & S. W. Matson, (1997) Nicking by transesterification: the reaction catalysed by a relaxase. Mol Microbiol 25: 1011-1022.

Camacho, E. M. & J. Casadesus, (2002) Conjugal transfer of the virulence plasmid of *Salmonella enterica* is regulated by the leucine-responsive regulatory protein and DNA adenine methylation. Mol Microbiol 44: 1589-1598.

Camacho, E. M. & J. Casadesus, (2005) Regulation of traJ transcription in the *Salmonella* virulence plasmid by strand-specific DNA adenine hemimethylation. Mol Microbiol 57: 1700-1718.

Camacho, E. M., A. Serna, C. Madrid, S. Marques, R. Fernandez, F. de la Cruz, A. Juarez & J. Casadesus, (2005) Regulation of *finP* transcription by DNA adenine methylation in the virulence plasmid of *Salmonella enterica*. J Bacteriol 187: 5691-5699.

Cameron, A. D. & C. J. Dorman, (2012) A fundamental regulatory mechanism operating through OmpR and DNA topology controls expression of *Salmonella* pathogenicity islands SPI-1 and SPI-2. PLoS Genet 8: e1002615.

Carte, J., R. Wang, H. Li, R. M. Terns & M. P. Terns, (2008) Cas6 is an endoribonuclease that generates guide RNAs for invader defense in prokaryotes. Genes Dev 22: 3489-3496.

Cashel, M., D. R. Gentry, V. J. Hernandez, & Vinella, (1996). The stringent response, p. 1458-96. In Neidhart, F. C., R. I. Crustiss, J. L. Ingraham, E. C. C. Lin, K. B. Low, B. Magasanik, & al., e. (ed.), *Escherichia coli* and *Salmonella*: cellular and molecular biology, American society for microbiology press, washintong press, Washington dc.

Cheah, K. C. & R. Skurray, (1986) The F plasmid carries an IS3 insertion within *finO*. J Gen Microbiol 132: 3269-3275.

Chen, C. C., M. Y. Chou, C. H. Huang, A. Majumder & H. Y. Wu, (2005) A cis-spreading nucleoprotein filament is responsible for the gene silencing activity found in the promoter relay mechanism. J Biol Chem 280: 5101-5112.

Chen, C. C., M. Fang, A. Majumder & H. Y. Wu, (2001) A 72-base pair AT-rich DNA sequence element functions as a bacterial gene silencer. J Biol Chem 276: 9478-9485.

Chen, C. C., M. Ghole, A. Majumder, Z. Wang, S. Chandana & H. Y. Wu, (2003) LeuO-mediated transcriptional derepression. J Biol Chem 278: 38094-38103.

Chen, C. C. & H. Y. Wu, (2005) LeuO protein delimits the transcriptionally active and repressive domains on the bacterial chromosome. J Biol Chem 280: 15111-15121.

Chen, D., R. Bowater, C. J. Dorman & D. M. Lilley, (1992) Activity of a plasmid-borne leu-500 promoter depends on the transcription and translation of an adjacent gene. Proc Natl Acad Sci USA 89: 8784-8788.

Chen, D., R. Bowater & D. M. Lilley, (1994) Topological promoter coupling in *Escherichia coli*: delta *topA*-dependent activation of the *leu-500* promoter on a plasmid. J Bacteriol 176: 3757-3764.

Cheng, X., (1995) Structure and function of DNA methyltransferases. Annu Rev Biophys Biomol Struct 24: 293-318.

Cherepanov, P. P. & W. Wackernagel, (1995) Gene disruption in *Escherichia coli*: TcR and KmR cassettes with the option of Flp-catalyzed excision of the antibiotic-resistance determinant. Gene 158: 9-14.

Cho, B. K., E. M. Knight, C. L. Barrett & B. O. Palsson, (2008) Genome-wide analysis of Fis binding in *Escherichia coli* indicates a causative role for A-/AT-tracts. Genome Res 18: 900-910.

Chubiz, J. E., Y. A. Golubeva, D. Lin, L. D. Miller & J. M. Slauch, FliZ regulates expression of the *Salmonella* pathogenicity island 1 invasion locus by controlling HilD protein activity in *Salmonella enterica* serovar Typhimurium. J Bacteriol 192: 6261-6270.

Chun, K. T., H. J. Edenberg, M. R. Kelley & M. G. Goebl, (1997) Rapid amplification of uncharacterized transposon-tagged DNA sequences from genomic DNA. Yeast 13: 233-240.

Crump, J. A. & E. D. Mintz, Global trends in typhoid and paratyphoid Fever. Clin Infect Dis 50: 241-246.

Dame, R. T., (2005) The role of nucleoid-associated proteins in the organization and compaction of bacterial chromatin. Mol Microbiol 56: 858-870.

Dame, R. T., M. C. Noom & G. J. Wuite, (2006) Bacterial chromatin organization by H-NS protein unravelled using dual DNA manipulation. Nature 444: 387-390.

Dame, R. T. & G. J. Wuite, (2003) On the role of H-NS in the organization of bacterial chromatin: from bulk to single molecules and back. Biophys J 85: 4146-4148.

Dame, R. T., C. Wyman & N. Goosen, (2000) H-NS mediated compaction of DNA visualised by atomic force microscopy. Nucleic Acids Res 28: 3504-3510.

Dame, R. T., C. Wyman & N. Goosen, (2001) Structural basis for preferential binding of H-NS to curved DNA. Biochimie 83: 231-234.

Dame, R. T., C. Wyman, R. Wurm, R. Wagner & N. Goosen, (2002) Structural basis for H-NS-mediated trapping of RNA polymerase in the open initiation complex at the rrnB P1. J Biol Chem 277: 2146-2150.

Darwin, K. H. & V. L. Miller, (1999) InvF is required for expression of genes encoding proteins secreted by the SPI1 type III secretion apparatus in *Salmonella typhimurium*. J Bacteriol 181: 4949-4954.

Darwin, K. H. & V. L. Miller, (1999) Molecular basis of the interaction of *Salmonella* with the intestinal mucosa. Clin Microbiol Rev 12: 405-428.

Darwin, K. H. & V. L. Miller, (2001) Type III secretion chaperone-dependent regulation: activation of virulence genes by SicA and InvF in *Salmonella typhimurium*. EMBO J 20: 1850-1862.

Datsenko, K. A. & B. L. Wanner, (2000) One-step inactivation of chromosomal genes in *Escherichia coli* K-12 using PCR products. Proc Natl Acad Sci USA 97: 6640-6645.

De la Cruz, M. A., M. Fernandez-Mora, C. Guadarrama, M. A. Flores-Valdez, V. H. Bustamante, A. Vazquez & E. Calva, (2007) LeuO antagonizes H-NS and StpA-dependent repression in *Salmonella enterica* ompS1. Mol Microbiol 66: 727-743.

de Vries, R., DNA condensation in bacteria: Interplay between macromolecular crowding and nucleoid proteins. Biochimie 92: 1715-1721.

De Wulf, P., O. Kwon & E. C. Lin, (1999) The CpxRA signal transduction system of *Escherichia coli*: growth-related autoactivation and control of unanticipated target operons. J Bacteriol 181: 6772-6778.

Deighan, P., A. Free & C. J. Dorman, (2000) A role for the *Escherichia coli* H-NS-like protein StpA in OmpF porin expression through modulation of micF RNA stability. Mol Microbiol 38: 126-139.

Deiwick, J., S. P. Salcedo, E. Boucrot, S. M. Gilliland, T. Henry, N. Petermann, S. R. Waterman, J. P. Gorvel, D. W. Holden & S. Meresse, (2006) The translocated Salmonella effector proteins SseF and SseG interact and are required to establish an intracellular replication niche. Infect Immun 74: 6965-6972.

Dempsey, W. B., (1987) Transcript analysis of the plasmid R100 *traJ* and *finP* genes. Mol Gen Genet 209: 533-544.

Dillon, S. C., A. D. Cameron, K. Hokamp, S. Lucchini, J. C. Hinton & C. J. Dorman, (2010) Genome-wide analysis of the H-NS and Sfh regulatory networks in Salmonella Typhimurium identifies a plasmid-encoded transcription silencing mechanism. Mol Microbiol 76: 1250-1265.

Dillon, S. C. & C. J. Dorman, (2010) Bacterial nucleoid-associated proteins, nucleoid structure and gene expression. Nat Rev Microbiol 8: 185-195.

Dillon, S. C., E. Espinosa, K. Hokamp, D. W. Ussery, J. Casadesus & C. J. Dorman, LeuO is a global regulator of gene expression in *Salmonella enterica* serovar Typhimurium. Mol Microbiol 85: 1072-1089.

Dorman, C. J., (2004) H-NS: a universal regulator for a dynamic genome. Nat Rev Microbiol 2: 391-400.

Dorman, C. J., (2007) H-NS, the genome sentinel. Nat Rev Microbiol 5: 157-161.

Dorman, C. J., J. C. Hinton & A. Free, (1999) Domain organization and oligomerization among H-NS-like nucleoid-associated proteins in bacteria. Trends Microbiol 7: 124-128.

Dostal, L., S. Shao & J. F. Schildbach, Tracking F plasmid TraI relaxase processing reactions provides insight into F plasmid transfer. Nucleic Acids Res 39: 2658-2670.

Dowman, J. E. & G. G. Meynell, (1970) Pleiotropic effects of de-repressed bacterial sex factors on colicinogeny and cell wall structure. Mol Gen Genet 109: 57-68.

Ehrbar, K. & W. D. Hardt, (2005) Bacteriophage-encoded type III effectors in *Salmonella enterica* subspecies 1 serovar Typhimurium. Infect Genet Evol 5: 1-9.

Eichelberg, K. & J. E. Galan, (1999) Differential regulation of *Salmonella typhimurium* type III secreted proteins by pathogenicity island 1 (SPI-1)-encoded transcriptional activators InvF and HilA. Infect Immun 67: 4099-4105.

Ellermeier, C. D., J. R. Ellermeier & J. M. Slauch, (2005) HilD, HilC and RtsA constitute a feed forward loop that controls expression of the SPI1 type three secretion system regulator HilA in *Salmonella enterica* serovar Typhimurium. Mol Microbiol 57: 691-705.

Ellermeier, C. D., A. Janakiraman & J. M. Slauch, (2002) Construction of targeted single copy lac fusions using lambda Red and FLP-mediated site-specific recombination in bacteria. Gene 290: 153-161.

Ellermeier, C. D. & J. M. Slauch, (2003) RtsA and RtsB coordinately regulate expression of the invasion and flagellar genes in *Salmonella enterica* serovar Typhimurium. J Bacteriol 185: 5096-5108.

Ellermeier, J. R. & J. M. Slauch, (2007) Adaptation to the host environment: regulation of the SPI1 type III secretion system in *Salmonella enterica* serovar Typhimurium. Curr Opin Microbiol 10: 24-29.

Elton, T. C., S. J. Holland, L. S. Frost & B. Hazes, (2005) F-like type IV secretion systems encode proteins with thioredoxin folds that are putative DsbC homologues. J Bacteriol 187: 8267-8277.

Fabrega, A. & J. Vila, *Salmonella enterica* serovar Typhimurium skills to succeed in the host: virulence and regulation. Clin Microbiol Rev 26: 308-341.

Fahlen, T. F., N. Mathur & B. D. Jones, (2000) Identification and characterization of mutants with increased expression of *hilA*, the invasion gene transcriptional activator of *Salmonella typhimurium*. FEMS Immunol Med Microbiol 28: 25-35.

Fahlen, T. F., R. L. Wilson, J. D. Boddicker & B. D. Jones, (2001) Hha is a negative modulator of transcription of *hilA*, the *Salmonella enterica* serovar Typhimurium invasion gene transcriptional activator. J Bacteriol 183: 6620-6629.

Fang, M., A. Majumder, K. J. Tsai & H. Y. Wu, (2000) ppGpp-dependent *leuO* expression in bacteria under stress. Biochem Biophys Res Commun 276: 64-70.

Fang, M. & H. Y. Wu, (1998) A promoter relay mechanism for sequential gene activation. J Bacteriol 180: 626-633.

Fang, M. & H. Y. Wu, (1998) Suppression of *leu-500* mutation in *topA*+ *Salmonella typhimurium* strains. The promoter relay at work. J Biol Chem 273: 29929-29934.

Feasey, N. A., G. Dougan, R. A. Kingsley, R. S. Heyderman & M. A. Gordon, Invasive non-typhoidal salmonella disease: an emerging and neglected tropical disease in Africa. Lancet 379: 2489-2499.

Fernandez-Mora, M., J. L. Puente & E. Calva, (2004) OmpR and LeuO positively regulate the *Salmonella enterica* serovar Typhi ompS2 porin gene. J Bacteriol 186: 2909-2920.

Fink, R. C., M. R. Evans, S. Porwollik, A. Vazquez-Torres, J. Jones-Carson, B. Troxell, S. J. Libby, M. McClelland & H. M. Hassan, (2007) FNR is a global regulator of virulence and anaerobic metabolism in *Salmonella enterica* serovar Typhimurium (ATCC 14028s). J Bacteriol 189: 2262-2273.

Finkel, S. E. & R. C. Johnson, (1993) The Fis protein: it's not just for DNA inversion anymore. Mol Microbiol 7: 1023.

Finlay, B. B., L. S. Frost, W. Paranchych & N. S. Willetts, (1986) Nucleotide sequences of five IncF plasmid finP alleles. J Bacteriol 167: 754-757.

Finlay, B. B., S. Ruschkowski & S. Dedhar, (1991) Cytoskeletal rearrangements accompanying salmonella entry into epithelial cells. J Cell Sci 99 (Pt 2): 283-296.

Finnegan, D. & N. Willetts, (1972) The nature of the transfer inhibitor of several F-like plasmids. Mol Gen Genet 119: 57-66.

Fortune, D. R., M. Suyemoto & C. Altier, (2006) Identification of CsrC and characterization of its role in epithelial cell invasion in *Salmonella enterica* serovar Typhimurium. Infect Immun 74: 331-339.

Foster, J. W. & H. K. Hall, (1991) Inducible pH homeostasis and the acid tolerance response of *Salmonella typhimurium*. J Bacteriol 173: 5129-5135.

Franch, T., M. Petersen, E. G. Wagner, J. P. Jacobsen & K. Gerdes, (1999) Antisense RNA regulation in prokaryotes: rapid RNA/RNA interaction facilitated by a general U-turn loop structure. J Mol Biol 294: 1115-1125.

Francis, C. L., T. A. Ryan, B. D. Jones, S. J. Smith & S. Falkow, (1993) Ruffles induced by *Salmonella* and other stimuli direct macropinocytosis of bacteria. Nature 364: 639-642.

Frost, L., S. Lee, N. Yanchar & W. Paranchych, (1989) *finP* and *finO* mutations in FinP anti-sense RNA suggest a model for FinOP action in the repression of bacterial conjugation by the Flac plasmid JCFL0. Mol Gen Genet 218: 152-160.

Frost, L. S., K. Ippen-Ihler & R. A. Skurray, (1994) Analysis of the sequence and gene products of the transfer region of the F sex factor. Microbiol Rev 58: 162-210.

Frost, L. S., J. Simon, (1993) Studies on the pili of the promiscuoud plasmid RP4. In: Kado, c. (ed.) promiscuous plasmids of Gram-negative and –positive bacteria. Kluwer Academic Publishers, Dordrecht, pp. 47-63.

Galan, J. E., (2001) *Salmonella* interactions with host cells: type III secretion at work. Annu Rev Cell Dev Biol 17: 53-86.

Gallego-Hernandez, A. L., I. Hernandez-Lucas, M. A. De la Cruz, L. Olvera, E. Morett, L. Medina-Aparicio, J. A. Ramirez-Trujillo, A. Vazquez, M. Fernandez-Mora & E. Calva, Transcriptional regulation of the *assT-dsbL-dsbI* gene cluster in *Salmonella enterica* serovar Typhi IMSS-1 depends on LeuO, H-NS, and specific growth conditions. J Bacteriol 194: 2254-2264.

Garcia Vescovi, E., F. C. Soncini & E. A. Groisman, (1996) Mg2+ as an extracellular signal: environmental regulation of *Salmonella* virulence. Cell 84: 165-174.

Garcia-del Portillo, F. & B. B. Finlay, (1995) Targeting of *Salmonella typhimurium* to vesicles containing lysosomal membrane glycoproteins bypasses compartments with mannose 6-phosphate receptors. J Cell Biol 129: 81-97.

Garcia-Del Portillo, F., M. G. Pucciarelli & J. Casadesus, (1999) DNA adenine methylase mutants of *Salmonella typhimurium* show defects in protein secretion, cell invasion, and M cell cytotoxicity. Proc Natl Acad Sci USA 96: 11578-11583.

Garcia-del Portillo, F., M. B. Zwick, K. Y. Leung & B. B. Finlay, (1993) *Salmonella* induces the formation of filamentous structures containing lysosomal membrane glycoproteins in epithelial cells. Proc Natl Acad Sci USA 90: 10544-10548.

Garcia-Quintanilla, M. & J. Casadesus, Virulence plasmid interchange between strains ATCC 14028, LT2, and SL1344 of *Salmonella enterica* serovar Typhimurium. Plasmid 65: 169-175.

Garcia-Quintanilla, M., A. I. Prieto, L. Barnes, F. Ramos-Morales & J. Casadesus, (2006) Bile-induced curing of the virulence plasmid in *Salmonella enterica* serovar Typhimurium. J Bacteriol 188: 7963-7965.

Garcia-Quintanilla, M., F. Ramos-Morales & J. Casadesus, (2008) Conjugal transfer of the *Salmonella enterica* virulence plasmid in the mouse intestine. J Bacteriol 190: 1922-1927.

Garneau, J. E., M. E. Dupuis, M. Villion, D. A. Romero, R. Barrangou, P. Boyaval, C. Fremaux, P. Horvath, A. H. Magadan & S. Moineau, The CRISPR/Cas bacterial immune system cleaves bacteriophage and plasmid DNA. Nature 468: 67-71.

Garvie, C. W. & C. Wolberger, (2001) Recognition of specific DNA sequences. Mol Cell 8: 937-946.

Glickman, B., P. van den Elsen & M. Radman, (1978) Induced mutagenesis in dam- mutants of *Escherichia coli*: a role for 6-methyladenine residues in mutation avoidance. Mol Gen Genet 163: 307-312.

Golubeva, Y. A., A. Y. Sadik, J. R. Ellermeier & J. M. Slauch, Integrating global regulatory input into the *Salmonella* pathogenicity island 1 type III secretion system. Genetics 190: 79-90.

Gong, H., G. P. Vu, Y. Bai, E. Chan, R. Wu, E. Yang, F. Liu & S. Lu, A *Salmonella* small non-coding RNA facilitates bacterial invasion and intracellular replication by modulating the expression of virulence factors. PLoS Pathog 7: e1002120.

Gottesman, S., (2004) The small RNA regulators of *Escherichia coli*: roles and mechanisms*. Annu Rev Microbiol 58: 303-328.

Graham, S. M., Nontyphoidal salmonellosis in Africa. Curr Opin Infect Dis 23: 409-414.

Grainger, D. C., H. Aiba, D. Hurd, D. F. Browning & S. J. Busby, (2007) Transcription factor distribution in *Escherichia coli*: studies with FNR protein. Nucleic Acids Res 35: 269-278.

Grainger, D. C., D. Hurd, M. D. Goldberg & S. J. Busby, (2006) Association of nucleoid proteins with coding and non-coding segments of the Escherichia coli genome. Nucleic Acids Res 34: 4642-4652.

Grainger, D. C., D. Hurd, M. Harrison, J. Holdstock & S. J. Busby, (2005) Studies of the distribution of *Escherichia coli* cAMP-receptor protein and RNA polymerase along the *E. coli* chromosome. Proc Natl Acad Sci USA 102: 17693-17698.

Grainger, D. C., T. W. Overton, N. Reppas, J. T. Wade, E. Tamai, J. L. Hobman, C. Constantinidou, K. Struhl, G. Church & S. J. Busby, (2004) Genomic studies with *Escherichia coli* MelR protein: applications of chromatin immunoprecipitation and microarrays. J Bacteriol 186: 6938-6943.

Grob, P., D. Kahn & D. G. Guiney, (1997) Mutational characterization of promoter regions recognized by the *Salmonella dublin* virulence plasmid regulatory protein SpvR. J Bacteriol 179: 5398-5406.

Groisman, E. A. & H. Ochman, (1997) How *Salmonella* became a pathogen. Trends Microbiol 5: 343-349.

Groisman, E. A., M. A. Sturmoski, F. R. Solomon, R. Lin & H. Ochman, (1993) Molecular, functional, and evolutionary analysis of sequences specific to *Salmonella*. Proc Natl Acad Sci USA 90: 1033-1037.

Guadarrama, C., A. Medrano-Lopez, R. Oropeza, I. Hernandez-Lucas & E. Calva, The *Salmonella enterica* serovar Typhi LeuO Global Regulator Forms Tetramers: Residues Involved in Oligomerization, DNA Binding, and Transcriptional Regulation. J Bacteriol 196: 2143-2154.

Gubbins, M. J., I. Lau, W. R. Will, J. M. Manchak, T. L. Raivio & L. S. Frost, (2002) The positive regulator, TraJ, of the *Escherichia co*li F plasmid is unstable in a *cpxA** background. J Bacteriol 184: 5781-5788.

Gulig, P. A. & R. Curtiss, 3rd, (1987) Plasmid-associated virulence of *Salmonella typhimurium*. Infect Immun 55: 2891-2901.

Gulig, P. A., H. Danbara, D. G. Guiney, A. J. Lax, F. Norel & M. Rhen, (1993) Molecular analysis of *spv* virulence genes of the *Salmonella* virulence plasmids. Mol Microbiol 7: 825-830.

Hale, C. R., P. Zhao, S. Olson, M. O. Duff, B. R. Graveley, L. Wells, R. M. Terns & M. P. Terns, (2009) RNA-guided RNA cleavage by a CRISPR RNA-Cas protein complex. Cell 139: 945-956.

Hanahan, D., (1983) Studies on transformation of *Escherichia coli* with plasmids. J Mol Biol 166: 557-580.

Harris, R. L., V. Hombs & P. M. Silverman, (2001) Evidence that F-plasmid proteins TraV, TraK and TraB assemble into an envelope-spanning structure in *Escherichia coli*. Mol Microbiol 42: 757-766.

Harris, R. L. & P. M. Silverman, (2004) Tra proteins characteristic of F-like type IV secretion systems constitute an interaction group by yeast two-hybrid analysis. J Bacteriol 186: 5480-5485.

Haurwitz, R. E., M. Jinek, B. Wiedenheft, K. Zhou & J. A. Doudna, Sequence- and structure-specific RNA processing by a CRISPR endonuclease. Science 329: 1355-1358.

Hederstedt, L. & L. Rutberg, (1981) Succinate dehydrogenase--a comparative review. Microbiol Rev 45: 542-555.

Heithoff, D. M., R. L. Sinsheimer, D. A. Low & M. J. Mahan, (1999) An essential role for DNA adenine methylation in bacterial virulence. Science 284: 967-970.

Hensel, M., (2000) *Salmonella* pathogenicity island 2. Mol Microbiol 36: 1015-1023.

Hensel, M., J. E. Shea, C. Gleeson, M. D. Jones, E. Dalton & D. W. Holden, (1995) Simultaneous identification of bacterial virulence genes by negative selection. Science 269: 400-403.

Hernandez-Lucas, I., A. L. Gallego-Hernandez, S. Encarnacion, M. Fernandez-Mora, A. G. Martinez-Batallar, H. Salgado, R. Oropeza & E. Calva, (2008) The LysR-type transcriptional regulator LeuO controls expression of several genes in *Salmonella enterica* serovar Typhi. J Bacteriol 190: 1658-1670.

Heroven, A. K. & P. Dersch, (2006) RovM, a novel LysR-type regulator of the virulence activator gene rovA, controls cell invasion, virulence and motility of Yersinia pseudotuberculosis. Mol Microbiol 62: 1469-1483.

Hertzberg, K. M., R. Gemmill, J. Jones & J. M. Calvo, (1980) Cloning of an EcoRI-generated fragment of the leucine operon of *Salmonella typhimurium*. Gene 8: 135-152.

Hizver, J., H. Rozenberg, F. Frolow, D. Rabinovich & Z. Shakked, (2001) DNA bending by an adenine-thymine tract and its role in gene regulation. Proc Natl Acad Sci USA 98: 8490-8495.

Hoch, J. A. & T. J. Silhavy, (1995) Two-component signal transduction. ASM Press, Washington, D. C.

Hofmann, A. F., (1998) Progress in idiopathic bile acid malabsorption. Gut 43: 738-739.

Hoiseth, S. K. & B. A. Stocker, (1981) Aromatic-dependent *Salmonella typhimurium* are non-virulent and effective as live vaccines. Nature 291: 238-239.

Hommais, F., E. Krin, C. Laurent-Winter, O. Soutourina, A. Malpertuy, J. P. Le Caer, A. Danchin & P. Bertin, (2001) Large-scale monitoring of pleiotropic regulation of gene expression by the prokaryotic nucleoid-associated protein, H-NS. Mol Microbiol 40: 20-36.

Howard, M. T., W. C. Nelson & S. W. Matson, (1995) Stepwise assembly of a relaxosome at the F plasmid origin of transfer. J Biol Chem 270: 28381-28386.

Hryniewicz, M. M. & N. M. Kredich, (1994) Stoichiometry of binding of CysB to the *cysJIH*, *cysK*, and *cysP* promoter regions of *Salmonella typhimurium*. J Bacteriol 176: 3673-3682.

Hueck, C. J., (1998) Type III protein secretion systems in bacterial pathogens of animals and plants. Microbiol Mol Biol Rev 62: 379-433.

Inamoto, S., H. Fukuda, T. Abo & E. Ohtsubo, (1994) Site- and strand-specific nicking at oriT of plasmid R100 in a purified system: enhancement of the nicking activity of TraI (helicase I) with TraY and IHF. J Biochem 116: 838-844.

Inamoto, S. & E. Ohtsubo, (1990) Specific binding of the TraY protein to oriT and the promoter region for the *traY* gene of plasmid R100. J Biol Chem 265: 6461-6466.

Inoue, H., H. Nojima & H. Okayama, (1990) High efficiency transformation of *Escherichia coli* with plasmids. Gene 96: 23-28.

Iuchi, S., A. Aristarkhov, J. M. Dong, J. S. Taylor & E. C. Lin, (1994) Effects of nitrate respiration on expression of the Arc-controlled operons encoding succinate dehydrogenase and flavin-linked L-lactate dehydrogenase. J Bacteriol 176: 1695-1701.

Jerome, L. J. & L. S. Frost, (1999) In vitro analysis of the interaction between the FinO protein and FinP antisense RNA of F-like conjugative plasmids. J Biol Chem 274: 10356-10362.

Jerome, L. J., T. van Biesen & L. S. Frost, (1999) Degradation of FinP antisense RNA from F-like plasmids: the RNA-binding protein, FinO, protects FinP from ribonuclease E. J Mol Biol 285: 1457-1473.

Johansson, J. & B. E. Uhlin, (1999) Differential protease-mediated turnover of H-NS and StpA revealed by a mutation altering protein stability and stationary-phase survival of *Escherichia coli*. Proc Natl Acad Sci USA 96: 10776-10781.

Johnston, C., D. A. Pegues, C. J. Hueck, A. Lee & S. I. Miller, (1996) Transcriptional activation of *Salmonella typhimurium* invasion genes by a member of the phosphorylated response-regulator superfamily. Mol Microbiol 22: 715-727.

Jones, B. D., (2005) *Salmonella* invasion gene regulation: a story of environmental awareness. J Microbiol 43 Spec No: 110-117.

Jones, B. D., N. Ghori & S. Falkow, (1994) *Salmonella typhimurium* initiates murine infection by penetrating and destroying the specialized epithelial M cells of the Peyer's patches. J Exp Med 180: 15-23.

Jones, G. W., D. K. Rabert, D. M. Svinarich & H. J. Whitfield, (1982) Association of adhesive, invasive, and virulent phenotypes of *Salmonella typhimurium* with autonomous 60-megadalton plasmids. Infect Immun 38: 476-486.

Kadner, R. J., (2005) Regulation by iron: RNA rules the rust. J Bacteriol 187: 6870-6873.

Kaniga, K., J. C. Bossio & J. E. Galan, (1994) The *Salmonella typhimurium* invasion genes *invF* and *invG* encode homologues of the AraC and PulD family of proteins. Mol Microbiol 13: 555-568.

Kim, M., S. Lim, D. Kim, H. E. Choy & S. Ryu, (2009) A *tdcA* mutation reduces the invasive ability of *Salmonella enterica* serovar Typhimurium. Mol Cells 28: 389-395.

Klauck, E., J. Bohringer & R. Hengge-Aronis, (1997) The LysR-like regulator LeuO in *Escherichia coli* is involved in the translational regulation of *rpoS* by affecting the expression of the small regulatory DsrA-RNA. Mol Microbiol 25: 559-569.

Klauck, E., M. Lingnau & R. Hengge-Aronis, (2001) Role of the response regulator RssB in sigma recognition and initiation of sigma proteolysis in *Escherichia coli*. Mol Microbiol 40: 1381-1390.

Kleckner, N., J. Bender & S. Gottesman, (1991) Uses of transposons with emphasis on Tn10. Methods Enzymol 204: 139-180.

Knapp, G. S. & J. C. Hu, Specificity of the *E. coli* LysR-type transcriptional regulators. PLoS One 5: e15189.

Knodler, L. A., B. A. Vallance, M. Hensel, D. Jackel, B. B. Finlay & O. Steele-Mortimer, (2003) *Salmonella* type III effectors PipB and PipB2 are targeted to detergent-resistant microdomains on internal host cell membranes. Mol Microbiol 49: 685-704.

Koraimann, G., C. Koraimann, V. Koronakis, S. Schlager & G. Hogenauer, (1991) Repression and derepression of conjugation of plasmid R1 by wild-type and mutated *finP* antisense RNA. Mol Microbiol 5: 77-87.

Koraimann, G., K. Teferle, G. Markolin, W. Woger & G. Hogenauer, (1996) The FinOP repressor system of plasmid R1: analysis of the antisense RNA control of traJ expression and conjugative DNA transfer. Mol Microbiol 21: 811-821.

Kroger, C., S. C. Dillon, A. D. Cameron, K. Papenfort, S. K. Sivasankaran, K. Hokamp, Y. Chao, A. Sittka, M. Hebrard, K. Handler, A. Colgan, P. Leekitcharoenphon, G. C. Langridge, A. J. Lohan, B. Loftus, S. Lucchini, D. W. Ussery, C. J. Dorman, N. R. Thomson, J. Vogel & J. C. Hinton, The transcriptional landscape and small RNAs of Salmonella enterica serovar Typhimurium. Proc Natl Acad Sci USA 109: E1277-1286.

Kullik, I., J. Stevens, M. B. Toledano & G. Storz, (1995) Mutational analysis of the redox-sensitive transcriptional regulator OxyR: regions important for DNA binding and multimerization. J Bacteriol 177: 1285-1291.

Laemmli, U. K., (1970) Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature 227: 680-685.

Lahiri, A., P. Das & D. Chakravortty, (2009) *Salmonella* Typhimurium: insight into the multi-faceted role of the LysR-type transcriptional regulators in *Salmonella*. Int J Biochem Cell Biol 41: 2129-2133.

Landgraf, J. R., J. Wu & J. M. Calvo, (1996) Effects of nutrition and growth rate on Lrp levels in *Escherichia coli*. J Bacteriol 178: 6930-6936.

Lang, S., K. Gruber, S. Mihajlovic, R. Arnold, C. J. Gruber, S. Steinlechner, M. A. Jehl, T. Rattei, K. U. Frohlich & E. L. Zechner, Molecular recognition determinants for type IV secretion of diverse families of conjugative relaxases. Mol Microbiol 78: 1539-1555.

Lau-Wong, I. C., T. Locke, M. J. Ellison, T. L. Raivio & L. S. Frost, (2008) Activation of the Cpx regulon destabilizes the F plasmid transfer activator, TraJ, via the HslVU protease in *Escherichia col*i. Mol Microbiol 67: 516-527.

Lawley, T. D., K. Chan, L. J. Thompson, C. C. Kim, G. R. Govoni & D. M. Monack, (2006) Genome-wide screen for *Salmonella* genes required for long-term systemic infection of the mouse. PLoS Pathog 2: e11.

Lawley, T. D., W. A. Klimke, M. J. Gubbins & L. S. Frost, (2003) F factor conjugation is a true type IV secretion system. FEMS Microbiol Lett 224: 1-15.

Lawrenz, M. B. & V. L. Miller, (2007) Comparative analysis of the regulation of *rovA* from the pathogenic yersiniae. J Bacteriol 189: 5963-5975.

Lee, C., C. Wozniak, J. E. Karlinsey & K. T. Hughes, (2007) Genomic screening for regulatory genes using the T-POP transposon. Methods Enzymol 421: 159-167.

Lee, S. H., L. S. Frost & W. Paranchych, (1992) FinOP repression of the F plasmid involves extension of the half-life of FinP antisense RNA by FinO. Mol Gen Genet 235: 131-139.

Lee, S. J., W. Boos, J. P. Bouche & J. Plumbridge, (2000) Signal transduction between a membrane-bound transporter, PtsG, and a soluble transcription factor, Mlc, of *Escherichia coli*. EMBO J 19: 5353-5361.

Leonard, P. G., S. Ono, J. Gor, S. J. Perkins & J. E. Ladbury, (2009) Investigation of the self-association and hetero-association interactions of H-NS and StpA from Enterobacteria. Mol Microbiol 73: 165-179.

Lilley, D. M. & C. F. Higgins, (1991) Local DNA topology and gene expression: the case of the *leu-500* promoter. Mol Microbiol 5: 779-783.

Lim, S., J. Yun, H. Yoon, C. Park, B. Kim, B. Jeon, D. Kim & S. Ryu, (2007) Mlc regulation of *Salmonella* pathogenicity island I gene expression via *hilE* repression. Nucleic Acids Res 35: 1822-1832.

Liu, M. Y., G. Gui, B. Wei, J. F. Preston, 3rd, L. Oakford, U. Yuksel, D. P. Giedroc & T. Romeo, (1997) The RNA molecule CsrB binds to the global regulatory protein CsrA and antagonizes its activity in *Escherichia coli*. J Biol Chem 272: 17502-17510.

Liu, M. Y. & T. Romeo, (1997) The global regulator CsrA of *Escherichia coli* is a specific mRNA-binding protein. J Bacteriol 179: 4639-4642.

Liu, M. Y., H. Yang & T. Romeo, (1995) The product of the pleiotropic *Escherichia coli* gene csrA modulates glycogen biosynthesis via effects on mRNA stability. J Bacteriol 177: 2663-2672.

Liu, X. & P. De Wulf, (2004) Probing the ArcA-P modulon of Escherichia coli by whole genome transcriptional analysis and sequence recognition profiling. J Biol Chem 279: 12588-12597.

Lopez-Garrido, J. & J. Casadesus, Crosstalk between virulence loci: regulation of *Salmonella enterica* pathogenicity island 1 (SPI-1) by products of the *std* fimbrial operon. PLoS One 7: e30499.

Lopez-Garrido, J. & J. Casadesus, Regulation of *Salmonella enterica* pathogenicity island 1 by DNA adenine methylation. Genetics 184: 637-649.

Lopez-Garrido, J., E. Puerta-Fernandez & J. Casadesus, (2014) A eukaryotic-like 3' untranslated region in *Salmonella enterica hilD* mRNA. Nucleic Acids Res 42: 5894-5906.

Lostroh, C. P., V. Bajaj & C. A. Lee, (2000) The cis requirements for transcriptional activation by HilA, a virulence determinant encoded on SPI-1. Mol Microbiol 37: 300-315.

Lostroh, C. P. & C. A. Lee, (2001) The *Salmonella* pathogenicity island-1 type III secretion system. Microbes Infect 3: 1281-1291.

Lucas, R. L. & C. A. Lee, (2001) Roles of *hilC* and *hilD* in regulation of *hilA* expression in *Salmonella enterica* serovar Typhimurium. J Bacteriol 183: 2733-2745.

Lucchini, S., G. Rowley, M. D. Goldberg, D. Hurd, M. Harrison & J. C. Hinton, (2006) H-NS mediates the silencing of laterally acquired genes in bacteria. PLoS Pathog 2: e81.

Lynch, A. S. & E. C. Lin, (1996) Transcriptional control mediated by the ArcA two-component response regulator protein of *Escherichia coli*: characterization of DNA binding at target promoters. J Bacteriol 178: 6238-6249.

Macian, F., I. Perez-Roger & M. E. Armengod, (1994) An improved vector system for constructing transcriptional lacZ fusions: analysis of regulation of the *dnaA*, *dnaN*, *recF* and *gyrB* genes of *Escherichia coli*. Gene 145: 17-24.

Maddocks, S. E. & P. C. Oyston, (2008) Structure and function of the LysR-type transcriptional regulator (LTTR) family proteins. Microbiology 154: 3609-3623.

Madhusudan, S., A. Paukner, Y. Klingen & K. Schnetz, (2005) Independent regulation of H-NS-mediated silencing of the *bgl* operon at two levels: upstream by BglJ and LeuO and downstream by DnaKJ. Microbiology 151: 3349-3359.

Madrid, C., C. Balsalobre, J. Garcia & A. Juarez, (2007) The novel Hha/YmoA family of nucleoid-associated proteins: use of structural mimicry to modulate the activity of the H-NS family of proteins. Mol Microbiol 63: 7-14.

Madrid, C., J. M. Nieto, S. Paytubi, M. Falconi, C. O. Gualerzi & A. Juarez, (2002) Temperature- and H-NS-dependent regulation of a plasmid-encoded virulence operon expressing *Escherichia coli* hemolysin. J Bacteriol 184: 5058-5066.

Majdalani, N. & S. Gottesman, (2005) The Rcs phosphorelay: a complex signal transduction system. Annu Rev Microbiol 59: 379-405.

Majowicz, S. E., J. Musto, E. Scallan, F. J. Angulo, M. Kirk, S. J. O'Brien, T. F. Jones, A. Fazil & R. M. Hoekstra, The global burden of nontyphoidal *Salmonella* gastroenteritis. Clin Infect Dis 50: 882-889.

Maloy, S. R. (1990). Experimental techniques in bacterial genetics. Boston, MA: Jones & Barlett.

Maneewannakul, S., K. Maneewannakul & K. Ippen-Ihler, (1992) Characterization, localization, and sequence of F transfer region products: the pilus assembly gene product TraW and a new product, TrbI. J Bacteriol 174: 5567-5574.

Margolin, P., L. Zumstein, R. Sternglanz & J. C. Wang, (1985) The Escherichia coli *supX* locus is *topA*, the structural gene for DNA topoisomerase I. Proc Natl Acad Sci USA 82: 5437-5441.

Marinus, M.G., (1996) Methylation of DNA. P. 782-791. In Neidhart, F. C., R. I. Crustiss, J. L. Ingraham, E. C. C. Lin, K. B. Low, B. Magasanik, & al., e. (ed.), *Escherichia coli* and *Salmonella*: cellular and molecular biology, American society for microbiology press, washintong press, Washington dc.

Marinus, M. G. & N. R. Morris, (1973) Isolation of deoxyribonucleic acid methylase mutants of *Escherichia coli* K-12. J Bacteriol 114: 1143-1150.

Marlovits, T. C. & C. E. Stebbins, Type III secretion systems shape up as they ship out. Curr Opin Microbiol 13: 47-52.

Marraffini, L. A. & E. J. Sontheimer, Self versus non-self discrimination during CRISPR RNA-directed immunity. Nature 463: 568-571.

Marraffini, L. A. & E. J. Sontheimer, (2008) CRISPR interference limits horizontal gene transfer in staphylococci by targeting DNA. Science 322: 1843-1845.

Maxon, M. E., B. Redfield, X. Y. Cai, R. Shoeman, K. Fujita, W. Fisher, G. Stauffer, H. Weissbach & N. Brot, (1989) Regulation of methionine synthesis in *Escherichia coli*: effect of the MetR protein on the expression of the *metE* and *metR* genes. Proc Natl Acad Sci USA 86: 85-89.

McClelland, M., K. E. Sanderson, J. Spieth, S. W. Clifton, P. Latreille, L. Courtney, S. Porwollik, J. Ali, M. Dante, F. Du, S. Hou, D. Layman, S. Leonard, C. Nguyen, K. Scott, A. Holmes, N. Grewal, E. Mulvaney, E. Ryan, H. Sun, L. Florea, W. Miller, T. Stoneking, M. Nhan, R. Waterston & R. K. Wilson, (2001) Complete genome sequence of *Salmonella enterica* serovar Typhimurium LT2. Nature 413: 852-856.

McEwen, J. & P. Silverman, (1980) Chromosomal mutations of *Escherichia coli* that alter expression of conjugative plasmid functions. Proc Natl Acad Sci USA 77: 513-517.

McEwen, J. & P. Silverman, (1980) Genetic analysis of *Escherichia coli* K-12 chromosomal mutants defective in expression of F-plasmid functions: identification of genes *cpxA* and *cpxB*. J Bacteriol 144: 60-67.

McFarland, K. A. & C. J. Dorman, (2008) Autoregulated expression of the gene coding for the leucine-responsive protein, Lrp, a global regulator in *Salmonella enterica* serovar Typhimurium. Microbiology 154: 2008-2016.

McGraw, B. R. & M. G. Marinus, (1980) Isolation and characterization of Dam+ revertants and suppressor mutations that modify secondary phenotypes of dam-3 strains of *Escherichia coli* K-12. Mol Gen Genet 178: 309-315.

McQuiston, J. R., R. Parrenas, M. Ortiz-Rivera, L. Gheesling, F. Brenner & P. I. Fields, (2004) Sequencing and comparative analysis of flagellin genes *fliC*, *fljB*, and *flpA* from *Salmonella*. J Clin Microbiol 42: 1923-1932.

Medina-Aparicio, L., J. E. Rebollar-Flores, A. L. Gallego-Hernandez, A. Vazquez, L. Olvera, R. M. Gutierrez-Rios, E. Calva & I. Hernandez-Lucas, The CRISPR/Cas immune system is an operon regulated by LeuO, H-NS, and leucine-responsive regulatory protein in *Salmonella enterica* serovar Typhi. J Bacteriol 193: 2396-2407.

Meresse, S., K. E. Unsworth, A. Habermann, G. Griffiths, F. Fang, M. J. Martinez-Lorenzo, S. R. Waterman, J. P. Gorvel & D. W. Holden, (2001) Remodelling of the actin cytoskeleton is essential for replication of intravacuolar *Salmonella*. Cell Microbiol 3: 567-577.

Messer, W., U. Bellekes & H. Lother, (1985) Effect of dam methylation on the activity of the *E. coli* replication origin, oriC. EMBO J 4: 1327-1332.

Miller, J. H. (1972). Experiments in molecular genetics. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.

Miller, S. I., A. M. Kukral & J. J. Mekalanos, (1989) A two-component regulatory system (phoP phoQ) controls *Salmonella typhimurium* virulence. Proc Natl Acad Sci USA 86: 5054-5058.

Moest, T. P. & S. Meresse, *Salmonella* T3SSs: successful mission of the secret(ion) agents. Curr Opin Microbiol 16: 38-44.

Mojica, F. J., C. Diez-Villasenor, J. Garcia-Martinez & E. Soria, (2005) Intervening sequences of regularly spaced prokaryotic repeats derive from foreign genetic elements. J Mol Evol 60: 174-182.

Mojica, F. J., C. Diez-Villasenor, E. Soria & G. Juez, (2000) Biological significance of a family of regularly spaced repeats in the genomes of Archaea, Bacteria and mitochondria. Mol Microbiol 36: 244-246.

Moller, T., T. Franch, P. Hojrup, D. R. Keene, H. P. Bachinger, R. G. Brennan & P. Valentin-Hansen, (2002) Hfq: a bacterial Sm-like protein that mediates RNA-RNA interaction. Mol Cell 9: 23-30.

Momany, C. & E. L. Neidle, Defying stereotypes: the elusive search for a universal model of LysR-type regulation. Mol Microbiol 83: 453-456.

Moorthy, S. & P. I. Watnick, (2005) Identification of novel stage-specific genetic requirements through whole genome transcription profiling of *Vibrio cholerae* biofilm development. Mol Microbiol 57: 1623-1635.

Mullineaux, P. & N. Willetts, (1985) Promoters in the transfer region of plasmid F. Basic Life Sci 30: 605-614.

Nagarajavel, V., S. Madhusudan, S. Dole, A. R. Rahmouni & K. Schnetz, (2007) Repression by binding of H-NS within the transcription unit. J Biol Chem 282: 23622-23630.

Nam, T. W., S. H. Cho, D. Shin, J. H. Kim, J. Y. Jeong, J. H. Lee, J. H. Roe, A. Peterkofsky, S. O. Kang, S. Ryu & Y. J. Seok, (2001) The *Escherichia coli* glucose transporter enzyme IICB(Glc) recruits the global repressor Mlc. EMBO J 20: 491-498.

Navarre, W. W., M. McClelland, S. J. Libby & F. C. Fang, (2007) Silencing of xenogeneic DNA by H-NS-facilitation of lateral gene transfer in bacteria by a defense system that recognizes foreign DNA. Genes Dev 21: 1456-1471.

Navarre, W. W., S. Porwollik, Y. Wang, M. McClelland, H. Rosen, S. J. Libby & F. C. Fang, (2006) Selective silencing of foreign DNA with low GC content by the H-NS protein in *Salmonella*. Science 313: 236-238.

Nelson, W. C., M. T. Howard, J. A. Sherman & S. W. Matson, (1995) The *traY* gene product and integration host factor stimulate *Escherichia coli* DNA helicase I-catalyzed nicking at the F plasmid oriT. J Biol Chem 270: 28374-28380.

Nelson, W. C., B. S. Morton, E. E. Lahue & S. W. Matson, (1993) Characterization of the *Escherichia coli* F factor *traY* gene product and its binding sites. J Bacteriol 175: 2221-2228.

Nicholson, B. & D. Low, (2000) DNA methylation-dependent regulation of *pef* expression in *Salmonella typhimurium*. Mol Microbiol 35: 728-742.

Nieto, J. M., C. Madrid, E. Miquelay, J. L. Parra, S. Rodriguez & A. Juarez, (2002) Evidence for direct protein-protein interaction between members of the enterobacterial Hha/YmoA and H-NS families of proteins. J Bacteriol 184: 629-635.

Nieto, J. M., C. Madrid, A. Prenafeta, E. Miquelay, C. Balsalobre, M. Carrascal & A. Juarez, (2000) Expression of the hemolysin operon in *Escherichia coli* is modulated by a nucleoid-protein complex that includes the proteins Hha and H-NS. Mol Gen Genet 263: 349-358.

Ochman, H. & A. C. Wilson, (1987) Evolution in bacteria: evidence for a universal substitution rate in cellular genomes. J Mol Evol 26: 74-86.

Ogden, G. B., M. J. Pratt & M. Schaechter, (1988) The replicative origin of the *E. coli* chromosome binds to cell membranes only when hemimethylated. Cell 54: 127-135.

Olekhnovich, I. N. & R. J. Kadner, (2002) DNA-binding activities of the HilC and HilD virulence regulatory proteins of *Salmonella enterica* serovar Typhimurium. J Bacteriol 184: 4148-4160.

Olekhnovich, I. N. & R. J. Kadner, (2006) Crucial roles of both flanking sequences in silencing of the *hilA* promoter in *Salmonella enterica*. J Mol Biol 357: 373-386.

Olekhnovich, I. N. & R. J. Kadner, (2007) Role of nucleoid-associated proteins Hha and H-NS in expression of *Salmonella enterica* activators HilD, HilC, and RtsA required for cell invasion. J Bacteriol 189: 6882-6890.

Oshima, T., S. Ishikawa, K. Kurokawa, H. Aiba & N. Ogasawara, (2006*) Escherichia coli* histone-like protein H-NS preferentially binds to horizontally acquired DNA in association with RNA polymerase. DNA Res 13: 141-153.

Ou, J. T., L. S. Baron, X. Y. Dai & C. A. Life, (1990) The virulence plasmids of *Salmonella* serovars typhimurium, choleraesuis, dublin, and enteritidis, and the cryptic plasmids of *Salmonella* serovars copenhagen and sendai belong to the same incompatibility group, but not those of *Salmonella* serovars durban, gallinarum, give, infantis and pullorum. Microb Pathog 8: 101-107.

Pallen, M. J., R. R. Chaudhuri & I. R. Henderson, (2003) Genomic analysis of secretion systems. Curr Opin Microbiol 6: 519-527.

Park, S. J. & R. P. Gunsalus, (1995) Oxygen, iron, carbon, and superoxide control of the fumarase *fumA* and f*umC* genes of *Escherichia coli*: role of the *arcA*, *fnr*, and *soxR* gene products. J Bacteriol 177: 6255-6262.

Parsek, M. R., R. W. Ye, P. Pun & A. M. Chakrabarty, (1994) Critical nucleotides in the interaction of a LysR-type regulator with its target promoter region. *catBC* promoter activation by CatR. J Biol Chem 269: 11279-11284.

Paytubi, S., C. Madrid, N. Forns, J. M. Nieto, C. Balsalobre, B. E. Uhlin & A. Juarez, (2004) YdgT, the Hha paralogue in *Escherichia coli*, forms heteromeric complexes with H-NS and StpA. Mol Microbiol 54: 251-263.

Pegues, D. A., M. J. Hantman, I. Behlau & S. I. Miller, (1995) PhoP/PhoQ transcriptional repression of *Salmonella typhimurium* invasion genes: evidence for a role in protein secretion. Mol Microbiol 17: 169-181.

Pelletier, J., K. Halvorsen, B. Y. Ha, R. Paparcone, S. J. Sandler, C. L. Woldringh, W. P. Wong & S. Jun, Physical manipulation of the *Escherichia coli* chromosome reveals its soft nature. Proc Natl Acad Sci USA 109: E2649-2656.

Penfold, S. S., J. Simon & L. S. Frost, (1996) Regulation of the expression of the *traM* gene of the F sex factor of *Escherichia coli*. Mol Microbiol 20: 549-558.

Penheiter, K. L., N. Mathur, D. Giles, T. Fahlen & B. D. Jones, (1997) Non-invasive *Salmonella typhimurium* mutants are avirulent because of an inability to enter and destroy M cells of ileal Peyer's patches. Mol Microbiol 24: 697-709.

Perez, J. C. & E. A. Groisman, (2009) Evolution of transcriptional regulatory circuits in bacteria. Cell 138: 233-244.

Peterson, K. R. & D. W. Mount, (1987) Differential repression of SOS genes by unstable lexA41 (tsl-1) protein causes a "split-phenotype" in *Escherichia coli* K-12. J Mol Biol 193: 27-40.

Petrone, B. L., A. M. Stringer & J. T. Wade, Identification of HilD-regulated genes in *Salmonella enterica* serovar Typhimurium. J Bacteriol 196: 1094-1101.

Pogliano, J., A. S. Lynch, D. Belin, E. C. Lin & J. Beckwith, (1997) Regulation of *Escherichia coli* cell envelope proteins involved in protein folding and degradation by the Cpx two-component system. Genes Dev 11: 1169-1182.

Pourcel, C., G. Salvignol & G. Vergnaud, (2005) CRISPR elements in Yersinia pestis acquire new repeats by preferential uptake of bacteriophage DNA, and provide additional tools for evolutionary studies. Microbiology 151: 653-663.

Prieto, A. I., F. Ramos-Morales & J. Casadesus, (2004) Bile-induced DNA damage in *Salmonella enterica*. Genetics 168: 1787-1794.

Prosseda, G., M. Falconi, M. Giangrossi, C. O. Gualerzi, G. Micheli & B. Colonna, (2004) The *virF* promoter in *Shigella*: more than just a curved DNA stretch. Mol Microbiol 51: 523-537.

Pruss, G. J. & K. Drlica, (1985) DNA supercoiling and suppression of the *leu-500* promoter mutation. J Bacteriol 164: 947-949.

Pucciarelli, M. G., A. I. Prieto, J. Casadesus & F. Garcia-del Portillo, (2002) Envelope instability in DNA adenine methylase mutants of *Salmonella enterica*. Microbiology 148: 1171-1182.

Pul, U., R. Wurm, Z. Arslan, R. Geissen, N. Hofmann & R. Wagner, Identification and characterization of *E. coli* CRISPR-cas promoters and their silencing by H-NS. Mol Microbiol 75: 1495-1512.

Queiroz, M. H., C. Madrid, S. Paytubi, C. Balsalobre & A. Juarez, Integration host factor alleviates H-NS silencing of the *Salmonella enterica* serovar Typhimurium master regulator of SPI1, *hilA*. Microbiology 157: 2504-2514.

Rahav-Manor, O., O. Carmel, R. Karpel, D. Taglicht, G. Glaser, S. Schuldiner & E. Padan, (1992) NhaR, a protein homologous to a family of bacterial regulatory proteins (LysR), regulates *nhaA*, the sodium proton antiporter gene in *Escherichia coli*. J Biol Chem 267: 10433-10438.

Rajashekar, R., D. Liebl, A. Seitz & M. Hensel, (2008) Dynamic remodeling of the endosomal system during formation of *Salmonella*-induced filaments by intracellular *Salmonella enterica*. Traffic 9: 2100-2116.

Rappleye, C. A. & J. R. Roth, (1997) A Tn10 derivative (T-POP) for isolation of insertions with conditional (tetracycline-dependent) phenotypes. J Bacteriol 179: 5827-5834.

Rathman, M., L. P. Barker & S. Falkow, (1997) The unique trafficking pattern of *Salmonella typhimurium*-containing phagosomes in murine macrophages is independent of the mechanism of bacterial entry. Infect Immun 65: 1475-1485.

Repoila, F. & S. Gottesman, (2003) Temperature sensing by the *dsrA* promoter. J Bacteriol 185: 6609-6614.

Rescigno, M., (2006) CCR6(+) dendritic cells: the gut tactical-response unit. Immunity 24: 508-510.

Richardson, S. M., C. F. Higgins & D. M. Lilley, (1988) DNA supercoiling and the *leu-500* promoter mutation of *Salmonella typhimurium*. EMBO J 7: 1863-1869.

Rimsky, S., (2004) Structure of the histone-like protein H-NS and its role in regulation and genome superstructure. Curr Opin Microbiol 7: 109-114.

Rimsky, S., F. Zuber, M. Buckle & H. Buc, (2001) A molecular mechanism for the repression of transcription by the H-NS protein. Mol Microbiol 42: 1311-1323.

Rodriguez-Maillard, J. M., D. Arutyunov & L. S. Frost, The F plasmid transfer activator TraJ is a dimeric helix-turn-helix DNA-binding protein. FEMS Microbiol Lett 310: 112-119.

Rodriguez-Morales, O., M. Fernandez-Mora, I. Hernandez-Lucas, A. Vazquez, J. L. Puente & E. Calva, (2006) *Salmonella enterica* serovar Typhimurium *ompS1* and ompS2 mutants are attenuated for virulence in mice. Infect Immun 74: 1398-1402.

Rohs, R., S. M. West, A. Sosinsky, P. Liu, R. S. Mann & B. Honig, (2009) The role of DNA shape in protein-DNA recognition. Nature 461: 1248-1253.

Romeo, T., M. Gong, M. Y. Liu & A. M. Brun-Zinkernagel, (1993) Identification and molecular characterization of *csrA*, a pleiotropic gene from *Escherichia coli* that affects glycogen biosynthesis, gluconeogenesis, cell size, and surface properties. J Bacteriol 175: 4744-4755.

Rotger, R. & J. Casadesus, (1999) The virulence plasmids of *Salmonella*. Int Microbiol 2: 177-184.

Rutherford, K., J. Parkhill, J. Crook, T. Horsnell, P. Rice, M. A. Rajandream & B. Barrell, (2000) Artemis: sequence visualization and annotation. Bioinformatics 16: 944-945.

Salcedo, S. P. & D. W. Holden, (2003) SseG, a virulence protein that targets *Salmonella* to the Golgi network. EMBO J 22: 5003-5014.

Sanderson, K. E., S. K. Kadam & P. R. MacLachlan, (1983) Derepression of F factor function in *Salmonella typhimurium*. Can J Microbiol 29: 1205-1212.

Schechter, L. M. & C. A. Lee, (2001) AraC/XylS family members, HilC and HilD, directly bind and derepress the *Salmonella typhimurium hilA* promoter. Mol Microbiol 40: 1289-1299.

Schell, M. A., (1993) Molecular biology of the LysR family of transcriptional regulators. Annu Rev Microbiol 47: 597-626.

Schmidt, H. & M. Hensel, (2004) Pathogenicity islands in bacterial pathogenesis. Clin Microbiol Rev 17: 14-56.

Schmieger, H., (1972) Phage P22-mutants with increased or decreased transduction abilities. Mol Gen Genet 119: 75-88.

Schroder, O. & R. Wagner, (2000) The bacterial DNA-binding protein H-NS represses ribosomal RNA transcription by trapping RNA polymerase in the initiation complex. J Mol Biol 298: 737-748.

Serna, A., E. Espinosa, E. M. Camacho & J. Casadesus, (2010) Regulation of bacterial conjugation in microaerobiosis by host-encoded functions ArcAB and *sdhABCD*. Genetics 184: 947-958.

Sheehan, B. J. & C. J. Dorman, (1998) In vivo analysis of the interactions of the LysR-like regulator SpvR with the operator sequences of the *spvA* and *spvR* virulence genes of *Salmonella typhimurium*. Mol Microbiol 30: 91-105.

Shen, J. & R. P. Gunsalus, (1997) Role of multiple ArcA recognition sites in anaerobic regulation of succinate dehydrogenase (*sdhCDAB*) gene expression in *Escherichia coli*. Mol Microbiol 26: 223-236.

Shi, X. & G. N. Bennett, (1994) Plasmids bearing *hfq* and the hns-like gene *stpA* complement *hns* mutants in modulating arginine decarboxylase gene expression in *Escherichia coli*. J Bacteriol 176: 6769-6775.

Shi, X. & G. N. Bennett, (1995) Effects of multicopy LeuO on the expression of the acid-inducible lysine decarboxylase gene in *Escherichia coli*. J Bacteriol 177: 810-814.

Shimada, T., A. Bridier, R. Briandet & A. Ishihama, Novel roles of LeuO in transcription regulation of *E. coli* genome: antagonistic interplay with the universal silencer H-NS. Mol Microbiol 82: 378-397.

Shimada, T., K. Yamamoto & A. Ishihama, (2009) Involvement of the leucine response transcription factor LeuO in regulation of the genes for sulfa drug efflux. J Bacteriol 191: 4562-4571.

Silverman, P. M. & A. Sholl, (1996) Effect of *traY* amber mutations on F-plasmid *traY* promoter activity in vivo. J Bacteriol 178: 5787-5789.

Silverman, P. M., E. Wickersham & R. Harris, (1991) Regulation of the F plasmid *traY* promoter in *Escherichia coli* by host and plasmid factors. J Mol Biol 218: 119-128.

Singer, H. M., C. Kuhne, J. A. Deditius, K. T. Hughes & M. Erhardt, The *Salmonella* Spi1 virulence regulatory protein HilD directly activates transcription of the flagellar master operon *flhDC*. J Bacteriol 196: 1448-1457.

Starcic, M., D. Zgur-Bertok, B. J. Jordi, M. M. Wosten, W. Gaastra & J. P. van Putten, (2003) The cyclic AMP-cyclic AMP receptor protein complex regulates activity of the *traJ* promoter of the *Escherichia coli* conjugative plasmid pRK100. J Bacteriol 185: 1616-1623.

Starcic-Erjavec, M., J. P. van Putten, W. Gaastra, B. J. Jordi, M. Grabnar & D. Zgur-Bertok, (2003) H-NS and Lrp serve as positive modulators of *traJ* expression from the *Escherichia coli* plasmid pRK100. Mol Genet Genomics 270: 94-102.

Stockwell, D., V. Lelianova, T. Thompson & W. B. Dempsey, (2000) Transcription of the transfer genes *traY* and *traM* of the antibiotic resistance plasmid R100-1 is linked. Plasmid 43: 35-48.

Stoebel, D. M., A. Free & C. J. Dorman, (2008) Anti-silencing: overcoming H-NS-mediated repression of transcription in Gram-negative enteric bacteria. Microbiology 154: 2533-2545.

Stratmann, T., S. Madhusudan & K. Schnetz, (2008) Regulation of the *yjjQ-bglJ* operon, encoding LuxR-type transcription factors, and the divergent *yjjP* gene by H-NS and LeuO. J Bacteriol 190: 926-935.

Stratmann, T., U. Pul, R. Wurm, R. Wagner & K. Schnetz, RcsB-BglJ activates the *Escherichia coli leuO* gene, encoding an H-NS antagonist and pleiotropic regulator of virulence determinants. Mol Microbiol 83: 1109-1123.

Strohmaier, H., R. Noiges, S. Kotschan, G. Sawers, G. Hogenauer, E. L. Zechner & G. Koraimann, (1998) Signal transduction and bacterial conjugation: characterization of the role of ArcA in regulating conjugative transfer of the resistance plasmid R1. J Mol Biol 277: 309-316.

Takaya, A., Y. Kubota, E. Isogai & T. Yamamoto, (2005) Degradation of the HilC and HilD regulator proteins by ATP-dependent Lon protease leads to downregulation of *Salmonella* pathogenicity island 1 gene expression. Mol Microbiol 55: 839-852.

Takaya, A., T. Tomoyasu, H. Matsui & T. Yamamoto, (2004) The DnaK/DnaJ chaperone machinery of *Salmonella enterica* serovar Typhimurium is essential for invasion of epithelial cells and survival within macrophages, leading to systemic infection. Infect Immun 72: 1364-1373.

Takeuchi, A., (1967) Electron microscope studies of experimental Salmonella infection. I. Penetration into the intestinal epithelium by *Salmonella typhimurium*. Am J Pathol 50: 109-136.

Tan, J., L. Shu & H. Y. Wu, (1994) Activation of the *leu-500* promoter by adjacent transcription. J Bacteriol 176: 1077-1086.

Tavendale, A., C. K. Jardine, D. C. Old & J. P. Duguid, (1983) Haemagglutinins and adhesion of *Salmonella typhimurium* to HEp2 and HeLa cells. J Med Microbiol 16: 371-380.

Tenor, J. L., B. A. McCormick, F. M. Ausubel & A. Aballay, (2004) *Caenorhabditis elegans*-based screen identifies *Salmonella* virulence factors required for conserved host-pathogen interactions. Curr Biol 14: 1018-1024.

Teplitski, M., R. I. Goodier & B. M. Ahmer, (2003) Pathways leading from BarA/SirA to motility and virulence gene expression in *Salmonella*. J Bacteriol 185: 7257-7265.

Tindall, B. J., P. A. Grimont, G. M. Garrity & J. P. Euzeby, (2005) Nomenclature and taxonomy of the genus *Salmonella*. Int J Syst Evol Microbiol 55: 521-524.

Torreblanca, J. & J. Casadesus, (1996) DNA adenine methylase mutants of *Salmonella typhimurium* and a novel dam-regulated locus. Genetics 144: 15-26.

Torreblanca, J., S. Marques & J. Casadesus, (1999) Synthesis of FinP RNA by plasmids F and pSLT is regulated by DNA adenine methylation. Genetics 152: 31-45.

Travers, A. & G. Muskhelishvili, (2005) DNA supercoiling - a global transcriptional regulator for enterobacterial growth? Nat Rev Microbiol 3: 157-169.

Troxell, B., M. L. Sikes, R. C. Fink, A. Vazquez-Torres, J. Jones-Carson & H. M. Hassan, Fur negatively regulates *hns* and is required for the expression of HilA and virulence in *Salmonella enterica* serovar Typhimurium. J Bacteriol 193: 497-505.

Tsai, M. M., Y. H. Fu & R. C. Deonier, (1990) Intrinsic bends and integration host factor binding at F plasmid *oriT*. J Bacteriol 172: 4603-4609.

Tupper, A. E., T. A. Owen-Hughes, D. W. Ussery, D. S. Santos, D. J. Ferguson, J. M. Sidebotham, J. C. Hinton & C. F. Higgins, (1994) The chromatin-associated protein H-NS alters DNA topology in vitro. EMBO J 13: 258-268.

Turnbull, A. L., W. Kim & M. G. Surette, Transcriptional regulation of *sdiA* by cAMP-receptor protein, LeuO, and environmental signals in *Salmonella enterica* serovar Typhimurium. Can J Microbiol 58: 10-22.

Ueguchi, C., T. Ohta, C. Seto, T. Suzuki & T. Mizuno, (1998) The *leuO* gene product has a latent ability to relieve *bgl* silencing in *Escherichia coli*. J Bacteriol 180: 190-193.

Uzzau, S., N. Figueroa-Bossi, S. Rubino & L. Bossi, (2001) Epitope tagging of chromosomal genes in *Salmonella*. Proc Natl Acad Sci USA 98: 15264-15269.

Valentin-Hansen, P., M. Eriksen & C. Udesen, (2004) The bacterial Sm-like protein Hfq: a key player in RNA transactions. Mol Microbiol 51: 1525-1533.

van Biesen, T. & L. S. Frost, (1994) The FinO protein of IncF plasmids binds FinP antisense RNA and its target, *traJ* mRNA, and promotes duplex formation. Mol Microbiol 14: 427-436.

van Biesen, T., F. Soderbom, E. G. Wagner & L. S. Frost, (1993) Structural and functional analyses of the FinP antisense RNA regulatory system of the F conjugative plasmid. Mol Microbiol 10: 35-43.

Van Engelenburg, S. B. & A. E. Palmer, Imaging type-III secretion reveals dynamics and spatial segregation of *Salmonella* effectors. Nat Methods 7: 325-330.

VanBogelen, R. A., E. R. Olson, B. L. Wanner & F. C. Neidhardt, (1996) Global analysis of proteins synthesized during phosphorus restriction in *Escherichia coli*. J Bacteriol 178: 4344-4366.

Venkatesh, G. R., F. C. Kembou Koungni, A. Paukner, T. Stratmann, B. Blissenbach & K. Schnetz, BglJ-RcsB heterodimers relieve repression of the *Escherichia coli bgl* operon by H-NS. J Bacteriol 192: 6456-6464.

Viswanathan, P., T. Ueki, S. Inouye & L. Kroos, (2007) Combinatorial regulation of genes essential for *Myxococcus xanthus* development involves a response regulator and a LysR-type regulator. Proc Natl Acad Sci USA 104: 7969-7974.

Wagner, M. A., K. Bischof, D. Kati & G. Koraimann, Silencing and activating type IV secretion genes of the F-like conjugative resistance plasmid R1. Microbiology 159: 2481-2491.

Waldminghaus, T. & K. Skarstad, ChIP on Chip: surprising results are often artifacts. BMC Genomics 11: 414.

Wallis, T. S. & E. E. Galyov, (2000) Molecular basis of *Salmonella*-induced enteritis. Mol Microbiol 36: 997-1005.

Walthers, D., Y. Li, Y. Liu, G. Anand, J. Yan & L. J. Kenney, *Salmonella enterica* response regulator SsrB relieves H-NS silencing by displacing H-NS bound in polymerization mode and directly activates transcription. J Biol Chem 286: 1895-1902.

Weber, R. F. & P. M. Silverman, (1988) The cpx proteins of *Escherichia coli* K12. Structure of the cpxA polypeptide as an inner membrane component. J Mol Biol 203: 467-478.

Wei, B. L., A. M. Brun-Zinkernagel, J. W. Simecka, B. M. Pruss, P. Babitzke & T. Romeo, (2001) Positive regulation of motility and *flhDC* expression by the RNA-binding protein CsrA of *Escherichia coli*. Mol Microbiol 40: 245-256.

Wei, Q., P. N. Minh, A. Dotsch, F. Hildebrand, W. Panmanee, A. Elfarash, S. Schulz, S. Plaisance, D. Charlier, D. Hassett, S. Haussler & P. Cornelis, Global regulation of gene expression by OxyR in an important human opportunistic pathogen. Nucleic Acids Res 40: 4320-4333.

Weilbacher, T., K. Suzuki, A. K. Dubey, X. Wang, S. Gudapaty, I. Morozov, C. S. Baker, D. Georgellis, P. Babitzke & T. Romeo, (2003) A novel sRNA component of the carbon storage regulatory system of *Escherichia coli*. Mol Microbiol 48: 657-670.

Wessler, S. R. & J. M. Calvo, (1981) Control of *leu* operon expression in *Escherichia coli* by a transcription attenuation mechanism. J Mol Biol 149: 579-597.

Westra, E. R., U. Pul, N. Heidrich, M. M. Jore, M. Lundgren, T. Stratmann, R. Wurm, A. Raine, M. Mescher, L. Van Heereveld, M. Mastop, E. G. Wagner, K. Schnetz, J. Van Der Oost, R. Wagner & S. J. Brouns, H-NS-mediated repression of CRISPR-based immunity in *Escherichia coli* K12 can be relieved by the transcription activator LeuO. Mol Microbiol 77: 1380-1393.

Will, W. R. & L. S. Frost, (2006) Characterization of the opposing roles of H-NS and TraJ in transcriptional regulation of the F-plasmid *tra* operon. J Bacteriol 188: 507-514.

Will, W. R. & L. S. Frost, (2006) Hfq is a regulator of F-plasmid TraJ and TraM synthesis in *Escherichia coli*. J Bacteriol 188: 124-131.

Will, W. R., J. Lu & L. S. Frost, (2004) The role of H-NS in silencing F transfer gene expression during entry into stationary phase. Mol Microbiol 54: 769-782.

Williams, R. M., S. Rimsky & H. Buc, (1996) Probing the structure, function, and interactions of the *Escherichia coli* H-NS and StpA proteins by using dominant negative derivatives. J Bacteriol 178: 4335-4343.

Wilmes-Riesenberg, M. R., J. W. Foster & R. Curtiss, 3rd, (1997) An altered *rpoS* allele contributes to the avirulence of *Salmonella typhimurium* LT2. Infect Immun 65: 203-210.

Wilson, R. L., S. J. Libby, A. M. Freet, J. D. Boddicker, T. F. Fahlen & B. D. Jones, (2001) Fis, a DNA nucleoid-associated protein, is involved in *Salmonella typhimurium* SPI-1 invasion gene expression. Mol Microbiol 39: 79-88.

Wilson, R. L., M. L. Urbanowski & G. V. Stauffer, (1995) DNA binding sites of the LysR-type regulator GcvA in the *gcv* and *gcvA* control regions of *Escherichia coli*. J Bacteriol 177: 4940-4946.

Wong, J. J., J. Lu & J. N. Glover, Relaxosome function and conjugation regulation in F-like plasmids - a structural biology perspective. Mol Microbiol 85: 602-617.

Wu, H. Y. & M. Fang, (2003) DNA supercoiling and transcription control: a model from the study of suppression of the *leu-500* mutation in *Salmonella typhimurium topA*- strains. Prog Nucleic Acid Res Mol Biol 73: 43-68.

Wu, H. Y., J. Tan & M. Fang, (1995) Long-range interaction between two promoters: activation of the *leu-500* promoter by a distant upstream promoter. Cell 82: 445-451.

Yoshioka, Y., H. Ohtsubo & E. Ohtsubo, (1987) Repressor gene *finO* in plasmids R100 and F: constitutive transfer of plasmid F is caused by insertion of IS3 into F finO. J Bacteriol 169: 619-623.

Zatyka, M. & C. M. Thomas, (1998). Control of genes for conjugative transfer of plasmids and other mobile elements. FEMS Microbiol Review 21: 291-319.

Zahrl, D., A. Wagner, M. Tscherner & G. Koraimann, (2007) GroEL plays a central role in stress-induced negative regulation of bacterial conjugation by promoting proteolytic degradation of the activator protein TraJ. J Bacteriol 189: 5885-5894.

Zhang, A., S. Rimsky, M. E. Reaban, H. Buc & M. Belfort, (1996) *Escherichia coli* protein analogs StpA and H-NS: regulatory loops, similar and disparate effects on nucleic acid dynamics. EMBO J 15: 1340-1349.

Zhang, A., K. M. Wassarman, J. Ortega, A. C. Steven & G. Storz, (2002) The Sm-like Hfq protein increases OxyS RNA interaction with target mRNAs. Mol Cell 9: 11-22.

TABLE S1

Table S1: LeuO LPM ChIP-chip sites

High Average Log2 Ratio	High Log2 Ratio for Spot	High Spot	Regulated Gene(s)	Location	E. coli	Length	Peak Start	Peak End	H-NS LPM chip-chip	H-NS LB chip-chip	RNAP LPM chip-chip	RNAP LB chip-chip
1.215832766	2.66489507	SL0012	dnaK/dnaJ	ORF 3'	yes	500	12800	13300			+	
1.715696889	3.679047941	SL0023	bcfC	ORF 5'	N/D	375	26250	26625	+		+	
1.438054949	2.366775772	SL0043	SL0043	ORF 3'	N/D	250	50750	51000	+	+	+	
1.72661667	3.985773528		tdcB/carA	ID	N/D	900	75000	75900	+	+	+	
1.978815464	5.665144913	SL0105	yabI	I	N/D	625	122500	123125			+	
1.881145596	3.98601467	SL0132	ftsA	ORF 5'	N/D	500	154250	154750			+	+
1.718101138	3.883594533		hpt/gcd	ID	N/D	1125	200625	201750			+	+
2.189759884	3.247400029	SL0176	stiC	ORF 5'	N/D	700	207300	208000	+		+	
1.726368084	4.240069723	SL0186	yadB	ORF 5'	N/D	750	215625	216375			+	+
1.32909758	2.744809139	SL0192	fhuA/fhuC	ORF 3'	N/D	500	225000	225500	+		+	
2.206122516	5.856299447	SL0232	dnaE/accA	ORF 3'	yes	625	272500	273125			+	+
1.43777357	2.219473542	SL0256	gloB/yafS	ID	N/D	900	301800	302700			+	
1.186524024	5.240956262	SL0295	safA	ORF 5'	N/D	250	341750	342000	+	+	+	
1.581422491	5.502605266	SL0317	proB	ORF 3'	N/D	375	366500	366875				
2.504425246	5.179564261	SL0375	ddl	ORF 3'	N/D	750	433000	433750	+		+	+
2.143132849	3.229614241	SL0384	aroM	I	N/D	700	440800	441500	+	+	+	+
1.128650179	3.279787046	SL0393	phoR	ORF 3'	N/D	400	451700	452100			+	
1.954639692	2.815297275	SL0434	cyoD/cyoE	ORF 5'	yes	500	493300	493800	+		+	+
1.593664262	4.490014046		cypD	I	N/D	500	507625	508125			+	+
1.473860032	3.342414421	SL0457	amtB/tesB	ORF 3'	yes	500	521000	521500			+	
1.424674037	2.644055699	SL0468	acrB/ybaJ	ORF 3'	N/D	625	529500	530125			+	
2.121129821	2.967289033	SL0531	SL0531	ORF 3'	N/D	500	600125	600625			+	
1.741960571	5.898979245	SL0539	fimD	ORF 5'	yes	625	605750	606375	+			
2.479889086	3.313836354	SL0555	SL0555/pheP	ORF 3'	N/D	750	622375	623125	+		+	
1.747095121	2.373761313		SL0565	I	N/D	500	635750	636250			+	
3.083331523	5.644543372	SL0638	SL0638/SL0639	ORF 3'	N/D	625	712000	712625	+	+	+	
2.880000747	5.144114752	SL0639	SL0639/SL0640	ORF 3'	N/D	875	713250	714125	+	+	+	
1.717286384	2.524590053	SL0667	nagE	ORF 5'	N/D	900	744700	745600			+	+
2.284851361	4.999979817	SL0671	citA/citB	ORF 5'	N/D	1600	750700	752300			+	
2.321171757	6.271817101	SL0682	SL0681	I	N/D	400	761200	761600			+	
1.741198819	2.272928031	SL0691	ybgH	ORF 5'	N/D	600	776500	777100			+	
2.294134891	3.161014091	SL0715	sdhD/sdhA	ORF 5'	yes	1625	797625	799250			+	+
2.031309684	4.410743597	SL0772	bioF/bioC	ORF 5'	N/D	500	861500	862000			+	
1.530156197	4.078206773		SL0814	I	N/D	300	906500	906800	+	+	+	
1.925688657	3.889661214	SL0839	dacC	ORF 3'	N/D	700	935200	935900			+	+
1.942587727	3.115527447	SL0865	artM/artQ	ORF 3'	N/D	750	958625	959375			+	+
1.985109939	3.962153763	SL0971	SL0971	ORF 5'	N/D	625	1076125	1076750			+	
1.21085326	3.458704294	SL0983	sodC/SL0984	ORF 5'	N/D	700	1087300	1088000	+		+	
2.045889093	3.474251314	SL0996	SL0995/SL0996/pepN	ID	N/D	750	1099625	1100375	+	+	+	
1.66699302	2.812796414	SL0997	pepN/pyrD	ORF 3'	N/D	700	1102700	1103400			+	
1.576927237	2.865671967		SL1036/hpaC	IC	N/D	375	1141400	1141775	+		+	+
1.128935235	2.789189872	SL1063	phoH	I	N/D	375	1169500	1169875	+	+	+	+
1.447038759	4.226668026	SL1066	SL1065/SL1066	ORF 3'	N/D	500	1172500	1173000	+	+	+	
2.075923745	5.293732252	SL1153	ycfS	I	N/D	750	1254500	1255250			+	+
1.543431019	2.413955652	SL1156	ycfW/ycfX	ORF 3'	N/D	600	1261400	1262000			+	
1.757486885	2.488525562	SL1160	potC	ORF 5'	N/D	700	1264800	1265500	+		+	
1.680318129	4.989302283	SL1161	sifA	ORF 5'	N/D	500	1266200	1266700	+	+	+	
1.74219223	3.60622162	SL1253	katE	ORF 3'	N/D	625	1354375	1355000			+	
2.28245557	6.07485467	SL1261	pfkB/ydiY	ID	N/D	875	1362375	1363250	+		+	+
1.754855326	3.467808775	SL1275	btuED	ORF 5'	N/D	625	1377500	1378125			+	
1.140675668	3.99706598	SL1284	pps/ydiD	ORF 3'	N/D	600	1386800	1387400	+		+	
1.921392953	3.485823393	SL1287	ydiR	ORF 5'	N/D	625	1390625	1391250	+		+	+
2.390921067	3.841415834	SL1307	sufS	ORF 5'	N/D	500	1413375	1413875			+	
1.903125477	3.043964409		SL1316	I	N/D	750	1422875	1423625	+	+	+	
1.575002565	3.617382669		SL1323	I	N/D	375	1431800	1432175	+		+	+
1.889836032	4.153909141	SL1377	slyB	I	N/D	300	1477500	1477800			+	+
1.983172882	3.829235985		add	I	yes	1125	1494750	1495875			+	+
2.514391799	5.952525559	SL1396	ydgA/add	ORF 3'	N/D	750	1496000	1496750			+	+
2.097195919	4.987479761		ompN	I	yes	750	1507900	1508650	+	+	+	+
1.747530325	2.651237256	SL1513	nhoA	ORF 3'	N/D	625	1625250	1625875			+	
1.853900708	3.82489817	SL1518	yncC/yncD	IC	N/D	625	1632375	1633000	+	+	+	
2.209442031	3.762021897		SL1562/SL1563	ID	N/D	500	1679600	1680100	+	+	+	
2.057745801	3.258534673	SL1587	zntB	ORF 5'	N/D	875	1707250	1708125	+		+	+
1.155654517	3.64084628	SL1588	SL1588	ORF 5'	N/D	250	1708875	1709125	+	+	+	+
1.387611021	2.89729655	SL1616	ycjX	I	N/D	1100	1736700	1737800	+		+	+
1.639981752	3.30788501	SL1644	acnA	I	N/D	600	1763700	1764300			+	
2.447198431	5.655033687		yciG	I	N/D	625	1781750	1782375	+	+	+	
1.174975111	2.20708573	SL1680	adhE	ORF 3'	N/D	300	1801300	1801600			+	+
1.761912128	2.539545493		rssB	I	N/D	750	1806175	1806925	+		+	+
2.072412536	3.229358663	SL1754	yeaB	ORF 5'	N/D	875	1879875	1880750			+	
1.677803252	3.645809464		SL1786	I	N/D	625	1911475	1912100	+	+	+	+
1.808305408	4.604024994	SL1788	SL1788	ID	N/D	500	1913250	1913750	+	+	+	+
1.129342118	2.987680204	SL1869	ftn/yecH	IC	N/D	400	1987375	1987775	+	+	+	
1.243257821	2.009125092	SL1879	sdiA	I	yes	500	1998250	1998750	+	+	+	+
1.93505121	2.587261914	SL1898	fliF	ORF 3'	N/D	600	2014700	2015300			+	
1.698891614	2.900798939	SL1910	rcsA	I	N/D	500	2024375	2024875	+	+	+	
1.909774996	3.856456781	SL1920	dcm	ORF 5'	N/D	625	2032250	2032875			+	+
2.733038072	4.297354248		cspB	I	N/D	625	2037250	2037875	+		+	+
1.542242664	3.610129756	SL1936	pdxA/SL1935	ORF 3'	N/D	300	2046700	2047000			+	
1.41259342	3.022516022		sbmC	I	N/D	500	2133250	2133750			+	+
1.376633869	2.03347227	SL2043	sopA	ORF 3'	N/D	625	2140625	2141250	+	+	+	+
1.241164315	2.256466107	SL2046	yeeY	ORF 5'	N/D	500	2145600	2146100			+	+
1.449308834	2.618823494	SL2050	hisC/hisB	ORF 3'	N/D	625	2150000	2150625			+	
1.816907674	3.700149039	SL2062	rfbN	ORF 5'	N/D	600	2163200	2163800	+	+	+	
1.991056021	2.93820532	SL2063	rfbU	ORF 5'	N/D	500	2164400	2164900	+	+	+	
1.899596892	3.614928765	SL2081	cpsG	ORF 5'	yes	875	2185375	2186250			+	
2.228016424	3.660921995	SL2117	yegS/fbaB	IC	N/D	750	2232125	2232875	+		+	
1.671241461	3.843237757	SL2145	dld	ORF 3'	N/D	500	2262250	2262750			+	
1.815951938	4.150982032	SL2156	SL2156/SL2157	ID	N/D	875	2274500	2275375			+	
1.544109928	2.361936133	SL2169	yeiB	ORF 5'	N/D	250	2287750	2288000			+	
1.42373574	3.287693612	SL2233	yojI	ORF 5'	N/D	500	2359250	2359750			+	
1.577217175	2.503680442	SL2254	glpB/glpC	ORF 3'	N/D	700	2390200	2390900			+	+
1.371767497	2.452502021	SL2291	nuoH	ORF 5'	yes	250	2429250	2429500				+
1.205199366	3.219120047		yfbU	I	N/D	600	2444200	2444800			+	+
1.66804273	2.214943637		SL2327	ORF 5'	N/D	375	2467250	2467625	+	+	+	
2.006978535	4.878393898	SL2330	SL2330	ORF 5'	N/D	500	2471000	2471500			+	
1.716730551	4.491555525	SL2371	glk/SL2372	ID	N/D	375	2516375	2516750			+	+
2.086802644	5.22039315	SL2378	yfeA	ORF 3'	N/D	600	2524700	2525300	+		+	

1.646248848	3.477273432	SL2397	SL2397	ORF 3'	N/D	500	2545125	2545625			+	+
2.452458629	3.803268157	SL2428	eutN	ORF 5'	N/D	600	2572700	2573300			+	
2.995178073	4.378480962		eutS	I	N/D	1500	2576375	2577875	+	+	+	
2.241847079	3.992365088	SL2448	SL2448/SL2449	ORF 5'	N/D	1875	2597875	2599750			+	+
1.959714483	6.084465607	SL2453	gcvR/bcp	ORF 3'	N/D	400	2603100	2603500			+	+
1.511380075	3.561241439	SL2474	shdA	ORF 3'	N/D	375	2625500	2625875			+	
1.42131918	3.249945266	SL2482	yfgL/engA	ORF 3'	N/D	625	2650750	2651375			+	+
1.597832565	2.822116916	SL2526	yfhK/yfhG	ORF 3'	N/D	500	2704100	2704600			+	+
1.61336384	3.394308494	SL2553	SL2553	ORF 5'	N/D	625	2737500	2738125			+	
1.790651792	3.9972218	SL2558	SL2557/SL2558	ORF 3'	N/D	250	2741000	2741250			+	
1.853106796	2.668164049	SL2563	gipA	ORF 3'	N/D	500	2746500	2747000			+	+
1.595701379	3.985737743	SL2572	SL2572	ORF 5'	N/D	875	2754125	2755000			+	
3.385881698	6.228042632	SL2641	SL2641/SL2642	ORF 3'	N/D	750	2822000	2822750			+	
2.650749097	3.673278534	SL2647	trmD/rplS	ORF 3'	N/D	600	2826400	2827000			+	
1.931461699	3.844402959	SL2650	ffh/rpsP	ORF 3'	N/D	500	2828500	2829000			+	+
1.820147532	3.115335364	SL2651	corE/corB	ORF 3'	N/D	400	2830400	2830800			+	+
2.001911886	4.390239913	SL2668	SL2668/SL2667	ORF 3'	N/D	625	2858125	2858750			+	
1.59301138	3.698162115	SL2672	SL2672	I	N/D	625	2862125	2862750	+	+	+	
1.555643111	5.877522378	SL2675	SL2675	ORF 5'	N/D	600	2863900	2864500	+	+		
1.871196241	3.728305458	SL2680	SL2679/SL2680	ORF 3'	N/D	625	2867750	2868375			+	
2.532604896	3.504363621	SL2701	SL2701/SL2700	ORF 3'	N/D	500	2881500	2882000			+	
2.056469769	3.677508207		SL2723	I	N/D	500	2900500	2901000				
2.292558539	3.558951506	SL2772	SL2772/SL2773	ORF 3'	N/D	875	2959000	2959875			+	
1.540414592	3.371085906		yqaAB	ORF 3'	N/D	600	2991200	2991800			+	+
2.085922088	3.536341356	SL2839	fhlA	I	N/D	750	3026125	3026875			+	
1.119512969	3.177954327	SL2856	hilA	ORF 5'	N/D	300	3042400	3042700	+	+	+	
2.478905209	6.007223042	SL2876	invE	ORF 5'	N/D	500	3063750	3064250	+	+		
1.77878247	2.653358091	SL2892	SL2892	ORF 3'	N/D	625	3078125	3078750			+	
2.312600132	3.838117279		CRISPR repeats	I	yes	1375	3099125	3100500	+		+	
1.983207165	3.365996777		SL2929	I	N/D	1500	3116625	3118125	+	+	+	+
2.316939271	3.652555582	SL2978	ppdA	I	N/D	625	3178750	3179375			+	
1.556278047	3.016233049	SL3022	ygfX	ORF 3'	N/D	375	3226750	3227125				+
1.360663603	2.273059277	SL3089	speC	ORF 3'	N/D	600	3294100	3294700			+	
1.728539861	3.69145102	SL3143	SL3143	ORF 5'	N/D	500	3352400	3352900	+	+	+	
1.953047435	6.015933561	SL3175	ygiF/glnE	ORF 3'	N/D	625	3388125	3388750			+	
2.091809837	5.462878725	SL3214	tdcD	ORF 3'	yes	1000	3429500	3430500	+	+	+	
2.200602091	3.292018942	SL3280	yrbA	I	N/D	500	3497600	3498100			+	
1.333753682	2.131148495		yhbL	I	N/D	400	3511800	3512200			+	+
2.64262714	4.789798093	SL3341	yhdP/tldD	ORF 3'	N/D	1125	3557500	3558625			+	+
1.740443198	3.583053976	SL3357	yhdG/fis	ORF 3'	N/D	1000	3577125	3578125			+	
1.488873905	2.952936824	SL3369	aroE/yrdC	ORF 5'	N/D	500	3595375	3595875	+		+	
2.229112661	3.249515275	SL3409	hopD	ID	N/D	625	3618375	3619000	+		+	+
1.614094168	4.095914762		ppiA/yhfC	ID	N/D	375	3643375	3643750			+	+
1.874210274	3.607746726	SL3459	yrfD/yrfC	ORF 3'	N/D	500	3667125	3667625			+	
1.428200095	3.05417105		hslO/yhgE	ID	N/D	500	3675750	3676250			+	
1.739387397	3.142390429	SL3466	yhgE	ORF 5'	N/D	375	3676750	3677125			+	
1.306992999	2.131765023	SL3479	gntT/malQ	IC	N/D	250	3693125	3693375			+	
1.3668705	2.08600416	SL3500	SL3500	ORF 5'	N/D	250	3719500	3719750	+		+	
1.553116518	2.463123198	SL3525	yhhV	I	N/D	500	3749625	3750125			+	
2.458158084	4.555804786	SL3549	nikR/yhhJ	IC	N/D	750	3772750	3773500			+	
2.732181092	3.480879749	SL3550	yhhJ	ORF 5'	N/D	750	3773625	3774375			+	
1.280460208	3.795334367		yhiI	I	N/D	500	3778125	3778625			+	+
1.712747204	2.331945431	SL3555	uspB/uspA	ID	N/D	400	3781400	3781800			+	+
1.970998072	5.963347494	SL3558	yhiQ/prlC	ORF 3'	N/D	500	3785000	3785500				
1.896490868	4.239601752	SL3561	yhiR/gor	ORF 3'	N/D	375	3789250	3789625			+	+
1.714947509	3.983470893	SL3566	SL3565	I	N/D	1100	3794500	3795600	+		+	
1.684260738	4.869572132		SL3567/treF	ID	yes	500	3796625	3797125			+	
2.514734924	3.27299842		SL3569/SL3570	ID	N/D	825	3799675	3800500	+	+	+	
1.547333448	3.613556704	SL3585	yhjQ	ORF 5'	N/D	600	3824800	3825400	+			
1.410504832	3.127241656	SL3591	yhjV	ORF 5'	N/D	600	3830200	3830800	+	+		
1.687450877	1.91849451		SL3643/SL3644	ID	N/D	500	3887100	3887600	+	+	+	
2.380208504	3.020394266	SL3658	lldR	ORF 5'	N/D	500	3908800	3909300			+	+
2.432710827	3.651319429	SL3705	ligB/gmk	ID	N/D	625	3953625	3954250			+	
1.746889291	3.661727502	SL3732	SL3731	I	N/D	750	3988875	3989625			+	
2.248657993	5.103046372	SL3795	dgoA	ORF 5'	N/D	300	4053000	4053300			+	
1.389622324	3.198953531	SL3820	phoU	ORF 5'	yes	750	4081625	4082375			+	
1.79259666	3.809958219	SL3827	SL3827	ORF 5'	N/D	700	4088500	4089200			+	
1.421961865	3.295209511	SL3828	glmS	ORF 5'	N/D	375	4091375	4091750			+	
1.626058871	2.509293181	SL3832	atpD	ORF 5'	N/D	500	4096125	4096625			+	+
2.541994591	3.552703101	SL3917	yigM/metR	ORF 3'	N/D	625	4189750	4190375			+	
2.370507123	3.797285438	SL4093	SL4093/SL4094	ORF 5'	N/D	750	4395250	4396000	+	+	+	
2.502721469	3.955537117		thiF	ORF 5'	N/D	750	4400625	4401375			+	
1.875772615	4.311334561	SL4121	SL4121	ORF 5'	N/D	500	4428125	4428625			+	
1.75513387	2.949000987	SL4197	siiE	ORF 3'	N/D	625	4514000	4514625	+	+	+	
1.74663411	4.477395887	SL4342	ytfM/ytfN	ORF 3'	N/D	625	4668000	4668625			+	
1.690017081	3.673048849	SL4362	SL4362	ORF 5'	N/D	375	4695500	4695875			+	
1.381204952	3.384317767	SL4422	SL4422	ORF 5'	N/D	625	4762250	4762875			+	+
1.678655258	4.012802413	SL4454	SL4453/SL4454	ORF 5'	N/D	500	4797500	4798000	+	+	+	+
1.612046225	2.955903368	SL4482	SL4482/SL4483	ID	N/D	1125	4830125	4831250	+	+	+	+
2.593344434	5.434679514	SL4515	creAB	ORF 5'	N/D	700	4864400	4865100	+		+	

Table S1 continued: LeuO pBAD ChIP-chip sites

High Average Ratio	High Ratio for Spot	High Spot	Length	Peak Start		LeuO LPM sites	LeuO pBAD LB BR1	LeuO pBAD LB BR2
1.715696889	3.679047941	SL0023		375	26250	+	+	+
1.602075405	3.173819215	SL0025		500	29500		+	+
1.484291234	4.053981161	SL0050		625	58000		+	+
1.72661667	3.985773528			375	75000	+	+	+
2.79919259	4.555309328			250	121375	+	+	+
1.978815464	5.665144913	SL0105		625	122500	+	+	+
1.994540802	4.276500802	SL0122		625	142875		+	+
1.881145596	3.98601467	SL0132		250	154250	+	+	+
1.770735652	3.191745276	SL0132		375	155125		+	+
2.189759884	3.247400029	SL0176		500	207500	+	+	+
1.32909758	2.744809139	SL0192		250	225375	+	+	+
2.263904074	5.097291808	SL0210		875	245000		+	+
2.069829204	5.011839285	SL0217		750	254125		+	+
2.206122516	5.856299447	SL0232		625	272500	+	+	+
1.674326271	4.916133133	SL0234		625	274750		+	+
2.74688146	6.097786376	SL0257		750	302375	+	+	+
1.227972456	1.893869393	SL0260		250	305000		+	+

2.223889338	4.367149329	SL0262	750	306875	+	+
1.559589716	3.007430735	SL0265	375	310250	+	+
2.344756419	3.145413014	SL0280	750	325250	+	+
2.159666571	3.201088649	SL0284	500	330250	+	+
1.634312301	3.797283783	SL0286	500	335250	+	+
1.508947197	2.698825385	SL0290	375	338875	+	+
1.186524024	5.240956262	SL0295	250	341750 +	+	+
1.080104336	5.240956262	SL0295	250	342125 +	+	+
1.236917034	3.566898702	SL0297	500	343000	+	+
1.951297415	3.593925006	SL0309	500	357875 +	+	+
1.321928133	2.717053033	SL0347	375	396500	+	+
1.874494151	4.229650883	SL0356	375	410500	+	+
1.418135419	2.893491327	SL0357	250	411000	+	+
1.468566527	3.444446417	SL0371	625	430000	+	+
2.504425246	5.179564261	SL0375	750	433000 +	+	+
1.570569882	4.002830608	SL0380	375	437500	+	+
2.143132849	3.229614241	SL0383	375	440125 +	+	+
1.12491344	3.374413066	SL0424	250	483375 +	+	+
1.954639692	2.815297275	SL0434	500	493375 +	+	+
1.527576613	3.279730782	SL0438	250	499250	+	+
1.593664262	4.490014046		500	507625 +	+	+
1.473860032	3.342414421	SL0457	500	521000 +	+	+
1.490649129	3.009066479	SL0496	625	563000	+	+
3.272255162	3.397271706	SL0510	625	577500	+	+
1.337360876	3.750927494	SL0524	250	593625	+	+
2.121129821	2.967289033	SL0531	500	600125 +	+	+
1.481648821	2.907092573	SL0561	750	632375	+	+
1.877939187	2.859382249	SL0561	500	633250	+	+
1.22034465	3.542926802	SL0574	250	644000	+	+
1.325944486	3.008408452	SL0576	500	648125	+	+
1.821633019	2.571767178	SL0581	250	654125	+	+
1.468056914	2.723967949	SL0584	500	657875	+	+
1.608519518	2.939230585	SL0594	500	668375 +	+	+
1.342831707	2.86950542		250	684625	+	+
1.594733696	2.86950542		250	685000	+	+
2.880000747	5.144114752	SL0639	875	713250 +	+	+
1.509266247	3.552422744		625	737625 +	+	+
1.663933895	4.358828136		250	744500	+	+
2.284851361	4.999979817	SL0671	1000	751000 +	+	+
2.321171757	6.271817101	SL0682	250	761375 +	+	+
2.067371223	3.29405721	SL0689	750	774125	+	+
1.814840361	5.194845678	SL0698	500	782125 +	+	+
2.294134891	3.161014091	SL0715	1625	797625 +	+	+
1.3083955	4.455185325	SL0718	375	801875	+	+
1.357488937	3.230056353	SL0723	500	811250 +	+	+
1.794920395	3.60313117		375	811875 +	+	+
1.867597707	3.165900426	SL0740	875	825000	+	+
1.102260386	3.481360307		375	833500 +	+	+
1.33866973	3.633348996	SL0768	375	856250	+	+
1.533743868	3.932971936	SL0777	250	868875 +	+	+
1.316552867	1.992918941	SL0793	250	882625	+	+
1.530156197	4.078206773		375	906000 +	+	+
1.925688657	3.889661214	SL0839	625	935375 +	+	+
1.684998978	3.762681405	SL0842	625	938125	+	+
1.957761268	3.324866702	SL0862	625	955500	+	+
1.075714263	2.160721112	SL0890	250	986000	+	+
2.112788288	6.748755773	SL0898	625	994375 +	+	+
1.527663371	4.511825261	SL0905	250	1006625 +	+	+
1.754131996	4.537760293	SL0927	750	1032750	+	+
1.12539719	2.923960483	SL0928	250	1034250	+	+
1.413966174	2.86043499	SL0928	375	1034625	+	+
1.489709789	3.491671896		375	1041625	+	+
1.13052502	4.157368276	SL0952	250	1063250 +	+	+
1.617684354	4.748132829	SL0954	375	1064625	+	+
1.534595982	3.097523704	SL0969	625	1074375	+	+
1.985109939	3.962153763	SL0971	625	1076125 +	+	+
1.699766686	3.103334154	SL0987	500	1089875	+	+
2.045889093	3.474251314	SL0996	750	1099625 +	+	+
1.446820848	3.055157111	SL0997	375	1101500	+	+
1.187161304	2.85055933		375	1122750	+	+
1.516455663	2.797725385	SL1015	375	1124750	+	+
1.416256184	4.222384096	SL1051	375	1155500	+	+
1.59812248	4.330392463		375	1180500	+	+
1.468442928	5.837153362	SL1093	250	1200375 +	+	+
1.543318958	3.286644248	SL1115	750	1217000	+	+
1.626831956	3.741015454		500	1224125 +	+	+
2.122875228	6.370588715		625	1227625 +	+	+
1.786620502	4.451307403	SL1136	375	1239625	+	+
1.48826676	2.715697313		500	1244000	+	+
2.075923745	5.293732252	SL1153	750	1254500 +	+	+
1.691001847	4.530768341	SL1155	375	1260500	+	+
1.680318129	4.989302283	SL1161	250	1266625 +	+	+
1.48138147	3.116620832	SL1240	625	1342250	+	+
1.912751163	3.980725797		500	1344000	+	+
2.212770344	3.980732922	SL1244	750	1346375 +	+	+
1.74219223	3.60622162	SL1253	625	1354375 +	+	+
1.794705996	3.322568891		500	1356000	+	+
2.928683984	3.95030537	SL1256	875	1358250	+	+
2.28245557	6.07485467	SL1261	875	1362375 +	+	+
1.908750437	4.531210792	SL1262	625	1363500	+	+
1.140675668	3.99706598	SL1284	375	1387875 +	+	+
1.921392953	3.485823393	SL1287	625	1390625 +	+	+
2.390921067	3.841415834	SL1307	500	1413375 +	+	+
1.903125477	3.043964409		750	1422875 +	+	+
1.723482821	3.172597309	SL1317	500	1425250	+	+
1.674479425	4.154146202	SL1319	750	1427500	+	+
2.094961551	2.848915499	SL1320	375	1429875	+	+
1.575002565	3.617382669		375	1431875 +	+	+
1.181923545	3.772572125		250	1465875	+	+
1.533172211	3.06960712	SL1373	500	1473625	+	+

1.889836032	4.153909141	SL1376	750	1477125 +	+	+
1.954947287	6.544579287	SL1390	375	1490750	+	+
1.55107786	3.331327663		250	1492500 +	+	+
1.983172882	3.829235985		1125	1494750 +	+	+
1.261537795	1.560057508	SL1397	250	1498125	+	+
1.515616468	5.417219714	SL1397	375	1498500	+	+
2.097195919	4.987479761		750	1508000 +	+	+
1.371064858	3.134418527		250	1538625	+	+
1.836676671	3.599506345	SL1450	375	1554500	+	+
1.45581143	2.743478364	SL1451	375	1555500	+	+
1.208099504	3.082796704	SL1472	250	1576000	+	+
1.332294982	3.662399129	SL1485	375	1589750	+	+
1.184619794	1.879806335		250	1592500	+	+
2.035359443	3.008194731	SL1500	625	1609750	+	+
1.860740398	3.989313782		750	1615625 +	+	+
1.747530325	2.651237256	SL1513	625	1625250 +	+	+
1.853900708	3.82489817	SL1518	625	1632375 +	+	+
2.209442031	3.762021897		500	1679875 +	+	+
2.057745801	3.258534673	SL1587	875	1707250 +	+	+
1.155654517	3.64084628	SL1588	250	1708875 +	+	+
1.323612674	3.695961767	SL1610	375	1730875	+	+
1.625076018	2.2201465	SL1632	250	1750500	+	+
1.639981752	3.30788501	SL1644	375	1763375 +	+	+
1.18289972	3.281545869	SL1644	250	1763875 +	+	+
1.527544285	2.719177742	SL1696	250	1823875 +	+	+
2.101873497	3.323012164	SL1704	625	1830625	+	+
2.514460234	3.457553489	SL1757	625	1884375	+	+
1.513410871	3.427636704	SL1774	500	1899250 +	+	+
1.677803252	3.645809464		625	1911875 +	+	+
1.345336839	3.510706055	SL1824	750	1943000	+	+
1.213399905	4.359496292	SL1828	250	1946875	+	+
1.411048632	4.678722539	SL1846	250	1965000	+	+
1.245110917	2.06667559	SL1858	250	1978625	+	+
1.485752752	3.625029149	SL1862	375	1982000	+	+
1.384491625	3.155250665	SL1918	250	2030625	+	+
1.909774996	3.856456781	SL1920	625	2032250 +	+	+
2.115196202	4.669762173	SL1923	500	2035875	+	+
2.733038072	4.297354248		625	2037250 +	+	+
1.622622357	3.197404076	SL1943	625	2054000	+	+
1.984618127	3.144143213	SL1992	500	2095625	+	+
1.849303159	2.278243417	SL1999	625	2100750	+	+
1.154531009	2.822449114		250	2110125	+	+
1.854646324	2.624678089		625	2111375	+	+
1.257744986	5.294784335	SL2026	250	2124000	+	+
1.331947177	5.125981671	SL2028	250	2125750	+	+
1.337529968	2.588752946	SL2054	250	2153375	+	+
1.816907674	3.700149039	SL2062	250	2163375 +	+	+
1.991056021	2.93820532	SL2063	500	2164625 +	+	+
4.10941681	8.303837193	SL2064	375	2165375	+	+
1.414279448	1.60394892	SL2065	250	2166625	+	+
1.899596892	3.614928765	SL2081	875	2185375 +	+	+
1.556859937	3.621399379	SL2093	625	2198250	+	+
1.719723114	3.718823014		375	2211625	+	+
1.380566141	2.568695434	SL2105	250	2216750	+	+
2.228016424	3.660921995	SL2118	750	2232125 +	+	+
1.98504832	3.356397277		500	2255000	+	+
1.244283614	3.02353048	SL2150	375	2267500	+	+
1.51660446	4.672361334	SL2151	375	2268875	+	+
1.815951938	4.150982032	SL2156	875	2274500 +	+	+
1.561013116	4.10042255	SL2168	500	2285625	+	+
2.079732118	4.152297814	SL2175	375	2293750	+	+
1.253694313	4.388916795	SL2195	250	2317000	+	+
1.700364373	3.89809243	SL2196	375	2319375	+	+
1.813308848	3.28780776	SL3784	1125	2349750	+	+
1.702255119	4.877526747	SL2241	500	2372500	+	+
1.418521863	3.475584722	SL2242	500	2375250	+	+
1.22462239	3.168254402		250	2416500	+	+
1.425970087	3.192875347	SL2290	250	2428875 +	+	+
1.371767497	2.452502021	SL2291	250	2429250 +	+	+
1.393736567	3.629358647	SL2302	500	2441625	+	+
1.66804273	2.214943637		375	2467250 +	+	+
2.006978535	4.878393898	SL2330	500	2471000 +	+	+
1.18367061	2.75031125		250	2475375	+	+
1.454777414	2.856841672	SL2341	625	2482250	+	+
1.306744516	3.323513011	SL2341	500	2483125	+	+
1.356785864	2.96629688	SL2363	375	2504250	+	+
1.716730551	4.491555525	SL2371	375	2516375 +	+	+
2.086802644	5.22039315	SL2378	1125	2524375 +	+	+
1.382730648	2.277518745	SL2382	500	2530125	+	+
2.17960399	3.967133553		625	2568750	+	+
2.452458629	3.803268157	SL2428	1375	2572375 +	+	+
2.995178073	4.378480962		750	2576375 +	+	+
1.517860678	2.659375933	SL2448	250	2597250	+	+
2.241847079	3.992365088	SL2448	1875	2597875 +	+	+
1.279433624	2.193915241	SL2476	375	2638000	+	+
1.42131918	3.249945266	SL2482	625	2650750 +	+	+
1.45674726	4.039472547	SL2492	500	2661375	+	+
1.489653767	2.47267974	SL2493	500	2664875	+	+
1.767089894	2.904058709		375	2675000	+	+
1.673276146	2.753155054	SL2517	375	2691750	+	+
1.810256102	2.973355592	SL2604	875	2780000 +	+	+
1.991172526	3.578435496	SL2611	625	2787625	+	+
3.385881698	6.228042632	SL2641	750	2822000 +	+	+
1.931461699	3.844402959	SL2650	500	2828500 +	+	+
1.820147532	3.115335364	SL2651	750	2830250 +	+	+
1.699801547	3.612566591	SL2661	375	2845250	+	+
2.33804392	3.895266433	SL2663	625	2853250	+	+
1.601889422	3.285499307	SL2668	375	2857250	+	+
2.001911886	4.390239913	SL2668	625	2858125 +	+	+
1.59301138	3.698162115	SL2672	625	2862125 +	+	+

1.852621916	2.96504373	SL2690	875	2871250	+	+
2.532604896	3.504363621	SL2701	375	2881750	+	+
1.352758648	4.302356866	SL2701	500	2882750	+	+
2.834526791	4.223116619	SL2712	375	2890000	+	+
2.289342949	3.542189931		1000	2896250	+	+
2.095549306	4.129628201	SL2722	1250	2898250	+	+
2.056469769	3.677508207		1250	2900500	+	+
1.156639253	3.125641596		250	2901875	+	+
1.767912154	2.18949946	SL2730	750	2909625	+	+
2.292558539	3.558951506	SL2772	875	2959000	+	+
2.12797871	4.588226003	SL2792	625	2975250	+	+
1.551700344	4.358816257	SL2802	375	2989000	+	+
2.085922088	3.536341356	SL2839	750	3026125	+	+
1.727620587	3.283402591	SL2841	500	3029125	+	+
2.312600132	3.838117279		1375	3099125	+	+
1.307431655	5.273624142	SL2924	375	3109250	+	+
1.983207165	3.365996777		1500	3116625	+	+
1.287184587	2.790685861	SL2932	250	3121750	+	+
1.385604716	3.661212519	SL2949	500	3140875	+	+
2.252819738	4.08757681	SL2972	1250	3168625	+	+
2.316939271	3.652555582	SL2978	625	3178750	+	+
1.447435739	4.852814543		250	3187875	+	+
1.321071735	2.737610361		250	3191625	+	+
1.364610953	2.204302902	SL2994	250	3197750	+	+
1.309551625	3.646117049		250	3206375	+	+
1.949967649	2.48329609	SL3018	500	3223500	+	+
1.802999086	3.326408793	SL3107	1000	3313250	+	+
1.381751388	3.138911616		375	3335125	+	+
1.726965241	3.031167449	SL3139	1125	3346125	+	+
1.728539861	3.69145102	SL3143	500	3352625	+	+
1.152398908	2.324486985	SL3145	250	3354250	+	+
1.341857035	3.135395904	SL3148	250	3359000	+	+
1.266064974	2.724754276	SL3161	250	3371625	+	+
1.866935599	4.239318433	SL3183	625	3394625	+	+
1.800151788	4.44408469	SL3196	625	3412625	+	+
1.685862935	3.289723923	SL3219	1375	3435750	+	+
1.672635176	3.261598519	SL3229	1000	3446250	+	+
2.200602091	3.292018942	SL3280	500	3497750	+	+
2.64262714	4.789798093	SL3341	1125	3557500	+	+
1.349550359	3.151992304	SL3345	375	3563750	+	+
1.487035216	2.770261339	SL3349	625	3568875	+	+
1.542398917	2.837161876	SL3355	250	3574250	+	+
1.740443198	3.583053976	SL3357	1000	3577125	+	+
1.488873905	2.952936824	SL3369	500	3595375	+	+
1.440205597	3.525820334	SL3386	750	3607125	+	+
1.967611726	3.292376644	SL3387	250	3608000	+	+
2.229112661	3.249515275	SL3409	625	3618375	+	+
1.177036833	2.840031178		250	3620500	+	+
1.728031842	2.665905484	SL3445	500	3651625	+	+
1.25766958	2.068582501	SL3477	250	3690500	+	+
1.891442193	2.879993965	SL3487	625	3704500	+	+
1.3668705	2.08600416	SL3500	250	3719500	+	+
1.185150961	3.881132581		250	3749125	+	+
1.26560238	3.489152262	SL3551	250	3775500	+	+
1.258923983	1.787026524	SL3551	250	3776625	+	+
1.712747204	2.331945431	SL3555	375	3781625	+	+
1.684260738	4.869572132		500	3796625	+	+
2.514734924	3.27299842		625	3799875	+	+
1.902853784	3.455187794	SL3574	500	3804625	+	+
1.833364201	3.928709341	SL3598	500	3839250	+	+
1.081640368	4.852464406		250	3933875	+	+
2.546736147	4.69713303	SL3683	625	3934250	+	+
2.432710827	3.651319429	SL3705	625	3953625	+	+
1.322129603	2.392430438	SL3711	250	3960250	+	+
1.791553695	3.710736537	SL3713	250	3962875	+	+
1.746889291	3.661727502	SL3732	750	3988875	+	+
1.088238948	2.331811545	SL3733	250	3990375	+	+
2.628362504	5.766935163	SL3755	2375	4009625	+	+
1.784204732	3.020677358	SL3762	1000	4018125	+	+
2.230546737	3.834761541	SL3781	625	4037125	+	+
1.304269727	3.450105426		375	4063250	+	+
1.487972969	3.319681521		375	4074875	+	+
1.863393624	3.198845329	SL3817	625	4078375	+	+
1.939603816	3.204782958		375	4113000	+	+
1.44203889	4.011174933		375	4130250	+	+
1.445892087	3.432553297	SL3889	250	4161750	+	+
2.541994591	3.552703101	SL3917	625	4189750	+	+
1.643724623	3.969957718	SL3919	375	4191000	+	+
1.343863898	3.288898568	SL3953	250	4235875	+	+
1.221414648	2.243359844	SL3962	375	4246750	+	+
1.708321793	3.322762867	SL3983	500	4265875	+	+
1.659415154	4.541583282	SL3996	625	4278375	+	+
2.284973839	6.379455282	SL4016	625	4299250	+	+
1.687824279	3.755024412	SL4049	500	4331875	+	+
1.623900199	2.470310805		625	4341500	+	+
1.309256962	3.551030672	SL4064	375	4352625	+	+
2.370507123	3.797285438	SL4093	750	4395250	+	+
2.071142557	5.04964696		500	4403750	+	+
1.083767181	1.882036481		250	4409125	+	+
1.875772615	4.311334561	SL4121	500	4428125	+	+
1.166435958	4.396659107	SL4170	375	4476125	+	+
1.183991898	3.743127577	SL4182	250	4488125	+	+
1.75513387	2.949000987	SL4197	625	4514000	+	+
2.130281608	6.171683994	SL4205	500	4529375	+	+
1.079941701	3.913162077	SL4217	250	4541250	+	+
1.524991889	3.913162077	SL4217	250	4541625	+	+
2.018387072	3.76815886	SL4217	1625	4542000	+	+
1.069292345	3.932716813		375	4583875	+	+
1.507918966	3.955054296	SL4282	375	4609125	+	+
1.666595083	3.481224911	SL4290	500	4619750	+	+

1.68387359	3.542740957		500	4648500	+	+
1.342631217	2.250141673	SL4328	375	4652625	+	+
1.74663411	4.477395887	SL4342	625	4668000 +	+	+
1.781979028	4.516162233	SL4359	250	4691375	+	+
1.211022945	1.559977511	SL4377	625	4709750	+	+
1.059823106	3.026457562		250	4774500	+	+
2.387739703	4.531088701	SL4446	500	4790625	+	+
1.678655258	4.012802413	SL4454	500	4797500 +	+	+
1.336888746	3.285040138	SL4463	500	4808125	+	+
1.72539318	4.358833834	SL4463	375	4809250	+	+
1.871547202	3.479929791	SL4465	375	4814250	+	+
1.668825318	2.703270406	SL4472	625	4820625	+	+
1.612046225	2.955903368	SL4482	625	4830125 +	+	+
1.469234041	2.438466265	SL4516	250	4865875	+	+

Table S2: H-NS LPM Chipotle peaks

High Average Log2 Ratio	High Log2 Ratio for Spot	High Spot	Length	Peak Start- SL1344 coordinate
1.689047578	2.076147738		250	250
1.857205972	2.123481739	SL0011	2000	9625
4.986759469	5.269741023	SL0014	4375	14250
4.460420209	4.976645412		3750	22500
1.098682964	1.235683015	SL0027	375	30500
5.18040438	5.702860142	SL0032	9125	31750
4.050858529	4.520105652	SL0038	3750	42250
4.77520677	5.140575911	SL0043	2000	50750
2.258723438	2.839412394	SL0054	2375	61250
4.082132303	4.556939578	SL0058	1750	67625
1.666817682	2.167372071		750	74625
4.207505974	4.585728533		1375	80000
4.360049593	4.724788208		1500	82000
4.085465704	4.817265884		1625	87750
4.63824468	4.971265923	SL0084	5500	93250
4.442641745	5.083482514		2375	115375
4.603939879	4.697896411		2750	133500
2.90522138	3.438583869		1125	139125
4.466294879	4.81198797	SL0160	2000	188125
1.440686797	1.689256512		875	202125
4.191023975	4.4293026		3500	207750
1.118496296	1.282620222	SL0188	500	217000
1.117398008	1.548695014	SL0192	375	225000
4.394529342	4.584346861		2750	229500
3.831697438	4.41442181	SL0209	1750	243250
1.679354171	1.956243704		875	248000
1.751480058	2.138547135	SL0235	750	276000
1.901631893	2.364428889		1625	285125
2.49763142	2.880846098		1250	310375
4.879376427	5.352893305	SL0273	3750	315625
4.323149436	4.508170418	SL0279	1875	322500
4.493189139	5.09201067		1750	328750
5.374368362	5.576631995		7500	335500
5.037970844	5.236918548	SL0300	5375	345750
2.519499964	2.764898955	SL0307	2250	354625
4.869453932	5.245478145	SL0309	2125	357125
2.461405731	2.90761827		2000	364000
1.672121012	3.560966444		625	368500
4.658937813	5.131317425	SL0323	2875	370250
3.823754745	4.308657493	SL0330	4250	376500
5.320990785	5.770969088	SL0334	9375	382750
3.0531653	3.456449069	SL0352	3625	402875
3.848540355	3.943190698		2000	406875
2.745022336	3.078806986		1625	414500
4.529308997	4.825452073	SL0368	2250	423875
4.314888293	4.565786974	SL0369	1875	427250
1.204309723	1.429616473	SL0374	500	432750
4.130297782	4.368570159		2500	435625
1.11243631	1.477437518		500	440000
2.22679638	2.456844951	SL0385	1125	441000
1.128520195	1.235037474		250	452375
5.298212301	5.912038595	SL0432	4250	489125
4.264276143	4.540179209	SL0437	1750	497125
1.334816655	1.715498628	SL0452	1250	515375
1.205893246	1.431603871	SL0461	375	524125
4.748698712	4.922746487		3625	525625
2.553256237	2.763280394	SL0470	1125	533250
2.312543051	2.688531012	SL0487	1625	552875
4.550622394	4.838427055	SL0490	1875	556125
3.346820041	4.113690591	SL0495	1750	561500

1.514655151	2.016841992	SL0502	625	569125
5.522138271	5.826775594	SL0515	10125	578125
4.424807606	4.772011924	SL0521	2625	588875
1.316965355	1.570886314	SL0530	500	598625
3.886825158	4.410634482	SL0538	2875	602750
5.121124069	5.450154027		10500	608250
4.394203547	5.001098813		2125	620375
4.02658746	4.420990829	SL0557	2750	624750
1.566913076	1.900954557	SL0559	875	629500
4.174128759	4.792722728	SL0560	3000	630500
3.53698769	3.801629908	SL0577	2125	648375
4.575808057	4.938475805	SL0594	3250	666125
4.583571489	5.056386499	SL0598	1750	672125
1.917814609	2.252280144		1000	677000
4.559231938	4.875614623		1875	686375
1.291799451	1.826483253	SL0614	625	689000
3.954772986	4.395279548		2125	690625
4.143596256	4.350670694	SL0622	1875	695875
4.217818584	4.383890303	SL0638	4625	711375
4.084157767	4.555531262	SL0642	1875	716500
1.340644038	1.583069374		750	719625
3.816825218	4.346476133	SL0648	1250	723000
2.907264459	3.406906457	SL0669	1750	748250
4.693742597	4.954089654		2000	764375
1.708568087	1.881589433	SL0689	1000	773375
3.865562472	4.047578538		1625	780125
5.502020916	5.733998286	SL0702	11125	782875
4.867723578	5.085491261		2500	807000
1.601446963	1.937168192	SL0732	500	817750
5.463706681	5.866278094	SL0739	7375	822250
4.22937201	4.642292735		1625	841125
4.02665038	4.326382914	SL0776	2500	865625
5.228854704	5.616554957	SL0785	3250	872750
1.343980444	1.611917951	SL0802	750	892875
1.060025242	1.477421893	SL0804	250	894750
3.464182224	3.776538499	SL0807	1750	896750
1.931279685	2.234873178	SL0809	1125	898875
4.370736509	4.906383613	SL0814	2875	905500
5.484765828	5.734803708	SL0834	9125	924500
1.567369752	1.834795929		750	937375
3.847771101	4.581149575		1625	943000
1.091333936	1.558246227	SL0854	375	948375
4.575715552	5.180441588	SL0861	3375	953000
2.052705302	2.442931247		1125	971625
2.756016002	2.853696842	SL0879	1375	974125
2.165009309	2.556720287		750	981750
4.570413763	4.841632628	SL0906	6375	1005875
3.991367183	4.551393551		1500	1014375
1.104897578	1.196014254	SL0916	750	1020250
2.117573868	2.519553534		1125	1047250
5.097576301	5.317070512		4500	1049375
3.619353227	3.885908574	SL0947	1750	1060000
1.859647144	1.985529958	SL0952	875	1062875
2.900136247	3.392368449		2125	1064875
3.677894323	4.241570322	SL0965	4250	1067875
1.917889653	2.311394552	SL0982	1125	1086000
4.41956032	4.709053003	SL0995	6625	1094875
4.619065524	4.876903334	SL0998	1875	1103250
1.281122477	1.710349148	SL1001	500	1107500
1.335666303	1.636644468	SL1012	500	1119375
4.638551791	5.094162304	SL1032	8750	1131125
2.926011435	3.354669542	SL1036	1375	1140375
4.574899208	5.331790126	SL1049	2375	1153250
2.752290877	3.225991012		1125	1161875
2.218212479	2.610281954		1125	1167750
3.324210284	3.693594482		2375	1169500
5.111999358	5.479126878	SL1068	7875	1172250
5.00768525	5.183837942	SL1080	5500	1183875
4.303350629	4.979476316	SL1086	2625	1190625
1.612586963	2.119476588		750	1199625
3.606914686	3.880965545	SL1095	3875	1201250
1.395187896	1.791263733	SL1101	625	1205625
1.22403843	1.405877677	SL1124	625	1229750

2.236419726	2.710096533		1000	1246000
1.166566692	1.58615836		500	1253125
4.350124752	4.651054437	SL1161	2750	1265500
1.546674842	1.784660642		1250	1268875
3.727718971	4.27080353	SL1165	2750	1270375
5.022026434	5.369153033	SL1179	14750	1281875
4.83788001	5.103734883		10000	1301625
4.747979508	5.105363596		3250	1314750
1.081472249	1.296815401		375	1320750
1.570442738	1.769210131		500	1336875
1.385251795	1.717106077		625	1338625
4.322672614	4.751866582		1875	1344750
5.091818987	5.255738524		5875	1347500
5.025529297	5.523215933		6625	1362750
4.088084172	4.400309349	SL1278	2250	1378625
1.659052334	1.740730599		750	1382000
2.446717599	2.87284918		1375	1383750
1.46667962	1.897684244	SL1284	875	1387250
2.462819914	2.764207944		1250	1388375
5.102946525	5.380184973	SL1294	12250	1390250
1.147277299	1.566181376		500	1403000
4.372530445	4.503393962	SL1302	2250	1407250
2.458273248	2.866873789		1000	1416250
5.236860577	5.694146179	SL1315	4375	1419375
4.794026648	5.05938364	SL1326	9500	1432125
3.850316606	4.1943438		10875	1442125
5.041115891	5.292688555	SL1356	5875	1453500
2.276392312	2.920147589	SL1357	2625	1459750
2.599533135	3.015278524		2625	1466125
1.453934243	2.06580349	SL1371	500	1472000
1.322892355	1.44122525	SL1382	250	1481750
2.863844269	3.377946611		1625	1491875
4.073522675	4.471592114	SL1404	3500	1506125
4.253449281	4.597231879		2250	1515750
1.204048059	1.440134857	SL1417	500	1520750
4.510121772	4.989354456	SL1437	2375	1540750
5.127025789	5.467548055		5125	1548000
1.922919018	2.26147866	SL1449	2125	1553750
4.358949045	4.925385992	SL1459	4500	1560875
1.973150725	2.32527237	SL1462	1375	1566000
5.225349038	5.621515917	SL1473	8500	1571125
4.902194089	5.262895884	SL1484	8500	1581000
4.093032215	4.529607866		3500	1599750
2.975213692	3.330261605		2625	1603875
4.39568573	5.00320951	SL1502	2625	1610125
3.075715813	3.998758238	SL1507	1375	1615625
2.268417725	2.588946902		1500	1626125
4.430893755	4.548823337		2500	1632125
4.931274003	5.269828828	SL1532	4000	1646875
2.362953018	2.634314103	SL1538	2125	1654875
1.264690998	1.644647972		750	1658250
4.707914402	5.304834097	SL1550	2875	1664250
5.535311877	5.952163731	SL1564	13125	1674875
2.457142818	2.780286499	SL1573	1375	1692875
1.295501711	1.772797935	SL1581	500	1700250
1.159215147	1.402418537	SL1581	250	1701500
3.961622152	4.310963552		2750	1702000
4.914572946	5.138932171	SL1588	7125	1708125
5.120198647	5.543126613	SL1601	8625	1715625
3.356335037	3.656463587		1750	1725750
3.660450644	4.129596987	SL1609	1875	1728500
3.246108012	3.496772963		1500	1736750
4.816477152	5.09798693	SL1628	3750	1745750
4.124524545	4.580118698	SL1637	2750	1755000
3.204728656	3.654408457		2750	1764000
4.936915175	5.507717384	SL1661	6250	1781750
2.387556646	2.714649708	SL1672	1500	1791250
2.514236304	3.092345586		4500	1795500
4.033496484	4.225415728		3875	1802750
1.353968533	1.624274887	SL1686	625	1808000
1.389787243	1.695404527	SL1688	750	1811875
1.262857224	1.523204408	SL1693	500	1819250
2.092770867	2.356592777	SL1699	2000	1825250

4.913629318	5.234239035	SL1713	2750	1839125
2.831589241	3.141510096		1125	1853750
1.7161577	1.978245774	SL1728	750	1856375
2.832025136	3.253874736		1625	1868000
3.070684871	3.473886087		1250	1870250
2.086426245	2.392516287		1000	1872000
3.864767597	4.808842547	SL1762	1500	1888625
4.213450765	4.546407616		3750	1893000
4.76952779	5.148207842	SL1784	6625	1908000
5.510719366	5.925575286	SL1793	8625	1915250
2.036564023	2.517045676	SL1806	1500	1924500
5.383237326	5.735286006	SL1831	3000	1948000
2.87923706	3.44203247		1375	1979500
3.644171524	4.002235652		1625	1983750
4.050810152	4.473362209	SL1868	2500	1985625
4.581681696	4.855105482	SL1873	3625	1989750
4.404442598	4.827213838	SL1879	3000	1995875
2.166119061	2.517303519	SL1887	1750	2003125
2.259530724	2.670550281	SL1889	2125	2005500
4.314483009	4.777816774	SL1896	1750	2012375
4.915501759	5.29542127		2250	2024000
1.725848814	2.169408521		1125	2029875
3.853333097	4.190542248		3625	2034250
5.15761893	5.433061414	SL1928	4625	2039250
1.096884752	1.43513683	SL1953	250	2061500
1.957370741	2.220803831	SL1958	1375	2063875
2.773079253	3.414374816	SL1970	1250	2074625
4.133236404	4.767622079	SL1976	3625	2077000
1.532200198	1.835229739	SL1978	625	2081375
4.543037284	4.939395174	SL1982	5000	2083375
1.317014727	1.49024271	SL1988	750	2090875
4.231835974	4.641200048	SL2012	3750	2111375
4.743712159	5.141940945	SL2043	2750	2138250
2.056485979	2.448520177		1000	2141500
4.661396502	5.116882896	SL2057	2625	2155125
5.296875528	5.797921642	SL2060	21000	2158000
3.776235625	4.08642497		1625	2180875
5.255639779	5.469018004	SL2089	3125	2191125
4.772508195	5.09485765		1875	2199750
4.245489202	4.835218854	SL2109	2375	2222500
1.692718869	1.951840178	SL2111	1000	2226375
4.841548685	5.154213588	SL2113	3500	2228625
5.312033448	5.835184725	SL2126	7125	2239750
3.638463849	4.057459452		2250	2249250
3.061566288	3.431978271		1250	2267750
4.580936954	5.162016533	SL2163	2875	2278250
4.170957786	4.763464987	SL2166	2875	2282000
1.191528851	2.786987838		375	2285375
1.128838541	1.456180215		375	2289000
4.978659876	5.284376428	SL2174	3000	2291125
4.578315457	5.07841881	SL2185	2375	2306125
1.739802928	2.178663587		875	2308750
3.824776974	4.235885411		1875	2310250
5.30026759	5.835083844	SL2208	4500	2329125
4.712630619	5.14742464	SL2214	2625	2335125
2.747010994	3.001678287		1500	2340750
4.458390375	4.623771118	SL2221	2250	2342625
3.86700451	4.266088663		1625	2363875
5.162393912	5.469518907	SL2243	4500	2374000
3.744961616	4.099472143	SL2250	3250	2383250
4.637547573	5.025978132	SL2256	2375	2391875
1.204554263	1.650823278		375	2397000
3.664183607	4.280392227	SL2265	1750	2400375
4.458535329	4.804669846		1625	2420625
4.258665021	4.52778449		1875	2438375
5.007035094	5.324956108	SL2312	1875	2453250
3.825453923	4.279718972	SL2328	3375	2466750
4.707515318	5.106481489	SL2346	3250	2483625
4.437056186	4.677217509		3375	2502375
3.937183778	4.435813668	SL2367	4875	2509125
2.228183752	2.643231369	SL2378	1625	2525375
1.204905889	1.605736623	SL2380	375	2527625
4.401140651	4.748143888		4250	2530375

2.476834895	3.04225516	SL2415	1000	2559750
4.211535585	4.667471993		2250	2575500
1.580233114	1.911364096		625	2583125
3.635488352	4.123630714	SL2441	2375	2584875
4.585340481	4.82176208		1500	2594125
1.962716935	2.617742027	SL2464	1125	2612375
4.632360005	5.067136182	SL2466	4375	2616125
4.329895666	4.601881923		1625	2631000
4.278011147	4.689395167		1875	2647750
3.83694926	4.178896022	SL2492	1500	2662250
4.742912784	5.067869986	SL2496	1750	2671125
4.312438789	4.612447279	SL2510	1750	2683375
4.969810297	5.469859088	SL2520	2375	2694875
1.369726865	1.719985114	SL2521	625	2697750
4.889962171	5.338288846	SL2536	4000	2716000
1.138035994	1.628540675		250	2723000
5.172003929	5.454368426	SL2547	7000	2726125
3.20109587	3.801964683	SL2574	1625	2755500
3.57521417	4.175540284	SL2577	3500	2757375
2.99742995	3.541817068	SL2586	2750	2762500
3.536829886	4.033323978	SL2594	2250	2768500
1.304731673	1.717528963		500	2771625
4.062306968	4.366441635	SL2629	2875	2812500
1.387067066	1.85634876	SL2632	875	2816250
2.583057772	2.952134306		1250	2818750
1.702678705	2.141320131	SL2644	750	2824750
1.264919801	1.459698251	SL2653	750	2832000
3.65949546	4.368926715		1750	2837625
4.985196054	5.333253725		3125	2862500
4.855606009	5.812319212	SL2696	4500	2876750
3.885401739	4.252100957	SL2702	2750	2883500
5.047110418	5.430219693	SL2710	7625	2887125
4.644600852	5.001602561		3625	2902375
4.481391594	4.72354413	SL2731	3500	2908125
4.873084979	5.508302754	SL2738	2750	2914375
5.250975838	5.553662801	SL2751	10250	2923375
3.995776497	4.78268633	SL2755	5000	2934250
5.054458841	5.45639005	SL2765	8500	2946125
4.378835502	4.611279674	SL2779	6375	2965625
5.007227959	5.069110707		2500	2977500
1.610272313	1.886609108		625	2983375
4.446952761	4.98497591	SL2801	2500	2987125
1.148349996	1.409656051		375	2999375
1.323750567	1.431459087		375	3000750
5.347616572	5.433433563	SL2856	20875	3031750
4.928096028	5.53396173		20000	3052875
2.166005183	2.37650448	SL2915	1250	3097750
1.421452951	1.67466998		625	3100000
4.936200719	5.536885021		3125	3107625
1.844058415	2.077963663		1375	3114500
2.434210357	2.887179307		1125	3117375
4.6652329	4.98154516		2000	3122375
5.173173042	5.411541604		2000	3147500
1.866825543	2.228712911	SL2962	1875	3155750
4.809503428	5.166570208	SL2966	2000	3158875
1.316352614	1.568575594		500	3184250
1.321729978	1.577018431	SL2984	500	3186125
2.613611892	2.77037624		1625	3198375
1.814500208	2.139558947	SL2996	1000	3200125
4.114219814	4.781447905	SL3000	2875	3203375
4.490909269	5.032249447	SL3005	2000	3207500
4.730720833	5.165617372	SL3009	4000	3212625
4.672535688	5.155889982	SL3028	2250	3231125
2.998494166	3.666362836	SL3043	1625	3249000
4.566087761	4.981433788	SL3056	4125	3261625
4.455078864	5.37337359	SL3061	1875	3268375
1.569491348	1.878435714	SL3080	1125	3285000
1.429022573	1.782154114		500	3287125
4.419788936	4.8375451	SL3092	5125	3295750
1.215322665	1.72043344	SL3096	500	3301750
3.63488202	3.91263887	SL3099	6125	3303500
4.702359853	4.94501608		4500	3311875
4.917204317	5.099160254	SL3112	3000	3320500

1.715596908	2.113444985	SL3125	875	3334375
4.520627898	5.097751297	SL3129	3125	3336375
1.684187043	2.220779548		750	3341250
1.138307956	1.467180115		250	3344500
4.4759903	4.892934372		1875	3348375
4.182687264	4.534414327	SL3144	3125	3352375
1.14766782	1.442572358	SL3147	375	3357125
4.514336683	5.102115002		3875	3374375
2.632993032	3.047016447		1500	3379875
1.813924876	2.168950975	SL3179	875	3391875
3.625430813	4.043704229	SL3189	1250	3402500
1.596509944	1.743568393		625	3404875
2.325286107	2.574429166	SL3205	1125	3419750
2.831526933	3.352129024	SL3211	1875	3423875
3.977312063	4.618633	SL3214	2500	3428875
4.779992126	5.127066015	SL3216	3750	3431500
4.186917196	4.38658217		1625	3438500
1.933194918	2.160943248	SL3224	1125	3440875
4.77896239	5.357197905	SL3227	2750	3443750
4.839163456	5.036550464	SL3251	2125	3463875
1.884574814	2.420943309		750	3485375
1.25871004	1.595828943	SL3277	375	3494625
4.05702504	4.481486686	SL3326	1625	3543250
1.055967816	1.229553592		250	3550500
1.087861877	1.517062824	SL3338	375	3554500
4.978335821	5.369634484	SL3362	2125	3581000
1.168180972	1.647204078	SL3368	250	3595375
3.808199333	4.27057826	SL3377	1875	3602000
2.439461431	3.016997966	SL3411	1250	3618875
1.808800585	2.432607842		750	3625875
1.253527832	1.476150057	SL3429	625	3633750
3.936854089	4.311581554	SL3445	1375	3650000
3.735052096	4.45580914		2000	3656500
1.627188218	2.163679459		625	3671375
1.324134548	2.020757047	SL3470	500	3681875
4.037102988	4.302012012		1625	3684625
2.791381313	3.078607516		1125	3697750
1.330009255	1.837991353	SL3495	500	3713375
3.536959103	3.917269025	SL3499	2750	3717875
4.646655327	4.864845025	SL3513	3500	3737000
2.309410151	2.730063414		1000	3754500
2.115973704	2.341458139		875	3765875
4.527595935	4.824745537	SL3565	4250	3791375
4.583642549	4.826155319		2250	3800250
1.269594288	1.618214402		625	3804000
4.26747348	4.510385112	SL3587	1750	3825375
4.562752672	4.710064694	SL3591	2125	3829875
1.793763194	1.968540207		750	3837500
2.894878269	3.189745008		1125	3844375
3.632632035	4.336732548		2750	3847625
3.765402644	4.289200886		5000	3856625
3.279598597	3.707498081	SL3623	2125	3864500
4.129263349	4.601741354		1625	3868750
4.181510956	4.856270345	SL3637	4375	3877750
3.469779911	3.691477063		1125	3886500
2.781678274	3.475225914	SL3647	1875	3890875
4.625788903	5.011717957	SL3655	2875	3900375
4.3210526	4.846243747	SL3663	1750	3913625
4.413841312	5.242294355	SL3673	2000	3922500
5.554765681	6.168015526	SL3679	11875	3929125
4.37834938	4.905379685	SL3717	2250	3969500
5.25900408	5.645714835		4125	3973000
4.173005158	4.616511776		5250	3978750
4.612833742	5.159064568	SL3729	2500	3985125
4.709912301	4.964388593		6500	4000375
3.364011492	3.934018778	SL3759	1625	4014250
5.035605752	5.296280801	SL3786	2500	4039875
4.702712479	5.187277379	SL3799	2500	4056000
4.580583519	4.740847623	SL3813	3000	4072250
1.276922587	1.729421524	SL3830	625	4094125
1.538462502	1.859740088		750	4101875
1.11574058	1.558711778	SL3867	500	4137375
2.204981711	2.600825911	SL3877	875	4148375

4.430831218	4.922964664	SL3896	2000	4170500
4.935434142	5.213077866	SL3907	2000	4180375
1.046642239	1.287528606		250	4201750
4.577519564	5.145422743		2000	4207000
1.920979518	2.35082654	SL3940	1250	4216500
1.64472752	2.080993685	SL3946	750	4226125
4.864976604	5.507046536	SL3962	8625	4240625
4.8281139	5.243391655	SL3988	3500	4270250
4.60982448	5.059937216	SL4000	2750	4283000
3.36492654	3.673421834		2250	4296250
2.899265208	3.42359851		2375	4303375
4.302420732	4.606635303	SL4025	4875	4306125
4.614475864	4.83929904		3375	4327875
4.555788684	5.05780434	SL4052	4500	4334500
1.336363527	1.70711326	SL4055	500	4340625
1.069383018	1.247906651	SL4057	375	4343500
4.737644469	4.914098689	SL4082	1750	4379375
5.169255911	6.623958348	SL4094	3375	4395375
2.441708408	2.827135053		1375	4422750
2.504843765	2.905630663	SL4127	1500	4435875
4.514100352	4.938821767	SL4131	3750	4438875
3.913801893	4.336614548	SL4136	1375	4443000
4.701560193	5.10786887	SL4139	4000	4445375
3.965365497	4.345230801	SL4148	1625	4454250
4.174608457	4.525642083	SL4151	3250	4456625
3.501912621	3.998873534		1250	4462875
1.883557111	2.22382932	SL4162	875	4467250
1.180041812	1.9228609		375	4483750
5.284552863	5.815161854	SL4194	10125	4497625
5.436241238	5.593606015	SL4197	12375	4513500
2.258871469	2.774601131		1000	4536750
2.063607612	2.470375446	SL4230	2000	4555500
4.411259956	5.038763405	SL4232	2250	4558375
3.941793527	4.413683927	SL4239	5125	4569250
4.874776116	5.185418379	SL4251	4875	4578625
4.919679443	5.155894661	SL4255	2375	4584000
1.178149198	1.406551721		250	4593125
4.306964869	4.6046043	SL4269	1875	4597750
2.101850138	2.292116766		1875	4600750
4.276648422	4.532562765	SL4282	1875	4607500
4.495154274	4.898156501		1750	4634500
3.222655715	3.972561938	SL4307	1250	4637500
1.349915561	1.506250207	SL4322	500	4650375
4.947498825	5.180912325	SL4345	3625	4672375
3.288192909	3.591352648	SL4351	2500	4679250
2.280873353	2.586135803		1000	4683000
4.608743687	5.076298197	SL4356	3875	4686250
4.656026923	4.974589592	SL4365	4500	4697000
3.100417172	3.335325668	SL4369	1500	4703375
4.612901323	4.778662023	SL4397	2250	4730125
4.960467547	5.307904306	SL4404	3375	4734375
1.441649912	1.737476841	SL4412	1000	4746125
4.6460048	5.178929586	SL4414	3125	4747500
3.447421051	3.605100798	SL4418	4125	4752125
1.333976687	1.635836928	SL4420	750	4757000
4.594197035	4.901411556	SL4424	3500	4763625
4.695558695	5.006559961		2625	4772375
5.270452222	5.524947986	SL4433	4625	4776250
4.432981706	4.952897177		2000	4783125
3.689227374	3.91890096		1750	4788875
1.132005712	1.49787598		375	4791125
4.84726153	5.244805658	SL4455	3875	4796125
4.900360926	5.064130363	SL4468	5125	4815250
1.17324579	1.65744056		500	4822375
4.774008199	5.06204473	SL4478	2625	4825750
3.412920327	3.931793748		1500	4830000
4.052513736	4.488771721	SL4500	6125	4846625
1.910911464	2.516460089		750	4864000
4.810844606	5.324475326	SL4523	7125	4869000
2.178585288	2.435605639		1125	4876750

Table S3: E. coli MG1655 LeuO motif matches

match	p-value	strand	E. coli MG1655 match start coordinate	E. coli MG1655 match end coordinate	alignment
1	8.00E-05	forward	11329	11356	CTGAATCATTCAGGTAATTAACATTCAT AAAATATATTCATTAAATGAATAATTAT + ++ ++++++ + ++++++ +++ ++
2	1.20E-07	reverse	11910	11937	CGATTCATTCTTTATATGAATAAAATTG ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ +++++++ ++++
3	8.60E-05	reverse	20619	20646	GTAGATATTCTTGTTCAGAATGTATCAG ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + + ++++++++ +
4	3.80E-05	reverse	29271	29298	TTTATTTTTGGTGTTATGTTTTTAAATT ATAATTATTCATTTAATGAATATATTTT +++++ ++ + + +++ + +++ ++
5	4.50E-05	forward	41989	42016	TGTTAACATTTAATATAATTATTATTAA AAAATATATTCATTAAATGAATAATTAT + +++++++ + ++++ ++++ ++++
6	5.70E-05	reverse	51217	51244	CGCCATATTCTTTTAATGAATGAGTGTG ATAATTATTCATTTAATGAATATATTTT ++++++ ++++++++++ + +
7	9.10E-05	forward	58362	58389	TATATTTTTACGTCTTAAAAATAAAAAA AAAATATATTCATTAAATGAATAATTAT ++ ++ + + + + ++ +++++++++
8	5.90E-05	reverse	71762	71789	GCTAAATTTATTACGCCGAATATTATCG ATAATTATTCATTTAATGAATATATTTT + +++ +++ ++ ++++++++
9	4.80E-06	forward	82472	82499	AAATTATATTCACTTTCTTTATACCCCA AAAATATATTCATTAAATGAATAATTAT ++++++++++++ + ++++++
10	1.40E-09	reverse	84011	84038	TTTGATATTGATTTGGTGAATATTATTG ATAATTATTCATTTAATGAATATATTTT ++ +++++ ++++ ++++++++++
11	2.10E-06	reverse	84058	84085	TAATGCATTAAATATATAAATTAATTAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + ++ +++ +++++
12	4.70E-05	forward	84293	84320	AAATCATATTCTTCAGGATTATTTCTCT AAAATATATTCATTAAATGAATAATTAT ++++ ++++++ + + ++++ + + +
13	3.20E-05	reverse	141247	141274	ATTAATATTTTAGTAGCAATTAATTATA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ + ++ ++ ++
14	9.40E-05	reverse	141312	141339	TTATTAACAGATTCCGCGAATGAATAGT ATAATTATTCATTTAATGAATATATTTT ++++ + + +++ ++ +++++ ++ +
15	5.90E-05	forward	149645	149672	CAGTCACATTGGTGGGGGCAATGATTTA AAAATATATTCATTAAATGAATAATTAT + + +++++ ++ ++++++++
					CAGAAATATATACATCACCAAAATCAAC

16	4.90E-05	forward	152024	152051	AAAATATATTCATTAAATGAATAATTAT + ++++++ ++ + ++ ++ +++
17	4.50E-05	forward	152238	152265	CCTTCTTATTGATAGATGAAATTAAACG AAAATATATTCATTAAATGAATAATTAT + ++++ ++ + ++++ +++
18	6.80E-05	reverse	152857	152884	AGAATAATAGATTGTGCTATTTTTTCTG ATAATTATTCATTTAATGAATATATTTT + +++ +++ +++ + + + +++ +
19	6.40E-05	reverse	156217	156244	GAGTTAATTAAAACAGGGAATAATATAA ATAATTATTCATTTAATGAATATATTTT ++ ++ +++++ + ++ +++++ +++++
20	2.70E-06	reverse	156263	156290	CTGTATATTCATTCAATCAATTTAACTG ATAATTATTCATTTAATGAATATATTTT + ++++++++++ +++ +++ +++ +
21	8.60E-05	reverse	156944	156971	ACACAAATAGGAGAAACAAATGTTAGAT ATAATTATTCATTTAATGAATATATTTT + + + +++ ++ +++++++ ++
22	5.00E-05	forward	157056	157083	AAATTAAATTTACTTAATTCAAAATTAA AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ ++++ + +++++
23	4.50E-08	forward	157228	157255	TATTTATATTCGCAATATAAATAAATTA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++ + ++++++++++++
24	2.70E-05	reverse	175073	175100	CATCTTATTTGTATGACCAATAAGTGAT ATAATTATTCATTTAATGAATATATTTT ++ ++++++ +++ + ++++ + ++
25	8.00E-05	forward	188088	188115	CAGAATCCTTCGCTGAAAATATGTTTTT AAAATATATTCATTAAATGAATAATTAT + ++ + +++ ++ ++ ++++++++++
26	3.30E-05	forward	208601	208628	TTGACTAATACAGGAATACTATGAGTCT AAAATATATTCATTAAATGAATAATTAT ++ + ++ ++ +++ +++++ + +
27	3.50E-05	reverse	222646	222673	TGATTATTTATTATCGTCATTAAGTTAG ATAATTATTCATTTAATGAATATATTTT +++ +++ ++++++ + ++ +++
28	5.50E-08	forward	234098	234125	TAATTACATTAATTAAATCAATATCTTC AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++++++ +++++ +++
29	1.80E-10	reverse	237203	237230	ATTTATATTGATTAAATGAATGTATATT ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ ++++++++++ ++
30	2.30E-05	reverse	237248	237275	GTTATTATTTAAGTGAGGTATATAATTA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + + +++++++++
31	4.40E-05	reverse	246234	246261	AATCATATTTAAATTCCTAATTTATCAA ATAATTATTCATTTAATGAATATATTTT +++ +++++++ ++ +++ +++ ++
32	5.20E-05	reverse	246573	246600	TGAGTAATTTAATAAACGGATGTTTTTA ATAATTATTCATTTAATGAATATATTTT + + +++++ + ++ + +++++++++
33	1.10E-06	forward	246612	246639	GAAATATATATGTTAATTTTATAATAAT AAAATATATTCATTAAATGAATAATTAT

33	1.10E-06	forward	246012	246039	++++++++ ++++ ++++++++++
34	4.20E-05	forward	247966	247993	GCATCATGTTGATTATATTTATATAAAT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++++++++++++++++
35	8.70E-06	forward	252474	252501	TGCTCATATTCATCTGGCAAATGAGAAT AAAATATATTCATTAAATGAATAATTAT + + ++++++++ ++++++ +++
36	2.40E-05	reverse	252694	252721	TTTTGAATTTATATTATGAATAACATAC ATAATTATTCATTTAATGAATATATTTT +++ ++++++++ +++++++ +++
37	6.10E-06	forward	253327	253354	TTTTTATATTTATATACTCTAAATAATT AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ + + ++ ++++++
38	8.30E-05	forward	259322	259349	CATTTTCATTCCTGATTTTAATTAACGC AAAATATATTCATTAAATGAATAATTAT + ++ +++++ ++++ +++++ ++ +
39	6.40E-06	reverse	259409	259436	AAAGATATATTACAGATTAATAATATTC ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ ++++ ++++
40	9.10E-05	reverse	265761	265788	AGTGTTTTACGTTTCATTATTTTTTTCC ATAATTATTCATTTAATGAATATATTTT + + ++ +++ ++++++ + + ++++
41	1.90E-05	forward	268601	268628	ACCAAATAATGACCGATGTAATGTATTT AAAATATATTCATTAAATGAATAATTAT + +++++ + ++ + ++++++++++
42	3.40E-05	reverse	274954	274981	GCGATTATTTTTGGTCTGAATGTTATCT ATAATTATTCATTTAATGAATATATTTT + +++++++ + ++++++++++ +
43	5.80E-06	forward	284452	284479	GAAATTTATTAATTTAAACAATTAGTTG AAAATATATTCATTAAATGAATAATTAT ++++ ++++ +++ ++ +++ + ++
44	1.40E-05	forward	289561	289588	AATTAAAATTCACTTTATATGTGTAATT AAAATATATTCATTAAATGAATAATTAT ++ +++ +++++++ +++++ +++++++
45	5.90E-05	reverse	293126	293153	AGTATTTTACCTCTCATAATTGTTTGTC ATAATTATTCATTTAATGAATATATTTT + ++++ +++ + ++++ + +++++ +
46	1.10E-05	forward	293270	293297	CCATTTCATTGACATGGTAAATATCAAT AAAATATATTCATTAAATGAATAATTAT +++ ++++ ++ +++++++ +++
47	3.30E-05	reverse	293431	293458	CTATGAATAAGAATAATGTTTGAATATC ATAATTATTCATTTAATGAATATATTTT +++ ++++ ++++++ ++ ++ +
48	2.90E-05	reverse	294119	294146	AATAAAATTAAATCTGTAATTTATTACA ATAATTATTCATTTAATGAATATATTTT +++++ +++++ + ++ + + ++ +
49	3.30E-05	reverse	310318	310345	CCATTCATTATCACGGTTTATAAATTCA ATAATTATTCATTTAATGAATATATTTT ++++++++ + ++ +++ +++ +
50	5.00E-05	forward	310735	310762	GGAATTCAATGGTTAAGTCAATATTTAG AAAATATATTCATTAAATGAATAATTAT +++ ++ + ++++ + ++++++++

51	8.30E-05	reverse	313318	313345	AGAAATATAACTTAGGTATCTATTTAAT ATAATTATTCATTTAATGAATATATTTT + ++++++++ ++ ++ +++++ ++
52	8.00E-05	reverse	313360	313387	GCTAAATTTTCCCCCATAAATAAAAATA ATAATTATTCATTTAATGAATATATTTT + +++ +++ +++ ++++ ++ ++
53	2.60E-06	reverse	316733	316760	TAAAACATTTTAATCCTGAATTTGTTCG ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ +++++ + ++
54	6.10E-06	forward	316773	316800	TGTAAAAATACATGATTGATATTAATCA AAAATATATTCATTAAATGAATAATTAT + +++ ++ ++++++ ++++ +++
55	3.90E-05	reverse	327907	327934	GGAGGTATAACCACCATGTATATAAAGC ATAATTATTCATTTAATGAATATATTTT + + +++++ + ++++ ++++++
56	4.20E-05	reverse	328628	328655	TGTGTCTTAATTGTTACGAATTTGATTT ATAATTATTCATTTAATGAATATATTTT + ++ +++ + + + ++++ + ++++
57	7.80E-05	reverse	331030	331057	GTGATATTTTATTGAATGTTTTAAATAT ATAATTATTCATTTAATGAATATATTTT ++ ++ ++++++ ++++ + +++++
58	9.70E-05	forward	343070	343097	CGATCAAATTAATGAAGCCTATGAGCGA AAAATATATTCATTAAATGAATAATTAT ++ + +++ +++++ +++++
59	5.40E-05	forward	344023	344050	ATTATTATTACACTTAAAAAATATCTAC AAAATATATTCATTAAATGAATAATTAT ++ ++ + ++++ ++ ++++++ +++
60	8.60E-05	reverse	344414	344441	TCATGCAGATGTTTTGTGAATGTGTTGG ATAATTATTCATTTAATGAATATATTTT ++ ++ ++ +++ ++++++++ ++
61	9.40E-05	forward	345959	345986	GGCAAATATTTATAAGAAGAAGTAATTC AAAATATATTCATTAAATGAATAATTAT +++++++ ++ + + +++ +++++
62	4.40E-07	forward	354032	354059	TGCACTCATTCATATAAAAAATATATTT AAAATATATTCATTAAATGAATAATTAT + + +++++++ ++ ++++++++++
63	3.70E-05	reverse	379193	379220	AATAAAATTTATCCGGTGAATGTGGTCG ATAATTATTCATTTAATGAATATATTTT +++++ ++++++ ++++++++ +
64	4.50E-05	forward	383168	383195	CTCAAAGAATCATTTTATGAATTACAAA AAAATATATTCATTAAATGAATAATTAT + +++ + +++++ +++++++ + ++
65	3.80E-06	reverse	384004	384031	CAATTCATATGTTAAGTGTTTGTATGTT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++++ +++++ ++
66	1.80E-09	reverse	384129	384156	GTTTATATACATTATGTGAATGTAATAT ATAATTATTCATTTAATGAATATATTTT ++++++++++++ ++++++++++++
67	2.00E-06	reverse	384178	384205	AGTGATATATACAATGCGAATATAATAG ATAATTATTCATTTAATGAATATATTTT + + +++++++ + + ++++++++++

68	8.50E-08	reverse	384384	384411	CGACTAATTCTTTTAATGAATGTTTTTA ATAATTATTCATTTAATGAATATATTTT + + ++++ ++++++++++++++++
69	8.80E-09	forward	389090	389117	ATTTTATATTCACTGAAAATATTTTTAA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++ ++++ ++++
70	4.90E-05	reverse	394201	394228	TCACGTATTGGTGTGATGAATTATATCC ATAATTATTCATTTAATGAATATATTTT + ++++ + + ++++++ +++
71	6.10E-06	reverse	400396	400423	TATTTCATAACTTTTATTTATAATAAAG ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ ++ +++ ++ +
72	8.00E-05	reverse	400440	400467	CTATATTTTGTGTGGGTAATTATTTAAA ATAATTATTCATTTAATGAATATATTTT +++++ ++ + ++ + +++++ ++
73	1.40E-05	forward	400497	400524	AAAAAATATTTGCGCAAAGTATTTCCTT AAAATATATTCATTAAATGAATAATTAT ++++++++++ ++ ++ ++++ + ++
74	1.80E-06	forward	406720	406747	GGAATACATTGACGAAGATAATATTTCC AAAATATATTCATTAAATGAATAATTAT ++++++++ +++++ ++++++++ +
75	8.30E-05	forward	407158	407185	AAAAATCATTGATGCCGGGAAAGAATTA AAAATATATTCATTAAATGAATAATTAT +++++ ++++ +++ +++ +++++
76	3.00E-05	reverse	411808	411835	GTATTCATTATCCTGCTGAATAGTTATT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + ++++++ ++ ++
77	3.30E-07	forward	424130	424157	CTAAAAAATTCATCGATTATATTCTATC AAAATATATTCATTAAATGAATAATTAT +++++ ++++++ + +++++ ++++
78	5.20E-05	forward	426486	426513	TAATATTAATAATGAGGGAAATTTAATG AAAATATATTCATTAAATGAATAATTAT +++++ ++ + ++++ ++++ ++++
79	4.60E-06	reverse	437485	437512	AATTATTTAGAGTCTATGAATAATTTCT ATAATTATTCATTTAATGAATATATTTT ++++++ ++ + + +++++++ +++ +
80	4.60E-06	reverse	439409	439436	CTATTAATACTTATTGTTTATTTATTAC ATAATTATTCATTTAATGAATATATTTT ++++ ++++ +++ ++ ++ +++++
81	5.90E-05	forward	450375	450402	CGATTTCATTCACGGTAGCAATGCCCTG AAAATATATTCATTAAATGAATAATTAT +++ ++++++++ ++ ++++ +
82	4.70E-07	forward	451067	451094	ATAAAACAATTATTTAACAAATAATTAT AAAATATATTCATTAAATGAATAATTAT ++++++++ + +++ ++ ++++++++++
83	2.80E-05	forward	451159	451186	AGAATTTATAAATGGCGCCAATAATTTC AAAATATATTCATTAAATGAATAATTAT + +++ +++ +++ +++++++++
84	4.90E-05	forward	478902	478929	AAAAATTATTACCGAGAAAAATGTTATA AAAATATATTCATTAAATGAATAATTAT +++++ ++++ +++ + +++++++++
					AACATAAATTCACCTGGTTAACTTATTC

85	4.10E-05	forward	500496	500523	AAAATATATTCATTAAATGAATAATTAT ++ +++ ++++++ ++++ +++++
86	3.50E-05	forward	502536	502563	CAATTTCATTGATGATGTTCATGAATAA AAAATATATTCATTAAATGAATAATTAT ++++ ++++ +++++ ++ +++++++
87	3.70E-05	forward	515652	515679	AAGTAATAAACATAACGTCAATGAGATG AAAATATATTCATTAAATGAATAATTAT ++ +++++ +++ + + +++++ ++
88	5.20E-05	reverse	522117	522144	TGTTTCATTGATGATGTTATTGAATTGG ATAATTATTCATTTAATGAATATATTTT +++++++ ++ ++ + ++ +++
89	1.80E-05	forward	522231	522258	CTAATAAAATCATAAATCATATGCGTTG AAAATATATTCATTAAATGAATAATTAT +++++ + ++++ ++ +++++ ++
90	1.40E-05	reverse	522263	522290	GATATTATCCATATAGTGAATTTGTTGA ATAATTATTCATTTAATGAATATATTTT ++++++++ ++++++++++++ + ++ +
91	3.70E-05	forward	522373	522400	CAAATAAGTTTATGTGAAAAATATATAA AAAATATATTCATTAAATGAATAATTAT +++++ ++ +++ + +++++++++
92	5.80E-06	reverse	527111	527138	GTATTTATTATAGAAATTAATAAGAAAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ ++++ + ++
93	3.90E-06	forward	527895	527922	TGATAATATTTATTTTTGCTATTATAAT AAAATATATTCATTAAATGAATAATTAT + ++++++++ +++ + +++ +++++
94	8.60E-05	forward	535790	535817	AAATTTAAAAGAGGTTAATTATGAAACT AAAATATATTCATTAAATGAATAATTAT +++++ + + + ++ ++++++++ +
95	6.60E-05	reverse	536768	536795	TCAGTATTAAAAATAATATTTTTATTTT ATAATTATTCATTTAATGAATATATTTT + + ++++ +++++ + ++++++
96	8.40E-06	reverse	545674	545701	AAAAATATAGTTAGAATTTATTTGATAA ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ +++ ++ + ++++
97	8.80E-05	reverse	558824	558851	CTGAAATTTCAGACCGTTAATGATTATG ATAATTATTCATTTAATGAATATATTTT + ++ ++++ + +++ ++++ ++ +
98	8.80E-05	forward	559834	559861	TTTTATTATCTATCAAAGCTATGTTTCC AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ +++ +++++++ +
99	5.20E-05	forward	561811	561838	GATAATTATAAATATATGCAATTACATG AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++ + +++ + ++
100	9.10E-06	forward	568057	568084	ATAAAAAATAAACAAAAATTATATCCCA AAAATATATTCATTAAATGAATAATTAT ++++++ ++ ++ +++ ++++++
101	1.80E-05	forward	568481	568508	CTATAATATTGACTCTTTGAATGAGCCA AAAATATATTCATTAAATGAATAATTAT +++++++++ +++ + +++++++
102	1.00E-05	reverse	569410	569437	GTGTAAATTCATTCAGTGATTTTTATGC ATAATTATTCATTTAATGAATATATTTT

102	1.00E-05	reverse	569410	569437	++ ++ +++++++ +++++ + ++++
103	7.00E-05	reverse	569502	569529	AAAATCATAATTAATACGGATAATAAAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ + + +++ ++ ++
104	9.40E-05	reverse	570849	570876	TATTTCCTTGTGGTTATGAATTTTATAT ATAATTATTCATTTAATGAATATATTTT +++++ ++ + ++++++ ++++++
105	9.70E-05	reverse	573569	573596	AATTGTTTACTAAAAATTATTAAAAATG ATAATTATTCATTTAATGAATATATTTT ++++ + +++ + +++ + ++ ++ +
106	5.00E-05	reverse	576020	576047	GCAGAAATTGCCACTGTTAATTTTTTCA ATAATTATTCATTTAATGAATATATTTT + + + +++ + ++ +++ ++++ +
107	4.10E-08	reverse	576097	576124	ATAAATATTCATCTAATCAATGTGATTA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ +++++ ++++
108	8.40E-06	forward	576247	576274	AATTTATATTAACGGCTGTTATTTATAA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ +++ ++++ ++++
109	3.60E-06	reverse	578191	578218	TTGAAATTTCATATTGTTAATATTTATT ATAATTATTCATTTAATGAATATATTTT + ++ +++++++ ++ +++++++ ++
110	7.00E-05	reverse	582042	582069	GTTATAGTTTTATTTGTGAATTAAATCA ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++ ++++++ +++ +
111	3.90E-05	reverse	582365	582392	GTATGTATATCATAGGTTATTAATTGTG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++ + ++ ++ +
112	8.60E-05	forward	582617	582644	TAAATTCAAACGGTTGACATATATATAG AAAATATATTCATTAAATGAATAATTAT +++++ ++ + + + +++++++++
113	3.90E-05	reverse	582757	582784	TTAATCTTAAATGAAATTTATTAAAATT ATAATTATTCATTTAATGAATATATTTT +++++ +++++ +++ ++ ++ ++
114	6.70E-06	forward	583304	583331	TAAATACATTTACCTGTAAAATTACTGG AAAATATATTCATTAAATGAATAATTAT ++++++++++ ++ ++++ + +
115	5.20E-05	forward	583551	583578	ATATTTCATATGTGCATTTAAAGATTAT AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++ + ++++ ++++++
116	2.90E-05	reverse	584924	584951	TTACATATTGCTCCACTGTTTATATTTT ATAATTATTCATTTAATGAATATATTTT ++ +++++ + + ++ ++++++++
117	4.10E-05	forward	592408	592435	ACCTTACATTAACGCTGGTTATGTTTAG AAAATATATTCATTAAATGAATAATTAT + +++++++ +++ + +++++++++
118	2.30E-05	reverse	593445	593472	CAAATCATTTATGTAATGAAGATGAAAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++++ ++ + ++
119	8.80E-05	reverse	605415	605442	TGTTTCATAACATTGTTAAATGTAAGTT ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ + +++++++ ++

120	1.20E-05	forward	611889	611916	AGTTATCAATAATATTATCAATATATTT AAAATATATTCATTAAATGAATAATTAT + ++ ++ + ++ +++ +++++++++
121	3.40E-08	reverse	617320	617347	TGATTTATAGGTTTGATGAATATTTCTC ATAATTATTCATTTAATGAATATATTTT +++++++ +++ ++++++++++ +
122	9.70E-05	reverse	617549	617576	AATGAAATTGATTTACTTAATCTAATCT ATAATTATTCATTTAATGAATATATTTT +++ + +++ +++++ + +++ ++++ +
123	2.10E-05	forward	618178	618205	TGCAAACATTCAGCGCCTCAATTATTCA AAAATATATTCATTAAATGAATAATTAT + +++++++++ + +++ +++
124	4.90E-05	forward	624056	624083	AAATATAAATGATAATCATTATTAAAGC AAAATATATTCATTAAATGAATAATTAT +++++ + + ++ ++ ++++ +++ +
125	5.80E-06	forward	635878	635905	ATTTTTCATTCGCGCTGTGAATAAATAG AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++ ++ + ++++++++++
126	4.50E-05	reverse	635945	635972	ACTCTCATTTAGACGGTCAATAAATCGG ATAATTATTCATTTAATGAATATATTTT + + +++++++ + ++ ++++ ++
127	1.40E-09	forward	636869	636896	ATGATATATTCACTTAATCAATGTTTTT AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ +++ +++++++++
128	3.20E-05	reverse	636900	636927	GTATATATTTTTATTGATTATGTTTTTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ + +++++++++
129	3.40E-05	reverse	637780	637807	AGTATCTTTTTTAACATTAATTTGTCCT ATAATTATTCATTTAATGAATATATTTT + ++++ +++ ++ +++ +++ + + +
130	2.90E-06	forward	641116	641143	ACAAATCATTCGCCATGATTATAATATT AAAATATATTCATTAAATGAATAATTAT + +++ +++++ + ++ ++++++++++
131	3.50E-05	forward	644236	644263	GGAACTCATACATACACTGAATACTATC AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ + ++++++ ++++
132	9.10E-05	forward	651061	651088	AAATATCATTGCCGAACATAATAAATAG AAAATATATTCATTAAATGAATAATTAT +++++ ++++ ++++ +++++++++
133	9.30E-08	reverse	651272	651299	TTTTTTATTTATTTAATGATTTTAAGTT ATAATTATTCATTTAATGAATATATTTT ++++++++++++++++ + +++ ++
134	2.00E-09	reverse	651341	651368	GATTTAATTGATTTAATGAATAAAATTT ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++++++++++++ +++++
135	5.30E-06	reverse	651372	651399	ACGATCATAATTAATATCTATGTATTTT ATAATTATTCATTTAATGAATATATTTT + +++++++ ++ ++ +++++++++
136	3.80E-05	reverse	655489	655516	TATATTATATACTTCGTTAAGATGATTG ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ ++ ++ +++

137	3.00E-05	reverse	655744	655771	AGTAGTAGATTTTTGATAAATGTTTTAT ATAATTATTCATTTAATGAATATATTTT + ++ ++ ++ +++ ++ ++++++++++
138	4.10E-05	forward	660612	660639	CAATTTTATTCATGGAAAAATAATATTT AAAATATATTCATTAAATGAATAATTAT ++++ ++++++++ ++ ++ ++++++
139	1.10E-05	reverse	661996	662023	CATTAATTTAATGTAATCAATGATTTTG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++++ ++++ ++++
140	7.30E-05	reverse	675663	675690	ATTATAATAAAACCCAACAATATATTGA ATAATTATTCATTTAATGAATATATTTT +++++ +++++ ++ ++++++++ +
141	4.10E-10	reverse	675896	675923	GCTAATATTCATTTAATGAATATTTAAG ATAATTATTCATTTAATGAATATATTTT + ++++++++++++++++++++ +
142	6.40E-06	forward	676919	676946	GCGATTCATTCAGCAATTAAATTATTGC AAAATATATTCATTAAATGAATAATTAT ++ ++++++ ++ +++++ +++ +
143	2.90E-05	forward	677891	677918	ATTATTAATTCAGGCGGCGAATTTTACC AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++ + ++++ +++ +
144	2.10E-05	forward	677995	678022	TCATTAAAATTATTTTCTATATTTTTAT AAAATATATTCATTAAATGAATAATTAT + ++++ + + +++ + +++++ +++++
145	3.10E-05	forward	678602	678629	CGAATATATACATTAATTTTTTATTCAT AAAATATATTCATTAAATGAATAATTAT +++++++ ++++++ +++ ++++ ++
146	9.10E-05	forward	678670	678697	AGTTTATACTCATCAATAATAAAAAAGT AAAATATATTCATTAAATGAATAATTAT + +++++ ++++ ++ +++ ++++ +
147	2.40E-05	reverse	678867	678894	GAATAAATAATCGTGATGATTTAATTCA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + ++++ + +++ +
148	5.00E-06	forward	679716	679743	GAAATTTATTCAGCAATTAAATACCTGG AAAATATATTCATTAAATGAATAATTAT ++++ ++++++ ++ ++++++ +
149	4.20E-05	forward	682501	682528	GTTAAATATTCACCGAACTTATTTGGAA AAAATATATTCATTAAATGAATAATTAT + ++++++++++ ++ ++++ + +
150	3.20E-05	reverse	702827	702854	AGTCTCATTATTCACCTCAATAAGTAAA ATAATTATTCATTTAATGAATATATTTT + + ++++++ + + + ++++ + ++
151	4.40E-05	reverse	703019	703046	CGTTTAATTTGCGATACGAATTAAATTT ATAATTATTCATTTAATGAATATATTTT +++ ++++ + ++++ +++++
152	1.80E-05	forward	707234	707261	GCAATTTATCCATAAAATAAATTTAAAA AAAATATATTCATTAAATGAATAATTAT +++ +++ +++ ++++++++ ++++
153	7.30E-06	forward	716161	716188	TTGTTTTATTAACCGTGTTTATTTTTCA AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++ + +++++ +++
					TTTGACATTTTTCATCTCTTTATTTTAG

154	4.90E-05	reverse	719676	719703	ATAATTATTCATTTAATGAATATATTTT ++ ++++++ + + +++++++
155	3.00E-05	forward	720122	720149	AATAAAAAATGATCAATCTTAATTTATT AAAATATATTCATTAAATGAATAATTAT ++ +++ + + ++ ++ +++ +++++
156	1.00E-05	forward	728195	728222	GTAACTTAATTACAGGATGAATGTAAAT AAAATATATTCATTAAATGAATAATTAT +++ ++ + ++ ++++++++++++
157	1.60E-11	forward	728668	728695	AACATATATTCATGAAATATATATAAAT AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++++++++++++++++
158	4.50E-05	forward	732857	732884	CTGATATATTCACACCTATAAATTTAGG AAAATATATTCATTAAATGAATAATTAT + ++++++++++ +++ +++
159	2.90E-05	reverse	733329	733356	AAGTTAATTGCTCTTATTATTATATGTA ATAATTATTCATTTAATGAATATATTTT ++ ++ +++ + + ++ + +++++ ++
160	5.60E-05	reverse	735375	735402	ACAAAAATGAGTCTTACGAATGTTTAAT ATAATTATTCATTTAATGAATATATTTT + +++ ++ + + + + ++++++++ ++
161	1.90E-05	forward	735460	735487	ACAAATTAATCATTGTGAAAAATTATAT AAAATATATTCATTAAATGAATAATTAT + +++ ++ +++++ + +++ +++++
162	9.40E-05	reverse	735645	735672	CCTTACATAAATAAGGTGAACAAATGGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ + ++ +
163	8.60E-07	forward	735675	735702	TTAAAAAATTGATGGAACATATTTCTAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ ++ ++++ + +++
164	9.40E-05	reverse	736025	736052	CCTTACATAAATAAGGTGAACAAATGGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ + ++ +
165	8.60E-07	forward	736055	736082	TTAAAAAATTGATGGAACATATTTCTAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ ++ ++++ + +++
166	3.80E-05	reverse	736783	736810	GAACTTATTGATTTCACGTTTGAATGGA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++++ + ++ ++ +
167	8.60E-07	forward	737322	737349	TTAAAAAATTGATGGAACATATTTCTAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ ++ ++++ + +++
168	8.80E-05	reverse	738050	738077	GAGCTTATTGATTTCACGTTTGAATAGA ATAATTATTCATTTAATGAATATATTTT ++ +++++ ++++++ + ++ ++ +
169	8.00E-05	forward	751380	751407	GATAAATATTCACGGTGTCCATACCTGA AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + + +++ +
170	1.40E-07	reverse	752135	752162	TAAATTATTGGTATCATGAATTTGTTGT ATAATTATTCATTTAATGAATATATTTT +++++++ ++++++++++ + ++ +
171	3.60E-06	forward	765136	765163	CCGATAAATTCATCCTGTAAATAATACA AAAATATATTCATTAAATGAATAATTAT

171	3.00E-06	forward	765130	765163	+++ ++++++ + +++++++++
172	7.50E-05	reverse	767276	767303	TCACGTATTCTGCTGGTCAATAATATGG ATAATTATTCATTTAATGAATATATTTT + +++++ + ++ ++++ +++
173	9.40E-05	forward	768010	768037	GGAATTTATTGATGGCAAATATATGCGC AAAATATATTCATTAAATGAATAATTAT +++ ++++ +++ + ++++++ +
174	8.60E-07	reverse	770083	770110	ATAATTATAAGTTAACTAAATGTTAATA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ + + +++++++ ++
175	4.70E-05	forward	770272	770299	TTTAAACATAAATGTCACTAAAGTTACC AAAATATATTCATTAAATGAATAATTAT ++ ++++++ +++ + +++ ++++ +
176	1.30E-05	forward	770496	770523	GTAATATATACGTGGGATCAATTTGAGT AAAATATATTCATTAAATGAATAATTAT ++++++++ + ++ ++ +++ + + +
177	1.20E-07	reverse	799529	799556	ATAAGCATTCATATCACGAATATTAAAA ATAATTATTCATTTAATGAATATATTTT ++++ ++++++++++ ++++++++ ++
178	8.60E-05	reverse	799961	799988	TTTTAAATTGAGGGCATTATTATGAAAA ATAATTATTCATTTAATGAATATATTTT ++++ +++ + +++ + +++ + ++
179	9.40E-05	forward	800076	800103	ATAAAATATTGATGGCAATTATGGGTTC AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++ + +++++ +++
180	1.40E-07	forward	812241	812268	CTAAAATAATCACGAAAAAAATTTTACT AAAATATATTCATTAAATGAATAATTAT +++++++ ++++++++ ++++ +++ +
181	8.60E-07	forward	819965	819992	TAAATTTATTGATGGTGAATATTAATAT AAAATATATTCATTAAATGAATAATTAT +++++ ++++ +++ + ++++ +++++
182	4.50E-05	reverse	820502	820529	ATAATAAGTTGCTTAATGATTGTGTTAT ATAATTATTCATTTAATGAATATATTTT +++++ + ++ +++++++ +++ ++++
183	3.40E-05	forward	837292	837319	ACCATTTATTTGTTGTACTTATGAACTT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ ++ ++ +++++++ ++
184	9.90E-06	forward	839325	839352	CTGTCATATTCAGTATGATAATTATCCA AAAATATATTCATTAAATGAATAATTAT + + +++++++ +++ ++++ ++
185	6.60E-05	reverse	841370	841397	CTTATTTTTTGAACGATATATTTTTACA ATAATTATTCATTTAATGAATATATTTT +++++ +++ + ++ ++ +++ +
186	9.10E-07	forward	848280	848307	TAGATATATTGATAAGAACAATTCTTAT AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ + + +++ ++++
187	4.50E-05	reverse	848425	848452	ATGTAAATTTAATTAATGTCTAATTCTT ATAATTATTCATTTAATGAATATATTTT ++ ++ +++++ ++++++ ++ ++ ++
188	1.30E-06	reverse	859339	859366	GATGAAATTGATGATGTGAATGATTTAG ATAATTATTCATTTAATGAATATATTTT +++ + +++ ++ +++++++ ++++

189	1.40E-05	forward	868609	868636	AGATAACATTCAGGCGGAGAATAAAATG AAAATATATTCATTAAATGAATAATTAT + +++++++++ + +++++++++
190	2.90E-05	reverse	872914	872941	TTTATAATAGCGAAGGTAATTATAATAT ATAATTATTCATTTAATGAATATATTTT ++++ +++ + ++ + ++++++++
191	8.00E-05	reverse	875210	875237	TTGCGTATAAAAAAGATGTTTATTTGCG ATAATTATTCATTTAATGAATATATTTT + ++++++ + +++ +++++
192	3.40E-06	reverse	877891	877918	TAAGTTTTTGTAAAAATGAATTTGTTAT ATAATTATTCATTTAATGAATATATTTT ++ ++ ++ + +++++++ + ++++
193	1.80E-05	reverse	880397	880424	TCATTTATTGGTCTGATGAATGGTTATG ATAATTATTCATTTAATGAATATATTTT +++++++ + + +++++++ ++ +
194	9.10E-05	forward	881195	881222	GTCATTAATACATCAACTTAATGCGCTG AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ ++ ++++++ +
195	4.40E-05	reverse	899892	899919	GATTAAATAATTTAAATGAAATAAAAAA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++++++ ++ ++
196	4.40E-05	reverse	913051	913078	AAAGTTATATTTAATATACATGTTTAAG ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ ++ ++++++ +
197	2.40E-05	forward	915281	915308	ATTAAAAATTGACCCTGTGAAAAATATG AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ ++ + ++++ +++++
198	1.40E-06	reverse	915390	915417	AGATAAATAAATCCAGTAAATTTGATTT ATAATTATTCATTTAATGAATATATTTT + +++ ++++++ +++ +++ + ++++
199	3.20E-06	forward	915503	915530	AAAAATAATTTATCATGCTAATTATTTG AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++ ++ ++++ ++++
200	1.10E-05	forward	918295	918322	GCGACATATTCATGAAATCAATGGTTAT AAAATATATTCATTAAATGAATAATTAT + ++++++++++++ ++++ ++++
201	7.50E-05	reverse	918439	918466	TGGAGTATTCAGAAAATTTATGAAAAAG ATAATTATTCATTTAATGAATATATTTT + ++++++ + +++ +++ ++ +
202	7.80E-05	reverse	925269	925296	AGAATTTTAATGATAATTATTGTTTGCT ATAATTATTCATTTAATGAATATATTTT + ++++ +++ +++++ + +++++ +
203	5.00E-05	reverse	949315	949342	AAAAAAATATAAGCGATTATTTAAAAAA ATAATTATTCATTTAATGAATATATTTT +++++ +++++ ++ + + ++ ++
204	6.70E-06	forward	953836	953863	AATAAAAATAAATTTTAAAAATTAACAA AAAATATATTCATTAAATGAATAATTAT ++ +++ ++ +++ ++ ++++ ++ +
205	2.90E-06	forward	953983	954010	TAATTACAATTATTTTATTAATGCAAAT AAAATATATTCATTAAATGAATAATTAT ++++++++ + +++ ++++++++ ++++

206	2.60E-06	reverse	959444	959471	TGATACATAATATTTATATATGATTAAT ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ ++ +++ ++ ++
207	2.20E-05	reverse	961042	961069	TTAAGCATTGAGCAAGTGATTGAAAAAG ATAATTATTCATTTAATGAATATATTTT +++ ++++ + +++++ ++ ++ +
208	5.00E-05	forward	970922	970949	CTTTTATATTGGCGCTCATTATGAAAGC AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ + ++++++++ +
209	6.10E-05	reverse	971023	971050	AGTCGTATTGAGTGCGTCAATGAAAAAG ATAATTATTCATTTAATGAATATATTTT + + ++++ + + +++ ++++ ++ +
210	9.10E-05	forward	974019	974046	CTGAAATATTCGGTAGCAGAAATTTTCG AAAATATATTCATTAAATGAATAATTAT + ++++++++ ++ +++ +++
211	2.70E-05	reverse	986484	986511	CTATTTATATGATTTCCTTATATTTAAA ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++++++ ++
212	1.80E-05	reverse	996817	996844	CCAAATATAAATTTTGTGTATCTTTTTC ATAATTATTCATTTAATGAATATATTTT ++++++++++++ +++ ++ +++++
213	6.40E-05	reverse	996867	996894	CTTTATATATCACGCATATTTATTTATT ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ +++++ ++
214	8.50E-11	forward	996942	996969	TTTAAATATTCATGAAATCTATAAATTA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++++++ ++++++++
215	4.70E-05	reverse	997624	997651	TTATTAATAGAACTCATTAATTGTTTTA ATAATTATTCATTTAATGAATATATTTT ++++ +++ + ++++ +++ +++++
216	6.10E-06	forward	1002267	1002294	TATTCATATTGGTGATTTTAATATCAGT AAAATATATTCATTAAATGAATAATTAT ++ + +++++ ++++ +++++++ + +
217	9.10E-05	reverse	1012242	1012269	GAATGCATTTGATTTATGAAGTTGTTGA ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++ +++++ + ++ +
218	2.00E-05	reverse	1020326	1020353	TCATTCTTTTATGTTATGATTTTAAAAG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++++ + +++ +
219	3.00E-05	forward	1030664	1030691	GTAATTAATTAAGCAGCATAATGATAAT AAAATATATTCATTAAATGAATAATTAT ++++ +++ + + ++++++++++
220	5.00E-05	forward	1042116	1042143	CAGAAATAAACAGGCCAAGAATAAAACC AAAATATATTCATTAAATGAATAATTAT + +++++ ++ + + ++++++++ +
221	5.40E-05	reverse	1063979	1064006	GAATTCATTAAAATGGTTGATAAAAAAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ ++ +++ ++ ++
222	9.70E-05	reverse	1084120	1084147	AAATATATTGTTGCAATAAATGCGAGAT ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++ ++++ + ++
					TTTTTAATTTGATTGGTCAATTGTATTA

223	6.10E-05	reverse	1087294	1087321	ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++ +++ +++++
224	1.70E-05	forward	1091751	1091778	CAAAATAAATTAGGATTAAAATAATTAA AAAATATATTCATTAAATGAATAATTAT ++++ + + + +++ +++++++++
225	1.70E-05	reverse	1091851	1091878	GATTTAATTGTTATTCCTAATGTATCTA ATAATTATTCATTTAATGAATATATTTT +++++ +++ +++ +++++++ ++
226	8.80E-05	forward	1092523	1092550	GCAATTTATTTTCCAAAAAAATGACTTT AAAATATATTCATTAAATGAATAATTAT +++ ++++ + +++ ++++++ +++
227	5.00E-05	forward	1092889	1092916	TGGTAATATTTATGTGCCATATATTCAG AAAATATATTCATTAAATGAATAATTAT + +++++++ +++ +++++++ +
228	5.60E-05	forward	1102652	1102679	AGGTTTTATTAAGTTTAGAAATGATAGA AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + + ++ ++++++++
229	5.40E-05	reverse	1102733	1102760	GATAACTTACTAATAATGCATATAAAAA ATAATTATTCATTTAATGAATATATTTT ++++++ +++ ++++++ ++++++ ++
230	1.30E-05	forward	1104118	1104145	AGTACTAATACATCATTTGTATTACAGA AAAATATATTCATTAAATGAATAATTAT + + ++ +++ ++ +++++ + +
231	2.40E-05	reverse	1118356	1118383	TTTATTTTTATTTCAATAATTTTGAATT ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++ +++ + + + + ++
232	5.00E-05	forward	1118538	1118565	AAAACACATAGATCAGATCCATAATTGC AAAATATATTCATTAAATGAATAATTAT ++++ ++++ ++ + ++ ++++++ +
233	5.90E-05	forward	1120312	1120339	TTTTAAGATTTATATGAACAATAAAACA AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ ++ + +++++++
234	2.70E-05	reverse	1124733	1124760	ATAGTAATACTTACAGCGTATTAAAGAC ATAATTATTCATTTAATGAATATATTTT +++ + ++++ ++ ++ + ++ ++ +
235	3.90E-06	reverse	1160831	1160858	GATTATATTTAGTGTGCGAATAATTTTG ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + +++++ ++++
236	9.90E-06	forward	1165073	1165100	CTCACAAATTCGCTCAAATAATAAACAA AAAATATATTCATTAAATGAATAATTAT + + + ++++ ++ ++ +++++++ +
237	6.60E-05	forward	1165272	1165299	AATTAACAATTGGTTAATAAATTTAAGG AAAATATATTCATTAAATGAATAATTAT ++ +++++ + + +++++++ +++
238	3.20E-06	forward	1168175	1168202	TAAATTAATTAATGATTGTTATAAAAAA AAAATATATTCATTAAATGAATAATTAT +++++ +++ +++++ +++++++++
239	9.40E-05	forward	1169609	1169636	AATAAATATAAGGTTATTGTAATAAACA AAAATATATTCATTAAATGAATAATTAT ++ ++++++ + + ++++ +++
240	8.00E-05	forward	1184944	1184971	GCTTTATATTCATTAAGGTAATGCTGAT AAAATATATTCATTAAATGAATAATTAT

240	8.00E-05	forward	1184944	1184971	+++++++++++++ +++++ + ++
241	3.90E-05	reverse	1195761	1195788	ATAGATATTCCTTAGCTTTTTATTATTG ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ + +++++++
242	3.10E-05	forward	1196292	1196319	CTTTTATATTGATTTACAATAAGAGTCT AAAATATATTCATTAAATGAATAATTAT + +++++++ +++ + +++ ++ + +
243	4.20E-05	reverse	1196711	1196738	GCGAATATTAACTCCGTGCATATTATAG ATAATTATTCATTTAATGAATATATTTT + ++++++++ + ++++ ++++++++
244	6.10E-05	forward	1197492	1197519	ATATTTAATTAAGTGTCATTATATACTT AAAATATATTCATTAAATGAATAATTAT +++++ +++ + + + +++++++ ++
245	2.20E-05	reverse	1209558	1209585	AGATTAATATTATGCATGTTTTTGATAA ATAATTATTCATTTAATGAATATATTTT + +++ ++++ + ++++ + + ++++
246	5.40E-05	reverse	1209780	1209807	ATATGCATTCTTTGGATGAAAGAAAAAT ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++ +++++ + ++ ++
247	7.00E-05	reverse	1210523	1210550	AAACACATGTTTATAATCAATGAGTTAT ATAATTATTCATTTAATGAATATATTTT +++ ++++ + ++++++ ++++ ++++
248	1.70E-05	forward	1211326	1211353	TAATTAAAATGATGGCTTATATAAAATA AAAATATATTCATTAAATGAATAATTAT ++++++ + + +++ ++++++++++
249	1.90E-06	reverse	1211784	1211811	GATAGTATTAGTCTGGTGATTATTTATG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + + ++++ +++++ +
250	8.80E-05	reverse	1213353	1213380	AAAATTGTACAAAGTATAAATAAGATTT ATAATTATTCATTTAATGAATATATTTT ++++++ ++++ + ++ ++++ ++++
251	4.90E-05	forward	1215726	1215753	CGATAATGTTAATAATAAAAATATTATC AAAATATATTCATTAAATGAATAATTAT +++++ ++ ++ +++ ++++++++++
252	3.40E-05	forward	1215887	1215914	AAAACTCATTCATCTTATTTTTGTCTGT AAAATATATTCATTAAATGAATAATTAT ++++ +++++++ +++++ +++ + +
253	9.90E-06	reverse	1215933	1215960	GCATAATTTTATTGGGTTAATATTTCTA ATAATTATTCATTTAATGAATATATTTT + +++ ++++++ ++ +++++++ ++
254	9.70E-05	forward	1218673	1218700	CCGACTTATTTATCATTTATATATTGTC AAAATATATTCATTAAATGAATAATTAT + ++++ ++ ++ ++++++++ ++
255	5.60E-05	reverse	1218712	1218739	ATTTAAATTTTTTGTGCTTTTGTTTTTG ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ + +++++++
256	6.40E-05	forward	1219624	1219651	AGGTAACATTGATATAAAAAATAGTTCT AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ ++ +++++ ++ +
257	3.50E-05	forward	1220094	1220121	GTCAAACATTTACCCAAGGAAAAACATT AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ ++ +++ ++ +++

258	2.90E-05	reverse	1222336	1222363	AATTATGTTTTTTACGTGAATGAGAATA ATAATTATTCATTTAATGAATATATTTT ++++++ +++ ++ ++++++++ + ++
259	2.90E-06	forward	1222378	1222405	ATAACTCATTGATTGACAATATTTTTAT AAAATATATTCATTAAATGAATAATTAT ++++ ++++ +++ + ++++ +++++
260	6.60E-05	reverse	1222447	1222474	AAGATAATCTGATTTATCAATATTATTG ATAATTATTCATTTAATGAATATATTTT ++ ++ ++ + ++ ++ +++++++++
261	3.40E-05	forward	1229615	1229642	CATAATCATTCGCCTCTTTAAATATATA AAAATATATTCATTAAATGAATAATTAT + ++ +++++ + ++++ ++++
262	8.00E-06	reverse	1229723	1229750	AATGTCTTTATTTCTATTAATATGATAA ATAATTATTCATTTAATGAATATATTTT +++ ++ +++ ++ ++ +++++ ++++
263	8.00E-05	reverse	1229902	1229929	ACAAATATTGATAGCCTGAATCAGTATT ATAATTATTCATTTAATGAATATATTTT + +++++++ +++ + +++++ + ++
264	5.90E-05	reverse	1244380	1244407	GGTGTGATTCAGAAAATAAATATTTTAG ATAATTATTCATTTAATGAATATATTTT + + + +++++ + +++ +++++++++
265	1.10E-05	forward	1246823	1246850	ATCATAAATTGGTGAAAAATATAACAGG AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ +++++ ++++++ +
266	1.90E-05	reverse	1255217	1255244	TGTCATTTTGTTTAAATCAATGAATAAT ATAATTATTCATTTAATGAATATATTTT + ++ ++ ++ +++ ++++ ++ ++
267	5.70E-05	forward	1255423	1255450	ACTATAAATATGGCAAAAATATTACAAC AAAATATATTCATTAAATGAATAATTAT + +++ ++ +++ ++++ + +++
268	5.90E-05	forward	1271109	1271136	GTAAAAAATAGGTAGGAAAAATAACAGA AAAATATATTCATTAAATGAATAATTAT +++++ ++ + + ++++++ +
269	3.20E-05	forward	1278854	1278881	TAAAAATCTTAATAGTTTAAATAACTAC AAAATATATTCATTAAATGAATAATTAT +++++++ ++ ++ + +++++++ +++
270	9.70E-05	reverse	1285066	1285093	GCACTAATGCAATTCCTGAATATGTTCT ATAATTATTCATTTAATGAATATATTTT + + + ++ ++ +++ +++++++ ++ +
271	5.40E-05	forward	1298720	1298747	AAATAATAATCAATTGTTAAATTATTGT AAAATATATTCATTAAATGAATAATTAT ++++++++ +++ + +++++ +++ +
272	4.10E-05	forward	1305657	1305684	ATCAAATATTCACGCGCCGAATAAGCCG AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++++++
273	4.10E-05	forward	1306216	1306243	AGATATAAAACACCATCTCAATATTATG AAAATATATTCATTAAATGAATAATTAT + +++ + +++ ++ + ++++++++
274	8.80E-05	reverse	1308349	1308376	ACATACATGCAGCGCGTGAATGTGTTAA ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ +++++++++ ++++

275	3.70E-05	forward	1311849	1311876	AGTTAATATTTGCGTAGCGAAAATATTT AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ + +++ ++++++
276	5.20E-05	forward	1314206	1314233	TATTAACAATTACCTGAGGAATAAGTGA AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ + ++++++ +
277	8.60E-05	reverse	1314358	1314385	ATAAATATTAAATGAATTTAGGATTTTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++ + + +++++
278	9.40E-05	forward	1331745	1331772	CACACCTATACACTAAGGCTATAAATGA AAAATATATTCATTAAATGAATAATTAT + + +++ ++++++ +++++++
279	6.10E-05	forward	1332949	1332976	CCCTCATATTTATAGGGTAAATTACCTG AAAATATATTCATTAAATGAATAATTAT + +++++ ++ +++++ + +
280	1.50E-05	forward	1336878	1336905	GGATTTTATTCAGCAGACCAATGTTACG AAAATATATTCATTAAATGAATAATTAT +++ ++++++ + + +++++++
281	5.40E-05	reverse	1344854	1344881	TTGTTTTTTTTATATATTTATTTGTAAT ATAATTATTCATTTAATGAATATATTTT + +++ +++ + ++ ++ + + ++
282	1.10E-05	forward	1347251	1347278	TTTTTATATTCATTTGATGAATCCATAC AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++++++ ++++
283	1.30E-05	forward	1355131	1355158	GCATAATATTAAGGGATTTTATGTAAAG AAAATATATTCATTAAATGAATAATTAT +++++++ + + + ++++++++++
284	8.80E-05	reverse	1368600	1368627	GAATGCAGTCATTTAATGTTTGATTTTG ATAATTATTCATTTAATGAATATATTTT ++++ ++ ++++++++++ ++ ++++
285	6.00E-08	forward	1369802	1369829	TAAAAATATTCAGCATGTAAATATTACT AAAATATATTCATTAAATGAATAATTAT ++++++++++ ++ +++++++++ +
286	5.70E-05	reverse	1390381	1390408	ATTGATATTCAGCTCACCATTGATTATG ATAATTATTCATTTAATGAATATATTTT +++ +++++++ +++ + ++ ++ +
287	5.00E-06	reverse	1403847	1403874	TACATTATTAATATCGTGAATGAATAAT ATAATTATTCATTTAATGAATATATTTT + ++++++++++++++++++ ++ ++
288	7.30E-05	reverse	1410864	1410891	TAAGATATCGCTATAACGAATATGTGAT ATAATTATTCATTTAATGAATATATTTT ++ ++++ +++++ ++++++ + ++
289	6.10E-05	reverse	1410908	1410935	AAATTATTATTCTGAGTGTTTTTAATTG ATAATTATTCATTTAATGAATATATTTT +++++ +++ + ++++ + +++++
290	8.60E-05	reverse	1411950	1411977	ATAATTTTTCTCATAAAAAATATTTCAA ATAATTATTCATTTAATGAATATATTTT ++++++ +++ ++++ +++++++ ++
291	4.90E-05	reverse	1416124	1416151	GAATATATAGTTTTCGCTTTTTAATATT ATAATTATTCATTTAATGAATATATTTT +++++++++ +++++ + ++ ++
					AAATTTTATACAGTATAATCATAATATT

292	3.50E-05	forward	1421742	1421769	AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++ ++++ + ++++++++
293	2.10E-05	reverse	1423210	1423237	CTTGAAATTTATCCTGTTATTATATTGT ATAATTATTCATTTAATGAATATATTTT ++ + ++++++ ++ + ++++++ +
294	2.90E-05	forward	1423273	1423300	GATTTATAATTGTGAGTTTAATATTATG AAAATATATTCATTAAATGAATAATTAT + +++++ + +++ ++++++++++
295	5.60E-05	reverse	1432009	1432036	ATTATATTACATTTTACCATTTAAATTT ATAATTATTCATTTAATGAATATATTTT +++++ +++++++ + + + +++++
296	2.20E-06	reverse	1435058	1435085	ATGATAATAAGTCTGGTGAATGTATCGA ATAATTATTCATTTAATGAATATATTTT ++ ++ ++++ + + ++++++++++ +
297	1.50E-05	forward	1435088	1435115	ATAATACATACAAAATAAAAATTATACT AAAATATATTCATTAAATGAATAATTAT +++++++++ ++ +++ ++++ +++ +
298	8.00E-05	forward	1442788	1442815	CCTAAACAATCACTGACCGTATTCCAGC AAAATATATTCATTAAATGAATAATTAT +++++ +++++ + ++++ + +
299	3.10E-05	forward	1443573	1443600	TAATTACCATCATGAAGAGAATATTTTT AAAATATATTCATTAAATGAATAATTAT +++++++ +++++++ ++++++++++
300	1.20E-05	forward	1461523	1461550	ATGATTCATAAATCACAACAATAACAAC AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ + + +++++ +++
301	2.10E-05	forward	1463109	1463136	TTTAATTATAAAGCAGAGTTATGTTTAA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ + + + +++++++++
302	6.60E-05	reverse	1463170	1463197	CCGTTTTTTCATCATATAATTATTTATA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++ + +++++ ++
303	5.00E-08	forward	1463226	1463253	ATATTATATACACAATTTATATATTTCA AAAATATATTCATTAAATGAATAATTAT +++++++++ +++ ++ +++++++++
304	3.50E-07	forward	1463259	1463286	TTTTTTTATTCACCTGAATTATAATTGT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++++ + ++++++++ +
305	8.00E-05	forward	1463389	1463416	TCTTTATATTCGCCAGAAGGATTTATTA AAAATATATTCATTAAATGAATAATTAT + ++++++++ + + + + ++ ++++
306	9.70E-05	reverse	1487676	1487703	TGGTTTATTTACAGTCTTAATGAGTGAA ATAATTATTCATTTAATGAATATATTTT ++++++++ + + ++++ + ++
307	1.20E-06	reverse	1489539	1489566	ATATTTATTTGTATGATAAATAAAACCA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ ++ ++++ ++ +
308	4.40E-05	reverse	1497214	1497241	AATCGTATTGAACCACTGAATAAAACCG ATAATTATTCATTTAATGAATATATTTT +++ ++++ + + ++++++ ++
309	4.80E-06	forward	1498555	1498582	ATTTCAAATATACTTTATAAATTAAACA AAAATATATTCATTAAATGAATAATTAT

309	4.80E-06	forward	1498353	1498382	++ + + ++ +++ +++++++ +++
310	7.30E-05	forward	1499465	1499492	TGTTTATCTTTACCAATTTTATTATTGC AAAATATATTCATTAAATGAATAATTAT + ++++ ++ ++ ++ +++++ +++ +
311	3.00E-05	reverse	1499602	1499629	AAAACTATTTTACTGATAAATATGAATT ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++ +++++ + ++
312	1.60E-05	forward	1518213	1518240	CACTTTAATACACCAGGTGAATTCCTTC AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ + +++++ +++
313	1.20E-05	forward	1524953	1524980	TAATTAAATTCATGGTATGTTTTTTAAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++++++ +++++ + +++++
314	1.80E-05	forward	1524993	1525020	CCTTTTCATTCAGCGTGTCTATTTCATT AAAATATATTCATTAAATGAATAATTAT ++ ++++++ + + +++ + +++
315	5.30E-06	forward	1525134	1525161	AATTAATATTAATACAAATAAAAATATC AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ ++ +++ ++++++
316	3.40E-08	forward	1525514	1525541	TTATTATATTCATCAGGTGAATTTAATA AAAATATATTCATTAAATGAATAATTAT ++++++++++++ + +++++ ++++
317	1.00E-05	reverse	1525679	1525706	GAATTATTTATTGTTGTGAATAAAAAGA ATAATTATTCATTTAATGAATATATTTT +++++ +++ + + +++++++ ++ +
318	3.50E-05	forward	1528091	1528118	CTGAAAAAAATATTATTTATAAAATAAT AAAATATATTCATTAAATGAATAATTAT + +++ + +++++ ++++ ++++++
319	8.30E-05	reverse	1528150	1528177	CATTTTATAAGTATAATGGTTAATAATT ATAATTATTCATTTAATGAATATATTTT +++++++++ +++++++ ++ ++ ++
320	3.10E-05	forward	1528203	1528230	TATAAATCTTAATTTTTTCAATGATATT AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ +++ + + +++++++++
321	2.30E-06	forward	1529847	1529874	TTAAAAAATTGATGGGACATATTTCTAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ + ++++ + +++
322	3.80E-05	reverse	1530575	1530602	GAACTTATTGATTTCACGTTTGAATGGA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++++ + ++ ++ +
323	5.70E-05	reverse	1542378	1542405	ACACTTATAGAATTAGTGATGATTTATT ATAATTATTCATTTAATGAATATATTTT + + +++++ + +++++++ ++++ ++
324	3.30E-05	forward	1542536	1542563	CTTTTATATTCATCTGGTTTACAACTTC AAAATATATTCATTAAATGAATAATTAT + ++++++++++ ++++ ++ +++
325	9.10E-05	forward	1542764	1542791	CAGAAACATTTAAAAAATTTAAGTTTTG AAAATATATTCATTAAATGAATAATTAT + +++++++ + +++++++ +++++
326	1.90E-05	reverse	1544079	1544106	AAACGTATTTTCTAAACGAATTTTAAAC ATAATTATTCATTTAATGAATATATTTT +++ +++++ + ++ ++++ +++ +

327	4.20E-05	reverse	1544176	1544203	GAAATAATATTATTTATCGATATGTGAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++ ++++ + ++
328	4.50E-05	forward	1564564	1564591	GGATTTTATAGATAATATCTATTTCCCA AAAATATATTCATTAAATGAATAATTAT +++ +++ ++ ++++ +++ +
329	5.70E-05	forward	1565146	1565173	TTTTAAAATACATCTCCATAATTCACAC AAAATATATTCATTAAATGAATAATTAT ++ +++ ++ +++ ++++ + ++
330	3.40E-05	reverse	1570368	1570395	TATTACATAAAAATAGCGAATATTGCTA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ +++++++ ++
331	4.10E-05	forward	1577408	1577435	ATGATTTACTGATGAAATTTATTTAAGT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ + ++++++++++ +++ +
332	7.30E-06	forward	1580729	1580756	CTAATTTATTGATATTTAATAAATTATT AAAATATATTCATTAAATGAATAATTAT ++++ ++++ ++ + +++ ++++++
333	4.20E-05	forward	1580838	1580865	GTCACTTATTTATTTCAATAAATATATC AAAATATATTCATTAAATGAATAATTAT + + ++++ +++ + +++ +++++
334	8.00E-05	reverse	1581976	1582003	GCATGCATTTCAAATATGTTTATTTAGC ATAATTATTCATTTAATGAATATATTTT + ++ +++++ + +++ +++++
335	6.60E-05	forward	1584699	1584726	TTAACATATTTTTCAATATAAAAAATAA AAAATATATTCATTAAATGAATAATTAT ++++ +++++ + ++ +++ +++++
336	7.50E-05	reverse	1587948	1587975	GAACAGATTAAAATAATCAATAAATTGT ATAATTATTCATTTAATGAATATATTTT +++ + +++++ +++++ ++++ +++ +
337	6.80E-05	reverse	1588784	1588811	ATATACATTATGCGCACCAATATAAACC ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ +++++++
338	5.90E-05	forward	1596104	1596131	TATTCATATAAACGCTCCATATACAAAC AAAATATATTCATTAAATGAATAATTAT ++ + ++++ +++ + +++++ ++++
339	7.50E-05	reverse	1596294	1596321	ATTTAAATATGAACTATGAGTTATTGTT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + ++++ + ++ ++
340	2.10E-05	reverse	1614228	1614255	GTACTCTTTCTGTTTCTGAATGATTTTA ATAATTATTCATTTAATGAATATATTTT +++ ++ +++ ++ ++++++ +++++
341	1.60E-05	reverse	1614633	1614660	TTGTTTTTATTTTTCGCCAATATGTTAT ATAATTATTCATTTAATGAATATATTTT + +++ +++ +++++ +++++ ++++
342	5.70E-05	reverse	1616177	1616204	GCGTTAATTTGGTCAATCATTATATTTC ATAATTATTCATTTAATGAATATATTTT + ++ ++++ + +++ + +++++++
343	3.90E-06	forward	1617068	1617095	TCAATTCATTCATTTGACTTATACTTGC AAAATATATTCATTAAATGAATAATTAT + +++ ++++++++ + +++++ ++ +

344	7.50E-05	forward	1621995	1622022	AAAACAAAATCAGCGGATAAAAAAGTGT AAAATATATTCATTAAATGAATAATTAT ++++ + + +++ +++++ ++ + +
345	5.90E-05	reverse	1622122	1622149	TTTATTTTTATTTCTGCAAATGAGTGAC ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++ + ++++ + +
346	6.40E-05	reverse	1622567	1622594	CTATTTTTATAATTGCCAAATAAGAATA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++++ + ++
347	6.80E-05	reverse	1622710	1622737	GGATTTATATGTTTGAAAATTATTATAT ATAATTATTCATTTAATGAATATATTTT + ++++++++ +++ + + ++++++++
348	5.60E-05	forward	1631308	1631335	AAATTTAAATGGTAAAATGTAATATAAT AAAATATATTCATTAAATGAATAATTAT +++++ + + + +++++++ +++++
349	2.10E-05	reverse	1635724	1635751	TTTTTCTTAAGTTCAATAATTTTTTTTG ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++ +++ + + +++++
350	5.70E-05	forward	1638706	1638733	AAAAAACATACACATTAAAAATGTGGGT AAAATATATTCATTAAATGAATAATTAT +++++++++ +++ ++ ++++++ +
351	1.70E-05	forward	1638758	1638785	ATAAAATAATAATACGAGAAATGTTTTC AAAATATATTCATTAAATGAATAATTAT ++++++++ + ++ + ++++++++++
352	8.40E-06	reverse	1639024	1639051	TTTTATATTTTAATAATATATTTAAAGC ATAATTATTCATTTAATGAATATATTTT +++++++++ +++++ ++ +++
353	7.70E-06	reverse	1639197	1639224	GTTAGCATACTTTTCCTGATTAAGATTT ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++++ +++ ++ ++++
354	8.00E-05	reverse	1640229	1640256	AATATAATAAGCAGACTCATTGTGTTTA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + + + + +++ ++++
355	6.10E-05	forward	1640278	1640305	ACATTTTAAACATCAGGCAAATAACCAA AAAATATATTCATTAAATGAATAATTAT + +++ ++ +++ + ++++++ +
356	7.80E-05	forward	1644143	1644170	TCAACTTATTCATCTATTTTTTGCTTTA AAAATATATTCATTAAATGAATAATTAT + ++ +++++++ + +++ ++ +++
357	5.40E-05	forward	1650721	1650748	ATGAAAAATTAATTTAATATTTATCAAA AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ +++ +++++ +++ ++
358	2.90E-05	reverse	1653342	1653369	TATCTTATTGATAAAATGGATTTATGTT ATAATTATTCATTTAATGAATATATTTT ++ +++++ +++ ++++ ++ +++ ++
359	5.90E-05	reverse	1653703	1653730	TCTCTTATTGACATCATGTATAGTTATA ATAATTATTCATTTAATGAATATATTTT + +++++ + ++++++ +++ ++ ++
360	2.60E-06	forward	1653805	1653832	TTTAATCATTCATACAGGGAATGAATTA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++++ + +++++++++
					CCTGTTATTGATTTAAGGAATGTAAGGA

361	4.70E-05	reverse	1654174	1654201	ATAATTATTCATTTAATGAATATATTTT + +++++ ++++++ ++++++++ +
362	1.60E-05	forward	1654769	1654796	CATTAATAATAATCGATCGTATTTTTGA AAAATATATTCATTAAATGAATAATTAT + +++++ + ++ + ++++ +++
363	3.90E-05	reverse	1656039	1656066	CTAAATATTCAATATATAAACTTTTATA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + ++ ++ +++ ++
364	2.00E-06	forward	1665266	1665293	CACAAATATAAACCAGGAAAATAATTAA AAAATATATTCATTAAATGAATAATTAT + ++++++ ++ + +++++++++
365	7.50E-05	forward	1674445	1674472	CGAAAATATTAATGCTGGCTATAAGCAC AAAATATATTCATTAAATGAATAATTAT ++++++++ +++ + +++++ ++
366	1.90E-05	reverse	1676318	1676345	ATTAAAATTGGCTTAAGGAATGTGATAT ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++++ ++++++ ++++
367	5.80E-07	reverse	1680159	1680186	GTTTTTATATCTACCGTGAATGTTATGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ ++++++++++++ +
368	4.10E-06	forward	1682615	1682642	CAGTCATATTCAGCACATCAATAAACTC AAAATATATTCATTAAATGAATAATTAT + + +++++++ + ++ ++++++ ++
369	5.40E-05	reverse	1690898	1690925	TTATTTTTATTGAATATTAATTAGTGAT ATAATTATTCATTTAATGAATATATTTT +++++ +++ + ++ +++ + ++
370	8.80E-05	reverse	1694358	1694385	TGACATATGGCTACAGTGAATATTTTGG ATAATTATTCATTTAATGAATATATTTT + ++++ ++ ++++++++++++
371	9.10E-05	forward	1710432	1710459	AACAAATATTGACCTACAAAACATTACA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ + +++ ++++
372	1.60E-05	reverse	1717735	1717762	AAATCAATAATCATCATGAATGTTTTGT ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++++++++++++++ +
373	3.20E-05	reverse	1718909	1718936	AATTGTATTGCTAAAACAAATGTATTGC ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++ ++ ++++++++
374	1.60E-05	reverse	1719444	1719471	GGACGTATTGTTGAGCTGAATATAAAAG ATAATTATTCATTTAATGAATATATTTT + + ++++ + +++++++++ +
375	3.50E-05	reverse	1739179	1739206	ACAAAATTTTGTTGTATGATTGAAATTA ATAATTATTCATTTAATGAATATATTTT + +++ +++ ++ ++++ ++ +++++
376	7.80E-05	reverse	1740911	1740938	CGATTATTTTCTGAGGTTAATATTTTCG ATAATTATTCATTTAATGAATATATTTT +++ +++ + ++ ++++++++
377	1.60E-05	reverse	1752822	1752849	AATAACATTATCGCTATAAATTAAAATA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ +++ ++ ++
378	4.10E-05	reverse	1753431	1753458	ATATTTTTTGAAACGCTGTTTTTGTTTT ATAATTATTCATTTAATGAATATATTTT

378	4.10E-05	reverse	1753431	1753458	++++++ ++ + + ++ + + ++++
379	4.40E-07	reverse	1755130	1755157	TGTAATATTGCTTTTGTGAATTAATTTG ATAATTATTCATTTAATGAATATATTTT +++++++ +++ ++++++ ++++
380	3.50E-05	forward	1755363	1755390	AAAAAATATTCTCAACATAAAAAACTTT AAAATATATTCATTAAATGAATAATTAT ++++++++++ + + +++++ ++ +++
381	6.80E-05	forward	1770774	1770801	TGATATTAATGGCAGTAATAATGTATCT AAAATATATTCATTAAATGAATAATTAT + +++ ++ + + ++ ++++++++ +
382	3.90E-05	forward	1773514	1773541	TATATTCAATCGTATTTAATAAAAATAT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ + + +++ ++++++
383	3.70E-05	reverse	1775473	1775500	TTTTAATTACCAACGGTCAATGTATTCA ATAATTATTCATTTAATGAATATATTTT ++++ +++ + ++ ++++++++ +
384	7.80E-05	forward	1776749	1776776	AATTATTATTCAGATAGAAAAGAATATC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++++ + +++ ++++++
385	8.30E-05	reverse	1780809	1780836	CAATGAATTCCATAAATTAATGAAAGCC ATAATTATTCATTTAATGAATATATTTT +++ ++++ + +++ ++++ ++
386	4.10E-05	reverse	1782565	1782592	CAAAATATAAATATCCTGAACATATCGT ATAATTATTCATTTAATGAATATATTTT ++++++++++++ ++++ ++++ +
387	3.90E-05	reverse	1785239	1785266	AAATATATTTTTTTACTTTTTAAGACTG ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ + ++ + +
388	1.30E-05	reverse	1787609	1787636	ATTGTTATATCAATTATTATTAATTTTT ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ ++ + ++ +++++
389	8.30E-05	forward	1801537	1801564	TAAAAAAATCCATAGAGAAAAAAACTAT AAAATATATTCATTAAATGAATAATTAT ++++++ ++ +++ + +++ ++ +++
390	6.60E-05	forward	1802272	1802299	AAAAAGAAATCATTGAAATAATAACTGC AAAATATATTCATTAAATGAATAATTAT +++++ + +++++ ++ ++++++ + +
391	2.20E-06	forward	1804282	1804309	TATATATATTTATCTGCAAAATTTTAAA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ ++++ ++++
392	2.60E-05	forward	1804316	1804343	TCCAATAAATCATATTGTTAATTTCTTC AAAATATATTCATTAAATGAATAATTAT + ++ + ++++ + +++++ + +++
393	6.80E-05	forward	1805483	1805510	GACTGAAATTAACGAGTTGAATAATTAC AAAATATATTCATTAAATGAATAATTAT + + + +++ ++++ ++++++++++
394	1.50E-05	reverse	1810876	1810903	TTATTAATTATTACTCTATATTTAACAT ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++ + ++ +++ ++
395	3.70E-05	reverse	1820481	1820508	AATGACATTGCAACAACAAATAATAAAG ATAATTATTCATTTAATGAATATATTTT +++ +++++ + ++ ++++ ++ +

396	1.20E-06	forward	1830020	1830047	GTAAATAATTCGTTATTTATATGTTAAT AAAATATATTCATTAAATGAATAATTAT ++++ ++++ ++++ ++++++++++
397	8.80E-05	forward	1840369	1840396	TATTAATATATAAGGGTTTTATATCTAT AAAATATATTCATTAAATGAATAATTAT ++ ++++++ + + +++++++ +++
398	9.70E-05	forward	1842929	1842956	TAATTTTATCCATGCAAAAAAAATATCC AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++++ ++ +++ ++++ +
399	8.60E-05	forward	1846719	1846746	GATATTTATTCACAAAATTAACACGAGA AAAATATATTCATTAAATGAATAATTAT + ++ +++++++ +++++++ + +
400	7.80E-05	forward	1855809	1855836	ATTAATTAATCGCTAATTTTAATAACGC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ ++++ ++++ ++ +
401	3.90E-05	forward	1857323	1857350	CAAACATACTCATGGTATTTAAAACAAT AAAATATATTCATTAAATGAATAATTAT +++ +++ +++++ ++++++ ++ +++
402	1.10E-05	reverse	1864499	1864526	TTAATCATTCCTTAAACAAATGTTTAGC ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++ +++++++
403	4.10E-05	forward	1864666	1864693	TCTTTACATTAATTATGCAAAATTTATG AAAATATATTCATTAAATGAATAATTAT + +++++++ +++++ +++ ++++
404	4.70E-05	forward	1868336	1868363	AGCTTACAATCGCTTTAAATATGACAGC AAAATATATTCATTAAATGAATAATTAT + +++++ ++ ++ ++ ++++++ + +
405	8.80E-05	reverse	1868435	1868462	GGGGTTATTCTTTAAATATTTTTTATCG ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ +++ + ++++
406	3.20E-05	reverse	1868591	1868618	CAGTTTATTGCTGACGTTAATTTTATTT ATAATTATTCATTTAATGAATATATTTT + ++++++ + +++ +++ ++++++
407	7.70E-06	forward	1875552	1875579	TTCATTTATTGATCTCACATATTTATCC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++ + ++++ +++ +
408	3.10E-05	forward	1875624	1875651	TTATTACATTCACTCAAAACATATTACG AAAATATATTCATTAAATGAATAATTAT ++++++++++++++ ++ + ++++++
409	2.40E-05	forward	1878777	1878804	CGAACACATTAACCTCTTTAATTATCTT AAAATATATTCATTAAATGAATAATTAT ++ +++++ ++ +++++ ++ ++
410	5.70E-05	forward	1879821	1879848	GTAAATTATTCATGATTCGTGTTTTATG AAAATATATTCATTAAATGAATAATTAT ++++ ++++++++++ ++ + ++++
411	3.00E-05	forward	1881141	1881168	TATTCTTAATTGTTTAATTTATGTAACA AAAATATATTCATTAAATGAATAATTAT ++ + ++ + ++ ++++++++++
412	7.80E-05	reverse	1887814	1887841	AATGATATACATGCCGTTAACATAATAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++++ +++ ++ +++++++

413	2.10E-07	forward	1891846	1891873	TATTTATATTTATAATTTCAATTTTATC AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ ++ + +++ +++++
414	6.10E-05	reverse	1892184	1892211	GATTTCATTGGTGCCATGGATGTATCAG ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++++ ++++++ +
415	7.80E-05	reverse	1899926	1899953	AAAATAATTTTTTCGATATCTAAAATAA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++ ++ +++++
416	2.10E-06	forward	1906105	1906132	CTAATAAATTAATGGGGTAAATATCTTT AAAATATATTCATTAAATGAATAATTAT +++++ +++ +++ +++++++ +++
417	8.80E-05	reverse	1906151	1906178	CAAATAAATAATATGATAATTATTTGAA ATAATTATTCATTTAATGAATATATTTT ++++ + ++++++ ++ + +++++ ++
418	2.50E-05	forward	1908269	1908296	GTTGATTATTCACCAAAGATATAAAATT AAAATATATTCATTAAATGAATAATTAT + + +++++++ +++ ++++++++++
419	8.80E-05	forward	1921018	1921045	ATCACATAATCTTAACAAGAATGTTAAA AAAATATATTCATTAAATGAATAATTAT ++ + +++ ++ + + + +++++++++
420	3.80E-05	forward	1925335	1925362	TCAAGATAATCATTAAACGTATTTTTCT AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++++++++ ++++ +++ +
421	7.00E-05	reverse	1928778	1928805	CCTCTCATAATAACTGTGATTTTATACA ATAATTATTCATTTAATGAATATATTTT + ++++++ + ++++ + +++ +
422	3.40E-05	forward	1932673	1932700	GCGTTTCATTCAGAGGATTTATGACTGA AAAATATATTCATTAAATGAATAATTAT ++ ++++++ ++++++++ +
423	8.00E-06	forward	1934947	1934974	TTGAATCATACACAGGGAAAATATTTGA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ +++ ++++++++
424	6.80E-05	reverse	1935565	1935592	AATCTTATACGACATCCGAATGAGATTA ATAATTATTCATTTAATGAATATATTTT +++ ++++++ +++++ ++++
425	9.40E-05	reverse	1944135	1944162	CAGGTTATATTGGAAGCAAATATTTTAA ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ ++++++++++
426	6.70E-06	forward	1944164	1944191	ATTACATATTCAGTGAAGAAATGCGTAA AAAATATATTCATTAAATGAATAATTAT ++ + +++++++ + ++ +++++ ++
427	2.60E-06	reverse	1944279	1944306	ATATTAATTACCCTGCTGAATATGAAAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + +++++++ + ++
428	5.20E-05	reverse	1955542	1955569	AGAAGTTTTGAAAGGATAAATATGTGCG ATAATTATTCATTTAATGAATATATTTT + ++ + ++ + + ++ +++++ +
429	1.20E-05	forward	1955867	1955894	CTAACAAATTCATGATAAATATCTTTAG AAAATATATTCATTAAATGAATAATTAT +++ + ++++++++++ ++++ ++++
					GCCTTTAATTTAGCAAATAAATAATCCA

430	4.10E-05	forward	1955897	1955924	AAAATATATTCATTAAATGAATAATTAT ++ +++ + ++++++++++
431	2.10E-05	forward	1956326	1956353	AATATATATTTATCAGTTTTAGTAATTT AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++ + ++++ +++++
432	5.20E-05	reverse	1956355	1956382	AATCCCATAATTAATGTGAATATATACA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++ ++++++++++ +
433	3.80E-07	reverse	1970329	1970356	GTTTTTATATTTTTCATCAATATTACGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++++ +++++++ +
434	3.30E-05	forward	1977426	1977453	CGTAAATAATCATCTGCTATAAATAATC AAAATATATTCATTAAATGAATAATTAT +++++ ++++ ++++ ++++++
435	3.80E-05	forward	1977608	1977635	TTCTTATAATTACATTTGAAATTATATG AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ + ++++ ++++
436	6.60E-07	reverse	1984729	1984756	AGTTACATTGATTTCATCAATGAAATGT ATAATTATTCATTTAATGAATATATTTT + +++++++ +++++++ ++++ +++ +
437	7.00E-05	reverse	1984759	1984786	AAATATATAAACTTGATGATTTAAGCAT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ ++++ + + ++
438	6.60E-05	forward	1986076	1986103	ATCACATAAATACCCCTTTAATGTTATA AAAATATATTCATTAAATGAATAATTAT ++ + +++ ++ ++++++++++
439	6.40E-06	reverse	1986640	1986667	TTTTTAATAATTGAAGTTTATATTTTAC ATAATTATTCATTTAATGAATATATTTT ++++ ++++ + +++ ++++++++
440	3.50E-05	forward	1987020	1987047	AACAATTAATCACCCAGAAAATTAACGA AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++++ + ++++ ++
441	7.50E-05	reverse	1987599	1987626	ACATTTATATTTACACCATATGTAACGT ATAATTATTCATTTAATGAATATATTTT + ++++++++ ++ + ++++++ +
442	5.80E-11	forward	1993668	1993695	AAAAAACATTCATGATAAAAATATTTAT AAAATATATTCATTAAATGAATAATTAT ++++++++++++++++ ++++++++++
443	8.80E-05	forward	1993699	1993726	TCATTATATTAACGTATTTTATAGCACT AAAATATATTCATTAAATGAATAATTAT + ++++++++ +++ + ++++++ + +
444	3.90E-05	reverse	1994173	1994200	GGTCTTATTTGGTGCATTAATTTTTTTC ATAATTATTCATTTAATGAATATATTTT + + ++++++ + +++ +++ +++++
445	1.00E-06	forward	1994909	1994936	CTATCACATAAATAAGATTTATATATAA AAAATATATTCATTAAATGAATAATTAT +++ ++++ ++ + ++++++++++
446	1.20E-06	forward	1994938	1994965	TTATATTATTCAGGCAATGAATTACTTT AAAATATATTCATTAAATGAATAATTAT +++++ ++++++ + +++++++ + +++
447	4.90E-05	forward	1996470	1996497	AGGAATCAATAACCAGTTGTATACTTTC AAAATATATTCATTAAATGAATAATTAT

447	4.90E-05	forward	1990470	1990497	+ ++ ++ + ++ + ++++++ ++++
448	8.80E-05	forward	1998482	1998509	ACATCTTATTCTTATTTAATATATATCA AAAATATATTCATTAAATGAATAATTAT + ++ +++++ + + ++++++++
449	5.00E-05	reverse	2006201	2006228	CTAACTATTATTTTTGTGAATTATTACC ATAATTATTCATTTAATGAATATATTTT +++ +++++ +++ ++++++ ++
450	9.90E-06	reverse	2006233	2006260	AAATAAATTTGCATGGTGTATGATTCGC ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ +++ +++ ++
451	1.90E-05	reverse	2009235	2009262	AATTAATTACATTTAATATTTAATTATG ATAATTATTCATTTAATGAATATATTTT +++++ ++++++++++ ++ ++ +
452	3.70E-05	reverse	2021635	2021662	GCGAACATTTATTCAGTGAAATTTTTAA ATAATTATTCATTTAATGAATATATTTT + ++++++++++ ++++++ ++++++
453	5.50E-08	forward	2023370	2023397	AGAAAATATTCGCCATATGAATGATTAA AAAATATATTCATTAAATGAATAATTAT + +++++++++ + ++++++++++++
454	2.30E-09	reverse	2031626	2031653	TTATTAATTCATTTAATCAATATATTAG ATAATTATTCATTTAATGAATATATTTT +++++ ++++++++++ +++++++++
455	5.60E-05	forward	2031808	2031835	AACAATCATTGATACCCCCTATGTTTCC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++ +++++++ +
456	7.60E-10	reverse	2031860	2031887	ACATTTATAATTTTCATGAATATTTATA ATAATTATTCATTTAATGAATATATTTT + ++++++++ ++++++++++++++ ++
457	2.30E-06	forward	2031893	2031920	AATTCATAATTATGAATTATATTAAATA AAAATATATTCATTAAATGAATAATTAT ++ + +++ + +++++ +++++ ++++
458	4.20E-05	forward	2031945	2031972	TAAATACATTTGTTACATGTAATCCTTA AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++ +++++ ++
459	1.20E-07	forward	2032034	2032061	TTGATATATTCATGAAGATTATAATCAC AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++++ +++++++ ++
460	1.90E-05	forward	2035115	2035142	CGATAACATTCGTTGTAGTAAAATTTTA AAAATATATTCATTAAATGAATAATTAT +++++++++ ++ ++ +++ +++++
461	3.00E-05	reverse	2040293	2040320	TCAATTTTTTAAATAACAAATTATTAAA ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++++ +++ ++ ++
462	9.40E-05	reverse	2054687	2054714	GTATGCTTTCAAAACACAATTATAAAAA ATAATTATTCATTTAATGAATATATTTT ++++ + ++++ + ++ + +++++ ++
463	2.60E-05	reverse	2055644	2055671	CATATAATTCTTATAAAAAATATAATAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ +++++ ++++++++++
464	4.20E-05	forward	2057090	2057117	CGCTAATAATAATATTAAGAATATTCAG AAAATATATTCATTAAATGAATAATTAT +++++ + ++ ++ +++++++ +

465	4.70E-05	reverse	2060778	2060805	GATGGCATACAACCTGCCAATATAAATC ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + +++++++ +
466	8.30E-05	forward	2063230	2063257	CAAAATAATTTACTCATTTGATTTTTAC AAAATATATTCATTAAATGAATAATTAT +++++ +++ +++ + ++ ++ +++++
467	2.00E-06	forward	2064014	2064041	ACATTTCATTCAGATAATGAATTAATGC AAAATATATTCATTAAATGAATAATTAT + +++ ++++++ +++++++ +++ +
468	6.60E-05	reverse	2066550	2066577	TGATATTTACAATTTATGAAGATGACAA ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++ +++++ ++ + ++
469	4.50E-05	forward	2066623	2066650	AGTAATCATTTGTACTTTGTATTAATGA AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + + +++++ +++
470	1.20E-07	reverse	2083550	2083577	AAATTAATTAACCAGATGAATGTTAATG ATAATTATTCATTTAATGAATATATTTT +++++ +++++ ++++++++++ +
471	5.40E-05	reverse	2087206	2087233	CTGACAATTCATTCTATGAATGAATCTG ATAATTATTCATTTAATGAATATATTTT + + +++++++ +++++++ ++ +
472	3.90E-06	reverse	2097771	2097798	GCTGATATTTATTAAGTTAATATTAAGC ATAATTATTCATTTAATGAATATATTTT + + +++++++++ +++ +++++++
473	7.00E-05	forward	2101191	2101218	CCTTTACATACGCCACCGCAATATTATT AAAATATATTCATTAAATGAATAATTAT ++++++ + + + +++++++++
474	2.20E-06	forward	2101398	2101425	TTATTATATATACCATTTCAATGTTCTT AAAATATATTCATTAAATGAATAATTAT +++++++++ ++ ++ + ++++++ ++
475	9.10E-05	reverse	2101712	2101739	TGAAATATTATAACAATGATCGATTTTT ATAATTATTCATTTAATGAATATATTTT ++++++++ + +++++ + +++++
476	8.00E-06	reverse	2102088	2102115	GCAGTATTTTTTTTAATGTTTATTTTAT ATAATTATTCATTTAATGAATATATTTT + + + +++ +++++++ ++++++++
477	2.50E-05	reverse	2102530	2102557	CCATAATTTGGTCTCATGATTGTATTTC ATAATTATTCATTTAATGAATATATTTT +++ ++ + ++++++ +++++++
478	5.80E-06	forward	2104056	2104083	AAATTTAAATCATTCAAAAAATACATTT AAAATATATTCATTAAATGAATAATTAT +++++ + +++++ ++ +++++ ++++
479	9.10E-06	forward	2104201	2104228	ATAAATAAAATATGAATAAAATATTTTC AAAATATATTCATTAAATGAATAATTAT +++++ + +++++ ++++++++++
480	4.50E-05	reverse	2104688	2104715	AGTATAATTGCAAAGATGAATACAATAA ATAATTATTCATTTAATGAATATATTTT + +++ +++ + +++++++ +++++
481	9.40E-05	forward	2105847	2105874	CTTAATAATAAATGCAGGCAATTCTTTT AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ + +++ ++++

482	5.40E-05	reverse	2105988	2106015	CTTTTTTTTCTGAGCATTAATGATATTT ATAATTATTCATTTAATGAATATATTTT +++++ +++ + +++ ++++ +++++
483	5.40E-07	forward	2106157	2106184	CATATATATTTATCATTGGTATGAAAAA AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ ++ +++++++++
484	1.40E-05	forward	2107596	2107623	TATTCGTATTCATGCAATTAATTTTAAT AAAATATATTCATTAAATGAATAATTAT ++ + ++++++++ +++++++ +++++
485	1.10E-05	reverse	2111336	2111363	GTTGTTATTCTGATGGTTTATATAAAAC ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ ++ ++++++ +
486	6.60E-05	forward	2112615	2112642	CTTTTTCATTCACCGCATGAACATTTGC AAAATATATTCATTAAATGAATAATTAT + ++ +++++++ +++++ ++++ +
487	9.40E-05	reverse	2112871	2112898	CAATTTATAAGCAAGATGAGTATTATCC ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++++ ++++++
488	1.50E-05	reverse	2126335	2126362	ACATGTATTATTCCTCTGTATTTTTGAA ATAATTATTCATTTAATGAATATATTTT + ++ +++++ + ++ ++ +++ ++
489	9.70E-05	reverse	2135770	2135797	TGTTTTATTATTACCACTTTTAATTCAG ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ ++ ++ ++ +
490	8.60E-05	forward	2141121	2141148	AAATTACGTTGATCAGTTTTATGTAAGG AAAATATATTCATTAAATGAATAATTAT +++++++ ++ ++ + +++++++++
491	1.10E-05	forward	2141293	2141320	AGCAAACAATCACAGCATGTATTAATTG AAAATATATTCATTAAATGAATAATTAT + +++++ ++++ ++++++ ++++
492	1.50E-05	forward	2148991	2149018	CTTTTATATTTGTTTTCATAATATTTCG AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ ++ +++++++++
493	7.50E-05	reverse	2149022	2149049	GTAGTTATATTATATTTCAATGAATAAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + + ++++ ++ ++
494	3.20E-06	forward	2149345	2149372	CCGATAAATTCATCGAGGTTATGAATAA AAAATATATTCATTAAATGAATAATTAT +++ ++++++ + +++++++++
495	8.60E-05	forward	2165599	2165626	ACAAAACAAACAGATAAAATAAAAACAT AAAATATATTCATTAAATGAATAATTAT + ++++++ ++ ++ +++ +++ ++
496	8.80E-05	reverse	2166287	2166314	ATAATAAAAATACTAATTAATGATATAG ATAATTATTCATTTAATGAATATATTTT +++++ + ++ ++++ ++++ ++++
497	8.00E-05	reverse	2166374	2166401	AAATATAATAATGGCATGATTATTATAA ATAATTATTCATTTAATGAATATATTTT +++++++ ++++ +++++ ++++++++
498	2.00E-05	forward	2183537	2183564	GTTAATAAATTATTTGATATATGAATCC AAAATATATTCATTAAATGAATAATTAT + ++ + + +++ ++++++++++ +
					TGATTTTGTTGACCTAATAAATTTTTAC

499	6.10E-05	forward	2185712	2185739	AAAATATATTCATTAAATGAATAATTAT + +++ + ++ ++ +++++++ +++++
500	8.00E-05	reverse	2186387	2186414	ACAGGCATAACCATCATCATTAATATAA ATAATTATTCATTTAATGAATATATTTT + + +++++ +++++ + ++ +++++
501	8.80E-05	forward	2189295	2189322	CCAGAACATTCAGATAAAAAATGCTTTC AAAATATATTCATTAAATGAATAATTAT + ++++++++ ++ +++++ ++++
502	2.00E-06	forward	2190358	2190385	AAAACAAATTAACCATTGCAATATAAAT AAAATATATTCATTAAATGAATAATTAT ++++ + +++ ++ ++ +++++++++
503	1.60E-05	reverse	2190448	2190475	AATGGTATTGTTGATATCAATAAAAAAG ATAATTATTCATTTAATGAATATATTTT +++ ++++ + ++ ++++ ++ +
504	9.40E-05	forward	2190515	2190542	CAATTAAAATCAGGTTGCCAAATTAATC AAAATATATTCATTAAATGAATAATTAT +++++ + +++ + + ++ +++++
505	5.30E-06	forward	2191011	2191038	AAAACTAATACACCGCATCAATGTAACA AAAATATATTCATTAAATGAATAATTAT ++++ ++ +++ ++ +++++++
506	8.60E-05	reverse	2201322	2201349	GCAGATTTTCATTCTCTGTTTGTTAATC ATAATTATTCATTTAATGAATATATTTT + + ++ ++++++ ++ +++++ +
507	5.40E-05	reverse	2202193	2202220	TGATTTATATAAGAGATGAGTGTATTGA ATAATTATTCATTTAATGAATATATTTT +++++++++ ++++ ++++++ +
508	8.00E-05	forward	2202556	2202583	GCCAAACATTTATTGCGCGTAAAATATC AAAATATATTCATTAAATGAATAATTAT +++++++ +++ +++ ++++++
509	5.50E-06	reverse	2202595	2202622	TAATACATTTCAGGGATGAATATATGTC ATAATTATTCATTTAATGAATATATTTT +++++++++ ++++++++++ +
510	6.80E-05	forward	2215922	2215949	GAATCACATTGAGCAGAGAAAAAATTGC AAAATATATTCATTAAATGAATAATTAT +++ +++++ + + + +++ ++++ +
511	5.40E-05	forward	2220126	2220153	TCAAAATATTCACTCGCTGAATTGTTAT AAAATATATTCATTAAATGAATAATTAT + ++++++++++ +++++ ++++
512	8.00E-05	reverse	2223693	2223720	AGTATAAGTCAGCTTGTGATTATTTTTT ATAATTATTCATTTAATGAATATATTTT + +++ + +++ + ++++ ++++++++
513	4.10E-08	forward	2226887	2226914	GAAAAATATACACTAAGTGAATGATATC AAAATATATTCATTAAATGAATAATTAT ++++++++ ++++++ ++++++++++
514	9.10E-06	forward	2231876	2231903	GTTAATTATTGAGAATAATTATTACTTC AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + +++ ++++ + +++
515	6.80E-05	reverse	2236718	2236745	GCGCTCTTTTAATTTACGAATAATAGTG ATAATTATTCATTTAATGAATATATTTT + ++ ++++ ++ + +++++ ++ +
516	3.40E-06	forward	2247664	2247691	TAATTATAAATATATAATCAATTTTATT AAAATATATTCATTAAATGAATAATTAT

516	3.40E-06	forward	2247664	2247691	++++++++ ++ +++ +++ +++++
517	1.70E-05	forward	2253046	2253073	GGCAAACATTCAGGCCATTAATTAATGT AAAATATATTCATTAAATGAATAATTAT +++++++++ + ++++++ +++ +
518	4.90E-05	forward	2256967	2256994	TGCTAATATTCATGTCATTTATAGCAAC AAAATATATTCATTAAATGAATAATTAT + +++++++++++ +++++++ +++
519	2.80E-05	forward	2257270	2257297	CATCAATATTCGCCGAACCTATAATTAC AAAATATATTCATTAAATGAATAATTAT + +++++++ + ++ +++++++++
520	9.40E-05	forward	2257642	2257669	CATTTAAATTCATAAAATTACATTCACA AAAATATATTCATTAAATGAATAATTAT + +++ ++++++ ++++++ + +
521	5.70E-05	reverse	2266861	2266888	ATAATTAGAGAAAATATGATTAAAAATT ATAATTATTCATTTAATGAATATATTTT +++++++ + + + ++++ ++ ++ ++
522	4.40E-05	forward	2267566	2267593	AACAAACATTTCCAAAACAAATAACTCA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ + +++ ++++++ +
523	3.90E-06	reverse	2267675	2267702	AAAATCATTCTCTAAGTAAATGAATGGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++ ++++ ++ +
524	6.80E-05	reverse	2276286	2276313	TCACAATTTGTTTACATCAATTTTAACA ATAATTATTCATTTAATGAATATATTTT + + ++ ++ +++ +++ +++ +
525	6.70E-06	forward	2276484	2276511	TACATAAATTGATTTTACATAAAATAAA AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ +++ ++ +++ +++++
526	5.30E-06	reverse	2301724	2301751	AAATATATTTATATAGCGATTGATTCAC ATAATTATTCATTTAATGAATATATTTT ++++++++++++++++ ++ ++ ++ +
527	3.40E-09	reverse	2301846	2301873	AAATTAATAAATCTGATGAATATGTTAA ATAATTATTCATTTAATGAATATATTTT +++++ ++++++ + ++++++++ ++++
528	5.80E-06	reverse	2304855	2304882	ATTTAAATAATGTTTATAAATTATATTC ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++ +++ ++++
529	3.30E-05	reverse	2304896	2304923	ATTATAATTTCGTTGATTAATTATAGGG ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++ +++ ++
530	7.80E-05	reverse	2313352	2313379	GTAAGTATTCATGAAATGGATAATTTGC ATAATTATTCATTTAATGAATATATTTT ++++ +++++++ ++++ +++ +++
531	1.60E-05	forward	2313684	2313711	AAGATTAATTAGTCAAGATTATGATATC AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ + ++ ++++++++++
532	6.80E-05	forward	2342135	2342162	TGCAATCATTGACGGGAGTAAAGATAAA AAAATATATTCATTAAATGAATAATTAT + ++ ++++ +++ + +++ +++++
533	8.80E-05	reverse	2342293	2342320	TTTTGTTATTATTTGATGAATAATATCA ATAATTATTCATTTAATGAATATATTTT +++ + ++++++ +++++++ +++ +

534	2.40E-05	reverse	2342370	2342397	AACTAAATTAAAGTCATGAATAATTTTC ATAATTATTCATTTAATGAATATATTTT ++ ++ +++++ +++++++++ ++++
535	9.10E-05	reverse	2347009	2347036	TTTCACATAGATATGGCGAACATAACAA ATAATTATTCATTTAATGAATATATTTT ++ +++++ ++++ + +++ ++++ ++
536	7.80E-08	forward	2350486	2350513	AGAAAACATTCATAAATTAAATGTGAAT AAAATATATTCATTAAATGAATAATTAT + ++++++++++ ++ +++++++ +++
537	6.40E-05	forward	2362421	2362448	AATAATTAAATGCCGAAAAAATAAACAC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ + ++ +++++++ ++
538	3.10E-05	forward	2374983	2375010	CTGTCACGTTCACCACATAAATAATAAA AAAATATATTCATTAAATGAATAATTAT + + ++ +++++ + ++++++++++
539	1.40E-05	forward	2377323	2377350	TACAAAAATAGATTATTGATATGAATCG AAAATATATTCATTAAATGAATAATTAT ++ +++ ++ +++++ ++++++++
540	5.00E-06	reverse	2383707	2383734	CTACTCATAAGCAACATGATTATATTTT ATAATTATTCATTTAATGAATATATTTT ++ ++++++ + +++++ ++++++++
541	3.30E-05	forward	2383777	2383804	ACATAAAATATACTCTTTGTATAATCCT AAAATATATTCATTAAATGAATAATTAT + ++++ ++ +++ + ++++++++ +
542	3.50E-05	reverse	2383885	2383912	AAAAAAATAATCTTTGCTTTTATTATAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ + ++++++++
543	2.10E-05	reverse	2383918	2383945	GTGTTTTTACTCCCTATGATTATTTTTT ATAATTATTCATTTAATGAATATATTTT ++ +++ +++ ++++ ++++++++
544	3.40E-05	reverse	2385832	2385859	TGTATTATAAGCATTTTGAATATGTCAT ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ +++++++ + ++
545	4.10E-07	reverse	2386308	2386335	CAATATATTGATTTGGTCAATATGAAAC ATAATTATTCATTTAATGAATATATTTT ++++++++ ++++ ++ +++++ + +
546	4.70E-07	forward	2386459	2386486	TTTAAATATTTATGATATTAAATATAAC AAAATATATTCATTAAATGAATAATTAT ++ +++++++ ++++++++++ +++++
547	2.30E-09	reverse	2386615	2386642	AATGTCATTCGTTTGATGAATATATTAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++ +++ ++++++++++++
548	5.70E-05	forward	2386689	2386716	TAATATCAATGGTGATGTTAATAATCCT AAAATATATTCATTAAATGAATAATTAT +++++ ++ + ++++ ++++++++ +
549	1.90E-05	forward	2403180	2403207	ACCTTACAATCACTGTAGAAATTCTTTT AAAATATATTCATTAAATGAATAATTAT + +++++ +++++ ++ ++++ ++++
550	4.90E-05	forward	2403272	2403299	TCTTCACATTAGTTTACATAATATCAAC AAAATATATTCATTAAATGAATAATTAT + + +++++ ++ + ++++++ +++

551	6.60E-05	reverse	2403535	2403562	GGTGATTTTTTTCAGGCGATTATTTGTG ATAATTATTCATTTAATGAATATATTTT + + ++ +++ + + ++ +++++ +
552	8.80E-05	reverse	2405407	2405434	AAGCATATACACCTCATTATTTTGTCAT ATAATTATTCATTTAATGAATATATTTT ++ +++++++ ++++ + + + + ++
553	6.80E-05	reverse	2406457	2406484	GTTATCAGAGCATCAGTGAATTTATTAC ATAATTATTCATTTAATGAATATATTTT +++++++ + + +++++++ +++++
554	2.90E-05	forward	2411302	2411329	TCGTCAAATTCATATACATTATGCCATT AAAATATATTCATTAAATGAATAATTAT + + + ++++++ + +++++ +++
555	6.10E-05	forward	2448592	2448619	CTGAATCATTGATTTATTCATTGATAAT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ +++ + + + +++++++
556	4.50E-05	forward	2453678	2453705	TTAAACTATAAATAATTAAAATATAAAC AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++ ++ ++++++++++
557	1.30E-05	reverse	2453863	2453890	GTAAATGTAGATTTAATTAATATATTGA ATAATTATTCATTTAATGAATATATTTT ++++++ ++ +++++++ ++++++++ +
558	2.90E-06	forward	2453917	2453944	TCTAAAAAAACACGAAATATATATTTAG AAAATATATTCATTAAATGAATAATTAT + +++ + ++++++++++++++++
559	9.70E-05	forward	2455984	2456011	GATTTTCAAACACCGCTTCAATAATCAG AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ + ++++++ +
560	7.30E-05	forward	2460125	2460152	CGATCTTAATCGTGCGTTTAATAACTAC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ +++++++ +++
561	5.90E-05	forward	2461093	2461120	AAATAACAATGATGAAGTTAATGGATTA AAAATATATTCATTAAATGAATAATTAT ++++++++ + +++++ ++++++ +++
562	6.10E-05	reverse	2462070	2462097	GTGTTAATTTTGATGATATTTAAAATTA ATAATTATTCATTTAATGAATATATTTT ++ ++ ++++ ++ ++ ++ +++++
563	3.20E-06	forward	2464219	2464246	GGAAAACATTAAGAAAAATTATAAAAAC AAAATATATTCATTAAATGAATAATTAT ++++++++ + +++ ++++++++++
564	5.20E-05	forward	2467362	2467389	TTCATATAGTTATATTTTGTATACATAC AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ + ++++++ ++++
565	5.30E-06	forward	2467455	2467482	AATATATATTTATTCATTATATGCGATA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ +++ + ++++++ ++
566	5.00E-05	reverse	2467730	2467757	TAGTGTATTCATATTATATTTTTTTTGA ATAATTATTCATTTAATGAATATATTTT + + +++++++++ ++ + ++++ +
567	6.60E-07	reverse	2468123	2468150	AAGAAAATTATTTCCATGTATATAAAAA ATAATTATTCATTTAATGAATATATTTT ++ ++ ++++ ++ ++++ ++++++ ++
					TATTTAAAAACATTAGATTTATATCATT

568	3.60E-06	forward	2468213	2468240	AAAATATATTCATTAAATGAATAATTAT ++ +++ + +++++ ++++++++ +++
569	2.20E-05	reverse	2468248	2468275	TTTTTTATTGCTTCTATTTTTATTAGAA ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ ++ +++++ ++
570	6.60E-05	reverse	2468410	2468437	TTATACATAACAGTCGTTTTTTTAATTT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++++ + ++++++
571	5.70E-05	reverse	2472005	2472032	CTAATTATTTATCTCATCACTGAATATC ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ + ++ ++ +
572	8.80E-05	forward	2479919	2479946	AAAAAAAAGTGACTGAAAGTAAAAATAA AAAATATATTCATTAAATGAATAATTAT ++++++ + + +++ ++ +++ +++++
573	2.30E-06	forward	2481373	2481400	ATTTCTCATAGATGAAATTTATGAATTG AAAATATATTCATTAAATGAATAATTAT ++ + +++ ++++++++++++++++
574	2.80E-05	forward	2481621	2481648	ACATTTCATTTATGCCGACTATTTATAT AAAATATATTCATTAAATGAATAATTAT + +++ ++++ +++ +++ +++++
575	3.30E-05	reverse	2483598	2483625	ACAAACATTAAAAAAAGGAATGAAAGTT ATAATTATTCATTTAATGAATATATTTT + +++++++++ + ++ +++++ ++ ++
576	6.40E-05	reverse	2487241	2487268	TGTAAAATCAATAACATGATTAATTATG ATAATTATTCATTTAATGAATATATTTT +++ ++ ++++ +++++ ++ ++ +
577	2.30E-05	forward	2492641	2492668	TGTAAATACTGATTAATTAAATGTAAAT AAAATATATTCATTAAATGAATAATTAT + +++++ + +++++ ++++++++++
578	6.40E-05	reverse	2493449	2493476	AAATATTTACTTTGCACGATTAATAATC ATAATTATTCATTTAATGAATATATTTT ++++++ +++ ++ ++ ++ ++ ++ +
579	6.10E-05	forward	2496512	2496539	TTAACATAATAATTTCAATAAATTTACT AAAATATATTCATTAAATGAATAATTAT ++++ +++ + +++ + +++ +++ +
580	6.10E-05	forward	2498237	2498264	CAATAAAATTGGCCTGCTGAATGTCCAT AAAATATATTCATTAAATGAATAATTAT +++++ +++ + +++++++ ++
581	6.10E-05	reverse	2506417	2506444	AATTGAATAAACTGTATGATTTAAAAGA ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++++ + ++ +
582	2.50E-05	forward	2511138	2511165	CAAAAAAATTCGTATCCGTTATGTTATT AAAATATATTCATTAAATGAATAATTAT +++++ ++++ + ++++++++++
583	6.80E-05	forward	2519665	2519692	GTGTTTCATAAACAATATATAAATCTGC AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++ +++++++ ++ + +
584	2.20E-06	forward	2520515	2520542	ATAATAAATACATCGTATTAAATTATCA AAAATATATTCATTAAATGAATAATTAT ++++++ ++ +++ ++++++ +++
585	4.70E-05	reverse	2520574	2520601	ACATACATAAACACAATGGATAATATAC ATAATTATTCATTTAATGAATATATTTT

585	4.70E-05	reverse	2520574	2520601	+ +++++++++ + ++++ +++ ++++
586	6.60E-05	reverse	2523009	2523036	GGATTTATATCTTTTCTCTATTAATCCA ATAATTATTCATTTAATGAATATATTTT + ++++++++ +++ + ++ ++ +
587	8.00E-05	reverse	2523895	2523922	CATCAAATTTAACTTCTGATTGATTACT ATAATTATTCATTTAATGAATATATTTT ++ + +++++ + +++ ++ ++ +
588	3.20E-05	reverse	2524851	2524878	CCTTTAATTGTTTTAAAGAATAATTCAT ATAATTATTCATTTAATGAATATATTTT +++ +++ +++++ +++++ ++ ++
589	6.10E-05	forward	2538809	2538836	TCTTAATATTGGCAATCTCAATGCTCAT AAAATATATTCATTAAATGAATAATTAT + +++++++ + ++ + ++++ + ++
590	7.30E-05	reverse	2570507	2570534	CCGTTCATTCAACCAGTGTTTGTAAACT ATAATTATTCATTTAATGAATATATTTT ++++++++ ++++ +++++ +
591	3.00E-05	forward	2573331	2573358	TTAAAATATTCACCCGGCGTATCAATAT AAAATATATTCATTAAATGAATAATTAT ++++++++++++ ++++ +++++
592	5.40E-05	reverse	2573962	2573989	TTTCATATGCAACGCATGAATATAAATA ATAATTATTCATTTAATGAATATATTTT ++ ++++ ++ ++++++++++ ++
593	3.70E-05	reverse	2574040	2574067	TCAGTAATAAGCTTTACTAATATATTGC ATAATTATTCATTTAATGAATATATTTT + + ++++ ++ + ++++++++
594	6.10E-05	forward	2589117	2589144	TCTTAATGTTTACGTTAAAAATGTTTAA AAAATATATTCATTAAATGAATAATTAT + ++++ ++ +++ ++ +++++++++
595	4.40E-05	reverse	2589145	2589172	TATTATTTAATAGTTGTTAATTTGAATA ATAATTATTCATTTAATGAATATATTTT +++++ +++ + ++ +++ + + ++
596	5.00E-05	forward	2589195	2589222	GATAATCATTTGCAGGCAAAATGTTTTC AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + +++++++++
597	2.30E-08	reverse	2590665	2590692	CTATTCATAAAATTAATGAATGTGTGAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++++++++ + ++
598	3.70E-05	reverse	2593835	2593862	CGTTTCATTTGCGCTGTTAATGTGTGAA ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ +++++ + ++
599	6.60E-07	forward	2594770	2594797	ACAATATATTCATTATAGAAATGATCGT AAAATATATTCATTAAATGAATAATTAT + ++++++++++++++ +++++++ +
600	4.10E-05	forward	2609820	2609847	TCAATTCATTCATCTGTTGGATGAAATT AAAATATATTCATTAAATGAATAATTAT + +++ +++++++ ++ ++++++++
601	6.40E-05	forward	2621950	2621977	TAATTTTAAAGACTTTATTAATTTCCCC AAAATATATTCATTAAATGAATAATTAT +++++ ++ +++ +++++++ + +
602	2.70E-05	forward	2624740	2624767	CGATTTCATTCAGCGTATCAATTAACGG AAAATATATTCATTAAATGAATAATTAT +++ ++++++ +++ +++ ++

603	8.60E-05	forward	2627125	2627152	TTATTACGTTTATCATGTTAATTCATCA AAAATATATTCATTAAATGAATAATTAT +++++++ ++ ++ ++ +++++ ++
604	6.80E-05	reverse	2627154	2627181	TATTACATCATCATTGTAAATAATTAAA ATAATTATTCATTTAATGAATATATTTT +++++++ + ++ ++ ++++ ++ ++
605	2.40E-07	reverse	2627650	2627677	ATAAATATAAAATTAATATATATGTTGT ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ ++++ ++ +
606	2.00E-06	reverse	2627693	2627720	TAAATTATTCCCTGCGTGAATTTTAATA ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++++++ +++ ++
607	9.10E-05	reverse	2627940	2627967	CAAGAAACTAAAACCGTTAATATTATTT ATAATTATTCATTTAATGAATATATTTT ++ + + +++ + +++ ++++++++++
608	7.80E-05	reverse	2633890	2633917	AAATACTTACGGATAATTATTTATTTTT ATAATTATTCATTTAATGAATATATTTT ++++++ +++ +++++ + + +++++
609	2.00E-06	reverse	2638596	2638623	ACGTTTATTCTCTTTCTGAATATAAAAA ATAATTATTCATTTAATGAATATATTTT + +++++++ ++ +++++++++ ++
610	8.00E-07	forward	2688333	2688360	GTTTTTAATTCATGAGATAAATGTCTTA AAAATATATTCATTAAATGAATAATTAT + ++ ++++++++ ++++++++ ++
611	8.00E-05	reverse	2689513	2689540	TTAGATAATATTAAAATCAATGAGTTAA ATAATTATTCATTTAATGAATATATTTT ++ +++ ++ ++ +++ ++++ ++++
612	3.40E-05	forward	2697997	2698024	CCATTATATTTATTTAATTGATGACATT AAAATATATTCATTAAATGAATAATTAT ++++++++ +++ ++++ ++++ +++
613	1.50E-08	forward	2698027	2698054	CATAATCATTCACTAAGTTAATTTATAT AAAATATATTCATTAAATGAATAATTAT + ++ ++++++++++ +++++ +++++
614	9.50E-06	forward	2711574	2711601	CAAAAAAATTCATCAGTGGTATTACCGC AAAATATATTCATTAAATGAATAATTAT +++++ ++++++ + ++++ + +
615	3.80E-05	forward	2713379	2713406	TAAAAACATTCATTTTTTTAAATGTTCC AAAATATATTCATTAAATGAATAATTAT ++++++++++++++ + ++++ ++ +
616	4.40E-05	forward	2723836	2723863	AAATATTATACATTTGTTGCATATCATT AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++++ ++ ++++ +++
617	9.70E-05	reverse	2727300	2727327	CCAGATTTTTAAAGAGCAAATATATCAA ATAATTATTCATTTAATGAATATATTTT + ++ ++++ + ++ +++++++ ++
618	1.60E-05	reverse	2732260	2732287	AAGGTTATTGACCAGATTAATGTGAAAA ATAATTATTCATTTAATGAATATATTTT ++ +++++ + ++ +++++ + ++
619	3.30E-05	forward	2739755	2739782	CCCACAAATAAATTAAACATAAGATTTT AAAATATATTCATTAAATGAATAATTAT + + ++ ++++++ +++ ++++++

620	3.80E-05	forward	2756520	2756547	AAAAATCATTCAGAGAAATCATAAAACC AAAATATATTCATTAAATGAATAATTAT +++++ ++++++ ++ + ++++++ +
621	8.60E-05	forward	2758322	2758349	ATGAATTAATTAGAATCTTAATTTCACA AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ + + ++ +++++ + +
622	8.60E-05	forward	2758910	2758937	GTGTTTCAATCAGGATGCTTATTATCAT AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ +++ ++++ ++ ++
623	5.60E-05	reverse	2771411	2771438	ATTTTTCTATATTTCCTCTATTTTTTTT ATAATTATTCATTTAATGAATATATTTT ++++++ ++++++++ + ++ ++++++
624	7.00E-05	reverse	2771691	2771718	TTAGACAATATAGCCATGAATAATATTT ATAATTATTCATTTAATGAATATATTTT ++ +++ ++ ++++++++ +++++
625	6.70E-06	reverse	2771750	2771777	GATTTTATTGTCACTGTTTATGTGTTTA ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++ ++++ ++++
626	3.60E-06	forward	2772419	2772446	AATAATAAATGATAAAAAATATAAAATT AAAATATATTCATTAAATGAATAATTAT ++ ++ + + ++ +++ ++++++++++
627	8.30E-05	forward	2772989	2773016	AAAATTCATTCATTCTTACTTTAAGAAT AAAATATATTCATTAAATGAATAATTAT +++++ ++++++++ + + +++ +++
628	9.10E-05	reverse	2781604	2781631	ATACATATTGTTTCAATCTACGTTATTA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++ +++ + +++++++
629	3.80E-05	reverse	2782589	2782616	CATTATTTTTATTCGATAATTTTTTAGT ATAATTATTCATTTAATGAATATATTTT +++++ ++++++ ++ + + +++ +
630	7.80E-05	forward	2783158	2783185	TTAATTAAATTAGCACAGGAATGTTAAA AAAATATATTCATTAAATGAATAATTAT +++++ + + + + + +++++++++
631	7.50E-05	forward	2783215	2783242	TGATAAAAAAAAACCGTTATAATTTATTA AAAATATATTCATTAAATGAATAATTAT + ++++ + ++ + ++++ ++++
632	7.80E-05	reverse	2784952	2784979	AGAAACATTTAAAATATTAATCAATCTA ATAATTATTCATTTAATGAATATATTTT + +++++++++ + ++ +++ ++ ++
633	2.40E-05	reverse	2787989	2788016	AAAGGAATTGAGCGGATGTATGATTTTG ATAATTATTCATTTAATGAATATATTTT +++ +++ + +++ +++ ++++
634	5.00E-06	forward	2796952	2796979	ATATCTAATTGATTTAATTAAAAATAAA AAAATATATTCATTAAATGAATAATTAT ++++ +++ +++ ++++++ +++++
635	6.10E-05	forward	2797041	2797068	TACAAAAACTGACTAAATAAAAATTTTT AAAATATATTCATTAAATGAATAATTAT ++ +++ + + ++++++++++ ++++++
636	1.80E-05	reverse	2802849	2802876	TTAGAAATTAAAAATCTTTATAAAATAT ATAATTATTCATTTAATGAATATATTTT ++ + +++++ + + +++ +++++
					AATTCTCAATAATCCGGCGAATGATTAT

637	6.60E-05	forward	2803589	2803616	AAAATATATTCATTAAATGAATAATTAT ++ + ++ + ++ ++++++++++
638	3.70E-05	forward	2806330	2806357	CAAAAATAATGACTAAACCTAATCATGA AAAATATATTCATTAAATGAATAATTAT +++++++ + ++++++ ++ ++
639	1.10E-06	reverse	2807585	2807612	TAAGATATTCATTCAGTCTATTTATAAT ATAATTATTCATTTAATGAATATATTTT ++ +++++++++ +++ ++ +++ ++
640	1.30E-05	forward	2830396	2830423	TAATTTTATTTATAGAGTAAAAACAATC AAAATATATTCATTAAATGAATAATTAT +++++ ++++ ++ + ++++ + ++++
641	5.70E-05	forward	2841809	2841836	TATAAACATCCACAGGGACAATTTTATC AAAATATATTCATTAAATGAATAATTAT ++ ++++++ +++ +++ +++++
642	5.70E-05	reverse	2842110	2842137	GTAAACATAGGCAGAACGTTTGATTTTT ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++ + ++ +++++
643	7.80E-05	forward	2859340	2859367	TAAAATAACACACAATGTTAATTTATGT AAAATATATTCATTAAATGAATAATTAT +++++ + +++ ++ +++++ +++ +
644	4.20E-05	forward	2859398	2859425	CGCTTATATTCACAATATCAAACAAAAT AAAATATATTCATTAAATGAATAATTAT ++++++++++ ++++ ++ +++++
645	8.60E-05	reverse	2867164	2867191	TGAAACATTATGTAAATCAAGATTTTTC ATAATTATTCATTTAATGAATATATTTT ++++++++ + +++ ++ ++++++
646	4.70E-05	reverse	2878737	2878764	ATAAATATTCGCGCCATGTTTGAATCGT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ ++ ++ +
647	9.70E-05	reverse	2880675	2880702	GCGGTTTTAACTCCCGTAAATGTTTGTA ATAATTATTCATTTAATGAATATATTTT + ++ +++ + +++ +++++++ ++
648	3.40E-08	forward	2882281	2882308	AAAATATATTCATTGGTTTAATACAATT AAAATATATTCATTAAATGAATAATTAT ++++++++++++ ++++++ ++++
649	7.80E-08	reverse	2882408	2882435	GTTATAATAATTACCATGAATTTTATTA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ +++++++ ++++++
650	3.90E-09	reverse	2882438	2882465	TAAAATATTCATACTGTGAATATAAAAT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++++++++ ++
651	4.10E-05	forward	2890085	2890112	AAAATAGATTAACCAACCTAATGAAAAA AAAATATATTCATTAAATGAATAATTAT ++++++ +++ ++ ++ +++++++++
652	5.70E-05	reverse	2890114	2890141	AAATGAATTTAGCCAATCATTAAGATAA ATAATTATTCATTTAATGAATATATTTT ++++ +++++ +++ + ++ ++++
653	1.60E-05	reverse	2897090	2897117	CTGCATATTCTCAATATCAATATTAATG ATAATTATTCATTTAATGAATATATTTT + ++++++ + ++ +++++++ +
654	5.40E-05	forward	2901659	2901686	TATCTTTATTCATAAGAACTATTCATCA AAAATATATTCATTAAATGAATAATTAT

654	3.40E-05	forward	2901059	2901086	++ + +++++++ + + +++ ++
655	6.80E-05	forward	2901832	2901859	TTAAAAAAATAATAGATTAAAATTTCTT AAAATATATTCATTAAATGAATAATTAT ++++++ + + ++ + ++++ ++ ++
656	5.20E-05	forward	2901881	2901908	ATAACACTTTGATTAAATTTAATTTTTT AAAATATATTCATTAAATGAATAATTAT ++++ ++ ++ ++++++++++ +++++
657	6.80E-05	reverse	2902436	2902463	CATAACCTATTATTAATTAATGATTTTT ATAATTATTCATTTAATGAATATATTTT +++++ +++ +++++ ++++ +++++
658	4.50E-05	reverse	2902537	2902564	CCATTGATTAAAAAGGTAAATATTTAAA ATAATTATTCATTTAATGAATATATTTT +++ +++++ + ++ +++++++ ++
659	9.90E-06	reverse	2902742	2902769	CCATTTATAACGCTTATAAATGTTTAAT ATAATTATTCATTTAATGAATATATTTT ++++++++ + ++ +++++++ ++
660	3.90E-09	forward	2903616	2903643	TCAAAACATTCACCAAAATTATATTTAT AAAATATATTCATTAAATGAATAATTAT + ++++++++++ +++ ++++++++++
661	2.10E-05	reverse	2903655	2903682	TAGTTTTTAATGATAACGAATATAAAAT ATAATTATTCATTTAATGAATATATTTT + +++ +++ ++++ ++++++++ ++
662	4.10E-05	forward	2915949	2915976	CAATTAAATTCAATGAATTAAAAAATGA AAAATATATTCATTAAATGAATAATTAT +++++ +++++ + ++++++ ++++
663	1.10E-07	reverse	2925759	2925786	CATTTCATTTGTTATATGAATGTTTCTT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++++++++++ ++
664	3.90E-05	reverse	2926126	2926153	CAAATTATTACGGCGGTAAATGATTAAG ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++++ ++ +
665	6.40E-06	forward	2927849	2927876	CAGTTTTATTCAGGATGTGAATACTCAT AAAATATATTCATTAAATGAATAATTAT + ++ ++++++ +++ ++++++ + ++
666	2.10E-05	forward	2947143	2947170	TTTTTATATTCACGGCATTACTGATAAA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++++ ++++++
667	1.20E-05	reverse	2949170	2949197	GTACTCATTGAACGCCTGAATGATTAAA ATAATTATTCATTTAATGAATATATTTT +++ +++++ + + ++++++ ++ ++
668	9.10E-05	reverse	2962944	2962971	GGTGACATTGTTTTCGTGTAGATAAGCA ATAATTATTCATTTAATGAATATATTTT + + +++++ +++++++ + ++++ +
669	3.10E-05	forward	2980388	2980415	AGATAAAATTCATAAAGTTCATTAATTG AAAATATATTCATTAAATGAATAATTAT + ++++ ++++++ ++ ++ ++ ++++
670	4.20E-05	reverse	2983673	2983700	AATTGTTTAAAAAAAGTGATTTTTATCA ATAATTATTCATTTAATGAATATATTTT ++++ + ++++ + +++++ + ++++ +
671	3.20E-05	forward	2986341	2986368	TACAAACAATAGTGGCATAAATGTTAAC AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ ++++++++++

672	3.80E-08	reverse	2986428	2986455	ATAAATATAAAATTAATATATATTTATG ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ ++++++ +
673	6.60E-05	forward	2986960	2986987	ATAACAAAATCCTCAAACATATAAAAAG AAAATATATTCATTAAATGAATAATTAT ++++ + + ++ + +++ +++++++++
674	3.70E-05	reverse	2987330	2987357	TTGATTATAAAAAAAACTTATTATTTAT ATAATTATTCATTTAATGAATATATTTT + ++++++++ + ++ ++ +++++
675	3.70E-05	forward	2987685	2987712	ACAACTTATTCCTGATTTTTATGTCTTT AAAATATATTCATTAAATGAATAATTAT + ++ +++++ ++++ +++++++ +++
676	7.50E-05	forward	2988214	2988241	AATTAACATTCACATATCTTGAATTTAA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ + ++ +++++
677	2.90E-05	reverse	2989089	2989116	AAGATAACTAATAAGGTGAATATTAGTA ATAATTATTCATTTAATGAATATATTTT ++ ++ + +++++ ++++++++++ ++
678	5.80E-06	reverse	2989204	2989231	CATAATTTAAAAAAGATAAATATAAAAA ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + ++ +++++++ ++
679	2.50E-05	reverse	2989880	2989907	AAGAGCATACTATAAATCATTATTTTTC ATAATTATTCATTTAATGAATATATTTT ++ + +++++ + +++ + +++++++
680	3.60E-06	forward	2990436	2990463	AACTAAAATTAATGAAGATAATACTTCA AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ +++++ +++++ ++
681	2.10E-05	reverse	2991507	2991534	AATTTTATTATTTAGATGTATGCAACTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ +++ +++ ++ ++
682	4.10E-05	forward	2992001	2992028	TTTGTATATTTATTACAAAAATGTCTTT AAAATATATTCATTAAATGAATAATTAT ++ ++++++ ++++ + ++++++ +++
683	7.70E-06	forward	2993204	2993231	ATGAAATAATAATGAAATATAATTAAAA AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++++++++++ ++++
684	3.70E-05	forward	2993264	2993291	ATTAAAAAATCATGAGATGATTAAAATA AAAATATATTCATTAAATGAATAATTAT ++ +++ + ++++++ ++++ ++++++
685	9.10E-05	forward	2993855	2993882	CCATCATAATAACCTTGAATAAATTTTT AAAATATATTCATTAAATGAATAATTAT ++ +++ + ++ + +++ ++++++
686	6.40E-05	forward	3006778	3006805	GAAAAATAATGGCTAAGAATATTCCATT AAAATATATTCATTAAATGAATAATTAT +++++++ + ++++ ++++ +++
687	3.20E-05	forward	3022328	3022355	TTTACTAATTCAGATGATCAAATTTACT AAAATATATTCATTAAATGAATAATTAT ++ + +++++ ++ ++ +++ +
688	7.80E-05	reverse	3023623	3023650	TAAAATATTGCCAGCCTCTATTTATGTA ATAATTATTCATTTAATGAATATATTTT ++++++++ + + + ++ +++ ++

689	7.80E-05	forward	3049000	3049027	AAAAAATAATGGCATTAGAAAATATAAT AAAATATATTCATTAAATGAATAATTAT ++++++++ + + ++ +++ +++++
690	4.70E-05	reverse	3061990	3062017	CAATATTTTGATTAAAGGAATTTTTATG ATAATTATTCATTTAATGAATATATTTT +++++ ++ +++ ++ ++++ +++ +
691	8.80E-05	forward	3066900	3066927	AATATTAATTGGCAATCAGAAAAACTAA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ + ++ +++ ++ ++
692	3.10E-05	reverse	3067242	3067269	GGAATCATACGCCACGCCAATAATAAAT ATAATTATTCATTTAATGAATATATTTT + ++++++++ ++ ++++ ++ ++
693	4.50E-05	forward	3069401	3069428	TCGAATTATTTAGAGTATGAAAAATTGC AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + ++++++ ++++ +
694	8.30E-05	forward	3073143	3073170	AGTTTTCATAAATGAAAATAAATTGTCC AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++++++ +++ + + +
695	8.70E-06	forward	3074764	3074791	TATTCACATACACCAGCTCAATGCCTTT AAAATATATTCATTAAATGAATAATTAT ++ + ++++ +++ + + ++++ +++
696	7.00E-06	reverse	3077206	3077233	GGAATCTTTAATTGCCTGAATGTAATTC ATAATTATTCATTTAATGAATATATTTT + ++++ ++++++ + ++++++++++
697	1.10E-05	forward	3077458	3077485	GTGAATTATTAATTTCTTATATAACATT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ +++ +++++++ +++
698	2.10E-05	reverse	3077543	3077570	TGATATTTATTGCATATAAATATTTGTG ATAATTATTCATTTAATGAATATATTTT ++++ +++ ++ +++++++ +
699	3.90E-05	forward	3083392	3083419	CGGATATATTCGCGGTCTTTATAACCGT AAAATATATTCATTAAATGAATAATTAT ++++++++ ++ + +++++++ +
700	1.90E-06	reverse	3086183	3086210	TAAATCATAACTAAGATAAATGTTAGTG ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++ +++++++ +
701	6.40E-06	reverse	3098815	3098842	TAAACAATTTACAACGTGAATATATTTT ATAATTATTCATTTAATGAATATATTTT +++ +++++ + ++++++++++++++
702	4.90E-05	forward	3108514	3108541	CAATAACCTTCACGAAAAAAATTAGCTT AAAATATATTCATTAAATGAATAATTAT ++++++ +++++++++ ++++ + ++
703	6.60E-05	forward	3126199	3126226	ATGTTAAATTGATGTAACATAATCACTT AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ +++ ++ +++ + ++
704	6.30E-09	forward	3132096	3132123	AAAACATATTAACCAAATAAATATTTTT AAAATATATTCATTAAATGAATAATTAT ++++ +++++ ++ ++++++++++++++
705	1.60E-06	forward	3132142	3132169	AGGATATATTCATGCAGTCAATAACACC AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + + +++++ + +
					CAACAAATAAATTTAGCATATATTAGAT

706	1.30E-05	reverse	3134375	3134402	ATAATTATTCATTTAATGAATATATTTT ++ + ++++++++++ ++++++ ++
707	5.50E-08	forward	3134570	3134597	TTAATATATTCACATATGAAATGAATAA AAAATATATTCATTAAATGAATAATTAT ++++++++++++ + +++++++++
708	2.90E-05	reverse	3134602	3134629	TGGAATATATAAATATTGAATATTTTGA ATAATTATTCATTTAATGAATATATTTT +++++++ +++ ++++++++++ +
709	4.20E-05	reverse	3144425	3144452	AGAAGCATTAGTGTAATTAATTAAAGCA ATAATTATTCATTTAATGAATATATTTT + ++ +++++ + ++++ +++ ++ +
710	1.00E-05	forward	3181599	3181626	ACTAAACATTTAGCGTATAAATTTCACA AAAATATATTCATTAAATGAATAATTAT + +++++++ + +++++++ + +
711	2.50E-06	reverse	3183270	3183297	GAAAGTATAATTGCAATGTATTTTTTAA ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++++ ++ ++++++
712	2.00E-05	forward	3183331	3183358	TTATAAAAAACACAAAATAAAATATCAT AAAATATATTCATTAAATGAATAATTAT ++++++ + +++ +++++++ ++ ++
713	9.40E-05	forward	3183416	3183443	TCTTTATATAAAGGAATATTATGTCCGC AAAATATATTCATTAAATGAATAATTAT + ++++++ + +++ ++++++ +
714	1.60E-05	forward	3186285	3186312	CCGTATTATTTATCAAGAAAATGTTCCT AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ ++ +++++++ +
715	5.80E-06	reverse	3186787	3186814	AAAAACTTTGTGACAATGAATGAATATA ATAATTATTCATTTAATGAATATATTTT ++++++ ++ + ++++++++ ++ ++
716	9.40E-05	forward	3188971	3188998	AACTTATAATGGGGTTGATTATGATTCT AAAATATATTCATTAAATGAATAATTAT ++ +++++ + + + ++++++++ +
717	9.90E-06	reverse	3190044	3190071	TTAAACATAACGTGCGTAAATATATTGT ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++ ++++++++ +
718	5.90E-05	reverse	3190148	3190175	TTATTATTAACACAGATAAATGTAAGCA ATAATTATTCATTTAATGAATATATTTT ++++ +++ ++ +++++++ +
719	3.20E-05	reverse	3190211	3190238	ATGGACATTGGAGTGATATATGATTTTA ATAATTATTCATTTAATGAATATATTTT ++ +++++ + ++ +++ +++++
720	8.30E-05	forward	3190856	3190883	GTAATTTATTAATCAAAAGGAAATTTAA AAAATATATTCATTAAATGAATAATTAT ++++ ++++ ++ +++ + + +++++
721	1.60E-05	reverse	3191078	3191105	CATGAAATAATCCCCATCAATATGAATA ATAATTATTCATTTAATGAATATATTTT ++ + ++++ +++ +++++ + ++
722	8.00E-05	forward	3197536	3197563	TGCACAAAATCACTAAAAGTAAGTACTG AAAATATATTCATTAAATGAATAATTAT + + + + ++++++++ +++ +++ +
723	4.70E-05	reverse	3199873	3199900	TTATTATTAGGAATTGTGTATTTGACGA ATAATTATTCATTTAATGAATATATTTT

723	4.70E-05	reverse	3199873	3199900	ATTACATATTCACGGTGGCAAAAAATAT AAAATATATTCATTAAATGAATAATTAT ++++ ++ ++ +++ ++ + + +
724	3.10E-06	forward	3204388	3204415	ATTACATATTCACGGTGGCAAAAAATAT AAAATATATTCATTAAATGAATAATTAT ++ + +++++++++ + ++ ++++++
725	5.60E-05	reverse	3214756	3214783	TCAGATATAAATTAGATATATCTAATTA ATAATTATTCATTTAATGAATATATTTT + +++++++++ ++ ++ ++++++
726	6.80E-05	reverse	3225543	3225570	GCGAATATTCTGACCATCATTTTTTATA ATAATTATTCATTTAATGAATATATTTT + +++++++ + +++ + + +++ ++
727	8.80E-05	reverse	3225741	3225768	GGGAAAATAGTTTCTGCCTTTATATTTT ATAATTATTCATTTAATGAATATATTTT + ++ +++ ++ + ++++++++
728	7.30E-05	reverse	3241378	3241405	ACGCGCATTGTTAAAGCAAATATTTTTC ATAATTATTCATTTAATGAATATATTTT + ++++ ++ ++ +++++++++
729	5.70E-05	reverse	3245623	3245650	ATTCAATTTGAATTTATGTTTTTGAATG ATAATTATTCATTTAATGAATATATTTT +++ + ++ + ++ +++ + + + +
730	3.90E-05	forward	3248474	3248501	AATCATCATTCACCACGTTTATGATTCT AAAATATATTCATTAAATGAATAATTAT ++ + +++++++ + +++++++++ +
731	3.10E-06	reverse	3250228	3250255	TTATTAATTCCTTGAACGAATATTTACT ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++ ++ ++++++++ +
732	1.50E-07	reverse	3250729	3250756	TTTATCATTATGTTGATGAATGAATAAT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ +++++++ ++ ++
733	4.50E-05	forward	3250758	3250785	TACTAATGTTTATTTAAAATATTTCAAT AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ +++ ++ ++++ + +++
734	8.00E-05	forward	3250790	3250817	TTATATAAATTACCTATAAAAAATAACC AAAATATATTCATTAAATGAATAATTAT +++++ + + ++ + +++ ++++ +
735	8.60E-05	reverse	3250910	3250937	CTTTTAATTAAAGGGATGTTTTTATGCA ATAATTATTCATTTAATGAATATATTTT ++++ +++++ +++ + +++ +
736	4.80E-06	reverse	3251318	3251345	TTTTTATTAACAATAATAAATATTATTT ATAATTATTCATTTAATGAATATATTTT ++++ +++ +++++ ++++++++++
737	6.40E-05	reverse	3264944	3264971	ATAATCTTCAATATCGTTAATGATTTTA ATAATTATTCATTTAATGAATATATTTT ++++++ + ++++++++ ++++ +++++
738	1.20E-08	reverse	3265493	3265520	ACAAACATTTATTTTATCAATATTTTAA ATAATTATTCATTTAATGAATATATTTT + ++++++++++++ ++ ++++++++++
739	1.20E-05	reverse	3266387	3266414	CCGATCATTTTAATAATGATTTTTATTG ATAATTATTCATTTAATGAATATATTTT +++++++ +++++++ + +++++
740	3.40E-05	forward	3267245	3267272	AAAATGAATTAACAAAAGAAATATATAA AAAATATATTCATTAAATGAATAATTAT +++++ +++ ++ +++ +++++++++

741	2.40E-05	reverse	3267646	3267673	TCTATTATTAATACCGTAGATATTTATT ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ ++++++ ++
742	1.60E-05	forward	3272854	3272881	CAATAAAAATAATCAGTAATATTAAATA AAAATATATTCATTAAATGAATAATTAT +++++ + + ++ + ++++ ++++
743	6.10E-06	forward	3273044	3273071	GAATAATAATCATTGTGCAAATGCTAAT AAAATATATTCATTAAATGAATAATTAT +++++++ +++++ + +++++ ++++
744	6.70E-06	forward	3282140	3282167	ATAATATATTTAAAAAAATTATATTATT AAAATATATTCATTAAATGAATAATTAT ++++++++++ + +++ ++++++++++
745	6.80E-05	forward	3282184	3282211	ATTACACAATGACCAGTCCAAATATTCT AAAATATATTCATTAAATGAATAATTAT ++ + +++ + ++ + ++ +++ +
746	4.90E-05	forward	3285086	3285113	ATGTAACAGTCACGCATTATATTAAATA AAAATATATTCATTAAATGAATAATTAT ++ +++++ +++++ + +++++ ++++
747	5.60E-09	forward	3285393	3285420	AACATATATTCACATTAAATATGATTAT AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++ ++++++++++
748	7.70E-06	reverse	3286605	3286632	ATATATATAACCCAACTGAATATTACGT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++++++++ +
749	2.60E-05	reverse	3296182	3296209	ATGATAATTGAGCGCGTGAATATTACGC ATAATTATTCATTTAATGAATATATTTT ++ ++ +++ + ++++++++++
750	7.50E-05	forward	3316465	3316492	AGTTCACTTTCATTTGTTGAATACTTTT AAAATATATTCATTAAATGAATAATTAT + + ++ ++++++ ++++++ ++++
751	1.30E-05	forward	3316577	3316604	AAAACTCATTTATTTTGCATAAAAATTC AAAATATATTCATTAAATGAATAATTAT ++++ ++++ +++ + +++ ++++++
752	2.90E-05	reverse	3319126	3319153	TTTTTTATTTTTTGCATCTTTATAAGCA ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ +++ +++++ +
753	9.40E-05	forward	3319779	3319806	GTAATTAAATAACATTATCAATGCGTCT AAAATATATTCATTAAATGAATAATTAT ++++ + + ++ +++ ++++ + +
754	5.60E-05	forward	3328394	3328421	TAAAGATATTTATCAGAACAATTAGTCA AAAATATATTCATTAAATGAATAATTAT ++++ +++++ ++ + + +++ + +
755	2.00E-05	reverse	3331732	3331759	ATGAATTTAGAAAAAATCAATGAGTTAA ATAATTATTCATTTAATGAATATATTTT ++ +++ ++ + + +++ ++++ ++++
756	4.10E-07	forward	3348507	3348534	GAAACACATTAATTTTTTTAATAAAAAT AAAATATATTCATTAAATGAATAATTAT +++ +++++ +++ + ++++++++++
757	9.90E-09	reverse	3358910	3358937	ATTAATATACAAAATATGAATATAAAAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + ++++++++++ ++

758	9.40E-05	forward	3358945	3358972	TATTATCCTTAATTATCTATATATTTTC AAAATATATTCATTAAATGAATAATTAT ++ ++ + ++ +++++ ++++++++++
759	5.60E-09	forward	3358984	3359011	CGCAAACATTCATGTAATGAATAATTAT AAAATATATTCATTAAATGAATAATTAT ++++++++++ ++++++++++++
760	2.10E-08	forward	3359058	3359085	CTATAAAATTCATTAAATAAATACATCC AAAATATATTCATTAAATGAATAATTAT +++++ ++++++++++++++++ ++ +
761	5.30E-06	reverse	3359155	3359182	TTTTTATTTTAAAAAATAAATTTGTTAT ATAATTATTCATTTAATGAATATATTTT ++++ ++++ + +++ +++ + ++++
762	1.00E-05	forward	3360070	3360097	GCATAACATATATTAACAATATGTTTCT AAAATATATTCATTAAATGAATAATTAT +++++++ +++++ ++++++++ +
763	1.00E-07	forward	3360144	3360171	ACATTACATTCACTGTATTTATAACAAC AAAATATATTCATTAAATGAATAATTAT + ++++++++++ +++++++++ +++
764	5.50E-06	reverse	3365698	3365725	CGTTTTATACGATCGGTTAATGTTTCAG ATAATTATTCATTTAATGAATATATTTT ++++++++ + ++ +++++++ +
765	2.30E-05	forward	3373211	3373238	AAAACTCATTCGCTCGCCGTATATTATT AAAATATATTCATTAAATGAATAATTAT ++++ +++++ ++ ++++++++++
766	3.10E-05	reverse	3383299	3383326	CATGTCATTCACACAATGAATACATAAG ATAATTATTCATTTAATGAATATATTTT ++ +++++++ + ++++++++ ++ +
767	5.90E-05	forward	3383415	3383442	TATTAAAATTCACATTTTTAACACTTAG AAAATATATTCATTAAATGAATAATTAT ++ +++ ++++++ + ++++ + +++
768	2.20E-05	forward	3399737	3399764	CTAAAGCATTCACTAAACGAATAACAGG AAAATATATTCATTAAATGAATAATTAT ++++ ++++++++++ ++++++ +
769	1.60E-05	forward	3408070	3408097	AATTTTCATTCATAAAGAAAAATTGAGA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++++ ++ +++ + +
770	7.50E-05	reverse	3410228	3410255	TGCGTTATTTGATGGATGAATATGAAAA ATAATTATTCATTTAATGAATATATTTT ++++++ + ++++++++ + ++
771	7.50E-07	reverse	3410581	3410608	CAGATTATTCATTTCGTGTATATTTCCT ATAATTATTCATTTAATGAATATATTTT + ++++++++++++++ ++++++ +
772	9.30E-08	reverse	3410837	3410864	TAATTCATTCGTTTGATGAATTAATTTC ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ ++++++ ++++
773	1.70E-08	forward	3411489	3411516	ATTAATTATTCAGGAAATAAATATATTC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++++ ++++++++++++++
774	7.30E-06	forward	3411599	3411626	TCGTTAAATAAATAATATATATTATTTA AAAATATATTCATTAAATGAATAATTAT + +++ ++ ++ ++++++++ ++++
					AAGATACATTCACTACATCAATATATAT

775	7.00E-09	forward	3411630	3411657	AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++++ ++ +++++++++
776	3.10E-05	reverse	3416343	3416370	AATGGCATTCAGCTCGTTAATAAGAGAG ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++++ ++++ + +
777	2.20E-05	reverse	3427102	3427129	ACAAGTATTTTTTTGATCTTTTTTTCTG ATAATTATTCATTTAATGAATATATTTT + ++ +++++ +++ ++ + +++ +
778	2.60E-05	forward	3427978	3428005	GGAAAACATACACATTTTTTATTCTCGT AAAATATATTCATTAAATGAATAATTAT +++++++ +++ + +++++ + +
779	5.60E-05	reverse	3434930	3434957	GATAATATTTACCGACTGATTGAGTATC ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++ ++ + +
780	2.60E-05	forward	3438736	3438763	CAGATTTATTCAAGGTAAGAATAACTTC AAAATATATTCATTAAATGAATAATTAT + ++ ++++++ + ++ ++++++ +++
781	7.30E-05	forward	3440119	3440146	ATTATTCAATCACCCCGATTATTTCTTG AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++++ ++++ + ++
782	8.80E-05	reverse	3451305	3451332	CCAATTATTTTATAAACGAAAATGATTA ATAATTATTCATTTAATGAATATATTTT ++++++++ + ++ +++ ++ ++++
783	1.10E-08	reverse	3453451	3453478	TTAATCATAAAAATAATGTATGTATTTA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++++ +++++++++
784	2.40E-07	forward	3453480	3453507	TAATTAAATACATATTACTAATATAAAT AAAATATATTCATTAAATGAATAATTAT ++++++ ++ +++ ++ ++++++++++
785	1.40E-06	forward	3453655	3453682	TCAATATATTGATTATATTTATAAGCAT AAAATATATTCATTAAATGAATAATTAT + ++++++++ ++++++++++++ ++
786	1.00E-05	reverse	3453687	3453714	TCGATTATTTTTAATGTGAATTATTTCC ATAATTATTCATTTAATGAATATATTTT +++++++ ++ ++++++ +++
787	2.80E-05	reverse	3453987	3454014	ACGTTTATTAGAAAAATAAATAAAACCA ATAATTATTCATTTAATGAATATATTTT + +++++++ + +++ ++++ ++ +
788	2.90E-05	forward	3454974	3455001	GCAAATTATTCATCTGGAATATGCGTCA AAAATATATTCATTAAATGAATAATTAT +++ +++++++ +++++ +
789	5.50E-08	reverse	3467841	3467868	CCAATCATAGATTTAGTAAATATATTTA ATAATTATTCATTTAATGAATATATTTT +++++++ +++++++ ++++++++++
790	1.30E-07	forward	3468016	3468043	CAGAAACATTCATATTTAAAATGTTAAA AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + +++++++++
791	9.30E-08	reverse	3468048	3468075	ATTGATATTTTAAATATGAATAATTTAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + +++++++ +++++
792	7.80E-05	forward	3483984	3484011	GTAATACATTGATGTACTGCATGTATGC AAAATATATTCATTAAATGAATAATTAT

792	7.80E-05	forward	3483984	3484011	++++++++ +++ + ++ ++++++ +
793	2.20E-05	reverse	3494984	3495011	TTTGTTTTATTTTTTGTTTTTATTTTTT ATAATTATTCATTTAATGAATATATTTT ++ ++ +++ +++ ++ ++++++++
794	9.10E-05	forward	3495020	3495047	ATCAAATGTTTACAGACACTATTAATAA AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ ++ + +++ ++++
795	4.60E-06	reverse	3497263	3497290	CTTTTTATATATTCAGCAAATAAAACAT ATAATTATTCATTTAATGAATATATTTT ++++++++++++ ++ ++++ ++ ++
796	1.40E-09	reverse	3497417	3497444	ATATTCATATAATCAATGAATATTAATT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + ++++++++++ ++
797	3.70E-05	forward	3497450	3497477	ATAATACATAGGGAATGTAAATGAACAA AAAATATATTCATTAAATGAATAATTAT +++++++++ ++ ++++++++ +
798	2.90E-05	forward	3509025	3509052	ATTAAATATTCATTTTTTTGAATATTTA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ + ++ + ++++
799	6.10E-05	forward	3518146	3518173	TTTTTTCATTAATGGTGACAATATGCGC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ +++ + +++++ +
800	5.80E-06	forward	3524246	3524273	TATTTACATTTATGTAACTTAATAAATA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ +++ ++ +++ ++++
801	4.10E-05	reverse	3538066	3538093	ATTATCATTGTGTTGTTGATTATTTAAT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ +++ +++++ ++
802	6.10E-05	forward	3556157	3556184	AAAATTAAATAAGCAGCTTAATTTTTTA AAAATATATTCATTAAATGAATAATTAT +++++ + + + + +++++ ++++
803	5.70E-05	forward	3558624	3558651	TTCATTTATAAATCCCTGGAATTATTTT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ ++++ +++++
804	5.60E-05	reverse	3560897	3560924	GAAATCAATTACCTGCTGAATGTGTATA ATAATTATTCATTTAATGAATATATTTT +++++++ +++ + +++++++ + ++
805	7.50E-05	reverse	3573079	3573106	CAGGGAATTTGAGTTATGAATGAAATCA ATAATTATTCATTTAATGAATATATTTT + ++++ + +++++++ +++ +
806	1.80E-05	reverse	3577667	3577694	ATTTGTATTCGCCCCCTGAATGATTTCG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + ++++++ +++
807	8.60E-05	reverse	3579714	3579741	GTATTTATTTGCCCAATACATATATTGA ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ +++++++ +
808	6.40E-05	reverse	3579769	3579796	TGTAATATTTTATTTTTTAATATATACG ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ + +++++++
809	8.60E-05	reverse	3580012	3580039	TCACTCTTAAATAATATTAATAATACGG ATAATTATTCATTTAATGAATATATTTT + ++ ++++++ ++ ++++ ++

810	2.80E-05	reverse	3580099	3580126	TTATTTATTAATTCCATTAACAATAATG ATAATTATTCATTTAATGAATATATTTT ++++++++++++ +++ ++ + ++ +
811	3.70E-05	forward	3580595	3580622	TTGATACATATACAGAAATAAATAGTTA AAAATATATTCATTAAATGAATAATTAT ++ ++++++ ++ ++ +++ + ++
812	2.10E-08	reverse	3581085	3581112	AAATTAATAAAAATGATGAATGATTTAG ATAATTATTCATTTAATGAATATATTTT +++++ +++++ ++ +++++++ ++++
813	9.90E-06	forward	3581137	3581164	AGGAATCATTTATTGAAAGTATAATCCA AAAATATATTCATTAAATGAATAATTAT + ++ ++++ +++ ++ +++++++
814	2.90E-05	reverse	3581353	3581380	AATTTTATAGAAATAATGATGATTTCAT ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++++++ ++++ ++
815	1.60E-05	forward	3582248	3582275	AGATAATATTGGCACAGAAAATATATTC AAAATATATTCATTAAATGAATAATTAT + ++++++++ + + ++++++++++
816	2.10E-08	forward	3582762	3582789	CAATAATATTTATTATAATTATGATTAC AAAATATATTCATTAAATGAATAATTAT +++++++++ ++++++ ++++++++++
817	4.40E-05	forward	3595908	3595935	AAAAATTAATCACCTGCCAAAAGAAATA AAAATATATTCATTAAATGAATAATTAT +++++ ++ ++++ +++ +++++
818	1.70E-05	forward	3597787	3597814	CTAAAACATACCCGATTTTTATGATATT AAAATATATTCATTAAATGAATAATTAT ++++++++ + ++++ ++++++++++
819	8.30E-05	forward	3611635	3611662	TACTTAAAATCGTCATACTTATTTCCGC AAAATATATTCATTAAATGAATAATTAT ++ +++ + ++ + +++ ++++ + +
820	8.60E-07	forward	3622408	3622435	TTAAAAAATTGATGGAACATATTTCTAT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ +++ ++ ++++ + +++
821	3.80E-05	reverse	3623136	3623163	GAACTTATTGATTTCACGTTTGAATGGA ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++++ + ++ ++ +
822	2.10E-05	reverse	3628831	3628858	ATACTCATAAGTGTGATCTATAAAACTG ATAATTATTCATTTAATGAATATATTTT +++ ++++++ + + ++ +++ ++ +
823	1.70E-05	forward	3628966	3628993	CATTAATATTCATGTTGTCTATGGTTCA AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + + ++++ ++
824	8.00E-05	forward	3629647	3629674	CATTTTCATTGATACTCATTATGCGTTT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ ++ + +++++ +++
825	8.00E-05	forward	3631532	3631559	AGGATATATTTATCACCAAAAATAGTAC AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ + +++ + +++
826	8.00E-05	forward	3631730	3631757	TTTAATAATTCACATAATAAACTCCAAC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++++ ++++++ +++

827	2.40E-05	forward	3632554	3632581	GATATAAAATAATAATACTTATATGTTC AAAATATATTCATTAAATGAATAATTAT + +++ + + ++ +++ ++++++ +++
828	6.40E-05	reverse	3632673	3632700	AGAATTAATCTTAGGATAAATTTTTATT ATAATTATTCATTTAATGAATATATTTT + +++++ ++ ++ ++ +++ +++ ++
829	1.60E-05	forward	3632791	3632818	TCATTATATTAACAGGATGAAATTATCA AAAATATATTCATTAAATGAATAATTAT + ++++++++ ++ +++++ +++
830	2.60E-05	reverse	3635167	3635194	GTGTTTATTGACCAGATCAATGAAATCC ATAATTATTCATTTAATGAATATATTTT ++ ++++++ + ++ ++++ +++
831	3.40E-05	reverse	3635523	3635550	CCTGAATTATATAAGATAATTATTTTTT ATAATTATTCATTTAATGAATATATTTT + + ++++++ ++ + ++++++++
832	3.60E-06	forward	3637921	3637948	TCAATATATTCATGTCGAAAATTTGTTT AAAATATATTCATTAAATGAATAATTAT + ++++++++++ ++++ + +++
833	1.80E-05	forward	3638774	3638801	TTAATCTATTCACCGCATCAATATTAAG AAAATATATTCATTAAATGAATAATTAT +++++ +++++++ ++ ++++++++
834	8.30E-05	forward	3648999	3649026	AAGATACCTTAACCCATTTTATTATTAC AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ ++ + +++++ +++++
835	6.40E-06	reverse	3649471	3649498	AAGGATATATCTCTGATCAATATGATTT ATAATTATTCATTTAATGAATATATTTT ++ ++++++ + + ++ +++++ ++++
836	9.40E-05	forward	3649646	3649673	ATCAATACTTAATCAGATTAATAACATT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ + ++++++++ +++
837	9.70E-05	forward	3649910	3649937	TGAAAATAAAAACAGGATGAAAGTCTTT AAAATATATTCATTAAATGAATAATTAT + ++++++ ++ +++++ ++ +++
838	3.50E-05	forward	3651296	3651323	AAATTATATAAAGATGGACAATATCTTG AAAATATATTCATTAAATGAATAATTAT +++++++++ + +++++ ++
839	8.80E-05	forward	3651442	3651469	TTCATACAATGACATATTAAAATATCAG AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ + ++++ ++ +
840	1.30E-05	reverse	3651767	3651794	ATAAAAATAGATTTTATGTACTTTTAAA ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++++ +++ + +++ ++
841	5.20E-05	forward	3652839	3652866	TTGATACATTAATGAATAATGTATTTCA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ +++++ ++ +++++
842	7.80E-05	forward	3653906	3653933	ATAATAAATTCTGCTGTCATATAAAAAT AAAATATATTCATTAAATGAATAATTAT ++++++ ++++ +++++++++
843	7.00E-05	forward	3654998	3655025	TAATTTTATAGGGTGGTTCTATGTTATA AAAATATATTCATTAAATGAATAATTAT +++++ +++ + + ++++++++
					GGAATCTTACTTAGGATCAATATATGGA

844	2.20E-05	reverse	3656195	3656222	ATAATTATTCATTTAATGAATATATTTT + ++++ +++ ++ ++ +++++++ +
845	3.50E-05	forward	3656772	3656799	GAAAAATAAAAATGAAAGCAATATCACG AAAATATATTCATTAAATGAATAATTAT +++++++ ++++++ +++++ +
846	3.40E-05	reverse	3662650	3662677	CTTATATTTCATACTGCGATTATTTCAA ATAATTATTCATTTAATGAATATATTTT ++++ ++++++ + ++ +++++ ++
847	3.80E-08	forward	3664069	3664096	AATAAACATTCATATAACATATATCTTA AAAATATATTCATTAAATGAATAATTAT ++ ++++++++++ ++ ++++++ ++
848	2.80E-05	forward	3665725	3665752	TATAAACATTTAACATGATAATATTAAA AAAATATATTCATTAAATGAATAATTAT ++ +++++++ + ++ +++++++++
849	2.30E-05	forward	3666041	3666068	TAGTCACATTCATACGACCAATATCCGC AAAATATATTCATTAAATGAATAATTAT ++ + ++++++++ + +++++ +
850	9.50E-06	reverse	3667339	3667366	ACATGAATATAAACTATCAATAAGATAG ATAATTATTCATTTAATGAATATATTTT + ++ +++++ + ++ ++++ +++
851	1.90E-05	reverse	3667461	3667488	ATTTTTATAAATTCCATTGATATTAGTG ATAATTATTCATTTAATGAATATATTTT ++++++++++++ +++ ++++++ +
852	8.00E-07	reverse	3669861	3669888	ACTGATTTTCATTCCATGAATAAATATT ATAATTATTCATTTAATGAATATATTTT + + ++ ++++++ ++++++++ ++ ++
853	5.20E-05	forward	3672630	3672657	CAGTTTTATCCACTATTTATAAAATTAT AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++++++ ++++ ++++++
854	7.00E-05	forward	3699578	3699605	CCGAATTATTGATACCAAGAAAATTAAC AAAATATATTCATTAAATGAATAATTAT ++ ++++ ++ + +++ ++++++
855	4.20E-05	forward	3706075	3706102	AAGTTTTATGCATTTAATGAAAAAAATC AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++++ ++++++ ++++++
856	7.80E-08	forward	3710167	3710194	GACAATTATTCACCAAATTTATTATTTG AAAATATATTCATTAAATGAATAATTAT + ++ +++++++ ++++++++ ++++
857	5.50E-06	forward	3717849	3717876	ATTAATCATAAATATGAAAAATAATTGT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ + ++++++++ +
858	9.40E-05	forward	3718044	3718071	CACACTTAATTATTAAAGGTAATACACT AAAATATATTCATTAAATGAATAATTAT + + ++ + ++++++ +++ + + +
859	1.30E-05	reverse	3718383	3718410	ATTATTATTTTTGTGAAGAATAAATTTG ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + + +++++ ++++
860	6.70E-06	reverse	3720232	3720259	AATCTCATAAAATTAATATATGAGATAA ATAATTATTCATTTAATGAATATATTTT +++ +++++++ +++++ +++ ++++
861	5.20E-05	reverse	3725389	3725416	GTATTCCTTTCATTCCTGAATATGTAAG ATAATTATTCATTTAATGAATATATTTT

861	3.20E-05	reverse	3725389	3725416	++++++ +++ +++ +++++++ + +
862	8.60E-07	forward	3725855	3725882	AGAATAAATTCATACTAAATATTAATTA AAAATATATTCATTAAATGAATAATTAT + ++++ ++++++ ++ ++++ ++++
863	5.90E-05	reverse	3735219	3735246	TTAATCATTCCAACACCTTATATTTTTC ATAATTATTCATTTAATGAATATATTTT +++++++++ + + ++++++++
864	9.40E-05	reverse	3742405	3742432	ATTGTATTTATAAACATTATTTTAAGAT ATAATTATTCATTTAATGAATATATTTT +++ + +++ + +++ + + +++ ++
865	3.20E-05	reverse	3742476	3742503	TTATTTATTTGTCTGGTTAACGTTTATT ATAATTATTCATTTAATGAATATATTTT +++++++++ + + ++ ++ ++++ ++
866	5.60E-05	forward	3749971	3749998	TTTATATAGTAATATATAAAATTATATA AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++ + ++++ ++++
867	7.80E-05	forward	3752101	3752128	TCAAAATAATCAGTAAATCCATAAGTAT AAAATATATTCATTAAATGAATAATTAT + ++++++ +++ +++++ ++++ +++
868	4.60E-06	reverse	3755777	3755804	ATATTCATTGCATCAGTCAATGAATCAG ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++ ++++ ++ +
869	4.40E-06	forward	3755917	3755944	CAGTATTATTGATTATCAAAATTAATCT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ +++++ ++++ +++ +
870	1.30E-05	reverse	3756008	3756035	TAATTTATTTTAAAACTTAATTAATCAT ATAATTATTCATTTAATGAATATATTTT +++++++++ + + + +++ ++ ++
871	5.40E-05	forward	3760086	3760113	GTGATATAAATATTTTCCTAATTATTTC AAAATATATTCATTAAATGAATAATTAT + +++++ +++ + ++++ +++++
872	8.00E-05	forward	3764726	3764753	CCAATTTATTCACCTAAAATAGTAGAAC AAAATATATTCATTAAATGAATAATTAT +++ +++++++ ++ +++ + +++
873	7.80E-05	reverse	3765057	3765084	AAAAAAATACTGTTTATGATGATATCAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++++ ++++ ++
874	3.20E-06	reverse	3767219	3767246	GCAAAAATTAAATGAGTTAATATTTTCA ATAATTATTCATTTAATGAATATATTTT + +++ +++++ + +++ ++++++++ +
875	3.20E-06	reverse	3767650	3767677	GATTGCATTGAAACAGTAAATAAAATAA ATAATTATTCATTTAATGAATATATTTT ++++ ++++ + + +++ ++++ +++++
876	1.40E-07	reverse	3767699	3767726	ATTGATATAAATTCAGTTAATATTTGTA ATAATTATTCATTTAATGAATATATTTT +++ +++++++++ +++ +++++++ ++
877	6.00E-08	reverse	3768154	3768181	GAACTTATTAACATAATGAATATTAAAG ATAATTATTCATTTAATGAATATATTTT +++ +++++++ ++++++++++++ +
878	8.40E-06	forward	3772421	3772448	TAAAAACATTGATGAAGGTTAATACTAT AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++++ +++ + +++

879	3.60E-06	forward	3791740	3791767	ATATCATAAATATTAATAGAATGTATAC AAAATATATTCATTAAATGAATAATTAT ++++ +++ +++++ ++++++++++
880	9.40E-05	forward	3791797	3791824	ATTTATCATACATCGGAATATTGATACT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ +++ + ++ +++++ +
881	6.80E-05	forward	3793450	3793477	AAATCATATACCTGTAATCAATTTTCGC AAAATATATTCATTAAATGAATAATTAT ++++ ++++ + ++ +++ +++ ++ +
882	1.70E-05	reverse	3795039	3795066	AATAACTTATATATTATGTTTTTTTTCA ATAATTATTCATTTAATGAATATATTTT ++++++ +++++++ +++ + ++++ +
883	1.10E-05	forward	3795086	3795113	ATAATACTTTCAGCATAAAAATATATAA AAAATATATTCATTAAATGAATAATTAT +++++++ ++++ +++ +++++++++
884	8.30E-05	forward	3795284	3795311	GTTATTTAAATACTGCCAAAATATTTAT AAAATATATTCATTAAATGAATAATTAT + ++ ++ +++ ++++++++++
885	7.50E-05	reverse	3795425	3795452	ATATTAATAGCATTCATGAAAATGACCG ATAATTATTCATTTAATGAATATATTTT +++++ +++ ++++++++ ++ +
886	8.00E-05	forward	3795667	3795694	TATAATAAATCACCCAAGAAATTCACTT AAAATATATTCATTAAATGAATAATTAT ++ ++ + ++++ ++ ++++ + ++
887	7.00E-05	reverse	3795724	3795751	GCTAGCATTGTTATTATATTTAATAAAC ATAATTATTCATTTAATGAATATATTTT + ++ ++++ +++ ++ ++ ++ +
888	4.10E-06	reverse	3796554	3796581	TCAAGTATTGGTATTGTCAATAAATCTT ATAATTATTCATTTAATGAATATATTTT ++ ++++ +++ ++ ++++ ++ ++
889	2.10E-05	forward	3797045	3797072	TTCTTTAATACAGAACTCAAATATATTT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ + ++++++++++
890	6.60E-07	reverse	3797180	3797207	AAGTTTATTATTATCATGAATAATAAGG ATAATTATTCATTTAATGAATATATTTT ++ +++++++ ++++++++++ ++
891	8.60E-05	reverse	3797241	3797268	TTATTTATTTTATTACGAAATAAAAAAG ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ ++++ ++ +
892	2.60E-05	reverse	3797276	3797303	ATTAATCTTGATTTTGTTTATATAAAAT ATAATTATTCATTTAATGAATATATTTT ++++++ ++ ++++ ++ ++++++ ++
893	3.90E-05	reverse	3797497	3797524	TGATAAATTATAAATATTAATATCTTTT ATAATTATTCATTTAATGAATATATTTT +++ ++++ + ++ +++++ ++++
894	2.70E-05	forward	3798675	3798702	AAATAAAAGTCATTGAGTGTATTTAACC AAAATATATTCATTAAATGAATAATTAT ++++++ + +++++ + +++++ +++ +
895	2.00E-05	forward	3798871	3798898	GAAAAACCTTGATGATATTTATATTATA AAAATATATTCATTAAATGAATAATTAT ++++++ ++ ++++++++++++++

896	3.70E-05	reverse	3799094	3799121	CTTTTTTTAAATTCAATAATTGATTTCG ATAATTATTCATTTAATGAATATATTTT +++++ ++++++ +++ + ++ +++
897	7.50E-05	forward	3799817	3799844	TCATTATAAACATCAGCAATAATATAAA AAAATATATTCATTAAATGAATAATTAT + ++++++ +++ + +++ ++++
898	7.30E-05	forward	3800876	3800903	CCAAAATAATCAGTAAAAATATGGAAAC AAAATATATTCATTAAATGAATAATTAT ++++++ +++ ++++ +++++ ++++
899	4.20E-05	forward	3801101	3801128	CAGAAATAATTACCTTATGTAATCTATC AAAATATATTCATTAAATGAATAATTAT + +++++ + ++ ++++++ ++++
900	4.40E-05	reverse	3801185	3801212	TATGAATTTCACCTGCTATATATTTATT ATAATTATTCATTTAATGAATATATTTT ++ + ++++ + + ++++++ ++
901	3.50E-05	forward	3801594	3801621	AAATTTCATACGCCCAACATAAATAAAC AAAATATATTCATTAAATGAATAATTAT +++++ +++ + + ++ +++ ++++++
902	3.00E-05	reverse	3802153	3802180	ATTTTCATAGAAACTCTCATTAATTGAG ATAATTATTCATTTAATGAATATATTTT +++++++++ + + + + ++ ++ +
903	2.20E-06	reverse	3802379	3802406	ACATTTATATTATTAGTAATTAATTTTT ATAATTATTCATTTAATGAATATATTTT + ++++++++ +++++ + ++ +++++
904	8.00E-05	forward	3802823	3802850	ATAAAATCTTCGCCAACAGTATTTCTTA AAAATATATTCATTAAATGAATAATTAT +++++++ +++ + ++ ++++ + ++
905	1.30E-05	reverse	3802855	3802882	CAAAACTTTATGACAGTTAATATTTTTT ATAATTATTCATTTAATGAATATATTTT +++++ +++ + +++ ++++++++++
906	7.80E-05	reverse	3803031	3803058	AGTTATATTTTTTTGGTGTTGTTATATT ATAATTATTCATTTAATGAATATATTTT + ++++++++ +++ +++ +++ ++
907	3.60E-06	forward	3803326	3803353	AATATTCATTGATGAGAAATATAAACCA AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++++ + +++++++
908	3.10E-05	forward	3806304	3806331	GATTTTTATACACAAAATATACTTTAAT AAAATATATTCATTAAATGAATAATTAT + ++ +++ +++ +++++++ +++++
909	5.70E-05	forward	3816976	3817003	TGGATACATTTGGCGTAATTATTATTGC AAAATATATTCATTAAATGAATAATTAT + +++++++ ++ ++++ +++ +
910	6.80E-05	reverse	3833416	3833443	TGGTTTATTATCACCGCCAATTAAATTA ATAATTATTCATTTAATGAATATATTTT +++++++ + ++ +++ +++++
911	1.60E-05	forward	3834706	3834733	AAGATTAATTTGTTCATTTAATATATCA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ + +++++++++
912	2.60E-06	reverse	3834787	3834814	TAATATATAAATTCGGTAATTAATTCTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ + ++ ++ ++
					GGTTCATATACACCGGGCGAATATACGT

913	4.70E-05	forward	3839027	3839054	AAAATATATTCATTAAATGAATAATTAT + ++++ +++ +++++++ +
914	1.60E-05	forward	3841954	3841981	TAATCAAATTGATAAAATCAAAATGAGA AAAATATATTCATTAAATGAATAATTAT ++++ + +++ ++ ++++ ++ ++ +
915	7.00E-05	forward	3851327	3851354	TTTATTTATACAGTAAACTTCTATAATA AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ ++++ ++ ++++++
916	3.30E-05	reverse	3851906	3851933	TGACTTATTCTAATTATTTTTATAAAAG ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ ++ +++++ +
917	5.60E-05	reverse	3858137	3858164	CATCTCATAGCCCTTATTTATGTTTATG ATAATTATTCATTTAATGAATATATTTT ++ +++++ + ++ ++++++ +
918	9.10E-05	reverse	3858569	3858596	TATTATATTCTTAAAGCCAATGGATATT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++ ++++ ++ ++
919	1.80E-05	forward	3858692	3858719	TATTTATAATGGCGAAATTTATAATCAG AAAATATATTCATTAAATGAATAATTAT ++ +++++ + ++++++++++++ +
920	9.10E-05	reverse	3865742	3865769	GAATTTATTATGATAAGAAATGTGTTGT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ +++++ ++ +
921	2.00E-05	reverse	3886456	3886483	TTATGAATATCTTACATATATGTGTGAC ATAATTATTCATTTAATGAATATATTTT +++ ++++ ++ +++ ++++ + +
922	4.40E-05	reverse	3886666	3886693	TTGCATATATATCTGGCGAATTAATCGG ATAATTATTCATTTAATGAATATATTTT + ++++++++ + + ++++ ++
923	3.80E-05	reverse	3899365	3899392	ATTGGTATTAATCTGCTGTTTGTTTTGC ATAATTATTCATTTAATGAATATATTTT +++ +++++++ + ++ ++++++
924	4.50E-05	reverse	3904826	3904853	TTATATATAACAAATCCCAATAATTAAG ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++++ ++ +
925	7.00E-05	reverse	3906339	3906366	GTTCAAATTACGAACCTGAATTTTACTC ATAATTATTCATTTAATGAATATATTTT +++ + ++++ + + +++++ +++ +
926	1.20E-05	forward	3913085	3913112	CTAATTCATTCGCAGCATCAATGACATG AAAATATATTCATTAAATGAATAATTAT ++++ +++++ + ++ +++++ ++
927	7.30E-05	forward	3920799	3920826	TAAAAACAGATACTGTTTTAATAAATGA AAAATATATTCATTAAATGAATAATTAT ++++++++ +++ + +++++++++
928	7.30E-05	reverse	3929079	3929106	CGGGAAATTCTTTCCGCTAATAAATGAG ATAATTATTCATTTAATGAATATATTTT + ++++ ++ ++ ++++ ++ +
929	1.80E-07	reverse	3929421	3929448	CGTTATATACACTTCGTGAATGTTTGTC ATAATTATTCATTTAATGAATATATTTT +++++++++ ++++++++++++ +
930	3.90E-05	forward	3929793	3929820	CTTTATTATTTATGATTCAAAAACATGG AAAATATATTCATTAAATGAATAATTAT

930	3.90E-05	forward	3929793	3929820	+ ++ ++++ +++++ +++ + ++
931	1.90E-05	forward	3932928	3932955	TGATTTCATTCGTCTGTTTAATGTGAAA AAAATATATTCATTAAATGAATAATTAT + +++ +++++ + +++++++ ++
932	2.90E-05	reverse	3937855	3937882	TTTTAAATAAATCTAATGAAATTAATGG ATAATTATTCATTTAATGAATATATTTT ++++ ++++++ +++++++ ++++
933	9.40E-05	reverse	3946004	3946031	AAATTATTTGTCGTTATGATTTAAATGT ATAATTATTCATTTAATGAATATATTTT +++++ ++ + ++++ + +++ +
934	6.40E-05	reverse	3948169	3948196	ACATTCATACTGAAATTGAATTTTTTTC ATAATTATTCATTTAATGAATATATTTT + ++++++++ + + +++++ +++++
935	3.80E-06	forward	3984140	3984167	ATTATTTATTTATCCAGAAAATGAATTG AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++ + +++++++++
936	9.10E-07	forward	3984302	3984329	TTTTATCATTCATAATAAGTATGTGTAG AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++++ +++ ++++++ ++
937	7.80E-05	forward	3984342	3984369	GTTAAATATTCACTCAGGAAGTTATTAC AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + ++ + +++++
938	4.20E-05	forward	3995914	3995941	CTGATATAATCAGCAAATCTGTATATAT AAAATATATTCATTAAATGAATAATTAT + +++++ +++ ++++ + +++++++
939	1.90E-05	reverse	4001134	4001161	ATGAAATTTATTAAAATAAATGAAAATA ATAATTATTCATTTAATGAATATATTTT ++ ++ +++ ++ +++ ++++ ++ ++
940	6.60E-07	reverse	4001200	4001227	ATAAATATACGTAACATAAATTTTACAT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ +++ +++ +++ ++
941	2.20E-05	reverse	4001285	4001312	ATATTTTTTCAGAATATATTTATTTTTT ATAATTATTCATTTAATGAATATATTTT ++++++ ++++ + ++ ++++++++
942	2.80E-08	forward	4002839	4002866	GAAAAATATTCACCTTATCAATAATTCG AAAATATATTCATTAAATGAATAATTAT ++++++++++++ +++ +++++++
943	8.60E-05	forward	4011052	4011079	TACATATAATTAGAGGAAGAAAAAATGA AAAATATATTCATTAAATGAATAATTAT ++ +++++ + + + +++ ++++
944	9.70E-05	reverse	4033167	4033194	GCTGAAATAAGCATAAAGAATAAAAAAT ATAATTATTCATTTAATGAATATATTTT + + + ++++ ++++ +++++ ++ ++
945	6.60E-05	reverse	4042077	4042104	AATTACATAAAGCCCGTGAATATTCACG ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++++++++
946	7.00E-06	forward	4042126	4042153	AATATAAATACATTCTGATAATGCATCC AAAATATATTCATTAAATGAATAATTAT ++ +++ ++ ++++ + +++++ ++ +
947	3.00E-05	forward	4044820	4044847	ATAAATTAAAAGCGATGTAAATAATTTA AAAATATATTCATTAAATGAATAATTAT +++++ ++ ++++ ++++++++++

948	7.30E-05	forward	4062472	4062499	GTTTTTCATTGAGTGTGTAAAAGAATCC AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + + + ++++ ++++ +
949	1.50E-05	reverse	4067366	4067393	ATTCTCATAAAACTGATATATAAAAACT ATAATTATTCATTTAATGAATATATTTT +++ +++++++ + ++ +++ ++ +
950	9.10E-06	forward	4076485	4076512	CTCTCTCATTCAGGTCATTTATATTAGT AAAATATATTCATTAAATGAATAATTAT + + ++++++ + ++++++++++ +
951	4.20E-05	forward	4076720	4076747	TTTTCTCATAAATATTTTTAAAATCTAT AAAATATATTCATTAAATGAATAATTAT ++ + +++ ++ + ++++ ++ +++
952	6.80E-05	reverse	4076819	4076846	TTATGAATAATTATGTTGTATGTTTGCT ATAATTATTCATTTAATGAATATATTTT +++ ++++ +++ ++ ++++++ +
953	2.10E-05	forward	4077108	4077135	ATAATATATTCATAGCACCCATAATTCA AAAATATATTCATTAAATGAATAATTAT ++++++++++++ + ++++++
954	2.70E-06	forward	4077276	4077303	CACATACATTAATGAGTAATATATGTAA AAAATATATTCATTAAATGAATAATTAT + +++++++ ++++ ++++++ ++
955	4.70E-05	reverse	4077534	4077561	AAAAATTTTTCATTCTTGAATATAAAAA ATAATTATTCATTTAATGAATATATTTT ++++++ +++ +++ +++++++++ ++
956	4.10E-08	reverse	4084907	4084934	GGACTTATTCATTTCGTGAATTTTATTA ATAATTATTCATTTAATGAATATATTTT + + ++++++++++++++++ ++++++
957	2.00E-05	reverse	4085002	4085029	CTATATATTTATAAGGCAATTAAATGAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + ++ ++ ++
958	5.60E-05	reverse	4090463	4090490	ATGAATAAATTCCTTGTGAATAATTTTG ATAATTATTCATTTAATGAATATATTTT ++ ++++ ++ + +++++++ ++++
959	2.50E-05	reverse	4090985	4091012	ATTTAAATAAACCACATGAATCATTAAT ATAATTATTCATTTAATGAATATATTTT +++++ +++++ +++++++ ++ ++
960	9.40E-05	forward	4096863	4096890	CTTTTACATTCATGCTGACGATAAACAC AAAATATATTCATTAAATGAATAATTAT + ++++++++++ + +++++ ++
961	1.30E-05	reverse	4098741	4098768	ATAATCATTTTCAATATCATTTAATTAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + ++ + + +++++
962	2.30E-05	forward	4099553	4099580	TAAAAACAATGATCCGATAAAAATAAAA AAAATATATTCATTAAATGAATAATTAT ++++++++ + ++ +++++ +++++
963	1.30E-07	forward	4099608	4099635	CACTTTTATTGATTAAATGAATGTCTAT AAAATATATTCATTAAATGAATAATTAT + ++ ++++ ++++++++++++ +++
964	4.80E-06	forward	4103681	4103708	GGATTTTATTCATTGTTTAAATACCTCC AAAATATATTCATTAAATGAATAATTAT +++ ++++++++ + ++++++ + +

965	5.90E-05	reverse	4109965	4109992	AGAAGCATACAAGTTCTCATTAATTTTA ATAATTATTCATTTAATGAATATATTTT + ++ ++++++ + + + ++ +++++
966	5.90E-05	reverse	4116308	4116335	TAGATCATTCGCGCAACAAATTTATTAA ATAATTATTCATTTAATGAATATATTTT + +++++++ ++ +++ ++++++
967	8.60E-05	reverse	4118365	4118392	TCAGTCATAATACGCGCCAATAAAAATG ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ ++++ ++ +
968	3.70E-05	reverse	4131711	4131738	AAAAGCTTAATTAAGATCAATTTGATCT ATAATTATTCATTTAATGAATATATTTT ++++ + +++ ++ ++ +++ + ++ +
969	1.10E-05	reverse	4137022	4137049	GGATGTATTTACCCGGTGATTGAATAAT ATAATTATTCATTTAATGAATATATTTT + ++ ++++++ ++++ ++ ++ ++
970	2.80E-05	forward	4148350	4148377	AAGGTATATTCAGAATTTGAATAAAATG AAAATATATTCATTAAATGAATAATTAT ++ ++++++++ ++ ++++++++++
971	3.70E-05	reverse	4153444	4153471	AATAAATTAAAAGAAGCGAATTTGATTG ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++++ + +++
972	1.80E-05	forward	4161916	4161943	TATTTTTATTCGCGGTACAAATGCCAGT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++++ ++ ++ +++++ + +
973	1.70E-05	forward	4170949	4170976	AGTTCTCATTAATGAAGACAATGCAAAA AAAATATATTCATTAAATGAATAATTAT + + ++++ +++++ ++++ +++
974	8.80E-05	reverse	4213367	4213394	TTTTTAATTAAAATGGAAATTGTTTTTG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++ + + +++++++
975	3.20E-05	reverse	4220004	4220031	ATTCTGATAAATATCATTAATATATTGT ATAATTATTCATTTAATGAATATATTTT +++ + ++++++++++ ++++++++ +
976	2.90E-05	forward	4220240	4220267	CGTTTTTATTAATTATCGTAATTTCTTT AAAATATATTCATTAAATGAATAATTAT ++ ++++ +++++ ++++ + +++
977	7.30E-05	reverse	4220523	4220550	TTGTTTATTGATGTCTTGAATTTTAACT ATAATTATTCATTTAATGAATATATTTT + ++++++ ++ ++ +++++ +++ +
978	2.20E-05	reverse	4233552	4233579	CAATTAATACATAGCACGATTGATTAAA ATAATTATTCATTTAATGAATATATTTT ++++ +++++++ ++ ++ ++ ++ ++
979	7.70E-06	reverse	4233735	4233762	TTTTATTTTAAGTTTATGATTTTTATTG ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++ ++++ + +++++
980	1.70E-05	forward	4238266	4238293	ACAAAACATACACAAAAAATATAGATCT AAAATATATTCATTAAATGAATAATTAT + +++++++ +++ +++ +++++ ++ +
981	5.20E-05	forward	4240410	4240437	ATCCAAAATTGATAAAAACAATACTATT AAAATATATTCATTAAATGAATAATTAT ++ ++ +++ ++ +++ ++++ ++++
					ACGAAAAAATCATGCAATAAATATGTTT

982	9.10E-06	forward	4248901	4248928	AAAATATATTCATTAAATGAATAATTAT + +++ + +++++ +++++++++ +++
983	4.60E-06	reverse	4249554	4249581	AATAACATTATAAAAATGATTGATACAT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++++ ++ ++ ++
984	6.80E-05	reverse	4249641	4249668	AAAATACTTAATATTGTTAATAAAAACT ATAATTATTCATTTAATGAATATATTTT +++++ +++++++ ++ ++++ ++ +
985	1.60E-05	forward	4249823	4249850	CGATTTTATTAACAGATTTAATACGAAT AAAATATATTCATTAAATGAATAATTAT +++ ++++ ++ + ++++++ +++
986	2.30E-05	reverse	4258465	4258492	TAAATAATATATATGGTAAATCTATTGA ATAATTATTCATTTAATGAATATATTTT ++++ ++++++++ ++ +++ ++++ +
987	8.80E-05	reverse	4258518	4258545	ATAATTATTGCAAAAATAGATTTGTTTA ATAATTATTCATTTAATGAATATATTTT +++++++++ + +++ ++ + ++++
988	5.60E-05	reverse	4258588	4258615	TGTGTTTTTAATTGTGCAAATAAATGAT ATAATTATTCATTTAATGAATATATTTT + ++ ++++++ + ++++ ++ ++
989	2.40E-05	reverse	4258703	4258730	GCTATTTTTCATTTCGCGATTAATAGTA ATAATTATTCATTTAATGAATATATTTT + ++++ +++++++++ ++ ++ ++ ++
990	5.00E-05	reverse	4259359	4259386	CATTATATAAAAGGACCCAATATTTATT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + +++++++ ++
991	7.00E-05	forward	4259477	4259504	GTTTATCATTGGCCTTAACAAAGTTAAC AAAATATATTCATTAAATGAATAATTAT + ++ ++++ + ++ ++ ++++++
992	5.90E-05	forward	4266820	4266847	TGATTTTGTTAACTAAATCAATAAATGC AAAATATATTCATTAAATGAATAATTAT + +++ + ++ +++++++ +++++++ +
993	7.30E-06	forward	4267211	4267238	TCATAATAAACGTAAAATTAATGTATCC AAAATATATTCATTAAATGAATAATTAT + ++++++ + + ++++++++++++ +
994	4.40E-05	reverse	4273181	4273208	TGTTTCATTAATTTTGTGAACTATATCA ATAATTATTCATTTAATGAATATATTTT ++++++++++++ +++++ +++ +
995	2.90E-06	reverse	4273322	4273349	AAATTAATTTTGAATATCAATGAATTAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ + ++ ++++ +++++
996	1.30E-05	forward	4279728	4279755	GGCTAACATTCATGATTCTAAAACAAAT AAAATATATTCATTAAATGAATAATTAT ++++++++++++ +++ + ++++
997	5.00E-05	forward	4280078	4280105	TGCTTAAATTGGCATTATTAAAATTAAC AAAATATATTCATTAAATGAATAATTAT + +++ +++ + ++++++ ++++++
998	3.00E-05	reverse	4280529	4280556	ATTAAAATTCGTTTTATACATATTACAG ATAATTATTCATTTAATGAATATATTTT +++++ ++++ +++ ++ ++++++ +
999	7.30E-05	reverse	4280813	4280840	CTATATCTATAAAATATTTATGTATTTT ATAATTATTCATTTAATGAATATATTTT

999	7.30E-05	reverse	4280813	4280840	+++++ ++++ + ++ +++++++++
1000	1.80E-05	reverse	4292492	4292519	GAAGTCATTCATATGAAAAATATAAAAT ATAATTATTCATTTAATGAATATATTTT +++ ++++++++++ + +++++++ ++
1001	6.10E-05	forward	4302139	4302166	GTCTCAAATAGATTAGAAAAATGCCAGC AAAATATATTCATTAAATGAATAATTAT + + + ++ ++++ + +++++ + +
1002	4.20E-05	reverse	4302495	4302522	ATGGCTATTTTCTTGATGAATAAAAATA ATAATTATTCATTTAATGAATATATTTT ++ +++++ ++ +++++++ ++ ++
1003	1.40E-07	reverse	4302559	4302586	TTATTTATTAATTGGCTGTATATATTTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ +++++++++
1004	2.40E-07	reverse	4304632	4304659	TTTATCATTTATGTCGTAAATATGTAAT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ +++++ + ++
1005	5.40E-05	forward	4307333	4307360	TAATATTATTGGTGGTCAGAAAATATTC AAAATATATTCATTAAATGAATAATTAT +++++ ++++ ++ + +++ ++++++
1006	2.60E-07	forward	4311095	4311122	AAATAAAATTTATAAAGTTTATTTTATT AAAATATATTCATTAAATGAATAATTAT ++++++ +++ ++ ++ +++++ +++++
1007	8.80E-05	reverse	4311147	4311174	ATTTTATTTCATTTAATTAGTTTAAAAA ATAATTATTCATTTAATGAATATATTTT +++++ ++++++++++ + + +++ ++
1008	6.60E-07	reverse	4311312	4311339	TAATTCATTAACATCACAAATGTTTTTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++++ ++++++++++
1009	4.20E-05	reverse	4324927	4324954	CTATTTATTATTTAAGATAATGTTAATG ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ ++ +++++++ +
1010	1.20E-05	reverse	4324969	4324996	TTTTTAATTCACATGATATTTTTATCTT ATAATTATTCATTTAATGAATATATTTT ++++ +++++ ++ ++ + +++ ++
1011	4.10E-05	reverse	4325061	4325088	AAATTATTTCTTGCAGTAATTATAAAAG ATAATTATTCATTTAATGAATATATTTT +++++ +++ + +++ + +++++ +
1012	9.40E-05	reverse	4335315	4335342	ATATTTTTACCGTCCATCATTAATTCAT ATAATTATTCATTTAATGAATATATTTT ++++++ +++ + +++ + ++ ++ ++
1013	1.70E-05	reverse	4335522	4335549	CGTAACATATACATCATTAATGAAACGA ATAATTATTCATTTAATGAATATATTTT +++++++++ +++++ ++++ ++ +
1014	2.90E-05	reverse	4335818	4335845	GATAATATTATTTTCACAATTTAATAAC ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++++ + + ++ +
1015	1.30E-05	forward	4336017	4336044	GTTATATAATTGTATGATGAATATAAAC AAAATATATTCATTAAATGAATAATTAT + +++++ + + ++++++++++++
1016	7.30E-05	reverse	4336086	4336113	ATAGTAATTTCTCATGTACATATTTTTT ATAATTATTCATTTAATGAATATATTTT +++ + ++++ + ++ +++++++++

1017	9.90E-06	forward	4338620	4338647	GAAAAACAAACATTTTTGAAATATTTAG AAAATATATTCATTAAATGAATAATTAT +++++++ ++++ + +++++++++
1018	3.70E-05	reverse	4338653	4338680	TAAACAATACGTTATGTGATTATTTTAA ATAATTATTCATTTAATGAATATATTTT +++ ++++ ++ ++++ ++++++++
1019	7.80E-05	reverse	4347291	4347318	TTTTGCATTACGGTAATAATTATTACTT ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++ + +++++ ++
1020	8.80E-05	forward	4350686	4350713	TAAGATCATTGATGTATGATATGAATTT AAAATATATTCATTAAATGAATAATTAT +++ + ++++ +++ + +++++++++
1021	6.10E-05	forward	4350944	4350971	CTAAAATATTAATTTTTTATGTGATTGG AAAATATATTCATTAAATGAATAATTAT +++++++++ +++ + +++ +++++
1022	1.60E-05	forward	4358299	4358326	TGGTTAAATTTATGTAATAAAAATTATG AAAATATATTCATTAAATGAATAATTAT + +++ +++ +++ ++++++ +++++
1023	3.30E-07	forward	4359336	4359363	AACTTTTATTTACCATATTAATGTCAAT AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ ++ ++++++++++ +++
1024	2.20E-05	reverse	4360034	4360061	ATTTACATATTATTGGTGAATGCAAGAC ATAATTATTCATTTAATGAATATATTTT +++++++++ ++ +++++++ ++ +
1025	5.90E-05	reverse	4371814	4371841	CGCATTATTAATTGCATGAATGATTGCT ATAATTATTCATTTAATGAATATATTTT +++++++++ ++++++++ ++ +
1026	7.00E-05	forward	4372280	4372307	TCAATTAAATAATTAATTTTAATTTATA AAAATATATTCATTAAATGAATAATTAT + +++ + + +++++ ++++ ++++
1027	1.70E-05	forward	4372390	4372417	GTTAATTATTGGTGTTAGCTATATAAAA AAAATATATTCATTAAATGAATAATTAT + ++ ++++ ++ ++ ++++++++
1028	8.30E-05	reverse	4398374	4398401	GTTTCTATTTATTTGGTGAATGGTATTA ATAATTATTCATTTAATGAATATATTTT ++++ +++++++++ +++++++ +++++
1029	5.90E-05	reverse	4402390	4402417	TTTTCTATAAGGATAATGAATGAATTCG ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++++++++ +++
1030	8.80E-09	forward	4408105	4408132	TGCAAATATTCATTTTATTAATATTTAA AAAATATATTCATTAAATGAATAATTAT + ++++++++++ ++++++++++++
1031	1.90E-07	reverse	4408237	4408264	GCATTAATTATTAAAATGAATGATTATG ATAATTATTCATTTAATGAATATATTTT + +++ ++++ ++ ++++++++ ++ +
1032	9.40E-05	reverse	4416496	4416523	TGATTTTTTTAGATGATATTTGAAATAG ATAATTATTCATTTAATGAATATATTTT ++++ ++++ ++ ++ ++ ++++
1033	1.70E-05	reverse	4417806	4417833	AATTCAATTAACTAAATGAATTTAAATG ATAATTATTCATTTAATGAATATATTTT ++++ +++++ + +++++++ +++ +

1034	9.10E-05	reverse	4418120	4418147	GTTATTATTAAAGGCACGATTAAAACCA ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ ++ ++ ++ +
1035	8.60E-05	reverse	4419308	4419335	ATTGTAATTGCACTGGCTTATATGTTCT ATAATTATTCATTTAATGAATATATTTT +++ + +++ + + ++++ ++ +
1036	1.40E-05	reverse	4422864	4422891	TCTGATTTAATTTTAATCAATGATAAAG ATAATTATTCATTTAATGAATATATTTT + ++ +++ ++++++ ++++ ++ +
1037	4.90E-05	reverse	4425137	4425164	ATTGTATTTCTGGGCGTGAATATTATCT ATAATTATTCATTTAATGAATATATTTT +++ + +++ ++++++++++ +
1038	1.20E-05	forward	4425402	4425429	GATAAATATGCAGGAAATGAATAAATAG AAAATATATTCATTAAATGAATAATTAT + ++++++ ++ ++++++++++++++
1039	4.20E-05	forward	4435584	4435611	TATAAATAAAAAGAGATTGTATTTAAAG AAAATATATTCATTAAATGAATAATTAT ++ +++++ + + +++++ ++++
1040	6.10E-05	forward	4435795	4435822	TACAAAAACACATTCAAACAATTTTTTT AAAATATATTCATTAAATGAATAATTAT ++ +++ + ++++ ++ +++ +++++
1041	4.10E-05	reverse	4436700	4436727	AATTATTTTTGCAGAATTTATGTTATTG ATAATTATTCATTTAATGAATATATTTT ++++++ +++ + +++ ++++++++
1042	7.00E-05	forward	4437332	4437359	GAGTTTTAATCATATGTGCTATTTATCG AAAATATATTCATTAAATGAATAATTAT + ++ ++ ++++ +++ +++
1043	3.00E-05	reverse	4437400	4437427	CAAATCATATGAAAAATGAATGCTTATA ATAATTATTCATTTAATGAATATATTTT +++++++++ + ++++++++ ++ ++
1044	6.40E-05	forward	4453607	4453634	ACAATAAATTCACCTAACGTTTTCATAA AAAATATATTCATTAAATGAATAATTAT + ++++ ++++++ ++ ++ + +++
1045	5.30E-06	forward	4474017	4474044	AAATAATAATCAGGAGTTAAATAATCTA AAAATATATTCATTAAATGAATAATTAT ++++++++ +++ ++ ++++++++ +
1046	4.60E-06	forward	4474089	4474116	AAATAATATACAGGGGTTAAATAATCCT AAAATATATTCATTAAATGAATAATTAT +++++++++ ++ + ++++++++ +
1047	1.10E-05	forward	4475016	4475043	TAATTTAAAATATGATTTAAATGATAAT AAAATATATTCATTAAATGAATAATTAT +++++ + +++++ ++++++++++
1048	8.80E-05	forward	4476389	4476416	ATTATTCATTTGCAAGTCTAAAGCATAA AAAATATATTCATTAAATGAATAATTAT ++ ++ ++++ + + +++ + +++
1049	1.30E-05	reverse	4477553	4477580	TTATTCATAGTTTAACCCAATAAAAATA ATAATTATTCATTTAATGAATATATTTT ++++++++ ++ + ++++ ++ ++
1050	8.70E-06	forward	4477582	4477609	AGTAATTATACATTTGTTTAATACCACT AAAATATATTCATTAAATGAATAATTAT + ++ +++ ++++ ++++++ + +
					GTATATATAAGTTATATCAATGGATTTT

1051	1.80E-05	reverse	4477707	4477734	ATAATTATTCATTTAATGAATATATTTT ++++++++++ ++ ++ ++++ +++++
1052	2.20E-06	reverse	4477825	4477852	TTTCTTATTTGTGTGGTGAATGTGTTGT ATAATTATTCATTTAATGAATATATTTT ++ ++++++ + + ++++++++ ++ +
1053	4.50E-05	reverse	4478500	4478527	GATCAAATATTAAATGCGTATGATAGTT ATAATTATTCATTTAATGAATATATTTT +++ + ++++ + + + +++ ++ ++
1054	5.20E-05	forward	4483665	4483692	CAGTATCATTCAGCGTATTAATGGTTTT AAAATATATTCATTAAATGAATAATTAT + ++ ++++++ ++++++++ ++++
1055	1.60E-05	reverse	4491247	4491274	GCAGTAATATCATTAATAATTATTTGTG ATAATTATTCATTTAATGAATATATTTT + + + ++++ +++++ + +++++ +
1056	3.60E-06	forward	4496096	4496123	TATTTATATACATTCAATAAAAAAGTAA AAAATATATTCATTAAATGAATAATTAT ++ ++++++ ++++ ++++++ ++ ++
1057	2.80E-05	forward	4504405	4504432	ATTAAACATACATCAGTAATGTAAAAAC AAAATATATTCATTAAATGAATAATTAT ++ ++++++ +++ + ++ +++++++
1058	1.30E-05	forward	4518429	4518456	TGATTTTATACAGATATTTTATTCTTTT AAAATATATTCATTAAATGAATAATTAT + +++ +++ ++ + +++++ ++++
1059	3.90E-05	forward	4519623	4519650	CACACATAAACATCGGTGATATTTTTGC AAAATATATTCATTAAATGAATAATTAT + + +++ +++ ++++ +++ +
1060	8.00E-05	reverse	4523005	4523032	GGTGGAATAATGCCGCTGAATTTTTTCA ATAATTATTCATTTAATGAATATATTTT + + ++++ +++++ ++++ +
1061	6.60E-05	reverse	4523725	4523752	GAATTTATTTAATAACTCCATATAACTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + + ++++++ ++
1062	3.50E-05	reverse	4529862	4529889	GTTGAAATAATGAGGATGAATAAAACGC ATAATTATTCATTTAATGAATATATTTT +++ + ++++ + +++++++ ++
1063	3.30E-07	reverse	4530358	4530385	TGATTAATAAACATACTGAATATGTATT ATAATTATTCATTTAATGAATATATTTT +++ +++++ +++ +++++++ + ++
1064	3.80E-05	reverse	4532236	4532263	AAAGGTATTTACGGAGCGAATATTAACA ATAATTATTCATTTAATGAATATATTTT +++ ++++++ ++ ++++++++ +
1065	5.90E-05	forward	4534852	4534879	AAATAATATTGGCTAAAACATTATTTTG AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++++ + ++++++
1066	9.70E-05	reverse	4535860	4535887	AGATGAATATCAGTGCTATATGATTTTT ATAATTATTCATTTAATGAATATATTTT + ++ ++++ + + +++ +++++
1067	9.40E-05	reverse	4537577	4537604	ATTAGCATTTATGTTGTGTAATATTTTT ATAATTATTCATTTAATGAATATATTTT ++++ +++++++ + +++ + +++++
1068	1.10E-05	reverse	4538108	4538135	TTAACTATTTGTTTTATAAATAATTTAT ATAATTATTCATTTAATGAATATATTTT

1068	1.10E-05	reverse	4538108	4538135	+++ +++++ +++ ++ ++++ +++++
1069	7.00E-05	reverse	4538635	4538662	GAATATTAAATTTTGCTGAATTTTTTAT ATAATTATTCATTTAATGAATATATTTT ++++++ ++ +++ +++++ ++++++
1070	7.50E-05	reverse	4538742	4538769	ATTCGTATCCGATTGATAAATATATAAA ATAATTATTCATTTAATGAATATATTTT +++ +++ + ++ ++ +++++++ ++
1071	5.00E-05	reverse	4539904	4539931	AGTGATATTTTATTTTTGTATGATATTT ATAATTATTCATTTAATGAATATATTTT + + ++++++ ++ ++ +++ +++++
1072	2.70E-06	reverse	4540802	4540829	TAAATTATTTCTATTGTAAATTAATTTC ATAATTATTCATTTAATGAATATATTTT +++++++++ +++ ++ +++ ++++
1073	3.40E-05	reverse	4553522	4553549	AATATAATTCCATTCACCATTTTTTAAT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ ++++ + + +++ ++
1074	4.70E-05	reverse	4554588	4554615	ATATTAATAATGCCTGTGAATGGTATTT ATAATTATTCATTTAATGAATATATTTT +++++ ++++ +++++++ +++++
1075	1.90E-05	reverse	4554642	4554669	TATATTATTTACAAACTAATTGTTTCAA ATAATTATTCATTTAATGAATATATTTT ++++++++++ + + + + +++++ ++
1076	3.70E-05	reverse	4561199	4561226	ATTTTTATTTTTTTGAGGATTTTTACTT ATAATTATTCATTTAATGAATATATTTT ++++++++++ +++ + ++ + +++ ++
1077	2.40E-05	forward	4566780	4566807	AGAAAATATACACCTTAAGTGTAATTAA AAAATATATTCATTAAATGAATAATTAT + +++++++ +++ ++ ++ ++++++
1078	5.70E-05	reverse	4569689	4569716	TGTTAAATAAAAGTAATATTTGAATCTG ATAATTATTCATTTAATGAATATATTTT +++ +++++ ++++ ++ ++ +
1079	4.70E-05	forward	4569978	4570005	TTTTTAAATTAAGTTATAAAAATTTTCC AAAATATATTCATTAAATGAATAATTAT ++ +++ +++ + + + +++ +++ +
1080	2.10E-05	forward	4570239	4570266	ATTATAAAATCAGGTGATAAATGAGTTG AAAATATATTCATTAAATGAATAATTAT ++ +++ + +++ + ++++++++ ++
1081	4.50E-05	reverse	4575138	4575165	GTTGATAAAGATTTTGCGAATGAAATTT ATAATTATTCATTTAATGAATATATTTT +++ +++ + ++++ + +++++ +++++
1082	6.40E-06	forward	4578015	4578042	TAAATATATTTATGTGGGTTATGATTGG AAAATATATTCATTAAATGAATAATTAT ++++++++++ +++ ++++++++
1083	5.90E-05	reverse	4578543	4578570	GCAAATTTTGATGTTGTAATTTTTTCAA ATAATTATTCATTTAATGAATATATTTT + ++++ ++ ++ + ++ + + +++ ++
1084	9.40E-05	forward	4579361	4579388	GGCAAATAATCATCTTTTAGATAATTTA AAAATATATTCATTAAATGAATAATTAT +++++ ++++ + ++ +++++++
1085	3.20E-06	forward	4584769	4584796	TGGATTTATTCATCATTGTTATTAATCC AAAATATATTCATTAAATGAATAATTAT + ++ +++++++ ++ ++++ +++ +

1086	8.50E-08	reverse	4589526	4589553	TCACATATTTATATTGTGAATAATTTAT ATAATTATTCATTTAATGAATATATTTT + ++++++++++ +++++++ +++++
1087	1.20E-06	forward	4589566	4589593	TTTTTAAATTCAGAGTGTGAATAAAATT AAAATATATTCATTAAATGAATAATTAT ++ +++ +++++ + ++++++++++
1088	3.20E-05	reverse	4594007	4594034	CGAATCATGTCTACGATGAATGTTTTAA ATAATTATTCATTTAATGAATATATTTT ++++++ + ++ ++++++++++++
1089	1.80E-05	reverse	4601063	4601090	AATATTATCATCATAATGAATTTATTGT ATAATTATTCATTTAATGAATATATTTT ++++++++ + +++++++++ ++++ +
1090	1.00E-09	reverse	4601218	4601245	TTAATTATAAATTAAATGAATGTGATTT ATAATTATTCATTTAATGAATATATTTT ++++++++++++ +++++++++ ++++
1091	1.30E-07	forward	4601400	4601427	ATAATTTATTCGCTTAATCTATTAATTT AAAATATATTCATTAAATGAATAATTAT +++++ +++++ ++ +++ +++ +++++
1092	8.00E-05	reverse	4617618	4617645	GAGAACATATGAAACGTGCATTTATTAT ATAATTATTCATTTAATGAATATATTTT ++ +++++++ + ++++ ++ ++++++
1093	5.20E-05	forward	4625724	4625751	AACTTTTAAATATCAGAAAAATATTCGC AAAATATATTCATTAAATGAATAATTAT ++ ++ ++ ++ + + +++++++ +
1094	5.00E-06	forward	4639120	4639147	TGATATTATTGATAATATTAAAGTTTTC AAAATATATTCATTAAATGAATAATTAT + +++ ++++ ++ +++++++ ++++++

Table S3 continued: Salmonella Typhimurium SL1344 LeuO motif matches

match	p-value	strand	S. Typhimurium SL1344 match start coordinate	S. Typhimurium SL1344 match end coordinate	alignment
1	8.50E-05	forward	11314	11341	TTTTGTAATCTTTTCTTTTTATTACAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++ +++ +++++ ++
2	2.60E-05	forward	11360	11387	CGTTATTTAATTTATTTCATGAATATTT TTTTAATTACGTTTTTTTACAGATATAA +++ +++ +++ ++++++ ++++++
3	7.50E-05	reverse	13634	13661	AAAACAGCGGAAGAGCGTGAAATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + + ++++ + + +++ ++++
4	2.30E-06	forward	14835	14862	TGTTGATATTTTGTTTTTACTGATAAAC TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ +++ +++++++ ++++ +
5	3.00E-05	forward	14883	14910	TTTTGTATACGCTTATTCTTTAAAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++++++ + +++ ++
6	9.00E-05	forward	15780	15807	TGAAATTAGCGCTTTTTTATAAAAATCA TTTTAATTACGTTTTTTTACAGATATAA + + + ++++++++++++ ++++ +

7	3.30E-06	forward	17741	17768	TTTTTATGATTTTTATATCATCTAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++++++ + +++ ++
8	3.70E-05	reverse	23495	23522	AGTTTTATTTACAGGCAAACGATGAACA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ ++ + ++++++++++ +
9	7.10E-06	reverse	24448	24475	TTATATTTAAAAGGAGCTTGAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++ + ++++++++
10	9.60E-05	forward	25002	25029	TTATTCCTGATTCCTTATCGGGATTTTT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ ++ ++ + +++++++
11	5.80E-05	reverse	32563	32590	AAAGAAAAGCACGAACAATAAAAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + + +++ ++ ++ ++ +
12	4.50E-05	reverse	34251	34278	TTATAAAAATGTCAAAAAACTGATATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++ +++++++ ++ +
13	8.50E-05	forward	34492	34519	TGATAATAATGTTAGCATCTACTTTAAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++++ + + ++ +++ ++
14	5.80E-05	forward	34644	34671	TCATTAGTGAGTTGTTTTTTATAAATAA TTTTAATTACGTTTTTTTACAGATATAA + + + ++ +++ ++++ +++++++++
15	4.20E-05	forward	34748	34775	TTTTATGTTTTTTAGCTCATTGGTCTTA TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ +++++ + + +++
16	3.00E-05	forward	35029	35056	CTTTGATTGATTTATTGTTGACATAAAA TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ +++ ++ + + +++ ++
17	3.90E-05	reverse	35321	35348	ATTAATCAGGAGAAACGTATGAATAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++ + ++++ +++ +
18	7.50E-05	forward	37150	37177	TGTTAACCTGCTTCATATAGTTAACTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++ ++ ++ +++ +++
19	4.20E-07	forward	38751	38778	TATTCATCAAGTTTATTAATTATTAAAA TTTTAATTACGTTTTTTTACAGATATAA + +++++++ +++++++ ++ +++ ++
20	6.20E-05	reverse	39603	39630	TTATACGTAGGTGATAGATGTCTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++ + ++ +++ + ++++
21	4.20E-05	reverse	39981	40008	ATAATTTTCTACGATAAAACGATGTTAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++ ++ +++++++++ ++
22	7.50E-05	reverse	43693	43720	TAAAAACGATCCGGGGATGTTAGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ + + ++ + +++++
23	5.10E-05	forward	47450	47477	TTATTATTTCTGGCATGTCTATAAAGAA TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ ++ ++ + ++++++ ++

24	3.00E-05	forward	51893	51920	TATTATTTTTATGTCGTTTCTGAATTTA TTTTAATTACGTTTTTTTTACAGATATAA + +++ ++ + + + ++ + +++++++
25	8.50E-05	reverse	52074	52101	TGAAATAAGAAAAGGAAAACAGTGAAAG TTATATCTGTAAAAAAACGTAATTAAAA + +++++ + +++ ++++++ +++++
26	5.10E-05	forward	59293	59320	TTTTCCTGTTGCCCTTATCTATTACAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++ + +++ ++ + +++++ ++
27	3.00E-05	forward	63479	63506	TCATACTTACTTTTCTTTCAGAAAAAAT TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++++++++ +++ +++ ++
28	6.60E-05	reverse	68259	68286	TTATAAAAATGAGAAAGTAATAAAGTAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++++ + + ++
29	8.80E-07	forward	68489	68516	TTTTAATTAATTTAATTATTTTTATTAA TTTTAATTACGTTTTTTTTACAGATATAA +++++++++ +++ +++ + +++++++
30	6.20E-05	forward	74998	75025	TGTTCTGCCGTTGTTTTCGCGTTAAGAA TTTTAATTACGTTTTTTTTACAGATATAA + +++ + ++ +++++ + ++++ ++
31	3.00E-06	forward	75408	75435	TCTTAATTTGCTGTTTTTGTTGATTTTA TTTTAATTACGTTTTTTTTACAGATATAA + ++++++ + +++++ + +++++++
32	3.40E-07	forward	75453	75480	TTTTTATATTTTTAATATATTGATTTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ ++++ ++ +++ +++++++
33	9.00E-05	forward	75485	75512	TTTTTTTGTCGTTAACTTTCTTGATTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++ + ++++ ++++ + + +++++
34	4.50E-08	forward	75555	75582	TTTTTATCGTTGTTTTTTGTTGTTTTAA TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++++++ ++++++ + +++++++
35	1.30E-06	reverse	75709	75736	TATAATGTGCAAAATAACATAAAAAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ ++++ +++++++ ++ +
36	3.00E-06	reverse	75839	75866	ATTAATATGCAAATAAAGTGAGTGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ +++++++ + ++++ +
37	8.00E-05	forward	75974	76001	TTTTCAATACTTCAATGACCGGTTATCA TTTTAATTACGTTTTTTTTACAGATATAA ++++++ +++++ ++ + +++++ +
38	2.30E-05	reverse	76774	76801	AAAGATATGGACAGAAACGTGGTAATGA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++++ + + +++++++ + + +
39	3.90E-05	forward	80478	80505	TTTTAATATGGCTTAGTTTTTATTAGTT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++++ ++ + +++ ++
40	2.30E-05	forward	82567	82594	TTATTTCAGATTTTTTTTGATTATTTTT TTTTAATTACGTTTTTTTTACAGATATAA ++ + + ++++++++ +++++++
					TATTAATGATTTGTTGATAAGTTTTTAA

41	6.50E-06	forward	88273	88300	TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++ ++ ++ +++++++
42	7.10E-05	forward	88420	88447	TATCAATTGATTGGTTGTGGTTTTTTAA TTTTAATTACGTTTTTTTACAGATATAA + + +++++ ++ ++ + +++++++
43	4.20E-05	reverse	89452	89479	ATTTAATTATCAGGGGATGTTATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ ++ + ++ +++++ +
44	2.80E-05	reverse	92796	92823	GTAAAAGAGTGCGAACAAATGATGATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++ +++++++++ +
45	7.50E-05	reverse	93812	93839	TGAAAAATATGAGCGAGCTGGATAATTA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++++++ +++ +++ + +
46	6.60E-05	reverse	94478	94505	ATCGAAAAATAAAAAGGGGAAATGGATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++++ + + ++++ + +
47	9.00E-05	forward	97965	97992	TGATATTACAGTCATTACAGGCAAATTT TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++ ++ ++ ++++++
48	2.40E-05	reverse	100817	100844	TTTTTTTTGTATCAGGAAATAATTAATG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++ + ++++++++++
49	2.40E-05	forward	106129	106156	TTTTTATACTGCTCTGCCGTGGAATAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + + + ++++ ++
50	9.00E-05	forward	115465	115492	TAATTATAACCTGTTTTAGGGGGTAATA TTTTAATTACGTTTTTTTACAGATATAA + + ++ ++ + ++++ + ++ ++
51	9.10E-06	forward	116446	116473	TTTGAATCATTTTTATTTACAGTTTTTA TTTTAATTACGTTTTTTTACAGATATAA +++ ++++++++++++++++++++++
52	2.30E-05	forward	116494	116521	TGTCAAGTCTGTTTTCATACATTAAGTA TTTTAATTACGTTTTTTTACAGATATAA + + ++ + +++++++ ++++++++ ++
53	4.80E-05	forward	126268	126295	TTTTCAGCTTGCTTTTATCGTAGACAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++ + +++++++ + + ++
54	4.80E-05	reverse	128909	128936	TAAAAATCGTATAAAAAATGCCGGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++++++ +++ +
55	5.10E-05	forward	132973	133000	CGTTCATGATGTCTTTGCGCACTTTAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++ +++ + ++ +++ ++
56	6.50E-06	reverse	134270	134297	TATTAATAATATAAACATTTAATTGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ +++ + +++++ +++
57	7.10E-05	forward	139455	139482	TTTTATTACCTTTCTTTTGTCCGAAATC TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ ++++ + ++ +
58	6.60E-05	forward	157696	157723	TATTATTGGTGCGTTTACCGCGTATAAA TTTTAATTACGTTTTTTTACAGATATAA

58	6.00E-05	forward	157690	157723	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT TTTTAATTACGTTTTTTTACAGATATAA + +++ + ++++ +++ + ++++ ++
59	5.80E-05	forward	161976	162003	TTATTAGCGATTTAATGTCGACATAATT TTTTAATTACGTTTTTTTACAGATATAA ++ + + ++ +++ ++ + + +++ ++
60	2.60E-08	reverse	173101	173128	AAAAATATCCGTATAAAAGTAATTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + +++++++++++++ +
61	2.80E-05	forward	174783	174810	TATTCATAACGCGCTTATTTTGAACGAT TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++ ++ + + +++ ++
62	4.20E-05	forward	174996	175023	TTTTATTTTCCCTTACAGATGTTAATTT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ + +++++ ++ +++++++
63	6.50E-06	forward	188692	188719	TTTTTACCATATTTATCTAAGAATTTAA TTTTAATTACGTTTTTTTACAGATATAA ++++ + +++ +++++ ++ ++++++
64	8.50E-05	forward	188769	188796	TATTTTTCTATTCCGCTCAGATAACATA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++ ++++ ++++ ++
65	1.30E-05	forward	188814	188841	TTTTCCTTCAGTGTGCTCGTTTTTATAC TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ ++ + +++ + ++++++
66	4.50E-05	reverse	189520	189547	TTTTTCCTCTACATAGCTGCGATAATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ ++ +++ +++++ + +
67	9.00E-05	reverse	193608	193635	AAAAACAACTGCGATCGCCCGCTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + ++ ++ ++ ++ ++++++
68	9.60E-05	reverse	202140	202167	TATATAAAGTGTAAGAACGTAAAGTAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ ++ +++++++ + ++
69	5.10E-05	reverse	202375	202402	TACGACCTGGAAAAAGACGTGGTTAACG TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ +++++ +++++ ++++
70	6.60E-05	forward	208918	208945	TTATCTTTGATCCTTTAAGATATTATAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ +++ ++ +++ ++++++
71	6.60E-05	forward	223579	223606	TATTAACCCTTCCTTTTCATCTGGTTAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + +++ +++++++ + ++++
72	6.60E-05	reverse	229690	229717	TTTGCTACGTAAACAGAGTCGGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++++ + + ++ + ++++
73	1.80E-05	reverse	230127	230154	AATTTTCATTATAAAACTTCGATAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ ++++ ++++ + ++
74	9.80E-06	reverse	230156	230183	ATATTATTTTTTATCGAAGTAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++ +++++++ ++++
75	3.60E-06	forward	230253	230280	TTTTAATGAAATTTATACCAAAAATAAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + +++++ + + +++ ++

76	2.00E-05	forward	230327	230354	TTTTATTCATTTTGACATGTTTATTGTT TTTTAATTACGTTTTTTTACAGATATAA +++++ +++++++ ++ + + ++++ ++
77	3.90E-05	reverse	230596	230623	GTATAACTCTGTGTGAATAGCGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ ++ + + ++++
78	2.10E-05	forward	248299	248326	TTATTCTGCGTTTTCTACAGGGATTTAT TTTTAATTACGTTTTTTTTACAGATATAA ++ + + ++++ + ++ +++++++
79	7.70E-06	reverse	268100	268127	GGTAATCTGAAAAAAAAAGGGATTAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++++++++ ++++++ +
80	3.00E-05	forward	301413	301440	TGTTTCTTTGTTTATTTCGTTAATTAAA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ +++ ++++ + +++ ++
81	5.80E-05	forward	301503	301530	TGTCATTTGTTTTTTTACACGTAACTCT TTTTAATTACGTTTTTTTTACAGATATAA + + + ++++++++++ +++ +++ + +
82	3.90E-05	forward	304353	304380	TTTTTATACATCCTGTGAAGTAAAAAAA TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ ++ + + + +++ ++
83	1.60E-06	reverse	316802	316829	ATCTATAAACAAAAAGATATAGATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++++ + +++ +++++
84	3.20E-05	reverse	316842	316869	TAAGTAAAACTTAATAAGGATATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + ++ ++ + ++ ++++
85	1.10E-05	forward	317391	317418	TTTTATTGTTTTGATTTTAAAGGAATTT TTTTAATTACGTTTTTTTTACAGATATAA +++++ + +++ +++++ ++ +++++
86	8.00E-05	reverse	318279	318306	TTAGTATACAAAGATGATGTCGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ ++++ + ++ ++++++
87	6.20E-05	reverse	323684	323711	AAATATACCTATATTAACAAAGATAAAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ ++++ + ++++
88	2.10E-05	forward	329573	329600	TATTAATCAAATTTCTATAAAATGCAAT TTTTAATTACGTTTTTTTTACAGATATAA + +++++++ +++ + ++ + + ++
89	8.50E-05	reverse	329617	329644	TAATAAAAATAAAATCATAATATTGTTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ + + +++ +
90	9.60E-05	forward	329681	329708	TTATGTGCTAATTTTTGTGTTTTTATTT TTTTAATTACGTTTTTTTTACAGATATAA ++ + + +++++ + + +++++++
91	5.80E-05	reverse	339516	339543	GGAATTGTGTTAACGAATGCAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++ ++ ++ ++++ +++++
92	9.10E-06	reverse	339739	339766	TTAAAATAATGAATCCATTATATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++++ + +++++++

93	6.00E-06	reverse	339775	339802	AAATAAAACCAAAAGGATTGAAACAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ + ++ ++++
94	1.20E-05	forward	340768	340795	TTTTCATCACGCGCTTTAACCGGACATA TTTTAATTACGTTTTTTTACAGATATAA ++++++++++++ +++ ++ + + ++
95	4.80E-05	forward	341197	341224	TTATAATTGCTTTTCTGTTTCGGAAAAC TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++++++ + + + + ++ +
96	1.30E-05	reverse	341570	341597	AAATACCAATAAGTACAAGCTGTTATTA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++++++ ++++ +++ +
97	2.10E-05	forward	363930	363957	TAATCATAGATTGTGTTAATAGATTGAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++ + ++ +++++++ ++
98	2.50E-06	forward	365501	365528	TTTTATTCATTTCCATTCCTGTTTTAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++++ ++++ + ++++ ++
99	9.60E-05	reverse	365536	365563	TATGATTTGTCGGGAAACCCGGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ + ++++ ++ + ++++
100	9.60E-05	forward	372043	372070	TTATCTGCCGGTTTATTTTCGCAAAATA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + ++++++++ + +++ ++
101	9.00E-05	forward	377290	377317	TATTACCGGATTTCTCACCTGGTTTTAA TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++ ++ + + +++++++
102	9.00E-05	forward	377986	378013	TTTTCTTTGATGGAGTCTATATAACTAT TTTTAATTACGTTTTTTTACAGATATAA +++++ +++ + + +++++++ +++
103	3.90E-05	forward	378265	378292	TAATAATACGTTCTACACATTAATTGAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ +++ +++ +++ ++
104	1.60E-05	forward	383315	383342	TATTTACCGTTTTAATCTGTAGTTTTTT TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++++++ ++ + +++++++++
105	4.20E-05	reverse	386070	386097	AGCAAACTGCGCAGAACGGGTATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ + + ++ + +++++++
106	9.60E-05	reverse	388880	388907	AATGAAATACATAAACAAAACGGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + +++ +++ ++++
107	9.10E-06	reverse	389212	389239	ATAAAAACAAAAGATAACGGTGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++ ++++ + ++++
108	7.50E-05	forward	390601	390628	TGATTATTATACTTATTTAGGCATCGCT TTTTAATTACGTTTTTTTACAGATATAA + + +++++ ++++++++ ++ +
109	3.00E-05	reverse	391288	391315	AAATAAGACTCAGAGAGCATATTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ ++++++ ++++++
					AACGATCTGAAAAACAAAGCTTATAAAA

110	7.50E-05	reverse	391680	391707	TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ ++++ +++++ +++++
111	7.10E-05	reverse	401143	401170	TTCTTTGCGTGAGATAATCCCCATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++ ++ + +++++
112	8.50E-05	reverse	405158	405185	ATTTTAAAGTAAAGTCGGGGCGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++ + + + ++++
113	9.60E-05	forward	407899	407926	TATTCTTAACTTTCAGCTACGCGTATTT TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++++ + +++ +++++
114	2.30E-05	forward	407959	407986	TTTTTTTGTTTTGCCGTTATTTTTATAA TTTTAATTACGTTTTTTTACAGATATAA ++++ + +++ ++++ +++++++
115	5.50E-05	reverse	408213	408240	TATTTTACACGAAGTGACTATATATAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++ ++ +++
116	7.50E-05	reverse	415119	415146	TGATAAAGCGATGATGGCGTAATAATAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ + ++ +++++++ + ++
117	6.60E-05	reverse	415329	415356	AGATTTAATCAAAAAGGCGGATGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ +++++ +++ + ++++
118	3.20E-05	forward	424382	424409	TTTATTTTGTTTTTCTTTAATCTATATT TTTTAATTACGTTTTTTTACAGATATAA +++ ++++++++ ++++ +++ ++
119	2.30E-05	forward	428269	428296	TATTAACCGTTTGCCCTCCGAATATTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++++ +++ + ++++++
120	2.80E-06	forward	428613	428640	TTTTCTTTAACTGTATGCGCTGATAAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ +++ + +++ + + ++++ ++
121	2.60E-05	reverse	431877	431904	TTATAACAGCAAGGAACCGGGCAAAACA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ ++ ++ + ++ +
122	1.30E-05	forward	436407	436434	TGATTATTGTTTTTTGATGGTTTATTAT TTTTAATTACGTTTTTTTACAGATATAA + + ++++++++++ + +++++++
123	8.00E-05	reverse	437609	437636	TTCTAAATGTTCCCAAAAATAATGAATG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++++ ++++++++++++
124	9.00E-05	forward	450965	450992	TTTTAATGCCTTTTCCGCCAGTAGAACA TTTTAATTACGTTTTTTTACAGATATAA +++++++ +++++ + + ++ + +
125	9.60E-05	forward	452435	452462	TTTTGTTCGCATGATTAGCCATAACTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++ + ++ +++++ +++
126	3.70E-05	reverse	458676	458703	AGATTTGCGTCCAGTGACGCGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ + +++++++ ++++
127	8.00E-05	reverse	465841	465868	TTTTTTGCGAAAAGTCGAGCACGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA

127	8.00E-05	reverse	403841	403868	++ +++ + +++ +++++ ++++
128	6.60E-05	forward	473324	473351	TTTTATCGCTTTCATCGTATAAATTTTT TTTTAATTACGTTTTTTTACAGATATAA +++++ +++ ++ ++++ ++++++
129	9.00E-05	reverse	490857	490884	TGCTTTACCTAAAGTAACCCTGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++++ +++ + ++++
130	2.40E-05	forward	491540	491567	CTTTAATGCGGCTTATTTCTATGAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++++++++ +++ +++++
131	3.00E-05	forward	492176	492203	TTTTAAAAAAGCTTATGAGAAAAAATTA TTTTAATTACGTTTTTTTACAGATATAA ++++++ + ++++++ + ++++++
132	8.50E-05	reverse	497858	497885	AATGTAAAAATAAAACAATTACTTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ ++ ++ ++++ +
133	8.50E-05	reverse	497928	497955	TTTAATCGGCTGAATCGTGTAAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ + ++++ +++++
134	3.00E-05	reverse	500489	500516	GATGATACGTGAGCAAATAGAAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ +++++ +++ + ++ ++++
135	7.50E-05	reverse	526785	526812	TGATTTCTGCGACATAGGGGTAGTAACA TTATATCTGTAAAAAAACGTAATTAAAA + +++++++ ++ + ++ + + +++ +
136	3.20E-05	reverse	527459	527486	GATATTATCGCAATAGAAGCAATAATAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ ++++ +++++++ + ++
137	9.60E-05	forward	531954	531981	TGTTATCCGCGGTAATTTCCTGTACTTT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++ + ++++ + +++ +++
138	2.40E-05	forward	545391	545418	TTATAATACCTTCTCTTTTCTGGATTTC TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ +++ + +++ + + ++++
139	2.60E-05	reverse	554019	554046	TTCGAATTCCGTAACGGCGAGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + ++ +++ ++++++++
140	3.20E-05	forward	559855	559882	TGTTCAAGACTTTCTTTCACGCGTTTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++++ ++++++ +++++
141	3.70E-05	reverse	569100	569127	TGATTTTTAGTAGCACAAATCATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ ++ + ++++ +++++++
142	3.20E-05	forward	575305	575332	TTTTCCTATGATTTTTAAGTAGTTTTAC TTTTAATTACGTTTTTTTACAGATATAA +++++ + +++++ ++++++++
143	8.50E-05	forward	582067	582094	TTTTTATACTGGGGCTATCAACATTTAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++ + + + ++++++
144	9.00E-05	reverse	586136	586163	ATCTTATTCCGTGGGAACGCATTAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + + ++++++ + ++ +

145	5.80E-05	reverse	587364	587391	GGCAAAATCCAACATAGCTAAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++ + +++ ++++++++
146	6.60E-05	reverse	587925	587952	AATATTTCCCGCAATGACATAGAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ +++++ +++++
147	9.60E-05	reverse	598837	598864	ATAAAATTATTAAACGCGCCAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ +++ +++++++++
148	3.60E-06	forward	601301	601328	TTTTATTCATATTGATTCCTTTTAATAT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++ ++ ++++ + +++++++
149	9.60E-05	reverse	610203	610230	TTCAATATCCAGAATGACAAGGTCAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + ++ +++ + + ++ +
150	9.00E-05	forward	610331	610358	TTACAATAGGGTGTTCGTCCATAATGAT TTTTAATTACGTTTTTTTACAGATATAA ++ +++ + ++ +++ + ++++++ ++
151	1.80E-05	reverse	610739	610766	GTTTTTAAGTATAAAAATAATATGAAAG TTATATCTGTAAAAAAACGTAATTAAAA + ++++ +++ +++++ + ++++++
152	3.00E-05	reverse	610911	610938	TATTTACATTTAATGGAAGTGAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++++ + ++
153	9.00E-05	forward	612546	612573	TTTTCTTTATCGCATTTATTACAAATAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++ +++ ++ ++++++
154	1.10E-05	reverse	614575	614602	TTATATATCCATAATGATTTTATATAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + ++ + + ++ +++
155	5.10E-05	forward	615345	615372	TTTATTTCTATTCATTATAAAGAAATAT TTTTAATTACGTTTTTTTACAGATATAA +++ ++ ++ ++ ++ ++++++++
156	3.30E-06	forward	617321	617348	TATTAATTGATCGTTGTTACCGATCAAT TTTTAATTACGTTTTTTTACAGATATAA + +++++++ ++ ++ ++++ +++ ++
157	8.00E-05	reverse	617910	617937	AAAAAACGACAGCTAAAAGGGATGTAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + ++++++ ++++ +++
158	3.20E-05	reverse	618797	618824	GAATTCACGGACAAAAGCTTTGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + + + ++++++ + ++++++
159	7.50E-05	reverse	631146	631173	AACGATAAACAAATTGCGTTAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ +++++++ +
160	5.80E-05	forward	631301	631328	TAATAATAATTTGATTATTAGTTTATAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++ ++ + +++++++
161	7.10E-05	forward	636374	636401	TTTAAATGTTATTTATTTTCAATAAATT TTTTAATTACGTTTTTTTACAGATATAA +++ +++ + +++++++ ++ +++ ++

162	3.20E-05	reverse	637776	637803	TATTCATCCGACATAAACACCATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + + ++++++++ ++ ++++
163	3.40E-05	reverse	643463	643490	AAAATTCATAATAAACACAGGGTTATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ +++ + +++ ++
164	7.50E-05	forward	648915	648942	TATTAATTCTTTTAACATAAGTGATACA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ ++++ ++ ++ + ++ +
165	4.80E-05	reverse	649452	649479	TTCTCCGTATGTCATGGATCAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++++ + ++ +++++++++
166	4.50E-05	reverse	652982	653009	TTAAAACCGCGGCGAGACTCAGTAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + + ++ ++ + + ++
167	5.50E-05	reverse	655559	655586	AGCGAACTAAAAATAGAAATAATAATCA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ +++++ +++++++ + +
168	9.00E-05	forward	660911	660938	TTTTTATGGGCTCTATATCGCCAAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + + +++ + +++ ++
169	6.20E-05	reverse	667481	667508	ATAAACATATACATTAAATTTATATTAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++++ ++ +++ + ++ ++
170	4.20E-05	reverse	667606	667633	ATAGAATTGTATGGGAGCAATGGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ ++++ + ++++ +++++
171	5.80E-05	reverse	668528	668555	TATTTAAACTAAAATACCACAGTTATGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++ + ++++ +++ +
172	6.60E-05	reverse	669509	669536	TAATATCAAAGCGAAAAGAGTATTAATG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + +++++ + +++++
173	9.00E-05	forward	672528	672555	TTTAACTGGAATTTTTCTGTTTTTTTAT TTTTAATTACGTTTTTTTACAGATATAA +++ + + + +++++ + + +++++++
174	6.20E-05	reverse	676004	676031	TAAGCAGCCGGAGGACAAGTAATGGAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ + +++ + ++++++++ +++
175	3.70E-05	reverse	686411	686438	GTCGATTTCGGTATAACAGTGATTAATA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + + ++++ +++++++++ +
176	7.10E-05	forward	687197	687224	TGATAACTTTTTCTTTTCAGTCAGAGTA TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++ ++++++ + + ++
177	3.00E-05	forward	687297	687324	TTTTGATTTATTTCACAAAGCGTTAGAT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ +++ ++ + ++++ ++
178	7.50E-05	forward	689111	689138	TTTTCTTTATTCCTTCCGAAAGTGAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++++ +++ + +++ + ++
					TTAATTTATTGTTATTTTATTGTTTTAT

179	4.20E-05	forward	691439	691466	TTTTAATTACGTTTTTTTACAGATATAA ++ + ++++ ++++++ +++++++
180	7.50E-05	forward	691594	691621	TTTTATTCAGGTTAATGTTGTTATTATC TTTTAATTACGTTTTTTTACAGATATAA +++++ +++ +++ ++ + +++ +
181	6.20E-05	forward	691711	691738	TATTCCTTCAGTCTCTGCGGCGGATAAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++ + + + + ++ ++
182	7.50E-05	reverse	692244	692271	TAAAAAGTCTTAAAAAACAATAAGTAGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++++++++ + + + +
183	4.70E-06	forward	692297	692324	TATTTATCACTTTTTCGCAAAGTTCGAC TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++++++ ++ ++++ +
184	5.50E-06	forward	693924	693951	TTATTATGATGTTTTTTTACGCAAAGCT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ ++++++++++ +++ +
185	2.10E-05	forward	696546	696573	TTAAAATTACTCTTATGAATGTATTTTT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++++++ ++ +++++++
186	9.60E-05	forward	698254	698281	TTTTGCTTTCTGTTTCACGGCCTTTATA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++ ++++ + +++ ++
187	9.00E-05	reverse	699110	699137	TACGACGTCCGTGATGAAATTAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + + ++ ++++ + ++++
188	2.40E-05	reverse	711694	711721	AATATAAAACAAGGGAAAATGATTATGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++++++++ +
189	1.10E-05	reverse	714337	714364	TTTTTACCTTACAGGGAAATGATAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ + +++++++ ++ +
190	3.70E-05	reverse	715955	715982	AACGATCCAAGAGGTGAAGTGATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ ++++++++++ +
191	4.50E-05	forward	723514	723541	TATTCACCAAATTTATTAGGTATTAATT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ ++++++ +++ ++
192	5.50E-05	reverse	723879	723906	ATCAATCAACAAGGGAGAATGGGTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++++ ++ ++
193	8.50E-05	reverse	737767	737794	TTCGAACCAGGGAATGCCGGTATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++ ++ ++ ++++
194	8.50E-05	reverse	737877	737904	TTCGAACCAGGGAATGCCGGTATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++ ++ ++ ++++
195	6.00E-06	forward	745729	745756	TGTTCAGCGCGGTTATTCGTATGTTTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++ ++++++ +++ +++++
196	8.00E-05	reverse	752225	752252	AATTTTCCGTAGGGAAGGGTGAGAAAGA TTATATCTGTAAAAAAACGTAATTAAAA

196	8.00E-05	reverse	752225	752252	TTTTTATTGGTGAAGAGATTATAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ + +++ ++++ ++ +
197	9.00E-05	reverse	765083	765110	AAAAATCAGTAAATTAGCTTTATTTTAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ +++ + +++ +
198	3.00E-05	forward	765642	765669	TTTTTATATCCTCTATAAAATATAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + + +++ + ++++++
199	4.70E-06	forward	772201	772228	TTTTCATTTCGCGCACGTCGATTTTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++ ++ + ++++++++
200	8.00E-05	reverse	773710	773737	TAAATCTGCTGGAAAAGCGTGAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++ ++++++++++ + ++
201	6.20E-05	forward	781021	781048	TTATGATGGATTTGTTTTGTGAAAAGAA TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ + +++ ++++ + +++ ++
202	1.20E-07	reverse	781723	781750	ATATAACAATAAAAAAACTAAGGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++++++ + +++++
203	8.00E-05	forward	784258	784285	TTATACTCGGATTACTGAGCACAAATAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++ +++ ++ + ++ ++++++
204	5.50E-05	reverse	784606	784633	TTTAACCGTCTTGAAAAATTAAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++++++ +++ ++++
205	1.10E-05	reverse	785595	785622	TTTTATTGGTGAAGAGATTATAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++ + + + ++++
206	1.70E-07	forward	786033	786060	TATTTATAAATTCTCTATAGAGAAAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ + ++ + + ++ +++++ ++
207	9.60E-05	reverse	786654	786681	GATAAATAGTATGTAAATATTATAGAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ +++ +++++ ++ ++ +++
208	8.50E-05	reverse	787364	787391	TTATTACTTTATGGAGATGCTCAGGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ + + + ++ + +++
209	9.10E-06	forward	788226	788253	TTTTAATATTCTTATTGCAGTATTTATA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + ++ ++ ++ +++ ++
210	3.90E-06	forward	788281	788308	TTATAATAGCGTTACCCCAGATAATATA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ +++++ + ++ +++++ ++
211	3.70E-05	forward	788517	788544	TTAACATCACTTTTTTTGCGGGTTAATA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++++++++ ++++ ++
212	3.40E-05	reverse	789231	789258	TTAGATACTTTTGATAATGAAAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + ++ ++ + ++ ++++
213	8.50E-05	forward	789962	789989	TATTAATGGTTTGTTTACGGCAGTCAAA TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++ +++ + + ++

214	1.70E-06	reverse	790003	790030	TTAAATCTGCAAAAAAAGAGATGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ +++++++ + + ++++
215	4.80E-05	reverse	790066	790093	ATAAAAAATTCAATAAAAAATCTGAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++++++ ++++ +
216	7.10E-06	forward	790142	790169	TTTTAATTATATGACTATGATAATCTTA TTTTAATTACGTTTTTTTTACAGATATAA ++++++++++ + + + ++ +++
217	8.00E-05	forward	790748	790775	TTTTGATGTTATTTATTACAGGAATTCT TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ + ++++++ +++++ +
218	3.00E-05	forward	790782	790809	CTTTCCTCGTGTTTATTCGATAAAAATT TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++++++++++++ +++ ++
219	6.60E-05	forward	790854	790881	TTTTTCTGGCCTTTTTTTATTCATTACC TTTTAATTACGTTTTTTTTACAGATATAA ++++ + ++ +++++++++ +++
220	3.20E-05	forward	791090	791117	TTTTCATAAAATTTCTTATATTGAAAAT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ + +++ ++ + ++ ++
221	2.30E-05	reverse	791448	791475	ATCGATCTGGAAATACAAATGGAGAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++++ +++++ +++ +
222	9.00E-05	reverse	792053	792080	TGAATACTTTTCAGAAGAACATGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ + + +++++++ +++++
223	3.40E-05	reverse	792379	792406	TTAAAACGGCCTGTGAAGGTTATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ ++ ++ ++ ++++
224	6.60E-05	reverse	793467	793494	TGTTACCCGGATAGAGACGCGGGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + + + + + +++++ +++++
225	3.70E-05	reverse	795296	795323	AATAATGAGGATAAGAAAAAAGGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++ ++++ + +++++
226	2.40E-05	forward	795433	795460	TTTTCATGCCGTCAGTGTGCATTTCATT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++ + + +++++ ++
227	8.00E-05	reverse	808355	808382	TAATAAGTATTGATAACCTGCAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++++ + + ++++
228	2.10E-05	reverse	808510	808537	TACTCTTTGCAAAAACAAAAAGTTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + ++ +++++ +++ + ++++ +
229	3.00E-07	reverse	808550	808577	TGCATTCAATGAATAAACATTATTAACA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++++++++++++ +++++ +
230	2.40E-05	reverse	808606	808633	ATTTAAATGTTGGAAAAGAGCATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++++ +++++ + ++ ++++

231	5.80E-05	forward	824152	824179	TATTACCAATATTAATGTATTATTATTT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++ ++ +++ ++++++
232	8.50E-05	forward	825509	825536	TCATAACAAGCTTTTTTTACAAGTTTTT TTTTAATTACGTTTTTTTACAGATATAA + +++ + ++++++++++ +++++
233	7.50E-05	reverse	827612	827639	TTAAACAGAAACAAAAGCAGTAAGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + + + +++++++ + +++ +
234	2.80E-05	forward	828086	828113	TATTGATTTTTCTTATTGGTGGAGTTAT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ ++++++++ + ++ ++++
235	5.80E-05	forward	840626	840653	TATCAATCGCGTGATCGTGCAGAATTTC TTTTAATTACGTTTTTTTACAGATATAA + + ++++++++ ++ + ++++++++
236	7.50E-05	reverse	844603	844630	GGAGTTGCCCATGTTAGAGTTATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + ++ +++++ +++++++
237	3.20E-05	forward	847623	847650	TTTTCATTGACCCTCCCTGCGCTTCTAT TTTTAATTACGTTTTTTTACAGATATAA +++++++++ + + + + + ++ +++
238	8.00E-05	forward	852283	852310	TTATATCAGCGGGTATACAGAGGAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ +++ +++ ++ ++ ++ ++
239	8.00E-05	forward	853690	853717	TTTCCATTCCATCATGGTGCATTATGAA TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ + + + + ++++++ ++
240	1.20E-05	reverse	869634	869661	ATATATCAATGTAAAAGTGTGATTTTCA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++ +++++ ++++++ +
241	1.30E-05	forward	871389	871416	TAATTTTCACCCTCATTTAAAGAAATAA TTTTAATTACGTTTTTTTACAGATATAA + + ++++ ++ +++++ ++++++++
242	7.50E-05	reverse	871879	871906	ATTTTAAGGTGGATGCGCATGATTAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ ++ ++++++++++
243	4.20E-07	forward	892165	892192	TATTCATCCCGTTTTCAAACTGAATAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ +++++++ ++ ++++ ++
244	8.00E-05	reverse	893138	893165	TAATTCCGGTACATTAGGGCAAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++ ++ ++ ++++ ++ +
245	5.50E-05	forward	905280	905307	TTTTGATAACGGTCCGCTGTTTAAAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ +++ + + + ++++ ++
246	1.20E-05	reverse	906213	906240	TTAAATGAAAGAAGAGGATCTATCATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ + ++ + ++ + ++
247	4.80E-05	reverse	908040	908067	GATTATTTGCGTAGTAAAGGGATTGAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ ++ + + ++++ ++++ +++
					TTAAAATAAGGTTAATGCAAGTTTAAAA

248	8.50E-05	forward	909516	909543	TTTTAATTACGTTTTTTTACAGATATAA ++ +++ + +++ ++ ++ ++++ ++
249	8.00E-05	forward	909619	909646	TATTCCTTTCGTTCAGCCACTTTTCATT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++++ + +++ +++ ++
250	5.50E-05	forward	925284	925311	TTTTATCTTTGTTATTGTAACAATAAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ ++ ++ +++ ++
251	6.50E-06	reverse	926703	926730	TTAAAAAACGAAGAAAAAGTAATTTAAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++++++++++ ++
252	2.40E-05	reverse	927283	927310	AAATTTATTAGCCAACATGTTAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + ++ + ++ + +++++
253	7.70E-06	reverse	928058	928085	ATATCACCGTAAGATAGATGAAGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ ++++++ +++ ++ ++++
254	4.20E-05	reverse	929349	929376	TTTTTCATCTGAGGGAGAAAGCTAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ ++++ ++++ + + ++ +
255	6.60E-05	reverse	931126	931153	TTTTTACAGGATAGTGAAACACAAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + + +++++ ++ +
256	9.60E-05	reverse	931816	931843	TTATATAGTGTAAGGAAATGGCTTAACA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ +++ + ++++ +
257	9.00E-05	forward	932112	932139	TGTTATGCTCCCTTCTTCACTGATAGCA TTTTAATTACGTTTTTTTACAGATATAA + +++ + + +++ +++++ ++++ +
258	2.60E-05	forward	936810	936837	TTAATATTACTCTTTTTTTCGCTATTTA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++++++++ + ++++++
259	9.00E-05	forward	943704	943731	TTACGCTACTGTTTTTATCATGAATTAA TTTTAATTACGTTTTTTTACAGATATAA ++ + +++++++ + +++++++
260	2.40E-05	reverse	947240	947267	TTTAACGCGGAAGAAGACGCGCAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + +++++ +++++ ++++
261	2.40E-05	forward	947347	947374	TTTTTATGCTGCTATTAACCTTTATTTA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ ++ + +++++++
262	6.20E-05	reverse	947409	947436	TTATCACATAGACAAAACCTGCATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ ++ +++++ ++ +++++
263	8.00E-05	forward	951017	951044	TGTTAATGTTGGTGATTTACTCGTTTAA TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++ + ++++++ +++++
264	1.60E-05	forward	952269	952296	TTTTAATTCTGTTTCTGCTGTTTATTCC TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++++ + + +++++
265	9.60E-05	reverse	952443	952470	AACTTTCCGCAAAAACAGCCGATTTACA TTATATCTGTAAAAAAACGTAATTAAAA

265	9.00E-05	reverse	952443	952470	++ ++++ + +++++ + +++++ + +
266	3.20E-05	forward	953524	953551	TTATCCCTTAACTATTTCATAAAAATAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + ++ +++++++ ++++++
267	4.50E-05	forward	953572	953599	TTTAATTCAATTGGTTGTATTTATATAT TTTTAATTACGTTTTTTTACAGATATAA +++ + +++ ++ ++ +++ +++++++
268	9.00E-05	forward	954141	954168	TGTTATTAGTTTTATTTGGCCGTTATAC TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++++ +++ + ++++++
269	3.20E-05	forward	957920	957947	TTTTCATGATGTCACTCCCGTAATCTTA TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++++ + + ++ +++
270	6.20E-05	reverse	958018	958045	TAAATATTTTAAAATGGATAAAAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++++ ++ ++ ++ +
271	4.50E-05	reverse	961147	961174	AACATAGCACAAAATAGCAGGAGGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ ++++ ++ +++ +
272	6.60E-05	reverse	961779	961806	TGATTTCCTTATAGGCGATCGAGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ ++ + ++ +++ ++++
273	6.20E-05	forward	964154	964181	TTTTTCTCATTTTTCTGTGATTTGTTCT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++++ + + ++ ++ +
274	7.50E-05	forward	975100	975127	TTTAGATACGGTTTACTTTCTGGTTAAA TTTTAATTACGTTTTTTTACAGATATAA +++ ++ ++++++++ + + ++ ++
275	2.60E-05	forward	991737	991764	TTTTACTTTTGTTACTGATTTGTAAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ ++++ + + ++++ ++
276	5.10E-05	forward	1011293	1011320	TTTTAATATTACTACCCAATTTTTTAAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + ++ + ++ ++++ ++
277	6.60E-05	reverse	1011511	1011538	TAAGAAGAATATATAGATCACATAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ +++ +++ + ++ + ++
278	1.10E-05	forward	1014996	1015023	TTTTGATTATCCTAATAAAAATAAATTT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++ ++ ++ + ++++++++
279	5.50E-05	reverse	1020617	1020644	GAAGATTAGTATGAAAAATAAATCATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ ++++++ +++ + +
280	2.30E-05	forward	1047440	1047467	TATTTATTACCCTCATTGGTTTTTTTAT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++++ ++ +++ + +++++++
281	2.40E-05	reverse	1047630	1047657	AATAATATGTAAACAAATGTTATTTTTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++++ +++ ++ +++ +
282	7.10E-06	forward	1047719	1047746	TTTTATATCCATGATTTTATTGAATTTA TTTTAATTACGTTTTTTTACAGATATAA +++++ + + + ++++++ +++++++

283	4.20E-05	forward	1047954	1047981	TTGTAATTAATTTTATTTACTTATTGAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++ ++++++++++ ++++ ++
284	8.60E-09	reverse	1050388	1050415	TTATTTCAATAAATAAACTTTAACAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++++++ + + ++++
285	9.00E-05	reverse	1051167	1051194	GTTATTTTGTTGAAAAAATGCAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ +++ ++++++ + +++++
286	5.50E-06	reverse	1052308	1052335	ATTATATTAAGAAAGGGCTCAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ ++++ ++ ++++ ++++
287	7.50E-05	forward	1061029	1061056	TATTAACTGCTTTCAGGTTCATTTCGAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++++ + + +++++ ++
288	1.40E-05	forward	1061254	1061281	TGTTTTTTACTTCTTTGCCTTCATCAAT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++ +++ + + ++ ++
289	7.10E-05	reverse	1061620	1061647	TTTTTTGAGGTCGTTAATTAGATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ ++ +++ ++++
290	5.50E-05	forward	1065466	1065493	TTACAACTATGCTTATTCTGGTAAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ ++++++++++ ++++ ++
291	1.20E-05	forward	1070255	1070282	TCTTAATTGTGTTCTTTATGAATAAATA TTTTAATTACGTTTTTTTACAGATATAA + ++++++++++ +++ + +++ ++
292	3.20E-05	reverse	1071208	1071235	TTATTACATGGAATTAACATTCTATAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ +++++ + +++
293	2.30E-06	reverse	1085970	1085997	TAATCAAAAAAAGGAAATGTTATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + +++ +++ ++ +++++++
294	5.10E-06	forward	1099283	1099310	TTTTTTGCACATTCATTTCTTTTAATAA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ ++ ++++ + +++++++
295	5.50E-05	reverse	1099341	1099368	TAATATATTATTAAACGCTTGATTATCA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ +++ ++ ++++++ +
296	2.10E-05	forward	1099553	1099580	TATTTTGAATGTGTCTTAACATAATATA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++ + ++ +++++++ ++
297	2.70E-07	reverse	1099652	1099679	TAATTATTATTTATGAAATTAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++ +++ +++++++++
298	3.60E-06	forward	1099745	1099772	TTTTTATTGTATTGTCGCATTTTTCTTA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++ ++ ++ +++ +++ +++
299	3.00E-06	forward	1100048	1100075	TAATAACTGTTTGTATATACAGTATTTT TTTTAATTACGTTTTTTTACAGATATAA + +++ +++++ +++ ++++++++++

300	3.00E-08	reverse	1100323	1100350	TAAAAACTATGAGTACATATTATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++++++++ + ++ ++ ++++
301	6.20E-05	reverse	1107642	1107669	AAAAACCCGTGAACGGCAAAAAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++++ ++ ++ +++++
302	5.80E-05	reverse	1111669	1111696	ATTGAAGGCGGAAAAACGACGATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++++ +++++ ++++
303	5.80E-05	forward	1113347	1113374	TGTTCAGTATGTGATTGCCAATAACAAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++++ ++ + ++++ ++
304	3.60E-06	reverse	1121941	1121968	ATAAAAAAGCAAATTAAGGTAATGATTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++ ++ +++++++ +
305	3.40E-05	reverse	1122139	1122166	GTATAACGGCGAATCAACGGACTTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++ ++++ + ++++ +
306	7.10E-05	reverse	1124335	1124362	TAAATAGTCTGACCCCAGGCGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ + +++++ ++++
307	1.90E-06	reverse	1131271	1131298	TGTAATTAATAAAGGAGAATAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ +++++ ++++++++ ++++
308	5.10E-05	reverse	1132525	1132552	ATTAATCTGTAGGTGACCGGAAGCATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++ ++ + ++ ++ + ++
309	9.60E-05	forward	1133129	1133156	TTTTGACAAATCTTCCCCCTGGAAATCT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + ++++ + + + +++++ +
310	5.10E-05	forward	1133223	1133250	TGTATATTATGTTTACTCATCAGTTTTA TTTTAATTACGTTTTTTTACAGATATAA + + ++++++++++++++ +++++
311	3.90E-05	reverse	1133934	1133961	GAAAATTTACTTAAAGAAAAAATAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++ +++ +++ +++ + ++
312	5.80E-05	reverse	1133998	1134025	GAATAAATGCGCGTAGATGGCGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + +++ + + + ++++
313	2.80E-05	reverse	1137677	1137704	GTTATCCTGCGAATAGGCTTGATGAAAG TTATATCTGTAAAAAAACGTAATTAAAA + ++ +++ +++++ ++ ++++++++
314	8.00E-05	forward	1143653	1143680	TGTTTCTTATTTGTTGTTCAATTGAATA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++ ++ ++ +++ + ++
315	1.10E-05	reverse	1152638	1152665	TAAGAAGAGTAAAAACATGATGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ +++++++ + + ++++
316	3.90E-05	reverse	1153713	1153740	ATTTTTATGCACAATAAAGGTAAGATGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ + ++ ++++ + ++ +
					TATTTATTTTATGCTCTTATTTTGTTTA

317	2.00E-05	forward	1154511	1154538	TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + + ++++++ ++ ++++
318	2.30E-06	reverse	1155936	1155963	AAAAATAGACGAGAAAATATCATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++++ ++ ++ ++++
319	1.70E-05	forward	1162291	1162318	TTTTAAGCGCTTTGATTTTCCCAAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++++++ ++++ + ++++++
320	9.00E-05	forward	1163706	1163733	CTTTGATAGGTTTCGTTCAGCTTTTTAT TTTTAATTACGTTTTTTTACAGATATAA +++ ++ + +++ ++++ +++++++
321	4.20E-05	forward	1168055	1168082	TTTTCTCTGCGGTAGTTAACACTTTTAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++ + ++ +++ ++++++
322	6.20E-05	forward	1170154	1170181	CGTTAATTATTCCATTTTAACCTTATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++++++ +++++ ++++++
323	9.10E-06	reverse	1173950	1173977	TTCAATTTCCGAAAAAACGGAATATAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++++++ +++ + +
324	8.00E-05	forward	1175477	1175504	TTTTATTAACTGCTTCCGGCATAAAGAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + +++ +++ ++++++ ++
325	8.00E-05	forward	1175684	1175711	TATTTTTAGCGCTTGGTCACATTTTGTC TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++++++ +++++++++ +
326	6.20E-05	forward	1176346	1176373	TTTTAATAAACCTGCCAAAGATTATTTT TTTTAATTACGTTTTTTTACAGATATAA +++++++ + ++ + + ++++++++
327	1.30E-05	reverse	1176719	1176746	TTTTATTCCCACGAAGGGATAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ + ++++ +++++
328	3.20E-05	reverse	1176927	1176954	ATTTATTAATAAAATAATTTTTTAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++ ++ + + ++ +
329	4.50E-05	reverse	1177076	1177103	GAATATGCTGATAGAACCAGAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + + ++ ++ ++++++ +
330	5.50E-05	reverse	1180818	1180845	TTAGTTTGGGGGATACATATAAGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ + + +++ + ++++ ++++
331	3.00E-05	forward	1183939	1183966	TATTGCTTTCTTTTGTTCCGGGAACATT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ +++++ +++ +++ ++
332	3.00E-05	forward	1186272	1186299	TTATATTATTGTTTTTGCGGCTTAAATT TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + +++++++ + ++++ ++
333	4.20E-05	forward	1186733	1186760	TATTAAAATGTTGTTTTTGGGTTTTTTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ +++++ +++++++
334	4.80E-05	reverse	1186810	1186837	ATTTAAAAAATCATACAAATTATAATAA TTATATCTGTAAAAAAACGTAATTAAAA

334	4.80E-05	reverse	1186810	1186837	++ ++++ + +++ ++++ ++ + ++
335	2.40E-05	forward	1187341	1187368	TTATGATCTGGCTCGTTCAGAGTATAAT TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ +++ ++++ +++++ ++
336	4.30E-06	forward	1188220	1188247	TATTAATTTAGCGTCTGCGCTAATAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ ++ + + + + +++ ++
337	3.90E-06	forward	1202227	1202254	TGATATTTATTTTTATTTCAATAATTTT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++++++++ ++++++++
338	9.00E-05	reverse	1204176	1204203	ATTTCTCTTTTTAAGAATTATATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ + ++ ++ +++++ +
339	5.50E-05	forward	1228112	1228139	TTTATCACCCGCTTACTCACAGTTTTTT TTTTAATTACGTTTTTTTACAGATATAA +++ + ++++++++++++++++++
340	7.70E-06	reverse	1228161	1228188	TTAATAACCAGCAAAACCGCAGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++ ++++ ++++++
341	5.50E-05	reverse	1236258	1236285	AGCACTATCGAAGAACGCGTTAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + +++ +++++ ++++ + +++++
342	5.80E-05	reverse	1253444	1253471	TTTATAAATTATATAACGATCATTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ ++++ ++ ++++ ++
343	4.50E-05	reverse	1254919	1254946	ATTTTTATAAAAGAGGAAATAAGAATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ ++++ ++++++ + +
344	8.00E-05	forward	1256020	1256047	TATTTTCGACGTCATTGTACAAATAGTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++ ++ ++++ +++ ++
345	5.50E-05	forward	1266996	1267023	TATTAATCTCACTTATACTGGAGTAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ + +++++ + ++ ++
346	2.30E-05	forward	1282708	1282735	TTTTTTGAAAGTGCCTTACCAGATTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ ++ +++++++++
347	5.80E-05	reverse	1282978	1283005	GAATATCTGGAAACAGATAAGGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ +++ + + + + ++++
348	3.40E-05	reverse	1283665	1283692	TTTTTTGAATTAAATGATAATGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++ + + + ++++
349	5.10E-05	forward	1284066	1284093	TTATTATCAGTCTCTTTAAAAGAGCTTT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++++ +++ +++ + +++ +++
350	2.80E-05	reverse	1284548	1284575	AGAAATGAGTAAAAAAAATGAAGAATGA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++++++++++ ++ + +
351	1.20E-05	forward	1285682	1285709	TTTTGCTGGATTTTTTGCATGTATTTCT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + ++++++ +++ +++++ +

352	4.50E-05	forward	1285933	1285960	TTATGCTGGTTTTATTTCGGATTTTTAC TTTTAATTACGTTTTTTTACAGATATAA ++ + + +++++ ++++ +++++++
353	5.50E-05	forward	1286897	1286924	TTATCATTACCCGTGCATGAATAAAGAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++++++ + + + + +++++ ++
354	7.10E-05	forward	1289112	1289139	TATTATTTTATCCACTTTAGTTATTACT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++ ++++ ++++ +
355	3.70E-05	forward	1290318	1290345	TTTTATTACTTGTGAGTTGTAGATTTTT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++ + + ++ +++++++++
356	9.00E-05	reverse	1291270	1291297	TTAATTCCCTGAAGAACGGGAGATAAAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ ++ + + ++++
357	7.50E-05	reverse	1292595	1292622	TGAATATTACGGGTAAACACACTGAAGA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ + +++++++++ ++++ +
358	7.10E-05	forward	1297620	1297647	TCTTCAGTCATTTTTTGCGGCTGATTAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++++++ + + +++++
359	3.00E-05	reverse	1303401	1303428	ATATTTCTGGCAATCAATATAAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ +++ ++ ++++ ++ +
360	3.20E-05	reverse	1306481	1306508	ATAAAACTGTAATAAAAAATCATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++++ +++++++ ++ ++++
361	1.80E-05	forward	1306592	1306619	TTTTTCTCACTCCAGTTTAAACGAATAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++ ++++ + +++++
362	8.40E-06	forward	1307846	1307873	TTATGTTTCCTTTTTTGTGCAATTTATT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ +++++++ + ++ +++ ++
363	6.20E-05	forward	1308984	1309011	TATTCATAAAACTTATGATTGGGTATTA TTTTAATTACGTTTTTTTACAGATATAA + +++++ + +++++ + + +++++
364	3.70E-05	forward	1315401	1315428	TTTTAATCGCTTTCGCCAACAGGGTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++++++++++ + ++++ ++++
365	2.80E-05	forward	1315787	1315814	TTATTTTTGCTTTGATTAATAATAATTT TTTTAATTACGTTTTTTTACAGATATAA ++ + +++++++ +++ +++ ++++++
366	3.40E-05	reverse	1316122	1316149	TAAATCATAGAAATAGACATAATGTTTA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++++ ++++++++ +
367	1.60E-05	reverse	1316151	1316178	TTAAATCAACGTAATAACGGAATTTAAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + ++ ++++ ++++ ++
368	2.80E-06	reverse	1323359	1323386	ATTGAAAAGGAAATGAAATCAGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ +++ ++ ++++++

369	8.40E-06	reverse	1337235	1337262	GAATTACTCCGAAGGCGCGGTAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++ +++ + +++++
370	4.80E-05	forward	1338839	1338866	TTTTTAGCCACCGATTATGCGGAAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + + ++ + + +++++++
371	9.00E-05	forward	1348985	1349012	TTTTTAATTTTTCCCGTCAAAGAGTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + +++ +++ +++ ++++
372	2.00E-05	forward	1349644	1349671	TATTATTCTCTCTATTATGGGGATTATT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++++ ++ + ++++ ++
373	9.60E-05	reverse	1351950	1351977	TATGATCTCTGCCAGCGAATGATTGATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ + ++++++++ + +
374	1.70E-06	reverse	1360107	1360134	TTAAATTTATGTATGCGCACAGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++ ++ +++++ ++++++
375	1.40E-05	reverse	1362912	1362939	TAATCCCCGGAAAGTGAAGGAATTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + + +++ +++ ++++++ +
376	4.30E-06	reverse	1362954	1362981	ATCTTTATTTAAAGAAGTGCGATGTAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ ++++ +++ ++++++ +++
377	4.30E-06	reverse	1365366	1365393	ATTATTAAGGAAGAAAAAGTGAACAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++++++++++ ++ +
378	6.60E-05	reverse	1366010	1366037	TTTATTCACCGGAATGGCGCCGTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ ++++ + ++++
379	9.60E-05	reverse	1367168	1367195	AGATATAACTAACCAAACTGGTGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ +++ ++++ + +++++
380	8.50E-05	reverse	1367244	1367271	TGATTTCTGTAGAATGCATCAGGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++++++ ++ + ++ +++++
381	4.80E-05	reverse	1367625	1367652	AGTATACAGTTAAATAAAACTATGGAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ +++ +++++ +++ +++
382	2.30E-05	reverse	1367903	1367930	TTTTCTTTGTGTGTAAAGATAAGAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + ++++ +++++ ++++ ++ +
383	7.10E-06	reverse	1368154	1368181	TTATAAGCATATAGAGCCTTTAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ + + + + + ++++
384	4.20E-05	reverse	1378043	1378070	AATAATGTCTCAATTGATGCAATTAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + +++ + +++++++++
385	5.10E-06	reverse	1384052	1384079	GAATTTCAGGTAAAACAATCGAGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++ ++ +++ +++++
					ATAATTATCTGAAAGCATAAATTAAAAG

386	7.50E-05	reverse	1384310	1384337	TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ +++++ + + + + +++
387	3.60E-06	reverse	1384488	1384515	TAAACAATCTGAAAAAATGAAAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++ ++++++++ + ++ + ++
388	7.10E-05	forward	1390495	1390522	TTTTATCTTTGTTAATTGCGACAATAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ +++ + +++ ++
389	2.60E-05	reverse	1392298	1392325	AAATATAAATACGGTAGTGAGAATAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++ + ++ + ++ +++ +
390	8.50E-05	reverse	1399372	1399399	AAAGTAACTAAAATAAATGCAGATAACA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ +++++++ +++ +++ +
391	8.40E-06	reverse	1401527	1401554	TTATATGAAAAAAGTGATGCTATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ + ++ ++ ++ +
392	6.20E-05	reverse	1401663	1401690	AACAATGCGGCGAAAAAAGTTAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++++++ + ++++
393	1.60E-05	reverse	1408474	1408501	ATTGATGGCGGAAAGAATAGAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++ ++ + ++ +++++
394	9.60E-05	forward	1416514	1416541	TATTACACAAACTTTTTTATGTTGAGAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ +++++++++ ++ + ++
395	4.80E-05	forward	1416544	1416571	TTTTTTTGATGGGAATGCACTTATTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ + +++ ++ +++ +++++++
396	5.10E-06	forward	1416748	1416775	TTTTAAACAAATTAATTCACACAACAAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ ++ +++++++ ++ ++
397	1.40E-06	reverse	1418436	1418463	TGAAATTTACAAAAAAGGAAAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ +++++++ + ++++++++
398	3.40E-05	forward	1421269	1421296	TTTTGCTTCTATTCCCGTAAAGGATAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + ++ + ++ ++ ++ ++
399	5.10E-05	reverse	1421517	1421544	TATTACCCTGGCGTAAGCAGGATAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + +++++++ +++ + ++
400	8.00E-05	forward	1422124	1422151	TTATTTTCTTGTTTGCCCAGACGAATAA TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ +++++ + ++ + +++++
401	8.50E-05	reverse	1430664	1430691	TAAAACGTATGACAAAACCGACAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++++ +++++ + ++ +
402	9.10E-06	forward	1431933	1431960	TATTCATGATTCCCCCTTATTGAAAGTA TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++ +++++ ++++ ++
403	2.10E-06	forward	1432027	1432054	TTTTGTCTAAGTTTTCGCGGAGATTTTT TTTTAATTACGTTTTTTTACAGATATAA

403	2.10E-06	forward	1432027	1432054	++++ ++ ++++++ + ++++++++
404	4.50E-05	reverse	1436365	1436392	ATAATTATTGTTGTTAATAAAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ ++ + ++ +++++
405	9.60E-05	forward	1436641	1436668	TAATAAATAATTTTTCAAATTGTAAGTT TTTTAATTACGTTTTTTTTACAGATATAA + +++ ++ ++++++ ++ ++++ ++
406	6.60E-05	reverse	1442124	1442151	TTTATCAATGATGATGACGTCATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + ++ ++++ +++++ +
407	3.40E-05	reverse	1444359	1444386	AAATAACAATCAATAGGTATGATGATGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++++ + +++++++ +
408	9.00E-05	reverse	1446368	1446395	TTTATTTTAAGGAAAAGCATTATGGATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ + ++++++++ +++ + +
409	3.90E-05	forward	1448447	1448474	TTTACTTCACTTCCTCTGACGGAAATTA TTTTAATTACGTTTTTTTTACAGATATAA +++ + ++++++ +++ ++ +++++++
410	2.60E-05	reverse	1455515	1455542	AAAATACAGCGTAAACCTGATAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + +++ + + +++++
411	7.10E-06	forward	1456889	1456916	TTTTCAGCCAGTTCTTGTGTGTTATTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++++ + +++ ++ + + +++++++
412	9.00E-05	reverse	1456992	1457019	TTTATTATTTGACCAGCAATTTTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++ + +++ ++++++
413	3.00E-05	forward	1457732	1457759	TCTTATCTTTGCCTTTTTCTTTTATTAT TTTTAATTACGTTTTTTTTACAGATATAA + +++ + +++ +++++ + +++++++
414	2.80E-05	reverse	1457898	1457925	TATTATAAGATTAGAAAAGATCTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++++ + ++++
415	6.20E-05	reverse	1465516	1465543	TAAAATCAGCGTATAGCCTTTCTGGAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + +++ + + ++ +++
416	1.40E-05	forward	1467242	1467269	TCTTCACTAAATCTTTATAGGCATAATA TTTTAATTACGTTTTTTTTACAGATATAA + ++++ ++ + +++ ++ +++ ++
417	1.20E-06	forward	1467603	1467630	TTTTTTTACGTTTTTTTTGCTGGTTTTA TTTTAATTACGTTTTTTTTACAGATATAA ++++ + ++++++++ + + +++++
418	5.50E-05	reverse	1467968	1467995	AAATCACTGCGCGGCAACCCGCTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++++ + + +++ ++ ++++++
419	5.50E-05	reverse	1469127	1469154	TTCAACGTCGATGACGACAGGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + ++ +++ +++ ++++
420	6.60E-05	reverse	1472243	1472270	TATTCTGAGCGCCGAACAGTCATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + + + ++ +++ +++++++

421	8.00E-05	forward	1484809	1484836	TTTACCTCTTTTTTACGCCCCGTATTAA TTTTAATTACGTTTTTTTACAGATATAA +++ + ++ +++++++ + + +++++++
422	9.60E-05	forward	1486103	1486130	TCTTCATTTTTTCATCAATAAGATATTT TTTTAATTACGTTTTTTTACAGATATAA + ++++++ +++ ++ ++++++++
423	3.40E-05	forward	1492813	1492840	TTTTTTTGCCGGTTTTTGACTTTTCTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ +++++ ++ +++ +++
424	5.20E-07	forward	1507651	1507678	TTTTCTTTTCATTTTTTTATCCTTAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ + +++++++++ +++ ++
425	6.50E-06	forward	1507954	1507981	TTTTAATTTAACTTTCTTGAGCGAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++++++ ++ ++
426	7.50E-05	reverse	1510794	1510821	AAAAATGAAATTGGAAGAATAATTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++++++++++ +
427	1.60E-05	forward	1511486	1511513	TTTTTTCGCATCTTGTTTATAGATAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++ ++++++++++ ++
428	4.50E-05	reverse	1512219	1512246	TAAATTTAATAAGTTAATTTAATGTTAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++++ ++ +++++ ++
429	8.40E-06	forward	1517233	1517260	TATATATTTCTTTCTTTTGCGGTAAAAA TTTTAATTACGTTTTTTTACAGATATAA + + +++ ++++ ++++ + ++++ ++
430	6.20E-05	forward	1519160	1519187	TTTTGATACCCTCGATTTGGTTTTCATT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + + ++++ +++ ++
431	3.90E-05	reverse	1520899	1520926	TTAATTGTCTCAAATAAGACGTTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + +++ ++ +++ + ++++
432	4.80E-05	forward	1523150	1523177	TGTTGATTCGTCTATTACAGGGTTAACA TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ +++ ++ ++ ++++ +
433	6.60E-05	reverse	1532775	1532802	GTATTTATCCAGAAACGGTTTATCAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ + + ++ ++ +
434	9.80E-06	reverse	1536279	1536306	ATTGATAACTATAACGAAATTATTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ ++ ++++ +++++ +
435	7.50E-05	forward	1536793	1536820	TTTTCATCCTGGTGATACGTGTGAAGAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++ + ++ + + + ++ ++
436	3.40E-05	forward	1536826	1536853	TTTTACTGACGTTATTGTGCATGATACT TTTTAATTACGTTTTTTTACAGATATAA +++++ + +++++ ++ + +++ ++ +
437	3.70E-05	forward	1541324	1541351	TCTTACTCACGTTTGCGAAATAATATAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++++++ + + ++++++

438	5.80E-05	forward	1542443	1542470	TATTCATAACTTTGCCGTGCTGGGATTA TTTTAATTACGTTTTTTTTACAGATATAA + +++++ +++++ + + + + ++++
439	2.00E-05	reverse	1550111	1550138	AAATTCATGTTTGTAAAAACTAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++++ ++++++++ + ++ +
440	2.00E-05	reverse	1550149	1550176	TTAATACGTCAAATAGACGTTATTAAGG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++ ++++ +++++
441	6.20E-05	reverse	1550973	1551000	AAAATAATTCCTAATACAACGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ + ++++++ ++++
442	7.70E-06	reverse	1552113	1552140	AGAAAAAACCGAATAGGCGCAGTTAATA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ +++++ +++++ ++++ +
443	4.80E-05	forward	1554121	1554148	TAATTTTTGCGCGATTTCCGTCATTTTA TTTTAATTACGTTTTTTTTACAGATATAA + + ++++++ ++++ ++++++
444	1.50E-07	forward	1562892	1562919	TTTTCATAACGCTAATTTAAAAATAAAT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++++ +++++ + +++ ++
445	1.40E-05	forward	1564453	1564480	CTTTATTATTGTTAATTTATTCTTTTAT TTTTAATTACGTTTTTTTTACAGATATAA ++++ + ++++ ++++++ ++++++
446	2.00E-05	forward	1571187	1571214	CTTTAATAATGGGTTTATCGGTAATTAA TTTTAATTACGTTTTTTTTACAGATATAA ++++++ +++ +++ + +++++++
447	8.00E-05	forward	1571983	1572010	TATTTATAACATGATGGGATTTTTTTAA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ ++ + + ++ +++++++
448	5.10E-05	reverse	1572168	1572195	TTTACAAACAAGGAGAGCATGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++ + ++ ++++++++++++
449	9.00E-05	forward	1574526	1574553	TTTTAATAGCGTCGATAACCTGATCGTC TTTTAATTACGTTTTTTTTACAGATATAA +++++++ ++++ ++ + +++ +
450	6.20E-05	forward	1580633	1580660	TTTTAATTGCTCTCGCATAATCGTTTCT TTTTAATTACGTTTTTTTTACAGATATAA ++++++++++++ + ++ +++ +
451	5.10E-05	reverse	1581519	1581546	TTCAATGCCGGAATAAGCAAAAGAAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++++++ ++ +++
452	8.50E-05	reverse	1581955	1581982	AAAACAAGACAGAATAGGTTAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + + ++ ++ +++++++++
453	7.10E-05	reverse	1582383	1582410	GTTGTCCAACAGAAAAATACAAACAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + + + + +++++ ++++ ++++
454	4.50E-05	forward	1583596	1583623	TTTTCAAGCCGTTCCCTTAGCTTTTTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++++ ++++ ++++ +++++++
					TTTTTATGTGCTTTATGTTCACTAAAAA

455	4.50E-05	forward	1587322	1587349	TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ +++++ + ++ +++ ++
456	2.10E-05	forward	1588025	1588052	TATTAAGCAATGTTTTTAATAATTCTTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ + +++++ +++ ++ +++
457	9.00E-05	reverse	1591581	1591608	AATAATAAGGAAACAAGATGGATTTTAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++ ++++ ++
458	7.50E-05	forward	1595791	1595818	TTTTCAGCGCGTTTAGGCCTGTTTCATC TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++++++++ + + +++ +
459	8.50E-05	forward	1599923	1599950	TTTTAAATAAACGTTCGCTGATAATGTA TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ + +++ + +++++ ++
460	4.50E-05	forward	1600446	1600473	TTTTGCTTAATTCACTCTGCGGGTTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ ++ + + + + +++++
461	9.80E-06	forward	1600734	1600761	TATTCATTGTTGTTGCTCCAATAATTAT TTTTAATTACGTTTTTTTACAGATATAA + +++++++++ ++ +++ ++++++++
462	9.60E-05	forward	1601747	1601774	TATATTTTATATGTATATTGAGATTTAT TTTTAATTACGTTTTTTTACAGATATAA + + ++++ + +++ + ++++++++
463	4.20E-05	forward	1611574	1611601	CTTTTATCTATTGCCTGTGCGTATTTAA TTTTAATTACGTTTTTTTACAGATATAA +++ +++ ++ + + + +++++++
464	3.90E-05	forward	1615938	1615965	TTTTTTATCTATTCTTTCACTCAATATT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + ++ ++++++ +++ ++
465	3.40E-05	forward	1633045	1633072	CATTAAGCAATTTTCTGTACAGATTAAC TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + ++++++++ +
466	3.90E-05	forward	1633563	1633590	TTTTCAACCTGTGTGGTCAGGCTTATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ + +++ + +++ ++++++
467	9.00E-05	reverse	1633880	1633907	GAATATAAGTAAAGCCGCAATTTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++++ +++ ++++++
468	3.20E-05	forward	1646665	1646692	TTTTCATTATTCGATCTCATTGAGCGCT TTTTAATTACGTTTTTTTACAGATATAA ++++++++++ ++++++ ++ +
469	2.00E-05	forward	1647217	1647244	TTTTCATTTGGTTTTGAGAAGGATCTTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++++ + +++ +++
470	6.20E-05	forward	1648815	1648842	TTTCATTCGTTTTATCTGACATATTTCA TTTTAATTACGTTTTTTTACAGATATAA +++ + +++++++ +++ ++++++++ +
471	7.10E-05	forward	1649104	1649131	CTTTCTTTACGTTACTATGGGAAAAGAT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++++ + + +++ ++
472	6.20E-05	forward	1649253	1649280	TTATCATCACCGTCATGCAGAGGAAATT TTTTAATTACGTTTTTTTACAGATATAA

472	6.20E-05	forward	1649253	1649280	++ +++++++ + ++ ++ ++ ++ ++
473	7.50E-05	reverse	1649866	1649893	TGCTATGTTTAAACGAGCTTACTGAATA TTATATCTGTAAAAAAACGTAATTAAAA + +++ + ++++ +++ ++ ++++ +
474	6.60E-05	forward	1653168	1653195	TTATCACTGCCGTTACCTACTGTATTAT TTTTAATTACGTTTTTTTACAGATATAA ++ +++ +++ ++++ +++ +++++++
475	8.50E-05	reverse	1660643	1660670	AAAATACCGTTTATGAAAGGACGCAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ ++++ + ++ +
476	1.70E-05	forward	1666144	1666171	TCTTCAAAATGCCATTTTGTTGATTTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++ ++++ + +++++++
477	5.50E-05	forward	1674462	1674489	TTTTCACAACATTCATTCCAGAAAATTC TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ ++ ++++ +++++
478	5.50E-05	reverse	1676412	1676439	TTTTTAATACCCAAAAGCGTCATCATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ ++++++++ ++ + +
479	5.80E-05	reverse	1677206	1677233	AAAGAAAATATAAAAAAATATATAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ +++++++ ++ + ++
480	8.50E-05	reverse	1678017	1678044	TTTTATTGGCGACGAAAAACTGTTAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ ++++++ +++++
481	5.10E-06	reverse	1679975	1680002	TAATTAACGGCTGTGAACACGATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ ++++++++++++
482	3.90E-06	forward	1680112	1680139	TATTAATCGTATTTATATTTATTACATA TTTTAATTACGTTTTTTTACAGATATAA + ++++++++ +++++ + +++++ ++
483	6.20E-05	reverse	1681326	1681353	TATTTTACCTTCAAAAATAAGAAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++++ + ++ ++ +
484	7.10E-06	forward	1681951	1681978	TTATCAATGAGTTTTCTTCTGTATTAAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++ ++ ++++++++ + ++++ ++
485	9.80E-06	forward	1683642	1683669	TTTTTATTTAGCGTTGATTAAGATTTTA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ ++ ++ + ++++++++
486	3.70E-05	forward	1684272	1684299	TTTTACACCCATTATTTCACCCTATTTA TTTTAATTACGTTTTTTTACAGATATAA +++++ + + ++ ++++++ ++++++
487	1.80E-05	reverse	1684887	1684914	TTTAAACCACTGGTAAACTATATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++++ +++++ +
488	7.50E-05	reverse	1686492	1686519	ATTTTATTTGTCATACAAATAAGTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ ++++++ ++ ++
489	1.20E-05	forward	1696812	1696839	TTATTTTTGATTTTTTGTAAGATAATTT TTTTAATTACGTTTTTTTTACAGATATAA ++ + +++ ++++++ ++ ++++++

490	5.80E-07	forward	1709073	1709100	TCTTCAATACTTTTCTTCACGGTATTAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++++++ +++++ +++++++
491	3.90E-05	forward	1711116	1711143	TATTCATCAAACTTATACTTGAATTATT TTTTAATTACGTTTTTTTACAGATATAA + +++++++ +++++ + + +++ ++
492	3.90E-05	forward	1712014	1712041	TATCGTTAAATTTTTCTCATTTATTGAT TTTTAATTACGTTTTTTTACAGATATAA + + + + ++++++++++ ++++ ++
493	3.90E-05	reverse	1721119	1721146	TTTATTCAGAAACGTCAAGCAATTTAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ ++++++++ +++
494	2.00E-05	forward	1722202	1722229	TATTAATATAGTTAACGTTTTGAAAGAA TTTTAATTACGTTTTTTTACAGATATAA + +++++ +++ ++ + + ++++ ++
495	4.50E-05	forward	1726494	1726521	TTTTAAGGTTGTTACTTAATATTGAATA TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++++ ++ +++++ + ++
496	5.80E-07	reverse	1726603	1726630	TTATATTTATACAAAAAGTTCATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++ +++++ + +++++ +
497	9.00E-05	forward	1729285	1729312	TTTTCTGATGGTTTTCTGAGGTATTGTA TTTTAATTACGTTTTTTTACAGATATAA +++++ +++++++ + ++++ ++
498	9.50E-08	reverse	1737230	1737257	ATAGATATGTGCAAAAACGTTATTATCA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++++++ ++++++++ ++++ +
499	6.60E-05	reverse	1741999	1742026	ATAGAAGCGTATGAGGAAGCGCAGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ +++ ++ +++++ +++ +
500	1.10E-05	reverse	1746594	1746621	ATCAATCAATAAAAACGATCAATATATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++++ ++ ++++ + +
501	2.80E-05	reverse	1746636	1746663	AAAACAATATATGTTAACTTCATGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++++++ ++ +++ + ++++ ++
502	4.50E-05	reverse	1748406	1748433	ATTATAATACACATGCAAACATATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ + ++ +++++ +++++
503	4.80E-05	forward	1750078	1750105	TGTTAACGATCGTTTTTTACTGGATTTA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ ++++++++ + +++++
504	3.30E-06	forward	1755424	1755451	TATTTTTCCCTTCTCTTTTCAGATTAAT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ +++ + +++ ++++++ ++
505	9.00E-05	forward	1782273	1782300	TTTTTTGTGCGTTATTTACGCGGTAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++ +++ + ++ ++
506	8.80E-07	forward	1782345	1782372	TTTTAATAGGGTGTCGACACGGTTAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + ++ + +++ ++++ ++

507	4.50E-05	forward	1798404	1798431	TGTTAACCAATTCTCTTTTATGGAAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ ++ + +++ + ++ ++
508	4.80E-05	reverse	1798475	1798502	TTTATTCTTTATAATCAATAAGTTGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ ++ ++ ++ + ++ +++
509	8.00E-05	reverse	1798694	1798721	AGTAATGTTGATAATAGTTTGATTAATA TTATATCTGTAAAAAAACGTAATTAAAA + +++ + + ++ ++ +++++++ +
510	4.50E-05	forward	1798740	1798767	TTATATTAGTATTTTTTATCATTTAAAC TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + ++ ++++++ ++++++ +
511	7.50E-05	reverse	1799460	1799487	AAAGAACTTAAAGTAAACAGGAAAATCA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++++ +++++++++ ++ + +
512	4.80E-05	forward	1799628	1799655	TGTTATTTATATGTACTCGTTATGCTAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++ + +++++ + + +++
513	6.20E-05	reverse	1800158	1800185	GGTATCGTGGAAGACAAAGTGATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++ ++++++++++++
514	3.40E-05	forward	1800205	1800232	TATTTACAACGCCTATAAAGATGAAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++++ +++ + ++ ++ ++
515	8.50E-05	reverse	1809084	1809111	GATAATCTGGATGAAGGCCCAATCATTA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ + +++ ++ ++++ + +
516	7.10E-05	reverse	1820857	1820884	ATATAAATCAAAGGAAAAGTCGTCATCA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ +++ ++++++ + + +
517	8.00E-05	forward	1825917	1825944	TTTTACGGAAATTAACTTTTTGTTATTT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++ ++++ + +++++++
518	1.70E-06	reverse	1826006	1826033	GTAAAACTACGTAAAAAACCACTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + ++++++ ++ + ++++
519	5.80E-05	forward	1840255	1840282	TTTAAAAAATCTTTTTTTGAATATAATT TTTTAATTACGTTTTTTTACAGATATAA +++ ++ ++ +++++++ +++++ ++
520	9.60E-05	forward	1840312	1840339	TAATTTTTTACTTTAGATGCAGATAAAT TTTTAATTACGTTTTTTTACAGATATAA + + ++ ++++ + ++++++ ++
521	8.40E-06	reverse	1840614	1840641	TTTAATATGATTAAGGAAATTATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ ++ ++++ +++++ +
522	5.80E-05	reverse	1841348	1841375	AAATCTACCCGAGGTCACTCGCTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ +++ ++ ++ + ++++
523	9.00E-05	reverse	1850334	1850361	TTAATTGTTTAAAAAAGTGTTAAATTTA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++++++ ++ + +
					TTCAATGTGGAGGAAACCGCAAAGAAAA

524	7.70E-06	reverse	1861042	1861069	TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ + ++++ +++++ +++++
525	3.90E-05	forward	1866976	1867003	TTTTCTTTGGATTTTTTCCTTCGTCTTC TTTTAATTACGTTTTTTTTACAGATATAA +++++ +++ +++++++ + + ++
526	8.00E-05	forward	1870598	1870625	TATTTACCGCAGTTACGTAAAGATATTC TTTTAATTACGTTTTTTTTACAGATATAA + ++ + +++ ++++ ++ +++++++
527	1.80E-05	reverse	1889402	1889429	TTTTATTGATGAATAAATCTAAATGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++++++ +++ + +++
528	5.10E-05	reverse	1892949	1892976	GAAAAACCAGAAAAAACAATGCTAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++++ ++++ + + ++
529	4.50E-05	reverse	1893871	1893898	TTTACAGAATGCCTTAAAATAATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + +++ + ++++++++++ +
530	3.40E-05	reverse	1895092	1895119	TAAGTACTGTTAAATAATATTTTAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++++++ +++ ++ ++ + + ++
531	1.80E-05	forward	1909447	1909474	TATCCATTTGATTTTTATATTAAAATAA TTTTAATTACGTTTTTTTTACAGATATAA + + ++++ +++++ +++ ++++++
532	4.80E-05	forward	1910342	1910369	TGTTTATATTTCTTGCTTTCAAAAAATA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ +++++ +++ ++ +++ ++
533	3.70E-05	forward	1910751	1910778	TTTTCATGACGTTCAGAAAAACTACAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++++ + + + ++ ++
534	6.20E-05	forward	1911072	1911099	TAATAATATCGCTTATTACATCTATTTT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ ++++++++ ++++++
535	3.30E-06	reverse	1913036	1913063	ATAAATAAGTTAATTAAATGTATCAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ +++ +++ ++ ++ +
536	9.50E-08	reverse	1913510	1913537	TTATACTTCGAAAAAGACGTTATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++++ ++++ ++ ++++
537	2.10E-05	reverse	1916160	1916187	AAATACCCATGTAGACGAAGGCTTAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++ + + +++ + ++++ +
538	3.70E-05	reverse	1916981	1917008	AAATTTTTATCTAAACATATAAAAAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ +++ + ++++ ++ +
539	4.80E-05	reverse	1920612	1920639	ATTTTTATTTAAGTTAAATATTTTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++++ +++ +++ ++
540	8.50E-05	forward	1922591	1922618	TATTTATTTCATTTTGCGATATTGATTA TTTTAATTACGTTTTTTTTACAGATATAA + ++ +++ + ++++ +++++ ++++
541	7.10E-05	reverse	1922630	1922657	AACAACACACAGAGAACATAAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA

541	7.10E-05	reverse	1922030	1922057	++ ++ + + + + ++ + ++++++++
542	4.20E-05	reverse	1923930	1923957	ATAACACCCCAACAACCCATGAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ ++ ++ +++++ +++++
543	4.50E-05	forward	1929148	1929175	TGTTAACCACTTTCCCGTTCGGTAAATA TTTTAATTACGTTTTTTTTACAGATATAA + ++++ ++++++ + + + ++++ ++
544	8.50E-05	reverse	1938846	1938873	AATATAATCGGCAAAACGCCTAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + ++++ + + +++++
545	7.50E-05	reverse	1948446	1948473	ATAACATTTTCTGTAAGAATAATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + + + ++++++++++ ++ +
546	2.00E-05	reverse	1954516	1954543	TTAGCTGTATGTCACAACTGGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ + ++++ + +++ ++++++++
547	9.60E-05	forward	1958137	1958164	TATTCCTTCCGCGCCGGCATTAAAAAAA TTTTAATTACGTTTTTTTTACAGATATAA + +++ ++ +++ +++ +++ ++ ++
548	7.50E-05	forward	1960006	1960033	CGTTTATTGAATGCTTATGCAGATTATT TTTTAATTACGTTTTTTTTACAGATATAA ++ ++++ + ++ + ++++++ ++
549	2.60E-05	reverse	1971531	1971558	TAAATTAACGGAGGAAAATTCAACATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++ ++++ + + + ++
550	2.30E-05	forward	1980036	1980063	TCTTTTTTGTTTCTCTCTGTTAAAATAA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++++++ + + + + ++++++
551	1.20E-05	reverse	1984427	1984454	TATTTTATTGAAATTAACATACTTGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ ++++ ++++++ ++ +++
552	5.10E-05	forward	1986837	1986864	TTTTATTCCCATTCGTATTTTTAATAAT TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++ + ++ + + + ++++ ++
553	5.50E-05	forward	1986871	1986898	TAATATTTTACCTTTTGCAAATAATAAA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ +++++ ++ +++++ ++
554	6.20E-05	forward	1996532	1996559	TTTTATCTCAACTTTGAAACGTAAAAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++ + ++++ ++ ++++ ++
555	3.00E-05	forward	1996575	1996602	TTTTGCTCTCGTTTTTGGAAATTATGTT TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ +++++++ + +++++ ++
556	3.20E-05	forward	2001132	2001159	TTTTGATCGTGCCTTCATTGCCTTTTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++ +++++++ +++ + ++++++
557	3.70E-05	forward	2004198	2004225	TTTTCCCAAATTTTATAGAGAATTAAAT TTTTAATTACGTTTTTTTTACAGATATAA +++++ + ++++++ + + +++ ++
558	4.20E-05	reverse	2012977	2013004	TTTTAATCAAAACATAAAACAATTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ + ++++++++++ +

559	3.90E-06	forward	2024633	2024660	TTTTGCGAACATTTATTCAGCGAAATTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++++++ +++++++
560	6.00E-06	forward	2024725	2024752	TTTTACTAAGGTTTATCCGAAAATAAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + + ++++++ + + +++ ++
561	4.50E-05	forward	2025230	2025257	TATTTATTGTTTTTATGGCAATTGCTAA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++++++ +++ +++
562	4.80E-05	reverse	2025277	2025304	TTATTAGTAAGACAAAACTTATTGATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ ++ +++++ ++ +++ +
563	1.60E-06	reverse	2025524	2025551	AAAGAAAGATAAAAACGCATAATAAACA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ +++++++ +++++++ ++ +
564	7.10E-05	reverse	2034907	2034934	ATCAAAAAACATAACCCATTGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + ++ + ++++ ++++
565	8.50E-05	reverse	2034984	2035011	TAAAAAACCAAACAGAAACAAATTGAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ + +++ ++++ +++
566	2.40E-05	forward	2035015	2035042	TTTAAATACCTTTGTTACATGTTATTTT TTTTAATTACGTTTTTTTACAGATATAA +++ +++ ++++ ++ +++ +++++++
567	4.80E-05	reverse	2039823	2039850	ATTAACTTATCTAATAACACGAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ ++ +++++++ ++++
568	3.00E-05	forward	2039873	2039900	TTTTCAGAAAGTTAGCCTACTTATCAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++ + +++ + +++ +++ ++
569	4.20E-05	reverse	2040308	2040335	AAATACTTATTCAAAAATGTAATTTTAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++++ ++++++ ++
570	8.50E-05	reverse	2041404	2041431	ATTGTTCTATACGGCACAATTATGAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++++ + + +++ +++++ +
571	1.40E-05	reverse	2041507	2041534	ATAATTATTTGCAAACGTATGATATAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ +++ + +++++ +++
572	6.60E-05	forward	2060844	2060871	TTAAATTTCATTTTTCGCGGGTATAAAA TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ ++++++ + ++++ ++
573	1.80E-05	forward	2064863	2064890	TTTTTTTACCTGTTTTCAAGATATTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ ++++ + ++++++++
574	3.70E-05	reverse	2072223	2072250	AAAAATTAATGTAATGAACGCATGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++ ++ +++++ +
575	8.00E-05	reverse	2077083	2077110	ATTAATCAGTGTGGAGGATGTATTGAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ + + ++ +++ + +

576	1.20E-05	forward	2080009	2080036	TTTTAACAGACCCTATTCGGGTAATTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++++ + + +++++ +++++++
577	9.00E-05	reverse	2085300	2085327	AGCTTTCTGCTCAGAGCTGGTATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ + + + +++++++
578	1.60E-05	reverse	2113107	2113134	GATAAAAAGTACAATGACAATATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ +++ ++ +++ ++ ++++
579	6.60E-05	forward	2139311	2139338	TTTTTCTACTATTCCTAACCAGGTTAAA TTTTAATTACGTTTTTTTTACAGATATAA ++++ + + ++ + +++ ++ ++
580	3.90E-05	reverse	2139575	2139602	AAATATTTCAGCAGAAGATGTCTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + + ++++ + ++++
581	2.00E-05	reverse	2141909	2141936	ATCAATCAACGACAAAATAAAAGAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ ++++ + ++ + ++
582	2.80E-05	forward	2146964	2146991	TTTTCATCCATTTTCTCCTGACTTTAAC TTTTAATTACGTTTTTTTTACAGATATAA ++++++++ ++++ + + + +++ +
583	2.80E-05	reverse	2147033	2147060	TTCATACTATAAATGCGAAATGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++++ +++ ++++
584	4.30E-06	forward	2156833	2156860	TTTTCATTATTCGCTCTCAGAATTAACT TTTTAATTACGTTTTTTTTACAGATATAA ++++++++++ +++++ + +++ +
585	1.40E-05	reverse	2156991	2157018	AATATTAAGCAAAAGCGATAAATCAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++ ++ +++ ++ +
586	3.60E-06	forward	2158596	2158623	TTTTACGCAGGCTAATTTATACAATTAT TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++ +++ +++++++ ++++++
587	4.20E-05	forward	2158624	2158651	TATTCAGTACTTCTCGGTAAGCTTAATA TTTTAATTACGTTTTTTTTACAGATATAA + ++++ +++++ + ++ +++ ++
588	4.80E-05	reverse	2159175	2159202	TAAATCATAAGTGGTGATGCAATTATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ + + + +++++++ ++
589	3.70E-05	forward	2161978	2162005	TTTTTTTAACATCTTGTACTGTATCTTT TTTTAATTACGTTTTTTTTACAGATATAA ++++ + ++ + ++ + + +++ +++
590	9.10E-06	forward	2162366	2162393	TGATAAATACTTTAATTCGTTTAAATAA TTTTAATTACGTTTTTTTTACAGATATAA + +++ ++++++ ++++ + +++++++
591	5.50E-05	forward	2164063	2164090	TTTTAATTGCACTCTGCCAGCTTTTTTC TTTTAATTACGTTTTTTTTACAGATATAA ++++++++++ ++ + ++ ++++++
592	5.10E-05	reverse	2164484	2164511	AAAATCAGATTTATTAACACTATTATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + ++ ++ +++++ ++++ ++
					TAAAAAGCGAAAATACACTTTCTGAATA

593	1.40E-05	reverse	2164619	2164646	TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++++ ++ + ++++ +
594	1.60E-06	reverse	2164737	2164764	AATTTTTTATTACCAAACTTAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ + ++++ +++++++++
595	7.50E-05	reverse	2165132	2165159	GTAAAACACTACAAAAACAATCATAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++++++ ++++
596	7.50E-05	forward	2165545	2165572	TTTTCAAATGCTCGTTTTAAAGATATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ + +++++ ++++++++
597	3.00E-06	reverse	2165599	2165626	TTTAAATATGCAATAAAATCAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++++ +++++++++
598	7.50E-05	forward	2166241	2166268	TCTAAATTAAATTTTTCCTGATTATTTA TTTTAATTACGTTTTTTTACAGATATAA + + +++++ +++++ + ++++++++
599	3.70E-05	reverse	2166304	2166331	TTATAAGTTGGAATACAAAATGATATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++++ +++ ++ ++
600	6.20E-05	reverse	2166572	2166599	AAATATATGCCAATTAACATAAAAGATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ +++ +++++++ + +
601	5.80E-05	forward	2166637	2166664	TGAAAATATCTGTTCTTTAAATAAATAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ ++ ++++ ++++++++
602	4.50E-08	reverse	2167307	2167334	GAAAAAATATAAAATAAAGCAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++++ ++++++++ ++++
603	7.10E-05	forward	2167389	2167416	TTTTGTTTTTGGCTCTGCATTCTGATAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++ + + +++ + ++++
604	2.30E-05	forward	2167960	2167987	TTTTCTATTTTCTAATATAGTTAAATAA TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ ++ ++ +++++++
605	9.00E-05	reverse	2172792	2172819	AATATTTGATGGAAAAATCTTAATAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ +++++ + + +++ +
606	2.10E-05	forward	2175260	2175287	TTTTAACATTGTTTACCCATTGAGTATT TTTTAATTACGTTTTTTTACAGATATAA ++++++ +++++++ +++ ++ + ++
607	1.30E-05	reverse	2175888	2175915	AACTTCATCAGTGGAAATATGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ + + +++ ++++++++++
608	9.60E-05	forward	2177559	2177586	TCATCATTGTTTCTTCCACCTGTAAAAT TTTTAATTACGTTTTTTTACAGATATAA + +++++++++ +++ + ++++ ++
609	2.80E-05	reverse	2181760	2181787	AATAATCATTAAAATAAAACTCAAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++ +++++ ++ +
610	4.20E-05	forward	2190058	2190085	CTATCATCATGTTTTCATAAATAAAATC TTTTAATTACGTTTTTTTACAGATATAA

610	4.20E-05	forward	2190058	2190085	+ ++++++++++++ ++ +++++ +
611	4.20E-05	reverse	2191656	2191683	ATTAATATCGAAATGGGCGCTGGTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ ++++ ++++ ++ ++
612	6.60E-05	forward	2195806	2195833	TTTTACTGGCGCGATCGAATTTATCTTT TTTTAATTACGTTTTTTTTACAGATATAA +++++ + ++++ ++ ++ +++ +++
613	9.00E-05	forward	2211923	2211950	TTTTTCTCCCTTCCCTGCTGACTACAAT TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ +++ + + + ++ ++
614	9.00E-05	forward	2220762	2220789	TTATTATCGCGCTACCGGCGATAATTTT TTTTAATTACGTTTTTTTTACAGATATAA ++ + ++++++++ + ++++++++
615	1.90E-07	forward	2229220	2229247	TTTTAATGCCGCTTTTACAAGGATTAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++++++ ++ ++++ ++
616	4.80E-05	forward	2230147	2230174	TTTTGACGGTTCTCATATACAAGATTAT TTTTAATTACGTTTTTTTTACAGATATAA ++++ + +++++ ++ ++++ +++++
617	6.60E-05	reverse	2230190	2230217	TTCATTGAATTTAAACACGAAAATATCA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++ +++ ++ ++ +
618	4.20E-05	reverse	2230661	2230688	TTTAATTTTAGTGAAAACTGTCTTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++++++ ++++ +
619	1.20E-05	forward	2234777	2234804	TTTTCACTAAGCGCTTTGGTATTAAAAA TTTTAATTACGTTTTTTTTACAGATATAA ++++++ ++ ++ +++ ++++++ ++
620	8.50E-05	forward	2234931	2234958	TTTCTACTACGTCACCGCCTACATTTAT TTTTAATTACGTTTTTTTTACAGATATAA +++ + +++++ + + ++ ++++++
621	2.30E-05	reverse	2241517	2241544	TAAAATCAATAACATCACGATAAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ + +++ + ++ +
622	4.80E-05	forward	2244359	2244386	TTTTATTCGATTCTGCATTGCGAATTTA TTTTAATTACGTTTTTTTTACAGATATAA +++++ +++ ++ + + + +++++++
623	1.70E-05	forward	2246107	2246134	TATTAATACATTCACTGCATCAATATAT TTTTAATTACGTTTTTTTTACAGATATAA + +++++ ++ + +++ ++++++
624	4.20E-05	reverse	2250594	2250621	AAATATCTGAACATAAACTACTTTATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ + ++++++ +++ ++
625	1.40E-06	forward	2259740	2259767	TTTTCACCGCCTCTTCATACAGGTTTAA TTTTAATTACGTTTTTTTTACAGATATAA ++++++ +++ + +++ +++++ +++++
626	2.40E-05	reverse	2268123	2268150	ATTTTTTGATGTAATACTTCAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ ++ + +++++++++
627	8.50E-05	forward	2271733	2271760	TATTCATGGGCTTTTTCCAGCGGAATAT TTTTAATTACGTTTTTTTTACAGATATAA + +++++ + +++++ ++ + +++++

628	6.50E-06	reverse	2275394	2275421	TTTTAAACTTGCCAAAAATTGAGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ +++++ +++ ++++
629	5.80E-05	forward	2276774	2276801	TTTTCATTGAAGTTTCACAAGTTGCATA TTTTAATTACGTTTTTTTACAGATATAA +++++++++ ++++ ++ ++ ++
630	9.60E-05	forward	2278880	2278907	TATTTATCTTCTTTTTTATCGTTAATCT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + ++++++ + +++++ +
631	4.80E-05	forward	2278986	2279013	TTTTTTGTGAATTCTTTCACAGAATACC TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++ ++++++++++
632	3.40E-05	reverse	2291953	2291980	TAATACCCGTAAATTAAGGGAGTTATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + ++++++ ++ + + +++ +
633	4.80E-05	forward	2291990	2292017	TATTTATTTTATTACTACACAGGATATC TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + ++ + +++++ ++ +
634	8.00E-05	reverse	2292270	2292297	TTTATTGCGGAAGAAGGCGTGGATGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++ +++++ + +++
635	9.60E-05	forward	2306106	2306133	TCATCTGTACGTTAATGTGGGGAACTAA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++ ++ + +++ +++
636	1.30E-05	forward	2307603	2307630	TCAAAATTCCTCTTTTTAATAGATAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++++++ +++++++ ++
637	6.20E-05	forward	2309158	2309185	TCTTTTTCACGTTTATTCGCCAGGATTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++++++++ + ++++
638	3.20E-05	forward	2312544	2312571	TAATGTCCGCGCCTTCTTATTGATTAAA TTTTAATTACGTTTTTTTACAGATATAA + + +++++ +++++++ ++++ ++
639	1.80E-05	forward	2320031	2320058	TTTACATAAATGGATTTTACATAAAATA TTTTAATTACGTTTTTTTACAGATATAA +++ +++ + + ++++++++++ ++
640	9.00E-05	forward	2324604	2324631	TATTCATACCTTTAAGCCGATTGAATAA TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++ + + + +++++
641	9.00E-05	forward	2324836	2324863	TATTTCCACCTTCTCTTTATGCGTCAAA TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + +++++ + ++
642	4.80E-05	reverse	2331319	2331346	AAATTCCTGAAGGATAACAAAGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ + ++ ++++ + + ++++
643	7.70E-06	forward	2341572	2341599	TTTTTATTTTTTTTCCGCTGTCATAATT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ +++++ + + +++ ++
644	9.00E-05	forward	2343717	2343744	TTTTTAACCGGCTAACATATTTAAAATT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + +++ ++ +++ ++++ ++

645	3.90E-08	reverse	2344030	2344057	ATAAAACCATAAATAAATTCAGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++++ ++ ++++++
646	4.80E-05	reverse	2357573	2357600	ATATTTATATAACGAAAACCACTAATAG TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++ ++++ ++ + + +
647	9.00E-05	forward	2358755	2358782	TTTTTTTGCCCTTTCGACAGTTTAAGAT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + +++ ++ ++++ ++
648	4.20E-05	reverse	2364487	2364514	TTTTAAAGCAAAAATCAAGTAAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++ ++++++ + ++
649	1.80E-05	reverse	2371203	2371230	TAAAACACCGAAACAAAGGCGATTAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++ +++ ++++++++ +
650	2.40E-05	forward	2375372	2375399	TATCAATAGCGCTCATTCCGGCATAAAA TTTTAATTACGTTTTTTTACAGATATAA + + +++ +++++ ++++ +++ ++
651	9.60E-05	reverse	2377133	2377160	AATGAAATATACAATAACAACAATAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++++ ++ ++++ + ++++
652	5.50E-05	reverse	2377233	2377260	TTAACCATGGAGGAGAAGAAAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++ + ++ ++ + ++++++++
653	7.50E-05	reverse	2377323	2377350	ATTAAAGAGAAAATAAGGGAGATGATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++++ + +++++ +
654	1.40E-05	forward	2377691	2377718	TTTTCATTATGTTTTTGTGAAATATGCC TTTTAATTACGTTTTTTTACAGATATAA ++++++++++++++ + + +++
655	7.10E-06	reverse	2384013	2384040	TACATAAAAAACAAAAAAGATAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++++++ + +++++
656	1.50E-08	reverse	2387931	2387958	AACGAACTGTGAGGAAAAACAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++++++ +++++++++++++
657	8.80E-07	forward	2392367	2392394	TAATAATAATATTTTTACAAATAATTAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ +++++ ++ ++++++++
658	3.90E-06	forward	2393254	2393281	TTTTATTGAAATGAATTTACAGAACAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + + + ++++++++++ ++
659	2.50E-06	reverse	2398040	2398067	ATATAAATGTGAATTAACGCACGTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++++++ ++++++ ++ +
660	6.20E-05	reverse	2401413	2401440	AGCTAACTTAATAGCAATACAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ + + ++ ++++++++++
661	4.50E-05	reverse	2437273	2437300	ATCGATTCATGGGGAGGAATAAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ + + ++++++ ++++
					TTTAACAAAAGTTCCTTCACATTAATTT

662	5.10E-05	forward	2437379	2437406	TTTTAATTACGTTTTTTTACAGATATAA +++ + + +++ ++++++++++++
663	6.20E-05	reverse	2439106	2439133	GGTTATGTATAAAATCGCGTCATGATAA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++++++ ++++ ++++ ++
664	8.40E-06	reverse	2439571	2439598	TTTAAACAGTTCGAAAGCGCGTTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ +++++++++ + ++++
665	3.40E-05	reverse	2445334	2445361	ATATAAAATTTAAAAAATTTGTGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++++ ++ ++++
666	4.50E-05	forward	2454242	2454269	TTTCTTTAATACTTTTTTAATGTTCATT TTTTAATTACGTTTTTTTACAGATATAA +++ + ++ ++++++++ +++ ++
667	9.00E-05	forward	2454316	2454343	TTTTCATTATTGTCACCTTTTAAAAGTA TTTTAATTACGTTTTTTTACAGATATAA ++++++++++ + ++ + + +++ ++
668	3.00E-06	reverse	2454375	2454402	TTATTTACCGCAAGAAAATGGAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++++ ++ +++++
669	8.00E-05	reverse	2464120	2464147	TTAAATTTGTTAATAAAACGTTGCAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ +++++++ ++ +
670	4.30E-06	forward	2467421	2467448	TTTTCTTCCAGCTTGCGTAGATTTATTT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ ++++ + ++ ++++++++
671	1.70E-06	reverse	2467596	2467623	ATATCAATTTGAGAAGGCGGAATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++ ++++++ +++ +++ ++ +
672	2.00E-05	reverse	2470453	2470480	TTTTATCAAAATAATCAATTAGTTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + ++ ++ ++ +++ ++
673	4.80E-05	reverse	2478085	2478112	ATCGATGTGCAGAATAAAATCAATAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ + ++ +++++ + +++ +
674	7.10E-05	forward	2484096	2484123	TTTTGCTTTCTTTCTGGCACTATTCTCA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + +++ ++ + +
675	2.30E-06	reverse	2485689	2485716	TAATATCGATGAAAAAACAAACAGATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++++++ + ++ ++
676	4.80E-05	forward	2487780	2487807	TTTTGATGATGTCTATTTTTCTAATGAC TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ +++++ + ++++ +
677	6.20E-05	forward	2493363	2493390	TGTCGTTTGCGTGTTTTAATCTTTATAA TTTTAATTACGTTTTTTTACAGATATAA + + ++++++ ++++ ++ +++++++
678	3.90E-05	reverse	2500072	2500099	AACATAGTTTGTATAAAAATAATCAATG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ ++++++++++ ++
679	2.10E-05	reverse	2508032	2508059	TAAAAAAGCGGAGTGGATGCGAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA

679	2.10E-05	reverse	2508032	2508059	+++++++ ++++ + ++++ +++++
680	9.60E-05	forward	2509537	2509564	TTTTATTTCTGTTGGCATCCAGAACAAC TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ ++++ + + +++++ +
681	5.80E-08	reverse	2511913	2511940	TTATCACTGTAAAAACAATGCATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++++++++++ ++ +++++++
682	9.60E-05	reverse	2526479	2526506	ATCATTATATAAGGCGCATGAATAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++++ + +++ + ++
683	1.70E-05	reverse	2526930	2526957	TTCAATCGCTGAAAAAGCATTCAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++++++++ + ++
684	6.50E-06	forward	2529288	2529315	TTTTCATGAAATGGCCTTACGTTTATAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + + +++++ +++++++
685	2.40E-05	forward	2531198	2531225	CTTTCATGCTGTGTCCTTGTTCATAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++ +++ + +++ + +++ ++
686	3.90E-05	forward	2533601	2533628	TATTTATAAATTGCCTCTTTTTAATTAA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ + ++ + + + +++++++
687	4.50E-05	reverse	2533790	2533817	AAAAAACCAGTAAAAAATCCCATAAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++++ + ++ ++ +
688	3.90E-06	reverse	2548602	2548629	TTAAAATTCCCGGTAAAAGCGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++++++++++++++
689	8.80E-07	reverse	2576657	2576684	GTAGATCACTAAGAGAAAGAAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++ ++++ ++ +++++
690	1.70E-05	reverse	2576787	2576814	TTCTTTGTATTACTACCATTGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ + ++ + ++++ ++++
691	7.50E-05	reverse	2585312	2585339	AATGTTGCGCAGAGTAAAATAATTATCA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + + ++++++++++ +
692	3.20E-05	forward	2593711	2593738	TATTAATCTTTGGTATGTCCGTAACAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ ++ +++ + + +++ ++
693	9.00E-05	reverse	2594967	2594994	AAATAACCATAAACGGCCACACTTATTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++ ++++ +++ +
694	9.00E-05	reverse	2603800	2603827	TGAACTGGCTGAAAGAAAACGCGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + +++++ ++++++ +++++
695	2.30E-05	forward	2618703	2618730	TTATCATTAATTTATTATTAATGTAAAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++ +++ ++ + ++ ++ ++
696	9.00E-05	forward	2619790	2619817	TCTTAAACTCGTTTTTGAAGATAGTGAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ + +++++++ + +++ + ++

697	3.30E-06	reverse	2620424	2620451	GAAAATTCATGAATGCACATAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++++++ ++++++ +++++
698	6.20E-05	forward	2623089	2623116	TTTTTCTACGCGTTTTTCGTGCATTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++++ + ++++++
699	3.90E-05	forward	2631693	2631720	CATTCATCCATTTAATAAATATTTATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ +++ ++ ++++++++++
700	1.90E-06	reverse	2639459	2639486	TTCATTCCATGAATACAAAAACGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++++ +++ + +++++
701	6.60E-05	forward	2648420	2648447	CTTTCATCATTTGCAGATGCAGAGTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++++++++ + + ++++ ++++
702	4.70E-06	reverse	2648604	2648631	ATATATTCCTAAAAAGAAAAGTTTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++++ +++ + ++++ +
703	9.00E-05	reverse	2648645	2648672	TAATATTGATATAATAAATAAAAAGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++ +++ ++ +++
704	2.80E-05	forward	2648682	2648709	TATTTCTAATATTAATTTTCGGGAATAA TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++ ++ ++++ + + +++++
705	5.50E-05	reverse	2648718	2648745	ATAAATAGTTGAATCAATAAAAAGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++ ++ + ++ +++ +
706	6.20E-05	reverse	2658306	2658333	TTTTAAAATAAAATGAGCATTAGCAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++ +++++ + ++ +
707	7.50E-05	reverse	2671921	2671948	ATTGAAACATTACAAAAATCTATTGATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ + +++++ + +++ + +
708	3.90E-06	forward	2684117	2684144	TTATTTTCATTTGTTTTTCCTGAATATT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++++++ +++++ + ++++ ++
709	5.80E-05	reverse	2711627	2711654	TGTTTACGCCGCAGAAGAAAGAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ + + +++++ ++ +++++
710	1.70E-05	reverse	2711758	2711785	TTAATTTCCTGACGACGCATACGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ + +++++ +++++
711	6.60E-05	forward	2716530	2716557	TGTTCATTACGCTATTAAAGGCTGCTTT TTTTAATTACGTTTTTTTACAGATATAA + ++++++++++ ++ + + +++
712	4.80E-05	reverse	2718581	2718608	TTATTTAAGCGAAAAGGTAGAGGAATTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ + + + + +
713	7.70E-06	reverse	2718626	2718653	ATTATTTTGCAACGACACGCTAACAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ ++ + ++++ + ++++

714	9.60E-05	forward	2720903	2720930	TAATCTTTCTTCGTTTTTACTGTGCGTT TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ +++ +++++++ ++ ++
715	8.00E-05	forward	2727105	2727132	CTTTCCCCGCATTACCTTATGGATTAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++ +++ ++ +++++ ++++ ++
716	1.10E-05	reverse	2727683	2727710	TATTATTTTTCAAAAAAAGATATTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++++++++ ++++ +
717	5.80E-05	reverse	2727763	2727790	TAATAAAGATGAGAAGATAGCAGAAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++ + + + ++ +
718	4.80E-05	reverse	2727830	2727857	TTATCTCAACATAAAAAATACAATATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + + ++++++ + ++ +
719	2.60E-05	reverse	2728506	2728533	AATTTTCGCTCAACAAACTTAATTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ ++++ ++++++ +
720	4.80E-05	reverse	2730592	2730619	ATTTTTATTTAAGTTAAATATTTTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++++ +++ +++ ++
721	5.10E-05	reverse	2740663	2740690	ATTTCACTCCACCGTGGCGGGATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ + +++ +++ ++++
722	1.90E-06	reverse	2755819	2755846	TAAAAACAGGAAATAAACAATAAGAAGA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++++++ + +++ +
723	3.20E-05	forward	2758110	2758137	TTTATAGAATGTTAATTCCATGTAATAA TTTTAATTACGTTTTTTTTACAGATATAA +++ + +++++ ++++ +++++++
724	3.70E-05	forward	2760148	2760175	TTTTAAAAAAAATGCTTTCCTACAACGAA TTTTAATTACGTTTTTTTTACAGATATAA ++++++ + + ++++ ++ ++ ++
725	2.30E-05	forward	2767219	2767246	TTTTAATATTGTCTTTTGTTAGTTTGTC TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++ ++++ ++++++ +
726	9.00E-05	forward	2770392	2770419	CCTTACTGATGTTTTTTTTAATCATATAC TTTTAATTACGTTTTTTTTACAGATATAA +++ + ++++++++++ +++++
727	4.20E-05	reverse	2772284	2772311	ATAACACCCCAACAACCCATGAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ ++ ++ +++++ +++++
728	5.80E-05	reverse	2780820	2780847	TTAGTAAATTAAACAAGAACCATGATGA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ ++++ ++++++ ++++ +
729	9.60E-05	reverse	2783203	2783230	AAAAAACGGCGACAGCGCCGGGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ + ++ + ++++++
730	6.60E-05	reverse	2786818	2786845	TTAAATCAATAAAAACCACACCACAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++ + ++++
					TTTTAATTCATCGTTCATGCTTTTCTCC

731	2.80E-05	forward	2788846	2788873	TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++ +++ + + +++ +
732	9.60E-05	forward	2792543	2792570	CTTTACTACCGTTATTTCAGCGAGATCA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++ +++++ ++ ++ +
733	1.90E-06	forward	2796169	2796196	TGTTAATTATTTGTTTGCTAATTTTTAT TTTTAATTACGTTTTTTTACAGATATAA + ++++++++++ +++ + ++++++++
734	9.10E-06	forward	2813188	2813215	TGATTATTTTTTCTCCGCACACATATTT TTTTAATTACGTTTTTTTACAGATATAA + + +++ +++ + + ++++ ++++++
735	1.60E-06	forward	2813393	2813420	TGTTAATGCGTTTTTCTCACCGATTTAT TTTTAATTACGTTTTTTTACAGATATAA + +++++ ++++++++++ +++++++
736	6.60E-05	forward	2813569	2813596	TCATCTGCGCGTTTTGTCAGGGTACTTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++++++ +++ +++ +++
737	3.00E-05	forward	2813727	2813754	TCATTATCCAGTTAATGCCTTGTTATTA TTTTAATTACGTTTTTTTACAGATATAA + + +++ +++ ++ + + +++++++
738	6.60E-05	reverse	2815336	2815363	ATAAAACAACTAGTTAAAGTAATTTTTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ +++++++++ +
739	4.80E-05	reverse	2816751	2816778	AACGAAAGAGTAAGAAGCAGAGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ +++++ + ++++++
740	4.80E-05	reverse	2819837	2819864	TACAAATTTTGAAAAAACTTCGGGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++++++ + +++ +
741	4.80E-05	forward	2822089	2822116	TTTTAACCCGGCTAACGCAGTGGAAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ + +++ ++ ++ + ++ ++
742	9.00E-05	forward	2828070	2828097	TTACCATAACATCCTCTTGTGTGAATAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++ ++ + ++++ + + +++++
743	4.20E-05	forward	2830198	2830225	TATTGTCTATGCTTTTGCGCTGATTAAC TTTTAATTACGTTTTTTTACAGATATAA + ++ +++++++++ + + ++++ +
744	7.10E-05	forward	2833344	2833371	TTTTCTGTTCTTTACTACTCATGAATTT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ + + +++ +++++
745	2.30E-06	forward	2834367	2834394	TTTTACGTTAGCCTCTTTACTGTATAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++ + +++++ ++++ ++
746	2.30E-05	reverse	2838381	2838408	TATGTTAAAAGAGAAAAAGAAGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++++++ + ++++
747	9.00E-05	reverse	2838418	2838445	ATTATAAAACATAAAGATAAATAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++ + + + ++++
748	2.60E-05	reverse	2842917	2842944	ATAATTCTCTACAATAATGGCAGTGAAA TTATATCTGTAAAAAAACGTAATTAAAA

748	2.00E-05	reverse	2842917	2842944	++++++++ ++ ++ ++ + + + +++
749	4.80E-05	forward	2853951	2853978	TATTGTTCTGATCTGCTCACTGTTATTT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ + + +++++ +++++++
750	8.50E-05	forward	2862834	2862861	TTTTTTGAAAGTTTCTGGAAAATAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++ + + + +++ ++
751	2.80E-05	reverse	2863062	2863089	TACTAAAAGAAAAATCAACCGAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++ ++ +++ ++++
752	5.50E-05	reverse	2864622	2864649	ATTTTTACGGGCGAAAGTCTGGTTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++++ ++ ++++ +
753	7.50E-05	forward	2870200	2870227	TTTTAACCATTTCATTTCGCTATACTCC TTTTAATTACGTTTTTTTACAGATATAA ++++++ +++++ ++++ + ++ +
754	4.20E-05	forward	2878034	2878061	TGTTAATTTATTTTTTAAAATTGATGTT TTTTAATTACGTTTTTTTACAGATATAA + ++++++ ++++++ + + ++ ++
755	2.70E-07	forward	2878579	2878606	TTTTTATTCTCTTTCTTTCCAATAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ + +++ +++ ++ ++++++
756	5.50E-06	forward	2879441	2879468	TTTTCATTTACCTTTCCCGCACTTAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++++ + ++ +++ ++
757	2.60E-05	forward	2879950	2879977	TAATAAAAAATTTCTTTCATTCATTTTT TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++ ++++++ ++++++
758	1.20E-05	forward	2884079	2884106	TTTTTATAATGTCCGTATGGATTGTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + + +++ ++++
759	5.50E-06	reverse	2885723	2885750	GAAGAACAAAAAAATCAAATTATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ ++++ +++++++
760	3.40E-05	forward	2886596	2886623	TATTTTTTTCTTTCTTTTCAATGTAGTT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++++ ++++ ++ ++ ++
761	9.00E-05	reverse	2888676	2888703	AACATATCAATAATTCAAATTATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ ++++ +++++++
762	4.20E-05	reverse	2888904	2888931	TATACAGAGTAAGAAAATCTGATAATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + +++++++++ ++++ + +
763	5.80E-05	reverse	2889582	2889609	GTAAATATCTAAGAAGAGGTAAAAAATG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ + ++++ ++
764	5.80E-05	reverse	2891480	2891507	TAATTTAACCTTATCAACAAACTTAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++++ + ++++ +
765	9.00E-05	reverse	2891600	2891627	ATCAATATCAAAGGAAAGATCAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++ +++ ++ + ++ +

766	3.90E-06	forward	2891938	2891965	TTTCTATCTCTTCTTTTTTCTTTAATAA TTTTAATTACGTTTTTTTACAGATATAA +++ +++ +++ +++++ + +++++++
767	2.00E-05	forward	2892139	2892166	CTTCAATATTTCTTACTCGCATATTTAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++ +++++++++ +++++++++
768	5.50E-05	forward	2892607	2892634	TTTTATCTATTTCAACATCATTTAAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ +++++ ++ + ++++ ++
769	2.80E-05	forward	2892886	2892913	TTATAATTAGGTTCAGACCGTCTTTAAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++ +++ + + +++ ++
770	4.20E-05	forward	2893100	2893127	TTATCATCGAATCATTACTTTGAAAGAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++++ + ++ + + ++++ ++
771	2.30E-05	forward	2893795	2893822	TTAATATTGTTTCTATTAGTTGTAATAT TTTTAATTACGTTTTTTTACAGATATAA ++ +++++++ ++++ + +++++++
772	6.20E-05	reverse	2894047	2894074	ATAGCAACTTAAGAAGAGTAAATGAACA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ ++++++ + ++++++ +
773	8.00E-05	reverse	2894199	2894226	ATCAATTGATATAACCAAAAAATTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ ++ +++ +++++ ++
774	2.80E-05	reverse	2896324	2896351	GAAAATATATAACTAAAGGAAATAGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++ ++++ + +++ +++
775	3.00E-05	forward	2896848	2896875	TTTTTATCGTTTCCAGGTATAGTTTTCC TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++++ + +++++++++
776	7.50E-05	reverse	2903995	2904022	TTTTTTCTTCACAAAAGCTGAAAATACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + ++++++ ++ + +
777	5.50E-05	reverse	2908380	2908407	AATGAAAATGGCGAAAAGGGAGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++++ + + ++++++
778	4.50E-05	reverse	2908597	2908624	ATATAATCATTGCTAACATTAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++ + ++++ ++++
779	8.40E-06	reverse	2908845	2908872	ATATTACTATGTATAGAGAAACAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++ +++ + + + ++++
780	9.60E-05	reverse	2910570	2910597	TTTATAACAAACAAGCAGATTATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + ++ + ++ ++ ++ +
781	3.20E-05	reverse	2910781	2910808	TTAATAAATTACATTCAAAAAAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ +++ ++ ++ +
782	1.30E-05	reverse	2915768	2915795	ATTTAATAGGCAAAAAAAGCGAAGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++++++++ +++ +

783	2.30E-05	reverse	2923943	2923970	TTTTAAATGCACAATAAAAGTATAGATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ + ++ ++++ ++ + +
784	3.70E-05	reverse	2924295	2924322	AACTATATAAAAATAGATCTTAGAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ +++++ + + + ++ +
785	6.00E-06	reverse	2924571	2924598	TATAATCATCAAATAAAGAAAAGTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++++ + ++ +++ +
786	6.60E-05	forward	2926662	2926689	TTTTCCGTAATTTTACGTCTTTTAAACT TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++ ++++++ + + ++++ +
787	4.20E-05	forward	2926710	2926737	TCTTAATTTCATTAATATGTATGTTTCT TTTTAATTACGTTTTTTTTACAGATATAA + ++++++ + ++ ++ + +++ +++ +
788	6.60E-05	reverse	2926880	2926907	TAAATAAATGGCATAAACGAAAATGATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++++ ++ + + +
789	4.80E-05	reverse	2926979	2927006	AAAAATGAATGGGCAAAATAAAATATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ + ++++ ++ ++ ++
790	1.10E-05	reverse	2927429	2927456	TTTTTACACCAAAGCAGAGCAATGATTA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ ++++++++++ +
791	1.70E-05	reverse	2927714	2927741	AAATTTCAGCACCATAAAGATAATAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + + ++++ + +++ +
792	8.50E-05	reverse	2928968	2928995	TATGTTCGGTTAAAGCGCTCAATAAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++ ++ ++++ +++
793	4.80E-05	reverse	2930269	2930296	TGAGAACAATATAAAAATGCATTTATCA TTATATCTGTAAAAAAACGTAATTAAAA + + +++ +++ +++++ +++ +++ +
794	3.00E-05	reverse	2931307	2931334	TATTTAAAACTAAGTGACTTTCTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ ++ + + ++++
795	3.40E-05	reverse	2931527	2931554	TGATTTTAGCGAATGAATGTACTCATAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ + ++++ ++ +++ + + ++
796	6.60E-05	forward	2932059	2932086	TTTTTATCAGCTCTCCCACTATTATTTA TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++++ + + + +++++++++
797	1.20E-05	forward	2934514	2934541	TAATGCTCAAGTTCTTTTATTTTTAGAT TTTTAATTACGTTTTTTTTACAGATATAA + + +++ +++ ++++++ ++++ ++
798	8.50E-05	reverse	2935789	2935816	GAATAAAACGAAATAAATTAACGTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++++++ + +++ +
799	5.50E-05	forward	2936463	2936490	TTTTAACTCCTGTACTTCTGTTTTAGTT TTTTAATTACGTTTTTTTTACAGATATAA ++++++ + ++ + +++ ++++ ++
					ATAAAAAAACGAATGAATTAAAATAAAA

800	1.40E-06	reverse	2937970	2937997	TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++ ++ ++ +++++
801	2.40E-05	reverse	2938045	2938072	TAAATAAACCGAAAGGGTATACAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ + +++ ++++
802	8.00E-05	reverse	2948438	2948465	ATAATAATTATCATTCAATTAAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ ++ +++ +++++
803	1.10E-05	reverse	2950709	2950736	TATTTAGAGTATATAACATCATTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ ++++ + ++ ++++++
804	3.90E-05	reverse	2952105	2952132	TTTTATTTGGTTAAGCAAAAAAATAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ ++ +++ ++ +++ +
805	6.60E-05	reverse	2952324	2952351	TTCTTCCACTATAAAGAAGATGATAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++ +++ +++ +++ +
806	2.60E-05	reverse	2952861	2952888	TTTGACGTATCTAATGGTGCAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ ++ + ++++++++++
807	7.50E-05	reverse	2953666	2953693	ATTGATAACGAAAGGCAAGCATGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ +++++ ++++
808	7.10E-06	forward	2968065	2968092	TTTTATTTAAATGTTCCTGGACTTTTTT TTTTAATTACGTTTTTTTACAGATATAA +++++ +++ + +++ + + ++++++
809	9.00E-05	reverse	2970179	2970206	TAAGTTCTGTAACATCAAATTCATATCA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++++++++ + ++++ ++ +
810	1.30E-05	forward	2970668	2970695	TTATAATGCATTGATTTAAAAGTAATTA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ ++ +++ + ++++++++
811	8.40E-06	reverse	2970750	2970777	TATTTTATCGACAAAAAGCCTATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + +++++ + ++ ++ +
812	8.00E-05	reverse	2972359	2972386	GAAGTAATATTGGTAAACGACAGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ +++++++ + +++++
813	2.30E-05	forward	2982623	2982650	TATTCAGCCTGTTTATTCACGATAAGCT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++++++++++ +++ +
814	6.60E-05	forward	2997744	2997771	TTTTCACCACTTTCACACGCGTTTCGCT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++++++ ++ + + +++ +
815	2.40E-05	reverse	3007555	3007582	AACTCAATACAAATCAATAAGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++++ ++++ ++ + ++++++++
816	9.00E-05	reverse	3010399	3010426	ATAACAATTTAAAATCAGAAAGATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++ +++++ + + + +++++
817	3.40E-05	forward	3013299	3013326	TTTTTATTTCATTGTTATTTAAGAATAT TTTTAATTACGTTTTTTTACAGATATAA

817	3.40E-05	forward	3015299	3015326	++++ +++ + ++ ++ + ++ +++++
818	2.30E-05	reverse	3017265	3017292	GAAGAACTGCATAAAGCCGGAGTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + +++ ++ + + ++++
819	7.10E-05	forward	3032231	3032258	TTTTGCGGGCGTTTATCTGTCTTTTTAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++++ + + +++++++
820	6.20E-05	reverse	3033464	3033491	TTATATATAAGAATTACTACTCAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ ++++ + ++ ++++
821	2.00E-05	forward	3035000	3035027	TTTTTATTGCTCGCTCAAGGAAATCAAA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++++ ++ + ++ ++
822	1.80E-05	reverse	3035057	3035084	TAAGATACATCAATGAGAAATATGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ ++ +++ ++++ +++++ +
823	2.30E-08	reverse	3035606	3035633	TTATATTCTTATAAACAAATAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++ ++++++++++++
824	2.60E-05	forward	3035764	3035791	TATTAATATAATCATTTCAGAATAAAAC TTTTAATTACGTTTTTTTACAGATATAA + +++++ + +++++ + +++ +
825	9.00E-05	reverse	3037666	3037693	GACATCACGGATAACAAAATAATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + + + ++ ++++++++ ++++
826	9.60E-05	reverse	3040385	3040412	TTAAAATAACATCAACAAAGGGATAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++ +++ + +++ +
827	1.60E-06	reverse	3041863	3041890	ATTATTTTGCAAAAAAATATAAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++++++ ++++ + ++
828	3.80E-07	forward	3042440	3042467	TTTTAATCCTGTTCCTGTATCGAATAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++++ + +++ ++++ ++
829	4.80E-05	reverse	3043368	3043395	ATTTTTGATAAACAAAACGCTATGATCA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++++++ ++++ +
830	9.60E-05	reverse	3044506	3044533	TAAAAAAATTTGGGAGAATTACAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + + ++ ++ +++++
831	2.10E-05	forward	3046169	3046196	TTATCAGTATTTTCCTTAGCAATATAAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++ ++++++ ++ ++ +++ ++
832	2.80E-05	forward	3046684	3046711	TTATAAGATTGCTTCTTCAAATTTAATC TTTTAATTACGTTTTTTTACAGATATAA ++ +++ +++++ ++++ +++++ +
833	4.70E-06	forward	3047230	3047257	TATTCATCGCATCTTTCCCGGTTAATTA TTTTAATTACGTTTTTTTACAGATATAA + ++++++++ + +++ + +++++++
834	5.10E-06	forward	3049456	3049483	TTTTCATATTTTCTTCCTGCGCTTTAAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ +++ +++ + + +++ ++

835	3.00E-05	forward	3051664	3051691	TTTTTCTCCCTTTATTTTGGCAGTTTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ ++++ +++++
836	8.50E-05	reverse	3054059	3054086	TGAACATTCAAAAAACGCCCAATGAATA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + + +++++ ++ +++++++ +
837	4.20E-05	forward	3054549	3054576	TTTTCATATCTTTCATGGTCAGGAAATA TTTTAATTACGTTTTTTTTACAGATATAA +++++++ ++++ ++ +++ ++ ++
838	4.80E-05	forward	3055011	3055038	TCTTAATTATCCCCATAAACTCATTAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++++++ + ++ ++ +++ ++
839	1.80E-05	forward	3060962	3060989	CCTTAATTAAGCCCTTATATTGTTTTTA TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++ ++ +++ +++++++
840	1.60E-05	reverse	3062084	3062111	AATTTAAAATAGAAGAGTACGCTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ ++ ++ +++ ++++++
841	1.80E-05	reverse	3068430	3068457	ATAAATTTGAAAAAAAATTTAATGTAGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++++++ +++++ + +
842	1.20E-05	forward	3069078	3069105	TAATCATTGTATTTTCGTATCTTAAATA TTTTAATTACGTTTTTTTACAGATATAA + +++++++ +++++ +++ ++++ ++
843	3.90E-05	reverse	3071999	3072026	AGTAATCTGGAAATAGAATTATATAATA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ +++++ ++ ++ +++ +
844	5.80E-05	reverse	3080463	3080490	TTAAATCAACAAGAAGCAGTTCGTTAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ +++ + +++
845	5.50E-05	forward	3106190	3106217	TTTTTCAAACTCGTCTTTATGTTTATTC TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++ + +++++ ++++++
846	4.30E-06	forward	3108755	3108782	TTTTTAATGGTCTTTTTTGTTGATATAC TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ ++++++++ + ++++++
847	7.50E-05	reverse	3109373	3109400	GAAGTTAACGTAGAGGATATAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ + ++++ +++++
848	7.50E-05	forward	3114817	3114844	TAATTATTAAATTTTCTGGAAATTCTTA TTTTAATTACGTTTTTTTACAGATATAA + + ++++ ++++++ + ++ +++
849	9.00E-05	forward	3117188	3117215	TTTTTTTCCTGTTCCTGTTCGGTTTATC TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + + + ++++ +
850	3.90E-06	forward	3117908	3117935	TTATCAGCGCTTTTATACACTCATCGAA TTTTAATTACGTTTTTTTACAGATATAA ++ +++ +++++++++ +++ ++ ++
851	3.90E-05	forward	3123045	3123072	TAATCATATAACTAATTTATTAAAAAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ ++++++ +++ ++

852	9.60E-05	forward	3123093	3123120	TATAAATAACATCAATTAAGTAAAAAAA TTTTAATTACGTTTTTTTACAGATATAA + + +++ ++ + +++ + +++ ++
853	2.60E-05	reverse	3136184	3136211	TTATTCACTGGCAGGAGAAGTATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + + + ++++ ++ ++++
854	7.50E-05	reverse	3138581	3138608	GTAAATTTTCATATGAAAGTGCGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + + ++ ++++++ ++++
855	3.90E-05	forward	3138612	3138639	TTTTAATTAGTTGTTTTATATAGACTTA TTTTAATTACGTTTTTTTACAGATATAA +++++++++ ++ ++++ + +++
856	4.20E-05	reverse	3142114	3142141	AATTATTACGGCGAAAAATTATATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++++ ++ +++++
857	4.20E-07	reverse	3148113	3148140	TTTTTTATGAAAATTAAAGTGATGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ ++++ ++++++++++ ++
858	8.00E-05	forward	3148184	3148211	TATTAAAAGGCCTTTTTTATTTGAAAAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + +++++++++ + ++ ++
859	3.40E-05	reverse	3148578	3148605	GGATTTTGATGAAAAAACTCAGTTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++++++++++ ++ +++ ++
860	7.10E-05	reverse	3159319	3159346	TTATAACAGGATATGGATAAGTGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + ++ + + + +++++
861	5.80E-05	forward	3159577	3159604	TTTTGATGATTGTCTCATGGTCATCTTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ +++ + ++ + ++ +++
862	2.00E-05	reverse	3164236	3164263	TGCACAGAGGGCAAAAACAGAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + + + + +++++++ +++ ++++
863	3.00E-05	reverse	3170224	3170251	TGCGCTCAGCTAAAAAACGCTGTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ + +++++++++ ++++++
864	8.00E-05	forward	3172839	3172866	TTTATCTATCCCTTTTTCACGTAACATA TTTTAATTACGTTTTTTTACAGATATAA +++ + + +++++++++ +++ ++
865	1.30E-05	reverse	3174165	3174192	TTCATACAATCAACGAGACTGATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ ++ +++ +++++++++
866	6.60E-05	reverse	3184725	3184752	AGAAACAACACAAAAAAGGCAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ + ++++++ +++++ ++++
867	2.40E-05	forward	3186958	3186985	TTTTTATTGTCCTTTGTCGGGAATTTCT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++ ++++ ++ ++++ +
868	8.40E-06	reverse	3198856	3198883	ATATTTCAATGAATTAAAGCATTGATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ ++++++ +++ +
					TTAAAATTAGTTTTCTTGATTGTTTAAA

869	2.30E-05	forward	3202341	3202368	TTTTAATTACGTTTTTTTACAGATATAA ++ +++++ ++++ ++ ++ ++++ ++
870	3.70E-05	forward	3215064	3215091	TGTTCATCTTCTTCTCTCCGGTTATTTT TTTTAATTACGTTTTTTTACAGATATAA + ++++++ + ++ ++++ +++++++
871	3.30E-06	reverse	3215249	3215276	ATTTAATAATAAATAAACTGGAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++++++ ++ + ++
872	9.80E-06	reverse	3216661	3216688	GAAATACCATGCAAACAATGCATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ +++ ++ ++ ++++
873	2.80E-05	reverse	3231610	3231637	TAATTTCAGTGAATCGACGGCAATATTA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ +++ + ++ +
874	6.20E-05	reverse	3232480	3232507	TTAAATTAATAACTTGATGAATTTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++ + + + + ++++ +
875	4.50E-05	reverse	3232592	3232619	TATTTTTATTAAATAACAGCAAGGTAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++++++ +++++ + +++
876	2.10E-05	reverse	3249029	3249056	TAAGAAAAGCTAATAAAGAGACTGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + ++++++ + + ++++ +
877	1.20E-05	reverse	3259359	3259386	TGATTCGTATGGAAGAGAAAAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ ++++ ++ ++++ ++++++++
878	6.00E-06	forward	3262140	3262167	TTTTGATACCATTCGCTTCCACAAATTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + ++ +++ ++ ++++++
879	7.50E-05	forward	3262950	3262977	TAATAATGTGGTTAACGTAAGGTAATAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++ ++ ++ +++++++
880	2.00E-05	forward	3264018	3264045	TTTCAATTCATTTTCTTTGACTAATATT TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ ++++ +++ ++++ ++
881	1.10E-05	reverse	3267069	3267096	ATTTAAAACAGGAAAAAATTGATGAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++++ +++++++ +
882	3.70E-05	forward	3267971	3267998	CATTCTTAACTCTTTCTTATGTAAATAC TTTTAATTACGTTTTTTTACAGATATAA +++ + ++++++++++++ ++++++
883	2.80E-05	forward	3273890	3273917	TATTAAAACTATTATTTTTCAGATAATT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++ ++++ ++++++ ++
884	5.50E-05	reverse	3281813	3281840	AAAATTATGTACAAGAGGGGGTGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++ ++ ++ + + +++++
885	8.50E-05	reverse	3287339	3287366	AGAGATGGATAACAAAATGCAGGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + ++ ++++ ++++ +++ ++++
886	2.00E-05	reverse	3288353	3288380	TTTATTAGGCTCAATAACGTCATTAATA TTATATCTGTAAAAAAACGTAATTAAAA

887	6.00E-06	forward	3295596	3295623	TATTCATTGATTTCATAAGCGCAAATAT TTTTAATTACGTTTTTTTACAGATATAA + +++++++ +++ ++ + ++++++
888	1.80E-05	reverse	3295976	3296003	TATTAACAGCTTAATCGCGTGATAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ +++++++ + ++
889	3.00E-05	reverse	3299380	3299407	TTATAAGCGGGTAATAACGTGTTCATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++ ++++++ + + ++
890	3.70E-05	forward	3300043	3300070	TATTCATTCCATTAATTCTTAATGCTAT TTTTAATTACGTTTTTTTACAGATATAA + ++++++ + ++ ++++ ++ + +++
891	6.20E-05	forward	3303011	3303038	TGTTACTTCTTTTTTCACGGCTTATTCT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ +++++++ + +++++ +
892	5.10E-05	reverse	3304640	3304667	ATCATTTATTTTCAAGATGTTATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ + ++ ++ ++++
893	1.70E-05	reverse	3312499	3312526	TAAAAAACACATCAAAAAGCAAATATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + +++++++++ ++ +
894	6.20E-05	reverse	3312563	3312590	TGATTTACATCAATTAACACACACAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ ++ +++ ++++++ ++++
895	3.00E-05	forward	3312636	3312663	TTTTATTTTTCTTAATACTCACATTATA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ + ++ ++ + ++ +++ ++
896	4.80E-05	reverse	3312676	3312703	TTATTATCCTGTGAAAACTAAAAAATGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ ++++++ ++ + +
897	7.10E-05	reverse	3316626	3316653	AAAATTGACACAGATCAAATAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++++++ +++++
898	3.90E-06	forward	3321582	3321609	TTATTTTACTGTTTATGTCTTTATTTAA TTTTAATTACGTTTTTTTACAGATATAA ++ + + +++++++ + + +++++++
899	1.20E-05	reverse	3322434	3322461	TTATCAACTCATGCTAACATAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + + ++++++++++++
900	9.00E-05	reverse	3322524	3322551	AAATAATTACAAGGTAAACTATTCAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++ +++ ++ + ++ +
901	1.10E-05	reverse	3331496	3331523	TTCAATCCAGAACATAGCGGAGTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ + ++++ + + ++++
902	6.60E-05	reverse	3336801	3336828	TGTTATATATCTGTGAACGCAGAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++++++ ++ ++++++ +++++
903	8.00E-05	reverse	3338216	3338243	TAATAGCAATATAATAACAGAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++ ++ ++++ +++ ++++

904	1.40E-05	forward	3344581	3344608	TTTTATCATTATTTTTTAAATGATTAAT TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++++ + ++++ ++
905	9.80E-06	forward	3347084	3347111	TTATTATGAATTTACTTAATGCATATAA TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ + +++ ++ ++ ++++++
906	3.70E-05	forward	3349480	3349507	TAATCATTAAGGTAATATATAATTAATT TTTTAATTACGTTTTTTTACAGATATAA + ++++++ + + ++ ++++ +++ ++
907	6.20E-05	forward	3352142	3352169	TCTTTCTTTGGTCTATTGATTAAATTAA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++ ++++ ++ ++++++
908	9.00E-05	reverse	3375032	3375059	TACTATCGACTCACTCAGGCAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + + ++++++++++
909	5.50E-05	forward	3375174	3375201	TATTTAGAAGTTGTATATAAGGAGATAT TTTTAATTACGTTTTTTTACAGATATAA + ++ + + ++ +++ ++ ++ ++++
910	4.70E-07	reverse	3376995	3377022	TTAAATAAATAACGGGAAGGAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ +++ ++++++ +
911	4.20E-05	forward	3378447	3378474	TTACCATTCAGCTTATTCGTCGTTCTTT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ ++++++++ + +++ +++
912	6.20E-05	reverse	3379203	3379230	GATTCATGGTAAAAAAACCTCATTAATA TTATATCTGTAAAAAAACGTAATTAAAA + + + ++++++++++ + +++++ +
913	9.00E-05	forward	3403125	3403152	TGTTACTAACTTTATGATATTGATCGCT TTTTAATTACGTTTTTTTACAGATATAA + +++ + +++++ + +++ +++ +
914	2.30E-06	reverse	3412961	3412988	TTTTTTGCATAGGGAGAAATAATGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ + + ++++++++++ +
915	4.80E-05	forward	3414026	3414053	TCACAATACTGTTAATATAAAGTTATAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++ ++ ++ ++++++++
916	6.20E-05	forward	3420245	3420272	TTTCATTCGCGGCTATTCTTAGTTTGAT TTTTAATTACGTTTTTTTACAGATATAA +++ + +++++ +++++ ++++++ ++
917	1.60E-05	reverse	3434455	3434482	TATAAACCGAAGGTAAATGCGCTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++++ +++ ++++++
918	2.50E-06	reverse	3434509	3434536	TTATTTGTTTGCAAAGAAACATTTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++ +++ +++++ ++++ +
919	2.10E-05	reverse	3434566	3434593	AATTTTCATTTAAAACAAATAATTTACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++ ++++++++ + +
920	4.50E-05	forward	3438848	3438875	TTATACCTTCGCTTATTTCTTTAATTCT TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + +++++++++ + +++++ +

921	2.10E-05	reverse	3439094	3439121	TAATCATTGTGCAAACGCTCATTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + ++++ +++ ++ ++ + ++++
922	2.80E-05	forward	3444218	3444245	TATTTAGCGATCCTTTACAGCCAAATAT TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++ ++ +++ ++ ++++++
923	2.30E-06	reverse	3464675	3464702	AAAAATTTTAAAATAAAAGCGATAAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++++++++++ ++ +
924	6.20E-05	reverse	3469483	3469510	ATCAAACGCTTCATAGGCAGCATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ +++ ++ ++++
925	1.20E-05	reverse	3485308	3485335	TATTTATGGTGAGTTAAAAAAATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++ ++++ +++ ++ +
926	5.80E-05	reverse	3493336	3493363	AAAAATCTCGATCAGACTGGTGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + + + + ++++++
927	8.00E-05	reverse	3494533	3494560	TTCAATGATTCAGAGCGCGCTATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ ++++ ++ ++ +
928	7.10E-05	forward	3495876	3495903	TTTTTAGAACATTCCTTCACGAAGCGTT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ ++ +++++ + ++
929	4.50E-05	reverse	3509498	3509525	ATAAAAACATTAAGAAAACCTTAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ ++++ + ++++
930	5.50E-05	reverse	3538564	3538591	ATTATTACCAACAAACACGTGATTAACG TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++++++++
931	8.50E-05	forward	3539196	3539223	TAATGATTTGATTATTTCGGTCAATAAT TTTTAATTACGTTTTTTTACAGATATAA + + +++ ++ ++++ +++ ++
932	8.00E-05	forward	3544478	3544505	TGTTAATGCCGTCTTCCAGCATTTTTTC TTTTAATTACGTTTTTTTACAGATATAA + +++++ +++ +++ ++++++++
933	9.60E-05	forward	3546904	3546931	TTTTCATTTTTTCGTTGCCAGCAACATT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++ ++ + ++ ++
934	2.10E-05	reverse	3547388	3547415	TTATTTCTGCTAAAGAGAGGAAATAACG TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ +++ ++++ ++ +++
935	6.20E-05	forward	3549345	3549372	CTTTCATAACATTATTTCAGCCTTAAAC TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ ++ +++++ +++ +
936	5.10E-05	forward	3550066	3550093	TATTAAGCAATTGATTTTCTTTTGTTTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++ ++ ++++ + ++ ++++
937	7.10E-05	reverse	3550262	3550289	GAATTCGACGAGGTAAAAATCATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + ++++++++ +++++++
					TTTGTATCTCAAATAAGTATAGTCATAA

938	8.00E-05	reverse	3551358	3551385	TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++++++ +++ + + ++
939	8.50E-05	reverse	3554639	3554666	GAATAATAGTATATTAACGTAATTGTTA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ ++ +++++++++ +
940	7.50E-05	reverse	3561679	3561706	TTATTCATATCGATAAAATCGATAATGA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++++ ++++++ ++++ + +
941	9.00E-05	reverse	3563674	3563701	AGAATCCAGTACAGTAAGATGAGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ + +++ + ++ ++++ ++++
942	7.10E-05	reverse	3582131	3582158	TAAAAACGATAAATACGCTGATAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++ ++ + ++ +
943	3.00E-05	reverse	3582239	3582266	ATCAATAATAAAAACAAATAAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++ +++ ++++++ +
944	8.50E-05	reverse	3584691	3584718	AAAAATATCTATCCACGAAGTGGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ + +++ +++++
945	1.80E-05	forward	3587758	3587785	TTTTTATCCACTCTACGAAGATGTTTAA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ + +++ + ++ +++++
946	5.10E-05	reverse	3599930	3599957	TATTTTATACATATGAAAAAACAAAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ + ++ ++++ + ++ +
947	5.80E-05	forward	3611593	3611620	TTTACTTCGCGTGCTTTCATTGATTGCT TTTTAATTACGTTTTTTTACAGATATAA +++ + ++++++ ++++++ ++++ +
948	6.60E-05	forward	3627278	3627305	TCTTTTCAGACTCTTTTTGTTTAAATTA TTTTAATTACGTTTTTTTACAGATATAA + ++ + + +++++ + +++++++
949	1.10E-05	reverse	3641191	3641218	AAATTATAATCACAAAATATGAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ + ++++ ++++ +++++
950	7.70E-06	reverse	3643427	3643454	AACATCACATTAAAAAATGCAATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++ ++++++ ++++++++ +
951	7.50E-05	forward	3647891	3647918	CCTTTTTTGTATTTTTTTTCATTTTAAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ +++++++ ++++++ ++
952	1.70E-05	reverse	3650417	3650444	TAAATACACCGGACAAATTTAAATAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + +++ +++ +++ +
953	4.50E-05	forward	3685241	3685268	TTATTTGTACATTCCGTCACATTTTAAT TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ ++ +++++++++ ++
954	9.60E-05	reverse	3697596	3697623	TTATTTCCCGTCAGGCGGCCAATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + + ++++ ++++
955	7.10E-07	reverse	3698013	3698040	ATAATCAAATGAATAAACAGAAATAACA TTATATCTGTAAAAAAACGTAATTAAAA

955	7.10E-07	reverse	3698013	3698040	+++++ + ++++++++++ ++ +++ +
956	3.90E-05	forward	3698260	3698287	TTTTAATACCGTTATTTAGAATTGTGAC TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++++ +++ +++ + +
957	1.10E-05	reverse	3698356	3698383	ATCTATTAATTACGAAGCGCAAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ + ++++++++ ++++
958	1.80E-05	forward	3706071	3706098	TTTTAATCTATTGATTTTTAATTGATTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++ ++++ +++ ++++
959	3.90E-05	forward	3709348	3709375	CTTTGATTATGTTGCTGAATAGTAAGAA TTTTAATTACGTTTTTTTACAGATATAA +++ ++++++++ + +++++++ ++
960	3.40E-05	forward	3720047	3720074	TCTTTTTCATATTATTATCAATTAATTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++ ++ ++ + ++++++++
961	2.60E-05	forward	3737566	3737593	TTTTCCGTAATTTTAGCAATATTAATAT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ +++++ ++++++++++
962	5.80E-05	reverse	3738179	3738206	TTATAAACTCATCAAAAATCCATAAAAG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ + ++ +++
963	6.60E-05	reverse	3738586	3738613	ATTATTCATCAGAAAGGCGTCAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++ ++++ + ++ +
964	8.50E-05	reverse	3747073	3747100	ATTGCAGCGCGGCAAAGAAGAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + + ++++++ +++ ++++
965	3.20E-05	reverse	3749093	3749120	TTTTTATTACAAAAAAAAGATAGTAAGG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++++++++ + +++
966	4.80E-05	forward	3754849	3754876	TTATATGTTTTGTTTTTTGCTGGTTAAA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ + ++ ++++++ + + ++ ++
967	7.50E-05	reverse	3755153	3755180	AATAACCTGGTAAATGACACAAAAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ +++ ++++++ ++ +
968	6.60E-05	reverse	3761569	3761596	ATATACATGGAAGCTAAAAAAATGATGA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++ ++++ +++++ +
969	6.00E-06	reverse	3763032	3763059	AAAAAATAACGAATTCAAGGAATTAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++ +++ ++++++ +
970	3.70E-05	reverse	3787255	3787282	TTAATTGCAGAAAAAGGCGGCAGTGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++++ +++ + + +++
971	1.20E-05	forward	3792354	3792381	TTTTCATTTTCTTCCTCTGAATTAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++ + ++ + + +++++ ++
972	5.10E-06	forward	3793086	3793113	TTTTTACTTTCTTTCTGCGCAGGTTTAA TTTTAATTACGTTTTTTTACAGATATAA ++++ + + + +++ + + +++ +++++

973	5.80E-07	forward	3794641	3794668	TATTCCTTGTTTGTCTTTACAATAAAAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++++ + ++++++ +++ ++
974	1.70E-05	reverse	3794679	3794706	TTTTTTATCCATCCTGATGTAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + + ++++++++ +
975	1.60E-05	reverse	3794770	3794797	ATTGTAAACGGGATAAACGTTATTAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++++++ ++++++
976	2.60E-05	reverse	3795752	3795779	TATGACATTTAAAGACATTTGATCAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++ ++++ + + ++++ ++ +
977	9.30E-15	forward	3800195	3800222	TTTTAATTATGTTTTTTCATAGATATAA TTTTAATTACGTTTTTTTACAGATATAA ++++++++++++++++++++++++++++
978	1.40E-06	forward	3800400	3800427	TTATAATCGCGCTTTTTATGAGAAAGAT TTTTAATTACGTTTTTTTACAGATATAA ++ +++++++++++++ +++++ ++
979	5.50E-05	reverse	3801699	3801726	AAAAATAAAGTAGCACATTTTGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ + + + ++++++
980	5.20E-07	forward	3812875	3812902	TTTTCATAGGGTGTCCTTGAAGTAAAAA TTTTAATTACGTTTTTTTACAGATATAA +++++++ + ++ + +++ +++++ ++
981	2.30E-05	reverse	3812979	3813006	ATCATAATTGAAACAAAAATGTTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++ +++++++ + ++++
982	5.10E-05	reverse	3826371	3826398	ATAAATGGCTGGAAAAAATGAATAAATG TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ ++++++ +++ ++
983	2.40E-05	reverse	3830479	3830506	ATATTTATCTAAAAACGTTATCTGAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++++++ + +++++
984	6.20E-05	forward	3830612	3830639	TATTTATTCCCTGTCGGTGGTGTTTGAT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + + + + ++++ ++
985	5.50E-05	reverse	3830928	3830955	TTCATTCAGGTGCTAAACCCAATGAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + +++++ +++++++ +
986	1.70E-05	forward	3831428	3831455	TATTATTCCCTTTTTCCTGATTTATAAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ +++++++ + ++++ ++
987	8.40E-06	reverse	3843750	3843777	GAAGATTTTTACAAAAAATCACTAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++ ++++++ ++ + ++++
988	6.20E-05	forward	3848734	3848761	TTATGATTGTCTGTATTAACGAAAATTC TTTTAATTACGTTTTTTTACAGATATAA ++ + +++++ + ++++ ++ +++++
989	8.50E-05	reverse	3849340	3849367	TGCATTCTGTGAGGAAATGGAGTGTATA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++++++ +++ + + ++ + +

990	4.70E-06	reverse	3849388	3849415	TAATTAGTATATATAAAAATAATTGTTA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++ ++++++++++++ +
991	3.00E-07	reverse	3849479	3849506	TATTAAGAATAAATTAATATAATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++ ++ ++++++++ +
992	3.90E-05	forward	3856737	3856764	TGTTAATACTCCTTTCACCCAAAAATAC TTTTAATTACGTTTTTTTACAGATATAA + +++++ + +++++ + ++ +++++
993	6.20E-05	forward	3856961	3856988	TATTTTTTTAATCTTTACAATTATTTTC TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ + +++ ++ ++++++
994	7.70E-06	reverse	3858715	3858742	ATAAAACGCCAACAAGATAAAATTAACA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ ++ + + ++++++ +
995	5.10E-05	forward	3860708	3860735	TCTTAAGTTCATCAATATCCTTAAATTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + + + ++ + + +++++++
996	2.60E-05	reverse	3869235	3869262	AAAAAACGCTGAAAACCACAGAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ + ++ +++++
997	4.20E-05	reverse	3878980	3879007	TTCTTACCGTTGGTAAACGTACTGGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++ +++++++++ ++ +++
998	4.80E-05	reverse	3879331	3879358	ATAAATATATTACGCGATGGTATTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++ + + + +++++ +
999	3.00E-06	forward	3886816	3886843	TTTTCAGGCAGCCTTTTTCCACAAATAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ +++++ ++ ++++++
1000	9.80E-06	forward	3887023	3887050	TTTCACTCGATCCATCTCACATTTTTAA TTTTAATTACGTTTTTTTACAGATATAA +++ + +++ ++ +++++++++++++
1001	7.10E-06	reverse	3896277	3896304	AAAATTCAACAAAGCACCAAAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ + ++ +++ ++++
1002	8.00E-05	forward	3901486	3901513	TCATGCCTGTTTGTATTTATACAATGAA TTTTAATTACGTTTTTTTACAGATATAA + + +++++ ++++++++ +++ ++
1003	2.00E-05	reverse	3901593	3901620	AAATCCCCATACATAAACATTATAATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + +++ ++++++++ ++ + +
1004	6.60E-05	reverse	3901999	3902026	TTAGAAAAACAACAAGCTACGATTATCA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + ++ ++ +++++++ +
1005	2.30E-05	forward	3902193	3902220	TGTTATTCATCTTGATTTAGTTAACTTA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++ ++ +++++ +++ +++
1006	8.00E-05	forward	3914086	3914113	TATTTTTATTTCTTGCTACCGTATTTAA TTTTAATTACGTTTTTTTACAGATATAA + ++ + +++++ ++ + +++++++
					ATTTTTACAGTAAAAAGCAAGCACAAAA

1007	4.80E-05	reverse	3923782	3923809	TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++++++++ + ++++
1008	9.60E-05	forward	3930728	3930755	TTTTTATATCGTTCGTGGCAATTTTGAA TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++ ++++ + +++++ ++
1009	7.50E-05	reverse	3931980	3932007	GAAAATATAGGAGTAACAGTAAATATGA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++++++ +++++ ++ +
1010	5.10E-05	reverse	3932044	3932071	AACTTTATAGAAAAAGAAATGTTATAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ +++++ +++++ + +++
1011	5.80E-05	forward	3932585	3932612	TAATTAAACAGTTTTCTTCAATATATTT TTTTAATTACGTTTTTTTTACAGATATAA + + + ++++++++ ++++++++
1012	4.20E-05	forward	3932863	3932890	TCTTCAGCCGTTCTTTTCGCAATAAGTT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ + ++ +++++ ++ +++ ++
1013	4.20E-05	forward	3933077	3933104	TGATCAGCGTTTTTCCTTACCCTTAATA TTTTAATTACGTTTTTTTTACAGATATAA + +++ +++++++ +++++ +++ ++
1014	5.10E-05	reverse	3933960	3933987	ATTTTTATAATAGATAACTGAAGGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ +++ +++ ++ ++ ++
1015	4.50E-05	reverse	3934108	3934135	ATAGTATTATACGGTCGCGGTAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ ++++ + +++ + ++++
1016	5.80E-05	forward	3935083	3935110	TAATAACTGAATCTTTTAATTCATAGTT TTTTAATTACGTTTTTTTTACAGATATAA + +++ ++ + ++++ ++ +++ ++
1017	3.20E-05	forward	3935230	3935257	TTTCAATCGCTTTCTTAGAGATATTTTC TTTTAATTACGTTTTTTTTACAGATATAA +++ +++++++++ ++ + +++++++
1018	5.80E-05	reverse	3935276	3935303	GTTAATTAAAATAAAACCGGCATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ + + ++++ ++ +++++++
1019	1.70E-05	forward	3935733	3935760	TTTTTATCAATCCCATAAGCTATATTAA TTTTAATTACGTTTTTTTTACAGATATAA ++++ ++++ ++ ++ + ++++++
1020	3.90E-05	reverse	3936967	3936994	ATATTAAATAGCAAAAATAGTAATATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ + + ++ ++
1021	3.20E-05	reverse	3940412	3940439	TTTTAATCATAAATTCAAAGAGATAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++++++ +++ + +++ +
1022	1.10E-05	forward	3940951	3940978	TGTTCAGCACGTTTACTTGCCTTATGAT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ ++++++++++ + ++++ ++
1023	4.20E-05	reverse	3945726	3945753	GATGAATTACTAATAAAAATGGTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ ++ ++++++++++ + ++++
1024	8.00E-05	reverse	3951646	3951673	TTAAATTATCTAAGTCAAAATAGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA

1024	8.00E-05	reverse	3951040	3951073	++++++ ++ +++ + ++++
1025	6.20E-05	reverse	3971190	3971217	AAAACCATGTTAATCAACAGGATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++++ +++ ++++ +++ ++ +
1026	3.00E-05	reverse	3980589	3980616	TAAATCATGAGAAAAAATATCCTGATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++++++ ++ +++ ++
1027	7.10E-05	reverse	3980924	3980951	ATAGAAACATTTATTCATAATATGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ ++ ++ + + +++++ +
1028	6.60E-05	reverse	3981773	3981800	TTATACCAAAGCGCAGGAAGTAGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + + + + + +++ + +++++
1029	7.10E-05	reverse	3985673	3985700	AATTATCTATGCATAAAAAAGGTTATTG TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++ +++++++ + +++
1030	7.10E-05	reverse	3986979	3987006	AAAATAAAACAACATGACGAGGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ + +++ + ++++
1031	4.80E-05	reverse	4005279	4005306	AGATATGCGTGTGTAAATTGACTGATAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ +++ +++++ + +++ ++
1032	1.40E-05	forward	4020969	4020996	TATTTTTTCTTTTTTTGAAAAGTAATCA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ +++++++ + ++++++ +
1033	4.80E-05	reverse	4028727	4028754	TTCATTGAGGAAAGAGATAAGAAGAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ + + + ++ +++ +
1034	4.70E-06	forward	4031779	4031806	TTTTAATCCGGCTTTTTTTTGCAGTTTA TTTTAATTACGTTTTTTTTACAGATATAA ++++++++ ++++++++ + + ++++
1035	7.10E-05	reverse	4055435	4055462	TTATAAGACGTAAACGAAAGACATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ +++ + +++++
1036	4.20E-05	reverse	4058132	4058159	ATTATCATCGGCATGGACCCGATGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ + ++ ++ +++++++ +
1037	9.80E-06	reverse	4058164	4058191	AGCTATCTGGGAAAAAATGCTCAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++++ +++++++ ++ ++++
1038	5.50E-05	forward	4060097	4060124	TTTTTATTCAGCTATGTCGATGAACATC TTTTAATTACGTTTTTTTTACAGATATAA ++++ +++ +++ + ++ +++ +
1039	1.40E-05	forward	4061884	4061911	TTTTATTCTTGTTCAGATATTCAACAAA TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++ ++++ + +++ ++ ++
1040	2.10E-05	reverse	4066817	4066844	TATTTTCCGCACAAAAAGGCGTGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + +++++ +++ +++++
1041	6.60E-05	reverse	4071066	4071093	AAATTACATCAAATGAACACAAAAAACG TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ +++++++ ++

1042	7.50E-05	reverse	4072360	4072387	TATGAATAATATGGAAAATATAACAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ + ++++ + ++ +
1043	3.40E-05	reverse	4072642	4072669	TTTTTCATCAACGGAAGACAAATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ + + ++++ +++ ++++
1044	1.40E-06	reverse	4072683	4072710	AAATCAATGTTTGAAGAAACTATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ +++++ +++ ++++ +++++++
1045	5.10E-06	reverse	4073367	4073394	ATTAATATTTCAACAAAAATTATTAACA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + ++ ++++++ +++++ +
1046	9.80E-06	reverse	4073745	4073772	ATAAAATTGCAAAAAGAAACTCAGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ +++++ ++++ ++ ++
1047	3.40E-05	reverse	4074207	4074234	ATTTAACCTTTTCAACAAATAATAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + ++ +++++++ ++ +
1048	8.50E-05	reverse	4074559	4074586	TAAATTACAAAAACAAAAAGACAAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ +++++ + + ++
1049	9.00E-05	forward	4074689	4074716	TAATCATAGATTTTCCAGAAAAATAAAT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++++ + + + +++ ++
1050	1.60E-05	reverse	4087494	4087521	TTTTAATTTAAAGAAAAAGCGGGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++++++++ ++++
1051	2.80E-05	reverse	4088376	4088403	ATCATCGGCTAAAAAGGGGATATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++++ + + +++++++
1052	6.20E-05	reverse	4093797	4093824	TTTTCATCGTAAAATGGAAGAAGGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + ++++++ +++ ++ ++ ++
1053	5.10E-05	reverse	4094055	4094082	TAATTACGCGACATAAAAATCCGCAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++++++ ++++
1054	5.50E-05	forward	4097163	4097190	TGTTAATAAATTTGTTGCTGACAATGTA TTTTAATTACGTTTTTTTACAGATATAA + +++++ + +++ ++ + + +++ ++
1055	8.80E-07	forward	4102456	4102483	TTTTTTTTCTATTTTTTTTGATAAAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ + +++++++ +++++ ++
1056	9.60E-05	forward	4103097	4103124	TGTTGAGCACGGTCATTACCTGTTAATA TTTTAATTACGTTTTTTTACAGATATAA + ++ + ++++ + +++ + ++++ ++
1057	9.00E-05	forward	4105465	4105492	CGATCTTTACATTTATTTGAGTAAATTA TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ +++++++ +++++++
1058	2.50E-06	forward	4106462	4106489	TTTCCATCGCTTTTTCTTATGCAGATTA TTTTAATTACGTTTTTTTACAGATATAA +++ ++++++++++++++ + ++++

1059	7.10E-05	forward	4116518	4116545	TGTTCAGGCTGTCTTCGCCCAGAACGAT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ +++ +++ + +++++ ++
1060	2.40E-05	forward	4120965	4120992	TCTTCCTTTCTCTTTCGTTTGGTTATTA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ +++++++ + + +++++++
1061	3.70E-05	reverse	4121066	4121093	ATTGATGAAAAAAGAGACACTCAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + +++ + ++++ +++++
1062	9.60E-05	reverse	4130252	4130279	TTCGAACAAGATGCAAGAATAGACAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + + +++++++ ++++
1063	7.10E-05	reverse	4141722	4141749	ATCTCCAACTGGAAAAACGATCTCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + ++ +++++++ + ++++
1064	7.70E-06	forward	4143487	4143514	TTTTCATTTAGCGCCTGTAGCGTAATTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++ + ++ +++++++
1065	5.80E-05	forward	4157540	4157567	TATTTTTCACTTTGTTGCGGCGTATTTT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++++++ ++ + +++++++
1066	3.40E-05	forward	4163125	4163152	TTTTTTTAATGCCTGCGCCTGTTTTTTA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++ + + + + +++++++
1067	5.80E-05	forward	4170976	4171003	TAATATTTTTTCTTATACAATTTATGTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ +++++++ ++ ++++ ++
1068	4.50E-05	reverse	4171837	4171864	ATCATTGCAGCAATGAAATCAAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + +++ +++ +++ +++++
1069	5.50E-05	forward	4172061	4172088	TATTCTTCTGGCTCTCCTGCGGAATTAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++ +++ ++ + + +++++++
1070	4.50E-05	forward	4173507	4173534	TTTTACGCCTTCTCCTGCGATGATAGAA TTTTAATTACGTTTTTTTACAGATATAA +++++ + ++++ + + ++++ ++
1071	7.10E-05	forward	4180733	4180760	TATTGATACCTTTAACCTCTTTTTCATA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++++ ++ + + +++ ++
1072	8.40E-06	reverse	4180905	4180932	ATAAATCCATGAGAAGAAAAAGGCAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ +++++++ +++ + ++ +
1073	2.80E-05	reverse	4181420	4181447	TTATATTTATTAGCGCGAATGATAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++ +++++++ + ++
1074	3.60E-06	forward	4183049	4183076	TCTTAATTGTTGTTTTCTACTTTAAGAA TTTTAATTACGTTTTTTTACAGATATAA + +++++++++ ++++ +++ ++++ ++
1075	5.50E-05	forward	4186610	4186637	TATTCACCTGATTATTTCGCGCTAATTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++ ++++ + ++++++
					TTTTTCTCATTTCCCTTTTTCTTATTTT

1076	3.40E-05	forward	4193671	4193698	TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++++ +++ + +++++++
1077	2.00E-05	forward	4198919	4198946	TTTTCATTCTGTGGCGTCAAAGTACGAT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++ +++ ++++ ++
1078	6.20E-05	reverse	4200632	4200659	AAATCAAACGGTAAAGAAGTGGTTATTA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + +++ +++++ +++ +
1079	3.40E-05	forward	4206305	4206332	TTTTGCGCCAGTTTATGTATACGAAATT TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++++ ++++ ++ ++
1080	7.10E-05	forward	4207174	4207201	TGTTAACCATCCGAATTTGCGTATTGAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ +++ + ++++ + ++++ ++
1081	1.70E-05	reverse	4207523	4207550	TGTATTGCGTGTAATAAATTAAGTAATA TTATATCTGTAAAAAAACGTAATTAAAA + +++ +++ ++ +++ +++ +++ +
1082	7.10E-05	forward	4208126	4208153	TGTTAAAAAGGTTTCCCCAGAATTTAAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ + ++++ + ++ + +++ ++
1083	5.10E-05	reverse	4213100	4213127	TATTTTGTGTTAAAAAAATGCAAATAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ +++++++ + +++
1084	8.00E-05	reverse	4217211	4217238	ATCGTCGGCAAAATAAACGCAAAGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++++++++++ +++ +
1085	3.40E-05	forward	4217263	4217290	TTTAAATTTCCTCTTGTCAGGCAAAAAT TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ + + ++ +++ +++ ++
1086	3.90E-05	forward	4225766	4225793	TTTTTCTCCTTCTACTGCCCACATTGTT TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ + + ++ +++ ++
1087	3.40E-07	forward	4226299	4226326	TTTTAATCTCTTCTATCTGTATATCTTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ +++ +++ + +++++ +++
1088	1.10E-05	reverse	4230427	4230454	AATTCCCTATGTAAAGAATGAAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++++ +++ ++ ++ ++++
1089	6.60E-05	forward	4243304	4243331	TAATAATCGCGTCGATATAGCTATCAAT TTTTAATTACGTTTTTTTACAGATATAA + +++++++++ ++ ++ +++ ++
1090	5.10E-05	forward	4243337	4243364	TATTATCTGCGCCAGTGCAGGTAAATAA TTTTAATTACGTTTTTTTACAGATATAA + +++ +++++ + ++ +++++++
1091	8.00E-05	reverse	4244792	4244819	GTTTTCCTGCTGAAGAACGCCATTAATA TTATATCTGTAAAAAAACGTAATTAAAA + ++ +++ ++ +++++ +++++ +
1092	9.00E-05	forward	4250966	4250993	TTTTGATGACGTCTTTGAACCAGTCGTA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++++ +++ ++ + ++
1093	2.40E-05	forward	4262866	4262893	CTTTGACTGTATGTATGTACAGTTTATA TTTTAATTACGTTTTTTTACAGATATAA

1093	2.40E-05	forward	4262860	4262893	+++ + +++ + +++ ++++++++ ++
1094	7.50E-05	reverse	4265154	4265181	ATCAACCAGTTGAAGGATGGGAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++ ++ + + ++ +++++
1095	3.60E-06	reverse	4269423	4269450	TTATATGGTTAAAAGAAAGTGAACAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++++ +++++++ ++ +
1096	5.80E-05	reverse	4271349	4271376	GTAAATATCTGCCTGGAGATTATTATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++ + + ++ ++++ ++
1097	7.50E-05	reverse	4271675	4271702	TATTTCATTATAATTAACATTATCAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++ +++ +++++ ++ ++ +
1098	1.80E-05	reverse	4271738	4271765	AAATATACAAAAGGCAATTAAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++ ++ ++++++++
1099	8.00E-05	reverse	4272315	4272342	AATATTATACCCAGGAAAACTATAAAGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++ + +++++ ++ ++ +
1100	5.50E-06	reverse	4272901	4272928	ATAAAATTACGCGATAACGCCAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++ + ++ +++++ + +++++
1101	3.40E-05	reverse	4283578	4283605	TTTGTTTTCTAAAATACCTTCATCATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + +++++ + + + ++ + ++
1102	3.70E-05	forward	4283710	4283737	TAATTATTTGGTTGTTTTATTTGTATTT TTTTAATTACGTTTTTTTACAGATATAA + + +++ +++ ++++++ + +++++
1103	2.60E-05	forward	4283811	4283838	TGTTGATGGTGTTTTGATTTTTATTTTA TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ +++++++ + + +++++++
1104	5.10E-06	forward	4283854	4283881	TTTCATTTATTTTATTTTGCTTTTTGAA TTTTAATTACGTTTTTTTACAGATATAA +++ + +++++++ ++++ + ++++ ++
1105	7.50E-05	forward	4284671	4284698	TAATCATTATCCCTGTTTATTATTTATT TTTTAATTACGTTTTTTTACAGATATAA + +++++++ + + +++++ +++ ++
1106	6.20E-05	forward	4287835	4287862	TTTTCAGCGGATGCCGTAACGTTTATAA TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ + + ++ +++++++
1107	6.60E-05	forward	4296805	4296832	TCTTATTGATTCTTATCCCGGTTTAAAA TTTTAATTACGTTTTTTTACAGATATAA + +++ + ++++++++ + ++++ ++
1108	4.20E-05	reverse	4296854	4296881	AAAAATATGTGAAATCGATCAAAAGATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++++++++ ++ +++ + +
1109	7.50E-05	forward	4303716	4303743	TTATTTTTTTATTTTTCAATAATTTGAA TTTTAATTACGTTTTTTTACAGATATAA ++ + ++ + +++++ +++ +++ ++
1110	6.60E-05	forward	4304868	4304895	TTTTGAACAATTTCTTTTTCAAAAAACA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++ +++ ++++ ++ +++ +

1111	4.20E-05	reverse	4304970	4304997	TGATTTGTGTGCAGAACATTTATAAAAG TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++++ + ++ + + ++ +++
1112	3.60E-06	reverse	4308532	4308559	AAAAAAATGGCAAGACACAGCATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ ++ + +++ +++++++
1113	5.10E-05	reverse	4317807	4317834	TTCGAAGTCCACAAAAAGATTGTAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + +++++ ++ + + ++
1114	1.80E-05	forward	4318377	4318404	TGTTAACACTTTTAAGTTATTGAATGAA TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++ + ++++ ++++ ++
1115	6.00E-06	forward	4328301	4328328	TTTTACTTTTACTATCTCGCTTTATTTT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ + ++ ++++ + +++++++
1116	8.00E-05	reverse	4330131	4330158	TATTATCGATAAAATGAATGTATATTAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++++ ++ ++ ++
1117	4.80E-05	reverse	4330167	4330194	TTTATCGGAGATGAAAAAACATTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + +++++++++ ++++++
1118	6.60E-05	forward	4334929	4334956	TTTTCATCCATTGCTTCCTTGATATTTT TTTTAATTACGTTTTTTTACAGATATAA ++++++++ ++ ++ + + ++++++
1119	2.10E-05	forward	4336720	4336747	TATTTATCCCTTGTTTTCCATAGAAAAT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ +++ +++++ ++ ++
1120	5.80E-05	reverse	4339915	4339942	ATAGATGTTTACAACACAACAAATAATA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ + ++ ++ + +++++ +++ +
1121	7.70E-06	reverse	4356593	4356620	TAAAATGCAGACAGAAATATATTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + + +++ +++ ++++++
1122	4.20E-07	forward	4366821	4366848	TATTACTCACCTGTTTTTATACATAAAA TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++ + ++++++++ +++ ++
1123	3.40E-05	forward	4372227	4372254	TTTAAATTTCCTCTTGTCAGGCAAAAAT TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ + + ++ +++ +++ ++
1124	4.50E-05	forward	4380159	4380186	TATTAACAGCTTCTTCTTTAGATAATTT TTTTAATTACGTTTTTTTACAGATATAA + ++++ ++++ +++++ ++++++
1125	1.60E-05	reverse	4392995	4393022	GTATCACTGAATATGAAAAAGATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++++ + ++ ++++ ++++++++
1126	2.40E-05	forward	4395741	4395768	TTTTTATTGTTTCTATCGTTATATATAC TTTTAATTACGTTTTTTTACAGATATAA ++++ +++++++ +++ ++++++++
1127	2.80E-06	forward	4395943	4395970	TTTTCATGACTCTTGTTTCTCGTATTAT TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++++++ +++ + +++++++

1128	6.20E-05	forward	4396453	4396480	CTTTGTTTGCTCTTATTACAGGAATTAT TTTTAATTACGTTTTTTTTACAGATATAA +++ ++++++++++ +++++++
1129	8.50E-05	reverse	4397338	4397365	ATATATCTTGATGCTGATATGATTATCA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + + + +++++++ +
1130	9.60E-05	forward	4397701	4397728	CAATAATCATGCTATTGAATACATAAAA TTTTAATTACGTTTTTTTTACAGATATAA ++++++++++ ++ +++ +++ ++
1131	3.40E-05	reverse	4409723	4409750	ATCTCTGCTTAAGTAAGGAAAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + + ++++++++ + +++ ++++
1132	8.00E-05	forward	4414644	4414671	CTTCTTTCACATTTTCTTCTATATAGAA TTTTAATTACGTTTTTTTTACAGATATAA ++ ++++ +++++++ ++++++ ++
1133	1.70E-05	forward	4421973	4422000	TCTTCACTCCTTTTTTGCTTACTTCTAT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ + +++++++ + ++ ++ +++
1134	4.20E-05	forward	4423173	4423200	TTATCAATAGGTTAATGCATAATTAAAT TTTTAATTACGTTTTTTTTACAGATATAA ++ +++ ++ +++ ++ ++++ +++ ++
1135	1.80E-05	forward	4426672	4426699	TTTCAACTCCGTTTATTGCCGGTTATTT TTTTAATTACGTTTTTTTTACAGATATAA +++ ++ + ++++++++ + +++++++
1136	4.20E-05	reverse	4433522	4433549	AATTTATCGCAAGTGAGCTTCAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ +++ + + +++++
1137	2.60E-05	reverse	4436455	4436482	AACTTCACCGATAATAACGTCATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + + ++ +++++ ++ ++++
1138	1.60E-06	forward	4439542	4439569	TTTTCATAAATTCATCCCACACATTTTT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ + ++ ++ ++++ ++++++
1139	3.20E-05	forward	4440014	4440041	TGTTCATATGGTTATCGAAGTTTTATTA TTTTAATTACGTTTTTTTTACAGATATAA + +++++ +++ ++ + +++++++
1140	1.80E-05	forward	4440057	4440084	TGTAATTTATTTGTTTATAATGTTATTA TTTTAATTACGTTTTTTTTACAGATATAA + + + ++++++ +++ ++ +++++++
1141	7.70E-06	forward	4440111	4440138	TTTTAATGATTGTTTTGTCTTTTATATT TTTTAATTACGTTTTTTTTACAGATATAA +++++++ +++ ++++ + + ++++ ++
1142	5.10E-05	forward	4440249	4440276	CCATAATCCAGTTTTTTTCTGTTTTTTT TTTTAATTACGTTTTTTTTACAGATATAA +++++ ++++++++ + +++++++
1143	1.60E-05	reverse	4457413	4457440	TAATCTCCTTTAGAGAAAAAAGTTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++ ++ + +++ ++++ + ++++++
1144	2.00E-05	forward	4459129	4459156	TATATATTTTTTTAATTTATAATTAAAT TTTTAATTACGTTTTTTTTACAGATATAA + + +++ ++++ +++++++ +++ ++
					TATTGATTTTATTTGTTTGTTAATTAAA

1145	7.10E-06	forward	4463366	4463393	TTTTAATTACGTTTTTTTACAGATATAA + ++ +++ + +++ +++ + +++ ++
1146	6.50E-06	reverse	4463522	4463549	TTCATTCAATGAAGGGAAGTTATGATGA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++ ++++ ++++ +
1147	7.90E-07	reverse	4467369	4467396	ATTGAACAAAATATAAACATAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + + ++++++++++ +++++
1148	6.60E-05	reverse	4486305	4486332	TTTTTCTTATATATCAATAATATAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++ ++ ++ + ++ ++ +
1149	3.90E-06	reverse	4491954	4491981	TTTGAATTTTAAGGGAAAACCATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++++ +++++ +++++++
1150	5.50E-05	forward	4494642	4494669	TTTTAATGACGTCCAGGTTGTGTTCGAT TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++++ + + +++ ++
1151	1.10E-05	reverse	4498391	4498418	ATTTTTTGACAACAAAAAGATATTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ ++++++ ++++ ++
1152	1.60E-05	forward	4498572	4498599	TTATTTGTGTATTTTTTTACACAATTCT TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ ++++++++++ ++++ +
1153	5.50E-05	forward	4499220	4499247	TCTTATGTTGGTGTTTGCACTTAATAAT TTTTAATTACGTTTTTTTACAGATATAA + +++ + ++ +++ +++ ++++ ++
1154	6.50E-06	reverse	4499251	4499278	ATTATTATGTATGACAACTCAATTAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++++++ ++ +++ ++++++++
1155	1.30E-05	reverse	4499969	4499996	AAATATTTCAGCAAAAGACATATTAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + + ++++++ +++++ +
1156	3.20E-05	reverse	4500419	4500446	TGTTTCTACGGAAATCAAAAAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++ ++++ +++ ++++++++
1157	1.70E-05	reverse	4500818	4500845	TATTATAGATAAAAAGAATGATTCAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++++++ ++ + + ++ +
1158	9.80E-06	reverse	4501504	4501531	AAAACTGACTATGAAAAAACAAAGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++++ + ++ ++++++++++ +++ +
1159	6.20E-05	reverse	4501598	4501625	TAAATCTGGAGAAAGAGTTTTATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + ++++ ++ + ++ ++++
1160	2.40E-05	reverse	4503761	4503788	ATATTATGGGAAATAAAAGCATACAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + ++++++++++ ++++
1161	5.80E-08	reverse	4504092	4504119	AAATAAGAAGGAAGAAGAGGAATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ +++++ ++++++++
1162	6.50E-06	reverse	4504421	4504448	AAAGTAATAGCAGTAAAAATGAGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA

1162	6.50E-06	reverse	4504421	4504448	+++ +++++ ++++++++++ +++++
1163	6.60E-05	reverse	4504963	4504990	TTATCTGAGGGCGAAAATAGTATAAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++++ + + + +++++ + ++ +++
1164	7.50E-05	reverse	4520890	4520917	AGTATAAGAGTAAAAAATATCATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ + ++++++ ++ ++ ++++
1165	7.70E-06	forward	4521320	4521347	TATTTCTCATTGTTATATATGTAAATTT TTTTAATTACGTTTTTTTACAGATATAA + ++ +++++ ++++ +++ +++++++
1166	9.10E-06	forward	4521534	4521561	TTTTGATTGGGTTAATACATCAAATGAA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++++ +++ ++ +++ +++ ++
1167	6.60E-05	forward	4523223	4523250	TTTCTATTTCATTGTTTTTGTGAACTAT TTTTAATTACGTTTTTTTACAGATATAA +++ +++ + ++ ++++ +++ +++
1168	2.40E-05	forward	4523366	4523393	TATTATTACTACTCTTTTATTTTTTTTC TTTTAATTACGTTTTTTTACAGATATAA + +++ + + ++ ++++++ ++++++
1169	3.90E-05	reverse	4525637	4525664	ATAATTCCTCAAGTTAACTTGAGGTAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++ +++ +++ + +++
1170	7.50E-05	reverse	4546475	4546502	TATTTAGGGTACGGAAAAGACAGTATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ +++ + +++++ + ++ ++
1171	4.80E-05	forward	4548783	4548810	TTTTCATCGGTTTCGCTCCAGTTAATCA TTTTAATTACGTTTTTTTACAGATATAA +++++++++ +++ +++ +++++ +
1172	2.80E-06	forward	4548859	4548886	TTTTTAGTATGGGCTTTCCCTGATATTA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++ ++++ + +++++++
1173	5.80E-05	reverse	4552258	4552285	AGCTATGCTGAAAAGGAAAAAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA + +++ ++++ +++ ++ +++++
1174	2.00E-05	forward	4557298	4557325	TTTTAAGAAAGCGCTTTAACATGTTGAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ + ++ +++ ++++ ++ ++
1175	5.50E-06	reverse	4558984	4559011	ATAAAACTCTTTAAACACGGAAATAAAG TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + +++ +++ ++ ++++
1176	1.10E-05	forward	4569870	4569897	TTTTTACAGAGTTGCTTTAAGTAATTAT TTTTAATTACGTTTTTTTACAGATATAA ++++ + + +++ ++++ +++++++
1177	6.20E-05	forward	4570273	4570300	TTTTGTTAGCGTTTTGAAATTAAAAACA TTTTAATTACGTTTTTTTACAGATATAA ++++ + +++++++ ++ +++ +
1178	8.00E-05	reverse	4573159	4573186	TGAGAAATAAAAAATGGAAATAAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + +++++ ++++ +++ + ++++
1179	9.60E-05	forward	4580565	4580592	TATAAATTAACTCTCTCTGTAATAATTA TTTTAATTACGTTTTTTTACAGATATAA + + +++++ + + + + ++ ++++++

1180	3.90E-05	forward	4582084	4582111	TGTTCATGAGTCTCTTCCATAGTGATAT TTTTAATTACGTTTTTTTACAGATATAA + +++++ + +++ ++ ++++++ ++++
1181	2.80E-05	reverse	4582386	4582413	AAATATTTCAAAAGAAAACTAATATATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ + +++ ++++ ++++ + +
1182	3.00E-05	reverse	4582523	4582550	TATGTCGCGTATAAAAAAAAGATGGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ +++++++ ++++ +++
1183	1.60E-05	forward	4582571	4582598	TTATTATCAATTTATCTCTTTAAAATTT TTTTAATTACGTTTTTTTACAGATATAA ++ + ++++ +++ ++++ + ++++++
1184	2.40E-05	forward	4585098	4585125	TTTTGTTTAACTTTTGTCCCCGATTATT TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ ++++ ++ + ++++ ++
1185	5.80E-05	reverse	4594447	4594474	TTTAAATTCAGACGACAAATGCGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++ + +++++ +++++
1186	3.40E-05	forward	4597506	4597533	TTTTCTTTTAGTCATCTTTTTAGTATAA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ ++ ++++ + +++++
1187	4.20E-05	forward	4598874	4598901	TTTTACTGCAATGTATTTGATATATAAA TTTTAATTACGTTTTTTTACAGATATAA +++++ + + +++++ +++ ++
1188	5.50E-05	reverse	4617690	4617717	TATAATTTACTGAAAAATATAGAAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ +++++ +++ ++++
1189	9.00E-05	forward	4620416	4620443	TTTTTACTACGCTGCGGCGTATTGTTAA TTTTAATTACGTTTTTTTACAGATATAA ++++ + ++++++ + ++++ ++++
1190	7.50E-05	forward	4631080	4631107	TTTTCCTTCCCCGAACTGAAATAAATTA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ + + +++ + ++++++++
1191	3.00E-05	reverse	4633861	4633888	GAAAAAGCGAAAAAAGGTGAAAGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ + +++++ + + ++ +++++
1192	7.50E-05	forward	4634949	4634976	TTTTTTTTTATCTTTGACTGGTAATATA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ +++++ + ++++ ++
1193	4.30E-06	reverse	4635009	4635036	TTATAAAAATGAGATAGAGATAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ ++++++ ++++ + ++ +
1194	3.90E-05	reverse	4635718	4635745	TTTACTCAACGAAGTGGCGGAAGAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++ + +++ +++ ++ ++ +
1195	9.60E-05	forward	4643984	4644011	TAATCACTACGCTTTCACCCGGGTTTAC TTTTAATTACGTTTTTTTACAGATATAA + +++ +++++++++ + + + ++++
1196	3.70E-05	forward	4645621	4645648	TTATGATTTTACTTATTTTAATGAAAAA TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ + +++++++ ++ ++ ++

1197	9.60E-05	reverse	4654766	4654793	GAAATACCTGGAAGAAAACCGCGAAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ +++ ++++ ++ ++++
1198	1.60E-06	reverse	4663806	4663833	AGATAATTCTGAATAACTGTAATCAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ + +++++++ +++++ ++++
1199	2.40E-05	reverse	4663944	4663971	AATACTCTGCAGGAGACAACAATGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ + ++++ + ++ + ++++++++++
1200	8.00E-05	reverse	4673550	4673577	TAAATACGCCGCCAAAAATATTTGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ ++++++
1201	3.70E-05	forward	4675205	4675232	TATTCATTCCGTGAATGTTAAATTAATA TTTTAATTACGTTTTTTTACAGATATAA + ++++++ +++ ++ + + +++ ++
1202	7.50E-05	forward	4677071	4677098	TTTTCATAACACTTTCCCTGCAATTGAT TTTTAATTACGTTTTTTTACAGATATAA +++++++ ++ +++++ + +++ ++
1203	5.50E-05	forward	4679654	4679681	TTTTAATTGACGGTATTGGCGGAATGTT TTTTAATTACGTTTTTTTACAGATATAA +++++++++ ++++ + ++++ ++
1204	1.70E-05	reverse	4680861	4680888	TAAAATACAGAACAAAATGCAGGGAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++ ++++ +++ +++ +
1205	2.10E-05	reverse	4681819	4681846	ATTTTTCTTCTAATGAATGCAAAAATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ +++ ++ ++++ + ++
1206	2.80E-05	forward	4686020	4686047	TTTCCATCTCTTTTTTATCCTCTTAAAC TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ +++++++ + + +++ +
1207	3.70E-05	reverse	4687204	4687231	AATTACTTCAAAAATAAAGTAGGGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ + ++++ ++++++ +++++
1208	1.60E-05	forward	4695085	4695112	TGTTTTTTGTTTTAATTGATTGATTATA TTTTAATTACGTTTTTTTACAGATATAA + ++ +++++++ +++ ++ ++++ ++
1209	3.70E-05	forward	4695199	4695226	TTTTGATCTCCTTCCCATAAATGAAATA TTTTAATTACGTTTTTTTACAGATATAA ++++ +++ + ++ + ++ ++ ++ ++
1210	2.60E-05	reverse	4701113	4701140	GTTGATATGGGCGTACAGGTGATTAATA TTATATCTGTAAAAAAACGTAATTAAAA + +++++ + +++ + ++++++++ +
1211	7.10E-05	reverse	4703835	4703862	TTAATAATAAAAAAGGAAGTGAGCAATG TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ ++++ ++++++ ++
1212	7.50E-05	reverse	4715503	4715530	AATTTTATTGATGTAGAACAAGGTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++++ + +++ ++ + +++++
1213	5.80E-05	forward	4725998	4726025	TTTTGTCCCTTCGTATTTCTGATTTTTA TTTTAATTACGTTTTTTTACAGATATAA ++++ + +++ +++++ + ++++++
					ATTTTTCAGTGAAATAACCATTACAATA

1214	8.50E-05	reverse	4728833	4728860	TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ ++++++ +++ ++ +
1215	1.30E-05	reverse	4731752	4731779	TTTTTCTCGTATAAAGAGAAAAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ +++ +++ + + ++ +++++
1216	5.10E-05	reverse	4731783	4731810	TGTTTTAACTAAGGGGATGCGATGATTA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++++ + +++++++ +
1217	8.50E-05	forward	4733368	4733395	TTAAAATTCACTTTATATGGATGATTAT TTTTAATTACGTTTTTTTACAGATATAA ++ ++++ +++++ + ++ +++++
1218	2.80E-05	reverse	4736159	4736186	AAATAAAAGGCGGAAAAATTAAACAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + ++++++ +++ ++++
1219	6.60E-05	reverse	4748303	4748330	AATATCCTGTTTATGGGTGACATTAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++ ++++ ++ + + +++++++
1220	9.00E-05	forward	4755718	4755745	TGATTACGGCGTGTTCACGTGGTATTAA TTTTAATTACGTTTTTTTACAGATATAA + + + ++++ +++ + + +++++++
1221	9.00E-05	forward	4756082	4756109	TCTTATCAGTGTTTCCCCAGGGTAAGAT TTTTAATTACGTTTTTTTACAGATATAA + +++ ++++++ + ++ ++++ ++
1222	2.30E-05	forward	4760255	4760282	TTTTACTGCCATCCCTTTATATTTCTTC TTTTAATTACGTTTTTTTACAGATATAA +++++ + + + +++++++++ ++
1223	1.30E-06	reverse	4764742	4764769	TAATTTATCTATAAAAATATTATTTATA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ ++ +++++ ++ +++ + +
1224	3.40E-05	forward	4765474	4765501	TTTTAATGCTATTTTTTCTCCAAGTTTT TTTTAATTACGTTTTTTTACAGATATAA +++++++ + +++++++ + + ++++
1225	6.60E-05	forward	4765626	4765653	TTTTCTTTACTTCTTCCCTACCATCTAT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++++ +++ + ++ +++
1226	2.80E-05	forward	4771957	4771984	CTTTGATCAAGTTGTTACCCATTTTTTT TTTTAATTACGTTTTTTTACAGATATAA +++ ++++ +++ ++ + +++++++++
1227	1.30E-05	forward	4773185	4773212	TTTTTATAACAGCTTTATAAATTAAACA TTTTAATTACGTTTTTTTACAGATATAA ++++ ++ ++ +++ ++ +++++ +
1228	1.60E-05	forward	4774145	4774172	TTTTCTTCTGGTTCTTTTTTTATTTTTA TTTTAATTACGTTTTTTTACAGATATAA +++++ ++ +++ ++++ + ++++++
1229	9.00E-05	forward	4776711	4776738	TATTGATTAAACTCATATACCCGATAAT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++++ ++ ++ +++ ++ ++
1230	9.60E-05	reverse	4778067	4778094	TGAGTTTTGCGAAAGCATGCGAATATTA TTATATCTGTAAAAAAACGTAATTAAAA + + ++ ++ ++++ + ++++ ++ +
1231	1.70E-05	reverse	4778433	4778460	ATTATTCCTTATATAAATATAAAGGAAA TTATATCTGTAAAAAAACGTAATTAAAA

1231	1.70E-05	reverse	4778433	4778460	++ ++++ ++ +++++ ++++ + +++
1232	4.50E-05	reverse	4778546	4778573	AATAAATTGAGTGAAGACTTACAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ ++ + +++ ++ ++ +++++
1233	7.50E-05	forward	4778713	4778740	TATTGATTTTGTTCGTCAGGATAATTTT TTTTAATTACGTTTTTTTTACAGATATAA + ++ +++ ++++ + ++++++++
1234	5.10E-05	reverse	4778750	4778777	AAAGTAGGTTGACAGGAAGTAATAATAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ +++ + +++++++ + ++
1235	2.40E-05	reverse	4783785	4783812	AACATTAAATATATTCACATAGTAAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ +++ ++ +++++ + ++ +
1236	1.80E-05	forward	4783946	4783973	TGATATTTCTTTTTTGATATGGTTCTTA TTTTAATTACGTTTTTTTTACAGATATAA + ++ ++ ++++++ +++ +++ +++
1237	1.70E-05	reverse	4784811	4784838	TGATTTTTACGCATAGCCGCTAATAAAA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ ++ + +++ +++ + +++++
1238	8.50E-05	forward	4789319	4789346	CCTAAATTTTACTTTTTTACTGTAATTT TTTTAATTACGTTTTTTTTACAGATATAA + ++++ + +++++++++ +++++++
1239	1.80E-05	reverse	4789410	4789437	TAAGAATCCTACGGGCAGGTAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ ++ + + +++++ ++++
1240	3.00E-05	forward	4796889	4796916	TTTTTCTCAATGTATTTTTCTGGTTTTA TTTTAATTACGTTTTTTTTACAGATATAA ++++ +++ + + ++++ + + +++++
1241	5.80E-05	reverse	4797102	4797129	TGTATAAGATAAGGAAAAGATAGAAATA TTATATCTGTAAAAAAACGTAATTAAAA + ++++ +++++ +++++ + ++ +
1242	5.80E-05	reverse	4797351	4797378	AAAAAAATCTCAGATAAAGCAAGCGAAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++++ + +++ +++++++ +++
1243	1.10E-05	reverse	4798033	4798060	AAATACCTGTACATAACATCAGTAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++++ ++++ + ++ + ++ +
1244	8.50E-05	reverse	4798129	4798156	GGTTATGATTGCGGGGAAATAATAAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++ ++ + +++++++ ++++
1245	2.00E-05	reverse	4807492	4807519	TACGTCATGGGAGAAAAAGGTCTGAATA TTATATCTGTAAAAAAACGTAATTAAAA ++ + +++ +++++++++ ++++ +
1246	5.10E-05	reverse	4810301	4810328	TAAAACCTGGTTGTAAGTTTAATTATCA TTATATCTGTAAAAAAACGTAATTAAAA +++++ +++ +++++ ++++++ +
1247	7.10E-05	reverse	4819111	4819138	TAAAATCTGAACAATCAGGAGAAAAATA TTATATCTGTAAAAAAACGTAATTAAAA +++++++++ + ++ + + ++ ++ +
1248	1.90E-06	reverse	4822739	4822766	TTAATAACAGGAAAAGACGAAGAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA +++++++ + +++++ +++ + +++++

1249	9.00E-05	forward	4826498	4826525	TCTTGCTTCTGGTTTTATGAGTAACTAT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++ ++++ + +++ +++
1250	3.20E-05	reverse	4826578	4826605	TATATTTTTAAAAATAAAACAAGGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++ +++ + ++++ +++++++ ++ ++
1251	2.00E-05	forward	4826620	4826647	TTATATTTCTTTGCGCTCATTGTTAATA TTTTAATTACGTTTTTTTACAGATATAA ++ ++ ++ +++ +++++ ++++ ++
1252	3.30E-06	reverse	4830382	4830409	GGAAATCAGTAAAAAAGAGAAATCATAA TTATATCTGTAAAAAAACGTAATTAAAA +++++ ++++++++++ +++ + ++
1253	2.80E-06	reverse	4830621	4830648	TGAGAAACAAGAAAAGACGTAAAGAAAA TTATATCTGTAAAAAAACGTAATTAAAA + + +++ + +++++ ++++++ +++++
1254	6.20E-05	reverse	4836166	4836193	TTTTATACGCACCGACAAGCGATTTTAA TTATATCTGTAAAAAAACGTAATTAAAA ++ ++++ + + + ++++++++ ++
1255	4.30E-06	forward	4851927	4851954	TTTTCAGAATATGTTGTTATGTTTAAAT TTTTAATTACGTTTTTTTACAGATATAA ++++++ ++ + ++ ++++ ++++ ++
1256	5.80E-05	forward	4853015	4853042	TTTTCCTTACCTTTATTAAGCCGTCATT TTTTAATTACGTTTTTTTACAGATATAA +++++ ++++ ++++++ + + ++
1257	8.50E-05	forward	4857150	4857177	TTTTAATACCACCAGCGCCTGGGAATAT TTTTAATTACGTTTTTTTACAGATATAA +++++++ + + + + + + +++++
1258	5.50E-05	forward	4872364	4872391	TTATTATCTGCTGATTTTTTATTTTTAA TTTTAATTACGTTTTTTTACAGATATAA ++ + +++ + ++++ +++++++++
1259	7.10E-05	forward	4873953	4873980	TGATTATTTTCTTATTAAACATATTAAT TTTTAATTACGTTTTTTTACAGATATAA + + +++ + ++ ++ +++++++ ++
1260	1.40E-05	forward	4873981	4874008	TGTTGCCTGATTCTATTCGCTGAAAAAT TTTTAATTACGTTTTTTTACAGATATAA + ++ ++ ++ +++++ + ++++ ++
1261	5.50E-05	reverse	4874009	4874036	AAAGATAGCCATATAAAATAAAATATTA TTATATCTGTAAAAAAACGTAATTAAAA +++ +++ + ++++++ ++ ++ +
1262	8.00E-05	forward	4874271	4874298	TCTATATTGCTTTATTTTTAATAATATA TTTTAATTACGTTTTTTTACAGATATAA + + ++++++++ ++++ +++++ ++
1263	3.00E-06	reverse	4877100	4877127	AAATTATCCTAAATAAACAGTAGGATAA TTATATCTGTAAAAAAACGTAATTAAAA ++++++ ++++++++++ + ++ ++

Table S4: H-NS and predicted LeuO binding site overlap

H-NS LPM ChIP-chip SL1344 start	H-NS LPM ChIP-chip SL1344	LeuO predicted	LeuO predicted site SL1344 end coordinate
9626	11625	11314	11341
9626	11625	11360	11387
14251	18625	14835	14862
14251	18625	14883	14910
14251	18625	15780	15807
14251	18625	17741	17768

22501	26250	23495	23522
22501	26250	24448	24475
22501	26250	25002	25029
31751	40875	32563	32590
31751	40875	34251	34278
31751	40875	34492	34519
31751	40875	34644	34671
31751	40875	34748	34775
31751	40875	35029	35056
31751	40875	35321	35348
31751	40875	37150	37177
31751	40875	38751	38778
31751	40875	39603	39630
31751	40875	39981	40008
42251	46000	43693	43720
50751	52750	51893	51920
50751	52750	52074	52101
61251	63625	63479	63506
67626	69375	68259	68286
67626	69375	68489	68516
74626	75375	74998	75025
80001	81375	80478	80505
82001	83500	82567	82594
87751	89375	88273	88300
87751	89375	88420	88447
93251	98750	93812	93839
93251	98750	94478	94505
93251	98750	97965	97992
115376	117750	115465	115492
115376	117750	116446	116473
115376	117750	116494	116521
133501	136250	134270	134297
139126	140250	139455	139482
188126	190125	188692	188719
188126	190125	188769	188796
188126	190125	188814	188841
188126	190125	189520	189547
202126	203000	202140	202167
202126	203000	202375	202402
207751	211250	208918	208945
229501	232250	229690	229717
229501	232250	230127	230154
229501	232250	230156	230183
229501	232250	230253	230280
229501	232250	230327	230354
229501	232250	230596	230623
248001	248875	248299	248326
315626	319375	316802	316829
315626	319375	316842	316869
315626	319375	317391	317418
315626	319375	318279	318306
322501	324375	323684	323711
328751	330500	329573	329600
328751	330500	329617	329644
328751	330500	329681	329708
335501	343000	339516	339543
335501	343000	339739	339766
335501	343000	339775	339802
335501	343000	340768	340795
335501	343000	341197	341224
335501	343000	341570	341597
364001	366000	365501	365528
364001	366000	365536	365563
370251	373125	372043	372070
376501	380750	377290	377317
376501	380750	377986	378013
376501	380750	378265	378292
382751	392125	383315	383342
382751	392125	386070	386097
382751	392125	388880	388907
382751	392125	389212	389239
382751	392125	390601	390628
382751	392125	391288	391315

382751	392125	391680	391707
402876	406500	405158	405185
406876	408875	407899	407926
406876	408875	407959	407986
406876	408875	408213	408240
414501	416125	415119	415146
414501	416125	415329	415356
423876	426125	424382	424409
427251	429125	428269	428296
427251	429125	428613	428640
435626	438125	436407	436434
435626	438125	437609	437636
452376	452625	452435	452462
489126	493375	490857	490884
489126	493375	491540	491567
489126	493375	492176	492203
497126	498875	497858	497885
497126	498875	497928	497955
525626	529250	526785	526812
525626	529250	527459	527486
552876	554500	554019	554046
569126	569750	569100	569127
578126	588250	582067	582094
578126	588250	586136	586163
578126	588250	587364	587391
578126	588250	587925	587952
598626	599125	598837	598864
608251	618750	610203	610230
608251	618750	610331	610358
608251	618750	610739	610766
608251	618750	610911	610938
608251	618750	612546	612573
608251	618750	614575	614602
608251	618750	615345	615372
608251	618750	617321	617348
608251	618750	617910	617937
630501	633500	631146	631173
630501	633500	631301	631328
648376	650500	648915	648942
648376	650500	649452	649479
666126	669375	667481	667508
666126	669375	667606	667633
666126	669375	668528	668555
672126	673875	672528	672555
686376	688250	686411	686438
686376	688250	687197	687224
686376	688250	687297	687324
689001	689625	689111	689138
690626	692750	691439	691466
690626	692750	691594	691621
690626	692750	691711	691738
690626	692750	692244	692271
690626	692750	692297	692324
695876	697750	696546	696573
711376	716000	711694	711721
711376	716000	714337	714364
711376	716000	715955	715982
723001	724250	723514	723541
723001	724250	723879	723906
764376	766375	765083	765110
764376	766375	765642	765669
773376	774375	773710	773737
780126	781750	781021	781048
780126	781750	781723	781750
782876	794000	784258	784285
782876	794000	784606	784633
782876	794000	785595	785622
782876	794000	786033	786060
782876	794000	786654	786681
782876	794000	787364	787391
782876	794000	788226	788253
782876	794000	788281	788308
782876	794000	788517	788544

782876	794000	789231	789258
782876	794000	789962	789989
782876	794000	790003	790030
782876	794000	790066	790093
782876	794000	790142	790169
782876	794000	790748	790775
782876	794000	790782	790809
782876	794000	790854	790881
782876	794000	791090	791117
782876	794000	791448	791475
782876	794000	792053	792080
782876	794000	792379	792406
782876	794000	793467	793494
807001	809500	808355	808382
807001	809500	808510	808537
807001	809500	808550	808577
807001	809500	808606	808633
822251	829625	824152	824179
822251	829625	825509	825536
822251	829625	827612	827639
822251	829625	828086	828113
892876	893625	893138	893165
905501	908375	906213	906240
905501	908375	908040	908067
924501	933625	925284	925311
924501	933625	926703	926730
924501	933625	927283	927310
924501	933625	928058	928085
924501	933625	929349	929376
924501	933625	931126	931153
924501	933625	931816	931843
924501	933625	932112	932139
943001	944625	943704	943731
953001	956375	953524	953551
953001	956375	953572	953599
953001	956375	954141	954168
974126	975500	975100	975127
1005876	1012250	1011293	1011320
1005876	1012250	1011511	1011538
1014376	1015875	1014996	1015023
1020251	1021000	1020617	1020644
1047251	1048375	1047440	1047467
1047251	1048375	1047630	1047657
1047251	1048375	1047719	1047746
1047251	1048375	1047954	1047981
1049376	1053875	1050388	1050415
1049376	1053875	1051167	1051194
1049376	1053875	1052308	1052335
1060001	1061750	1061029	1061056
1060001	1061750	1061254	1061281
1060001	1061750	1061620	1061647
1064876	1067000	1065466	1065493
1067876	1072125	1070255	1070282
1067876	1072125	1071208	1071235
1094876	1101500	1099283	1099310
1094876	1101500	1099341	1099368
1094876	1101500	1099553	1099580
1094876	1101500	1099652	1099679
1094876	1101500	1099745	1099772
1094876	1101500	1100048	1100075
1094876	1101500	1100323	1100350
1107501	1108000	1107642	1107669
1131126	1139875	1131271	1131298
1131126	1139875	1132525	1132552
1131126	1139875	1133129	1133156
1131126	1139875	1133223	1133250
1131126	1139875	1133934	1133961
1131126	1139875	1133998	1134025
1131126	1139875	1137677	1137704
1153251	1155625	1153713	1153740
1153251	1155625	1154511	1154538
1161876	1163000	1162291	1162318
1167751	1168875	1168055	1168082

1169501	1171875	1170154	1170181
1172251	1180125	1173950	1173977
1172251	1180125	1175477	1175504
1172251	1180125	1175684	1175711
1172251	1180125	1176346	1176373
1172251	1180125	1176719	1176746
1172251	1180125	1176927	1176954
1172251	1180125	1177076	1177103
1183876	1189375	1183939	1183966
1183876	1189375	1186272	1186299
1183876	1189375	1186733	1186760
1183876	1189375	1186810	1186837
1183876	1189375	1187341	1187368
1183876	1189375	1188220	1188247
1201251	1205125	1202227	1202254
1201251	1205125	1204176	1204203
1253126	1253625	1253444	1253471
1265501	1268250	1266996	1267023
1281876	1296625	1282708	1282735
1281876	1296625	1282978	1283005
1281876	1296625	1283665	1283692
1281876	1296625	1284066	1284093
1281876	1296625	1284548	1284575
1281876	1296625	1285682	1285709
1281876	1296625	1285933	1285960
1281876	1296625	1286897	1286924
1281876	1296625	1289112	1289139
1281876	1296625	1290318	1290345
1281876	1296625	1291270	1291297
1281876	1296625	1292595	1292622
1301626	1311625	1303401	1303428
1301626	1311625	1306481	1306508
1301626	1311625	1306592	1306619
1301626	1311625	1307846	1307873
1301626	1311625	1308984	1309011
1314751	1318000	1315401	1315428
1314751	1318000	1315787	1315814
1314751	1318000	1316122	1316149
1314751	1318000	1316151	1316178
1336876	1337375	1337235	1337262
1338626	1339250	1338839	1338866
1347501	1353375	1348985	1349012
1347501	1353375	1349644	1349671
1347501	1353375	1351950	1351977
1362751	1369375	1362912	1362939
1362751	1369375	1362954	1362981
1362751	1369375	1365366	1365393
1362751	1369375	1366010	1366037
1362751	1369375	1367168	1367195
1362751	1369375	1367244	1367271
1362751	1369375	1367625	1367652
1362751	1369375	1367903	1367930
1362751	1369375	1368154	1368181
1383751	1385125	1384052	1384079
1383751	1385125	1384310	1384337
1383751	1385125	1384488	1384515
1390251	1402500	1390495	1390522
1390251	1402500	1392298	1392325
1390251	1402500	1399372	1399399
1390251	1402500	1401527	1401554
1390251	1402500	1401663	1401690
1407251	1409500	1408474	1408501
1416251	1417250	1416514	1416541
1416251	1417250	1416544	1416571
1416251	1417250	1416748	1416775
1419376	1423750	1421269	1421296
1419376	1423750	1421517	1421544
1419376	1423750	1422124	1422151
1432126	1441625	1436365	1436392
1432126	1441625	1436641	1436668
1442126	1453000	1442124	1442151
1442126	1453000	1444359	1444386
1442126	1453000	1446368	1446395

1442126	1453000	1448447	1448474
1453501	1459375	1455515	1455542
1453501	1459375	1456889	1456916
1453501	1459375	1456992	1457019
1453501	1459375	1457732	1457759
1453501	1459375	1457898	1457925
1466126	1468750	1467242	1467269
1466126	1468750	1467603	1467630
1466126	1468750	1467968	1467995
1472001	1472500	1472243	1472270
1491876	1493500	1492813	1492840
1506126	1509625	1507651	1507678
1506126	1509625	1507954	1507981
1515751	1518000	1517233	1517260
1520751	1521250	1520899	1520926
1540751	1543125	1541324	1541351
1540751	1543125	1542443	1542470
1548001	1553125	1550111	1550138
1548001	1553125	1550149	1550176
1548001	1553125	1550973	1551000
1548001	1553125	1552113	1552140
1553751	1555875	1554121	1554148
1560876	1565375	1562892	1562919
1560876	1565375	1564453	1564480
1571126	1579625	1571187	1571214
1571126	1579625	1571983	1572010
1571126	1579625	1572168	1572195
1571126	1579625	1574526	1574553
1581001	1589500	1581519	1581546
1581001	1589500	1581955	1581982
1581001	1589500	1582383	1582410
1581001	1589500	1583596	1583623
1581001	1589500	1587322	1587349
1581001	1589500	1588025	1588052
1599751	1603250	1599923	1599950
1599751	1603250	1600446	1600473
1599751	1603250	1600734	1600761
1599751	1603250	1601747	1601774
1610126	1612750	1611574	1611601
1615626	1617000	1615938	1615965
1632126	1634625	1633045	1633072
1632126	1634625	1633563	1633590
1632126	1634625	1633880	1633907
1646876	1650875	1647217	1647244
1646876	1650875	1648815	1648842
1646876	1650875	1649104	1649131
1646876	1650875	1649253	1649280
1646876	1650875	1649866	1649893
1664251	1667125	1666144	1666171
1674876	1688000	1676412	1676439
1674876	1688000	1677206	1677233
1674876	1688000	1678017	1678044
1674876	1688000	1679975	1680002
1674876	1688000	1680112	1680139
1674876	1688000	1681326	1681353
1674876	1688000	1681951	1681978
1674876	1688000	1683642	1683669
1674876	1688000	1684272	1684299
1674876	1688000	1684887	1684914
1674876	1688000	1686492	1686519
1708126	1715250	1709073	1709100
1708126	1715250	1711116	1711143
1708126	1715250	1712014	1712041
1715626	1724250	1721119	1721146
1715626	1724250	1722202	1722229
1725751	1727500	1726494	1726521
1725751	1727500	1726603	1726630
1728501	1730375	1729285	1729312
1736751	1738250	1737230	1737257
1745751	1749500	1746594	1746621
1745751	1749500	1746636	1746663
1745751	1749500	1748406	1748433
1755001	1757750	1755424	1755451

1781751	1788000	1782273	1782300
1781751	1788000	1782345	1782372
1795501	1800000	1798404	1798431
1795501	1800000	1798475	1798502
1795501	1800000	1798694	1798721
1795501	1800000	1798740	1798767
1795501	1800000	1799460	1799487
1795501	1800000	1799628	1799655
1825251	1827250	1825917	1825944
1825251	1827250	1826006	1826033
1839126	1841875	1840255	1840282
1839126	1841875	1840312	1840339
1839126	1841875	1840614	1840641
1839126	1841875	1841348	1841375
1870251	1871500	1870598	1870625
1888626	1890125	1889402	1889429
1893001	1896750	1893871	1893898
1893001	1896750	1895092	1895119
1908001	1914625	1909447	1909474
1908001	1914625	1910342	1910369
1908001	1914625	1910751	1910778
1908001	1914625	1911072	1911099
1908001	1914625	1913036	1913063
1908001	1914625	1913510	1913537
1915251	1923875	1916160	1916187
1915251	1923875	1916981	1917008
1915251	1923875	1920612	1920639
1915251	1923875	1922591	1922618
1915251	1923875	1922630	1922657
1948001	1951000	1948446	1948473
1979501	1980875	1980036	1980063
1983751	1985375	1984427	1984454
1985626	1988125	1986837	1986864
1985626	1988125	1986871	1986898
1995876	1998875	1996532	1996559
1995876	1998875	1996575	1996602
2003126	2004875	2004198	2004225
2012376	2014125	2012977	2013004
2024001	2026250	2024633	2024660
2024001	2026250	2024725	2024752
2024001	2026250	2025230	2025257
2024001	2026250	2025277	2025304
2024001	2026250	2025524	2025551
2034251	2037875	2034907	2034934
2034251	2037875	2034984	2035011
2034251	2037875	2035015	2035042
2039251	2043875	2039823	2039850
2039251	2043875	2039873	2039900
2039251	2043875	2040308	2040335
2039251	2043875	2041404	2041431
2039251	2043875	2041507	2041534
2063876	2065250	2064863	2064890
2077001	2080625	2077083	2077110
2077001	2080625	2080009	2080036
2083376	2088375	2085300	2085327
2111376	2115125	2113107	2113134
2138251	2141000	2139311	2139338
2138251	2141000	2139575	2139602
2141501	2142500	2141909	2141936
2155126	2157750	2156833	2156860
2155126	2157750	2156991	2157018
2158001	2179000	2158596	2158623
2158001	2179000	2158624	2158651
2158001	2179000	2159175	2159202
2158001	2179000	2161978	2162005
2158001	2179000	2162366	2162393
2158001	2179000	2164063	2164090
2158001	2179000	2164484	2164511
2158001	2179000	2164619	2164646
2158001	2179000	2164737	2164764
2158001	2179000	2165132	2165159
2158001	2179000	2165545	2165572
2158001	2179000	2165599	2165626

2158001	2179000	2166241	2166268
2158001	2179000	2166304	2166331
2158001	2179000	2166572	2166599
2158001	2179000	2166637	2166664
2158001	2179000	2167307	2167334
2158001	2179000	2167389	2167416
2158001	2179000	2167960	2167987
2158001	2179000	2172792	2172819
2158001	2179000	2175260	2175287
2158001	2179000	2175888	2175915
2158001	2179000	2177559	2177586
2180876	2182500	2181760	2181787
2191126	2194250	2191656	2191683
2228626	2232125	2229220	2229247
2228626	2232125	2230147	2230174
2228626	2232125	2230190	2230217
2228626	2232125	2230661	2230688
2239751	2246875	2241517	2241544
2239751	2246875	2244359	2244386
2239751	2246875	2246107	2246134
2249251	2251500	2250594	2250621
2267751	2269000	2268123	2268150
2278251	2281125	2278880	2278907
2278251	2281125	2278986	2279013
2291126	2294125	2291953	2291980
2291126	2294125	2291990	2292017
2291126	2294125	2292270	2292297
2306126	2308500	2306106	2306133
2306126	2308500	2307603	2307630
2308751	2309625	2309158	2309185
2329126	2333625	2331319	2331346
2340751	2342250	2341572	2341599
2342626	2344875	2343717	2343744
2342626	2344875	2344030	2344057
2363876	2365500	2364487	2364514
2374001	2378500	2375372	2375399
2374001	2378500	2377133	2377160
2374001	2378500	2377233	2377260
2374001	2378500	2377323	2377350
2374001	2378500	2377691	2377718
2383251	2386500	2384013	2384040
2391876	2394250	2392367	2392394
2391876	2394250	2393254	2393281
2400376	2402125	2401413	2401440
2438376	2440250	2439106	2439133
2438376	2440250	2439571	2439598
2453251	2455125	2454242	2454269
2453251	2455125	2454316	2454343
2453251	2455125	2454375	2454402
2466751	2470125	2467421	2467448
2466751	2470125	2467596	2467623
2483626	2486875	2484096	2484123
2483626	2486875	2485689	2485716
2509126	2514000	2509537	2509564
2509126	2514000	2511913	2511940
2525376	2527000	2526479	2526506
2525376	2527000	2526930	2526957
2530376	2534625	2531198	2531225
2530376	2534625	2533601	2533628
2530376	2534625	2533790	2533817
2575501	2577750	2576657	2576684
2575501	2577750	2576787	2576814
2584876	2587250	2585312	2585339
2594126	2595625	2594967	2594994
2616126	2620500	2618703	2618730
2616126	2620500	2619790	2619817
2616126	2620500	2620424	2620451
2631001	2632625	2631693	2631720
2647751	2649625	2648420	2648447
2647751	2649625	2648604	2648631
2647751	2649625	2648645	2648672
2647751	2649625	2648682	2648709
2647751	2649625	2648718	2648745

2671126	2672875	2671921	2671948
2683376	2685125	2684117	2684144
2716001	2720000	2716530	2716557
2716001	2720000	2718581	2718608
2716001	2720000	2718626	2718653
2726126	2733125	2727105	2727132
2726126	2733125	2727683	2727710
2726126	2733125	2727763	2727790
2726126	2733125	2727830	2727857
2726126	2733125	2728506	2728533
2726126	2733125	2730592	2730619
2755501	2757125	2755819	2755846
2757376	2760875	2758110	2758137
2757376	2760875	2760148	2760175
2768501	2770750	2770392	2770419
2812501	2815375	2813188	2813215
2812501	2815375	2813393	2813420
2812501	2815375	2813569	2813596
2812501	2815375	2813727	2813754
2812501	2815375	2815336	2815363
2816251	2817125	2816751	2816778
2818751	2820000	2819837	2819864
2837626	2839375	2838381	2838408
2837626	2839375	2838418	2838445
2862501	2865625	2862834	2862861
2862501	2865625	2863062	2863089
2862501	2865625	2864622	2864649
2876751	2881250	2878034	2878061
2876751	2881250	2878579	2878606
2876751	2881250	2879441	2879468
2876751	2881250	2879950	2879977
2883501	2886250	2884079	2884106
2883501	2886250	2885723	2885750
2887126	2894750	2888676	2888703
2887126	2894750	2888904	2888931
2887126	2894750	2889582	2889609
2887126	2894750	2891480	2891507
2887126	2894750	2891600	2891627
2887126	2894750	2891938	2891965
2887126	2894750	2892139	2892166
2887126	2894750	2892607	2892634
2887126	2894750	2892886	2892913
2887126	2894750	2893100	2893127
2887126	2894750	2893795	2893822
2887126	2894750	2894047	2894074
2887126	2894750	2894199	2894226
2902376	2906000	2903995	2904022
2908126	2911625	2908380	2908407
2908126	2911625	2908597	2908624
2908126	2911625	2908845	2908872
2908126	2911625	2910570	2910597
2908126	2911625	2910781	2910808
2914376	2917125	2915768	2915795
2923376	2933625	2923943	2923970
2923376	2933625	2924295	2924322
2923376	2933625	2924571	2924598
2923376	2933625	2926662	2926689
2923376	2933625	2926710	2926737
2923376	2933625	2926880	2926907
2923376	2933625	2926979	2927006
2923376	2933625	2927429	2927456
2923376	2933625	2927714	2927741
2923376	2933625	2928968	2928995
2923376	2933625	2930269	2930296
2923376	2933625	2931307	2931334
2923376	2933625	2931527	2931554
2923376	2933625	2932059	2932086
2934251	2939250	2934514	2934541
2934251	2939250	2935789	2935816
2934251	2939250	2936463	2936490
2934251	2939250	2937970	2937997
2934251	2939250	2938045	2938072
2946126	2954625	2948438	2948465

2946126	2954625	2950709	2950736
2946126	2954625	2952105	2952132
2946126	2954625	2952324	2952351
2946126	2954625	2952861	2952888
2946126	2954625	2953666	2953693
2965626	2972000	2968065	2968092
2965626	2972000	2970179	2970206
2965626	2972000	2970668	2970695
2965626	2972000	2970750	2970777
3031751	3052625	3032231	3032258
3031751	3052625	3033464	3033491
3031751	3052625	3035000	3035027
3031751	3052625	3035057	3035084
3031751	3052625	3035606	3035633
3031751	3052625	3035764	3035791
3031751	3052625	3037666	3037693
3031751	3052625	3040385	3040412
3031751	3052625	3041863	3041890
3031751	3052625	3042440	3042467
3031751	3052625	3043368	3043395
3031751	3052625	3044506	3044533
3031751	3052625	3046169	3046196
3031751	3052625	3046684	3046711
3031751	3052625	3047230	3047257
3031751	3052625	3049456	3049483
3031751	3052625	3051664	3051691
3052876	3072875	3054059	3054086
3052876	3072875	3054549	3054576
3052876	3072875	3055011	3055038
3052876	3072875	3060962	3060989
3052876	3072875	3062084	3062111
3052876	3072875	3068430	3068457
3052876	3072875	3069078	3069105
3052876	3072875	3071999	3072026
3107626	3110750	3108755	3108782
3107626	3110750	3109373	3109400
3114501	3115875	3114817	3114844
3117376	3118500	3117908	3117935
3122376	3124375	3123045	3123072
3122376	3124375	3123093	3123120
3147501	3149500	3148113	3148140
3147501	3149500	3148184	3148211
3147501	3149500	3148578	3148605
3158876	3160875	3159319	3159346
3158876	3160875	3159577	3159604
3184251	3184750	3184725	3184752
3198376	3200000	3198856	3198883
3212626	3216625	3215064	3215091
3212626	3216625	3215249	3215276
3231126	3233375	3231610	3231637
3231126	3233375	3232480	3232507
3231126	3233375	3232592	3232619
3249001	3250625	3249029	3249056
3261626	3265750	3262140	3262167
3261626	3265750	3262950	3262977
3261626	3265750	3264018	3264045
3287126	3287625	3287339	3287366
3295751	3300875	3295976	3296003
3295751	3300875	3299380	3299407
3295751	3300875	3300043	3300070
3303501	3309625	3304640	3304667
3311876	3316375	3312499	3312526
3311876	3316375	3312563	3312590
3311876	3316375	3312636	3312663
3311876	3316375	3312676	3312703
3320501	3323500	3321582	3321609
3320501	3323500	3322434	3322461
3320501	3323500	3322524	3322551
3336376	3339500	3336801	3336828
3336376	3339500	3338216	3338243
3344501	3344750	3344581	3344608
3348376	3350250	3349480	3349507
3374376	3378250	3375032	3375059

3374376	3378250	3375174	3375201
3374376	3378250	3376995	3377022
3402501	3403750	3403125	3403152
3419751	3420875	3420245	3420272
3431501	3435250	3434455	3434482
3431501	3435250	3434509	3434536
3431501	3435250	3434566	3434593
3438501	3440125	3438848	3438875
3438501	3440125	3439094	3439121
3443751	3446500	3444218	3444245
3463876	3466000	3464675	3464702
3543251	3544875	3544478	3544505
3554501	3554875	3554639	3554666
3581001	3583125	3582131	3582158
3581001	3583125	3582239	3582266
3650001	3651375	3650417	3650444
3684626	3686250	3685241	3685268
3697751	3698875	3698013	3698040
3697751	3698875	3698260	3698287
3697751	3698875	3698356	3698383
3717876	3720625	3720047	3720074
3737001	3740500	3737566	3737593
3737001	3740500	3738179	3738206
3737001	3740500	3738586	3738613
3754501	3755500	3754849	3754876
3754501	3755500	3755153	3755180
3791376	3795625	3792354	3792381
3791376	3795625	3793086	3793113
3791376	3795625	3794641	3794668
3791376	3795625	3794679	3794706
3791376	3795625	3794770	3794797
3800251	3802500	3800400	3800427
3800251	3802500	3801699	3801726
3825376	3827125	3826371	3826398
3829876	3832000	3830479	3830506
3829876	3832000	3830612	3830639
3829876	3832000	3830928	3830955
3829876	3832000	3831428	3831455
3847626	3850375	3848734	3848761
3847626	3850375	3849340	3849367
3847626	3850375	3849388	3849415
3847626	3850375	3849479	3849506
3856626	3861625	3856737	3856764
3856626	3861625	3856961	3856988
3856626	3861625	3858715	3858742
3856626	3861625	3860708	3860735
3868751	3870375	3869235	3869262
3877751	3882125	3878980	3879007
3877751	3882125	3879331	3879358
3886501	3887625	3886816	3886843
3886501	3887625	3887023	3887050
3900376	3903250	3901486	3901513
3900376	3903250	3901593	3901620
3900376	3903250	3901999	3902026
3900376	3903250	3902193	3902220
3913626	3915375	3914086	3914113
3922501	3924500	3923782	3923809
3929126	3941000	3930728	3930755
3929126	3941000	3931980	3932007
3929126	3941000	3932044	3932071
3929126	3941000	3932585	3932612
3929126	3941000	3932863	3932890
3929126	3941000	3933077	3933104
3929126	3941000	3933960	3933987
3929126	3941000	3934108	3934135
3929126	3941000	3935083	3935110
3929126	3941000	3935230	3935257
3929126	3941000	3935276	3935303
3929126	3941000	3935733	3935760
3929126	3941000	3936967	3936994
3929126	3941000	3940412	3940439
3929126	3941000	3940951	3940978
3969501	3971750	3971190	3971217

3978751	3984000	3980589	3980616
3978751	3984000	3980924	3980951
3978751	3984000	3981773	3981800
3985126	3987625	3985673	3985700
3985126	3987625	3986979	3987006
4000376	4006875	4005279	4005306
4056001	4058500	4058132	4058159
4056001	4058500	4058164	4058191
4072251	4075250	4072360	4072387
4072251	4075250	4072642	4072669
4072251	4075250	4072683	4072710
4072251	4075250	4073367	4073394
4072251	4075250	4073745	4073772
4072251	4075250	4074207	4074234
4072251	4075250	4074559	4074586
4072251	4075250	4074689	4074716
4101876	4102625	4102456	4102483
4170501	4172500	4170976	4171003
4170501	4172500	4171837	4171864
4170501	4172500	4172061	4172088
4180376	4182375	4180733	4180760
4180376	4182375	4180905	4180932
4180376	4182375	4181420	4181447
4207001	4209000	4207174	4207201
4207001	4209000	4207523	4207550
4207001	4209000	4208126	4208153
4216501	4217750	4217211	4217238
4216501	4217750	4217263	4217290
4226126	4226875	4226299	4226326
4240626	4249250	4243304	4243331
4240626	4249250	4243337	4243364
4240626	4249250	4244792	4244819
4270251	4273750	4271349	4271376
4270251	4273750	4271675	4271702
4270251	4273750	4271738	4271765
4270251	4273750	4272315	4272342
4270251	4273750	4272901	4272928
4283001	4285750	4283578	4283605
4283001	4285750	4283710	4283737
4283001	4285750	4283811	4283838
4283001	4285750	4283854	4283881
4283001	4285750	4284671	4284698
4296251	4298500	4296805	4296832
4296251	4298500	4296854	4296881
4303376	4305750	4303716	4303743
4303376	4305750	4304868	4304895
4303376	4305750	4304970	4304997
4306126	4311000	4308532	4308559
4327876	4331250	4328301	4328328
4327876	4331250	4330131	4330158
4327876	4331250	4330167	4330194
4334501	4339000	4334929	4334956
4334501	4339000	4336720	4336747
4379376	4381125	4380159	4380186
4395376	4398750	4395741	4395768
4395376	4398750	4395943	4395970
4395376	4398750	4396453	4396480
4395376	4398750	4397338	4397365
4395376	4398750	4397701	4397728
4422751	4424125	4423173	4423200
4435876	4437375	4436455	4436482
4438876	4442625	4439542	4439569
4438876	4442625	4440014	4440041
4438876	4442625	4440057	4440084
4438876	4442625	4440111	4440138
4438876	4442625	4440249	4440276
4456626	4459875	4457413	4457440
4456626	4459875	4459129	4459156
4462876	4464125	4463366	4463393
4462876	4464125	4463522	4463549
4467251	4468125	4467369	4467396
4497626	4507750	4498391	4498418
4497626	4507750	4498572	4498599

4497626	4507750	4499220	4499247
4497626	4507750	4499251	4499278
4497626	4507750	4499969	4499996
4497626	4507750	4500419	4500446
4497626	4507750	4500818	4500845
4497626	4507750	4501504	4501531
4497626	4507750	4501598	4501625
4497626	4507750	4503761	4503788
4497626	4507750	4504092	4504119
4497626	4507750	4504421	4504448
4497626	4507750	4504963	4504990
4513501	4525875	4520890	4520917
4513501	4525875	4521320	4521347
4513501	4525875	4521534	4521561
4513501	4525875	4523223	4523250
4513501	4525875	4523366	4523393
4513501	4525875	4525637	4525664
4555501	4557500	4557298	4557325
4558376	4560625	4558984	4559011
4569251	4574375	4569870	4569897
4569251	4574375	4570273	4570300
4569251	4574375	4573159	4573186
4578626	4583500	4580565	4580592
4578626	4583500	4582084	4582111
4578626	4583500	4582386	4582413
4578626	4583500	4582523	4582550
4578626	4583500	4582571	4582598
4584001	4586375	4585098	4585125
4597751	4599625	4598874	4598901
4634501	4636250	4634949	4634976
4634501	4636250	4635009	4635036
4634501	4636250	4635718	4635745
4672376	4676000	4673550	4673577
4672376	4676000	4675205	4675232
4679251	4681750	4679654	4679681
4679251	4681750	4680861	4680888
4686251	4690125	4687204	4687231
4697001	4701500	4701113	4701140
4703376	4704875	4703835	4703862
4730126	4732375	4731752	4731779
4730126	4732375	4731783	4731810
4734376	4737750	4736159	4736186
4747501	4750625	4748303	4748330
4752126	4756250	4755718	4755745
4752126	4756250	4756082	4756109
4763626	4767125	4764742	4764769
4763626	4767125	4765474	4765501
4763626	4767125	4765626	4765653
4772376	4775000	4773185	4773212
4772376	4775000	4774145	4774172
4776251	4780875	4776711	4776738
4776251	4780875	4778067	4778094
4776251	4780875	4778433	4778460
4776251	4780875	4778546	4778573
4776251	4780875	4778713	4778740
4776251	4780875	4778750	4778777
4783126	4785125	4783785	4783812
4783126	4785125	4783946	4783973
4783126	4785125	4784811	4784838
4788876	4790625	4789319	4789346
4788876	4790625	4789410	4789437
4796126	4800000	4796889	4796916
4796126	4800000	4797102	4797129
4796126	4800000	4797351	4797378
4796126	4800000	4798033	4798060
4796126	4800000	4798129	4798156
4815251	4820375	4819111	4819138
4822376	4822875	4822739	4822766
4825751	4828375	4826498	4826525
4825751	4828375	4826578	4826605
4825751	4828375	4826620	4826647
4830001	4831500	4830382	4830409
4830001	4831500	4830621	4830648

4846626	4852750	4851927	4851954
4869001	4876125	4872364	4872391
4869001	4876125	4873953	4873980
4869001	4876125	4873981	4874008
4869001	4876125	4874009	4874036
4869001	4876125	4874271	4874298
4876751	4877875	4877100	4877127