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Evolutionary History and Biological Regulation of CD93

Jack W D Blackburn
The University of Western Ontario

Supervisor
Dr. Bryan Heit
The University of Western Ontario

Graduate Program in Microbiology and Immunology
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Abstract

CD93 is a transmembrane C-type lectin expressed on myeloid, endothelial, and B cells. First identified as a developmental B cell marker and a phagocytic C1q receptor, little is known about the role and mechanism of CD93 in efferocytosis (the phagocytosis of apoptotic cells). CD93 knockout mice develop chronic inflammatory diseases characterized by a lack of efferocytosis such as atherosclerosis and a lupus-like autoimmune disease. In humans, a cleaved form of CD93 (sCD93) is elevated during inflammation and autoimmune responses, and CD93 polymorphisms are associated with enhanced susceptibility to atherosclerosis and lupus. Despite these clinical associations, no comprehensive bioinformatic analysis of CD93's evolution and regulation have been performed to date. To this end evolutionary analysis of CD93 was performed, demonstrating that CD93 evolution is characterized by conservation but with several amino acid residues showing recent positive selection. Promoter analysis of CD93 revealed several interactions with transcription factors involved in regulation of cell growth, differentiation, and apoptosis, consistent with the known expression profile of CD93 and cell types known to engage in efferocytosis. Shedding assays using human monocytes and monocyte-like THP-1 cells show that CD93 expression is lost during monocyte-to-macrophage differentiation and in response to PMA stimulation. The cleavage was not dependent on the TAPI-2-inhibitable proteases which includes select MMPs and other proteases such as ADAMs and ACE secretases. Importantly, apoptotic cell mimics opsonized with sCD93 containing supernatants show increased phagocytic uptake, suggesting that sCD93 acts as an opsonin for apoptotic cells.

Keywords: CD93, Shedding, Protease cleavage, Efferocytosis, Opsonisation

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List of Abbreviations

AIC	Akaike Information Criterion
AICc	Corrected Akaike Information Criterion
BIC	Bayesian Information Criterion
CAD	Coronary Artery Disease
CI	Confidence Interval
CRD	Carbohydrate Recognition Domain
CTLD	C-type Lectin Domain
DMEM	Dulbecco's Modified Eagle's Medium
EGF	Epidermal Growth Factor
GTR	General Time Reversible
GWAS	Genome-wide Association Study
ICAM3	Intracellular Adhesion Molecule 3
ICD	Intracellular Domain
LPC	Lysophosphatidylcholine
MASP	MBL-associated Serine Proteases
MBL	Mannose-binding Lectin
MEC	Mechanistic Empirical Combination
MI	Myocardial Infarction
MMP	Matrix Metalloproteinase
PAMP	Pattern-Associated Molecular Pattern
PBS	Phosphate Buffered Saline
PDBu	Phorbol 12,13-dibutyrate
PI	Phosphatidylinositol
PI	Phagocytic Index
PI(3)P	Phosphatidylinositol-3-phosphate
PLF	Peritoneal Lavage Fluid
PMA	Phorbol 12-myristate 13-acetate
PS	Polystyrene
PtdChol	Phosphatidylcholine
PtdSer	Phosphatidylserine
RA	Rheumatoid Arthritis
RPMI	Roswell Park Memorial Institute
S1P	Sphingosine-1-phosphate
SAPK/JNK	Stress-activated Protein Kinases
sCD93	Soluble CD93
SFM	Serum Free Media
SLE	Systemic Lupus Erythematosis
SNP	Single Nucleotide Polymorphism
SPA	Surfactant Protein A
TAPI-2	N-(R)-(2-(Hydroxyaminocarbonyl)methyl)-4-methylpentanoyl-L-t-butyl-glycine-L-alanine 2 aminoethyl amide
TIM	T cell Immunoglobulin Mucin
TLR	Toll-like Receptor
TM	Transmembrane

Introduction

1.1 Phagocytosis and Efferocytosis

Phagocytosis plays a central role in maintenance of immune homeostasis and tissue remodelling through removing pathogens, apoptotic bodies and cellular debris. Phagocytosis is the receptor-mediated, actin-dependent engulfment of large particles ($>0.5 \mu\text{m}$) into plasma-membrane derived vacuoles. These vacuoles undergo a tightly regulated maturation process comprised of acidification and sequential fusion to endosomes and lysosomes, eventually maturing into phagolysosomes – highly acidic, hydrolase containing organelles specialized in the degradation of internalized particles¹⁻³. While many cell types can engage in phagocytosis under certain circumstances, phagocytosis is primarily performed by professional phagocytes such as macrophages, dendritic cells and neutrophils². Nonprofessional and paraprofessional phagocytes (such as retinal epithelial cells responsible for clearing damaged or otherwise worn retinal rods) display reduced phagocytic range and uptake capacity when compared to more specialized immune system counterparts (reviewed in 4). This difference in phagocytic capacity is primarily explained by the expression of a broad repertoire of phagocytic receptors by professional phagocytes, which provide an expansive recognition system for various ligands found on infectious agents, senescent cells and cellular debris^{1,2}.

Phagocytosis is initiated by the binding of phagocytic receptors to their cognate ligands, and can be driven by upwards of 20 individual receptors (reviewed in 5) – allowing for a range of highly defined and regulated immune responses to various targets, while preventing self-reactivity. The receptors themselves function either as Pattern Recognition Receptors, binding directly to Pathogen-Associated Molecular Patterns (PAMPs) on infectious agents, to specific “eat me” signals on cellular debris, or by recognizing targets via opsonins such as immunoglobulins, which bridge receptors to ligands on the phagocytic target (Figure 1). Following this, kinase and phosphatidylinositide signalling mediates the formation of the phagocytic cup – an actin-dependant extension of the plasma membrane – around the phagocytic target. Formation of this cup is dependent on Rho-family GTPases which mediate actin polymerization directly under the site of receptor-ligand interaction⁶⁻⁸, causing ruffling of the plasma membrane and pseudopodia protrusions which engulf the target particle and fuse to form the nascent phagosome^{9,10}. The maturation of the nascent phagosome into the highly acidified and hydrolytic enzyme-rich phagolysosome is then driven by changes in membrane phospholipids and recruitment of key regulatory proteins. First, the small GTPase Rab5 is recruited to the nascent phagosome, where it mediates recruitment of early endosomes and various Rab5 effectors¹¹⁻¹³. A major component of this fusogenic system is the Rab5 effector Vps34, which phosphorylates phosphatidylinositol (PI) to form phosphatidylinositol-3-phosphate (PI(3)P), which in turn promotes fusion of early endosomes to the nascent phagosome¹⁴⁻¹⁷. Following this, exchange of Rab5 for Rab7 is mediated by Mon1/Ccz1 binding to PI(3)P. Mon1/Ccz1 binding recruits PI5-kinase, which phosphorylates PI(3)P to form PI(3,5)P₂ and subsequently recruits Rab7¹⁸. Rab7 then mediates fusion of late endosomes and lysosomes with the maturing phagosome^{19,20}, completing the

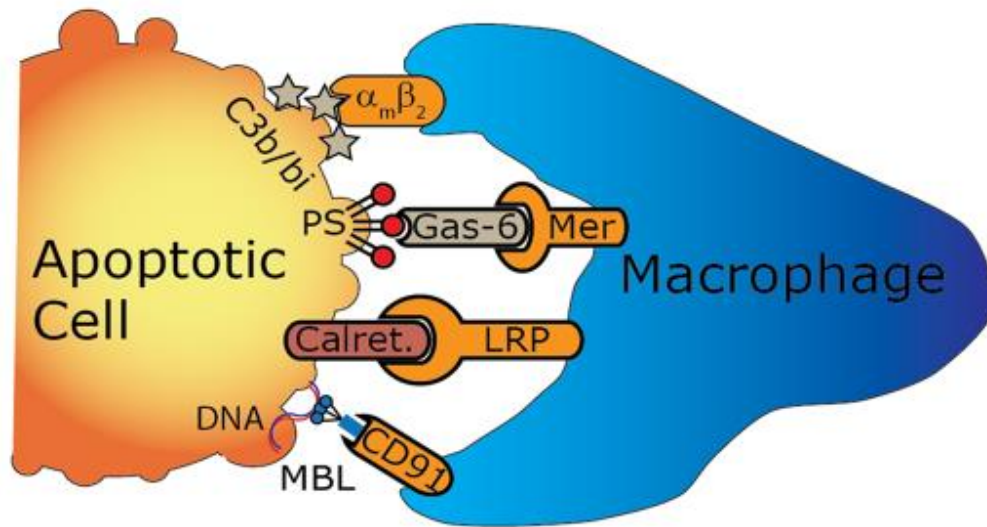


Figure 1: Macrophages bind to apoptotic cells. Macrophages bind to apoptotic cells through direct ligand receptor interactions, such as lrp and calreticulin, or through use of opsonins as with MerTK and Gas-6.

maturation of the phagosome to a phagolysosome and providing the requisite phagosome acidification and delivery of hydrolytic enzymes required to break down the phagocytic target^{5,18}.

Efferocytosis, the phagocytosis of apoptotic cells, differs from phagocytosis in several aspects: lack of antigen presentation, initiation by distinct ligand-receptor pairings, and the lack of release of pro-inflammatory signals following target engulfment. Removal of apoptotic bodies proceeds through a stepwise process, initiated by the release of diffusible extracellular “find-me” signals by apoptotic cells which act to recruit phagocytes. “Eat-me” signals such as phosphatidylserine (PtdSer) are then displayed on the surface of apoptotic cells, which are recognized by efferocytic receptors on the recruited phagocytes. Apoptotic cells are then internalized through receptor mediated signaling pathways thought to be similar to those mediating phagocytosis. Finally, apoptotic bodies are degraded within a phagosome-like vacuole termed the efferosome, through a process thought to be similar to the phagocytic maturation pathway²¹. The importance of efferocytosis is highlighted by the association between single nucleotide polymorphisms (SNPs) in efferocytic receptors with defective apoptotic cell clearance, and the onset of numerous inflammatory and autoimmune diseases including atherosclerosis and systemic lupus erythramatosis (SLE) (Figure 2).

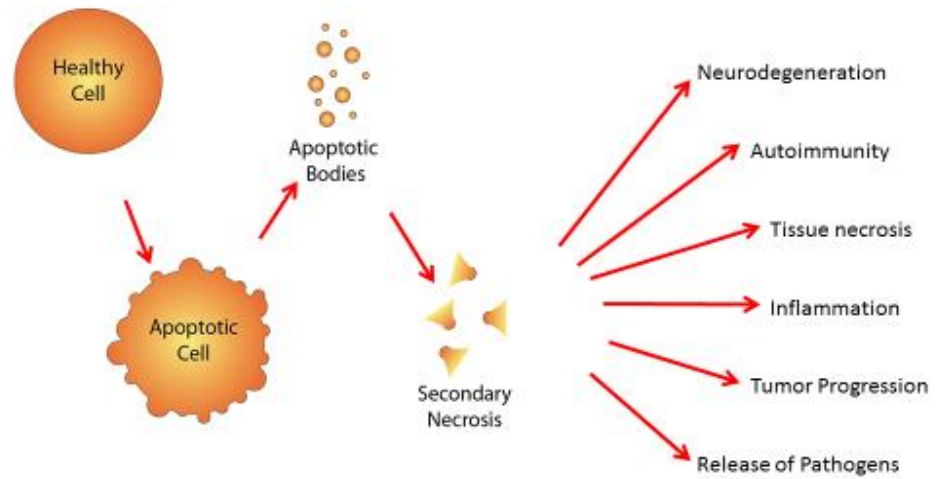


Figure 2: Importance of the efficient clearance of apoptotic bodies. Failure to efficiently and timely clear apoptotic bodies allows apoptotic bodies to degrade through secondary necrosis, releasing cellular contents into the extracellular milieu, a process which can drive the development and progression of numerous detrimental pathologies.

1.2 CD93

CD93 is a 120kDa , type-1 transmembrane glycoprotein expressed on the surface of endothelial cells, stem cells, platelets, and select leukocytes²²⁻²⁷. Part of the group XIV family of transmembrane glycoproteins, CD93 shares a common structure with the other group XIV family proteins, thrombomodulin and endosialin, containing five distinct domains²⁸: An N-terminal C-type lectin-like domain, an epidermal growth factor (EGF)-like domain containing five EGF-like repeats, a heavily glycosylated mucin domain rich in serine and threonine amino acids, a transmembrane helix, and a short cytosolic tail (Figure 3). Additionally, a soluble form of the protein (sCD93) which retains the C-type lectin-like and EGF-like domains, and a portion of the mucin domain is detected in human plasma²⁹. In mice, this soluble form of CD93 is generated by cleavage within the mucin domain by an unidentified matrix metalloproteinase (MMP)³⁰. Homologs of CD93 in mouse and rat (designated AA4) are 67% and 77% similar to the human protein respectively, and 87% similar to each other^{23,31-33}. Numerous clinical associations have been observed linking CD93 to various inflammatory and auto-immune diseases characterised by chronic inflammation and/or deficits in efferocytosis, including atherosclerosis, coronary artery diseases, rheumatoid arthritis, and SLE. Moreover, these clinical associations are replicated in mouse knockout models, demonstrating that the role of CD93 has been broadly conserved. Despite these interactions, many questions regarding CD93's basic biology most notably the mechanisms by which it functions within the context of inflammation and efferocytosis remain unanswered. To date there has been no investigation into CD93's evolutionary history,



Figure 3: Structural domains of CD93. CD93 contains a C-type lectin domain (CTLD), five epidermal growth factor (EGF) repeats, a mucin domain, transmembrane helix (TM) and intracellular domain (ICD). Domains are shown aligned with approximate amino acid position.

representing a gap in our current knowledge which given the apparent conserved function of CD93 between mice and humans may provide crucial insight into the biological function of CD93.

Clinical Associations

Numerous studies have shown that CD93 is differentially regulated in various human diseases and in murine disease models, in addition to direct *in vivo* observations and GWAS (Genome-wide association study) data linking mutations to increased disease risk in specific patient cohorts. Elevated levels of CD93 have been observed on activated neutrophils²⁹ and in ROS/neutrophil dependent inflammation. Neutrophils collected from hypoxic patients show significantly increased chemotaxis and phagocytosis, along with upregulation of CD93 expression when stimulated with *E. coli*. in comparison to control neutrophils³⁴. Taken together, these studies suggest that CD93 is present in neutrophil granules, and demonstrate that hypoxia-induced degranulation upregulates CD93 expression on activated neutrophils. Concordant with these observations, increased plasma levels of sCD93 are observed in many inflammatory conditions, including atherosclerosis, with increased sCD93 levels correlating with increased risk and worsened prognosis. Indeed, sCD93 has been investigated as a possible diagnostic and prognostic biomarker of Coronary Artery Disease (CAD) and Myocardial Infarction (MI). This linkage is further strengthened by the identification of two specific single nucleotide polymorphisms (SNPs) in CD93 that increase risk of CAD and MI. An A → G mutation in the 3' UTR (rs2749812) leads to increased mRNA expression and correlates with an increased risk of CAD/MI³⁵, while an A to G mutation (rs3746731) in the mucin domain produces a Q541P substitution which results in a 24% increased risk of CAD³⁶. However, as the 541 mutation is also

linked to elevated mRNA levels – and may be in linkage disequilibrium with the 3' UTR mutation, it is unclear if the increased risk of CAD and MI is due to a change in function from the missense 541 mutation, from the change in mRNA levels caused by the 3' UTR mutation, or a combination of the two. Additionally, increased levels of sCD93 correlates with an increased risk of rheumatoid arthritis (RA) with synovial fluid sCD93 concentrations significantly elevated in RA patients compared to those with osteoarthritis³⁷.

CD93 Expression

CD93 is expressed on the surface of numerous cells types involved in embryogenesis, hematopoiesis, immune and inflammatory responses. In mice, CD93 expression is observed in hematopoietic stem cells in the embryonic yolk sac³⁸, the liver, and adult bone marrow^{39,40}. In humans, CD93 expression is observed primarily on endothelial cells, but also observed on hematopoietic stem cells, platelets, and selected leukocytes including monocytes and neutrophils^{22–27}. CD93 is first detected during embryogenesis on the endocardium and vascular endothelium^{24,41}, as well as on the surface of circulating cells in the foetal liver, suggesting a role in angiogenesis and hematopoiesis⁴². In adults, CD93 is found during the early stages of B cell differentiation, and has been shown to be necessary for the development of B lymphocytes from hematopoietic stem cells *in vivo*^{39,43}. While down-regulated during B cell maturation and absent from mature IgM⁺IgD⁺ B cells⁴⁴, CD93 is re-expressed on plasma cells where it plays a role in maintenance of stable plasma cell populations and antibody titre⁴⁵. CD93 is expressed on monocytes, neutrophils, immature DCs²⁴, and possibly platelets²³. Single-cell gene-expression performed by Gren *et al.* demonstrated that CD93 expression is highest on 'classical'

(CD14^{hi}CD16⁻) and lowest on 'non-classical' (CD14⁺CD16⁻) monocytes, although expression was heterogeneous within each monocyte subpopulation⁴⁶. Although monocytes which give rise to macrophages express CD93, whether macrophages themselves express CD93 is still debated. Macrophage expression has been demonstrated on both murine peritoneal and bone marrow derived macrophages^{24,47}, but in contrast, human and rat tissue macrophages show low or no CD93 expression⁴¹. Indeed, data from our lab shows that CD93 surface expression is lost as primary human monocytes are differentiated to tissue-resident (M0), inflammatory (M1), and alternatively-activated (M2) macrophage phenotypes (J. Ellins, unpublished data, Figure 4). However, it is currently unclear whether CD93 expression is truly lost on macrophages, or whether it is continuously expressed and shed from the cell surface.

Structure and Functional Domains of CD93

CD93 is a 652 amino acid, heavily glycosylated, type 1 transmembrane protein containing a C-type lectin like domain. Unglycosylated CD93 is 66 kDa in size, but its mass increases to roughly 126 kDa with glycosylation⁴⁸. Like the other group XIV family members endosialin and thrombospondin, CD93 contains an N-terminal C-type Lectin-like domain (CTLD), an epidermal growth factor domain (EGF) containing 5 individual EGF-like repeats, a highly glycosylated mucin-like domain, a transmembrane helix, and a short C-terminal cytoplasmic tail (Figure 3). Despite sharing sequence and structural homology with the Ca²⁺ dependent Carbohydrate-Recognition Domains (CRDs) found in other C type lectins, neither the CD93 CTLD nor the CTLD of the other

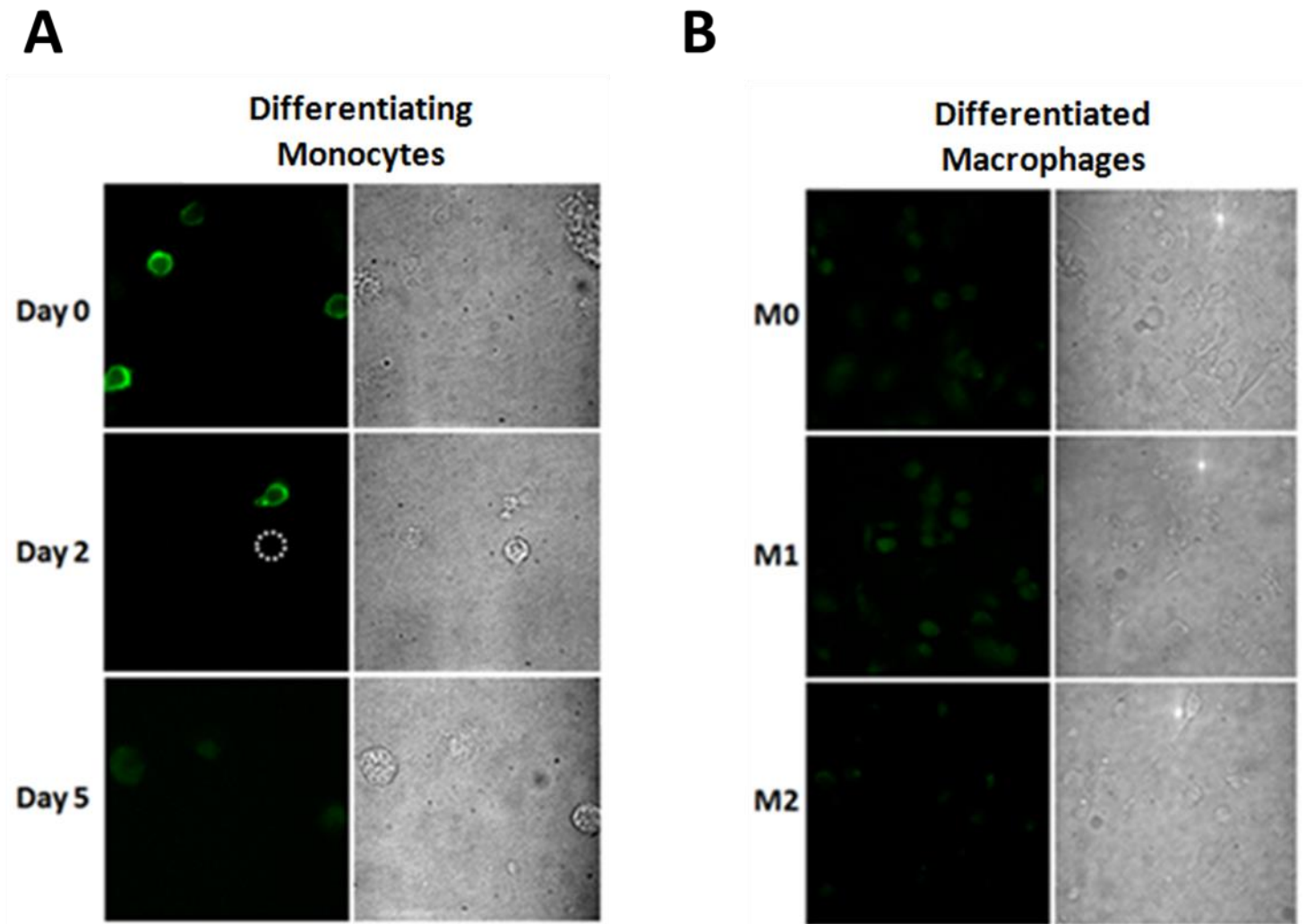


Figure 4: CD93 expression is lost during from the surface of monocytes during macrophage differentiation. Human peripheral mononuclear cells were isolated and stained for CD93. A) Freshly isolated monocytes (Day 0) displayed ring-like plasma membrane fluorescence on approximately 95% of cells. Monocytes on Day 2 of differentiation to M0 macrophages displayed CD93 expression on approximately 40% of cells. Dotted ring indicates a cell lacking CD93. Monocytes on Day 5 of differentiation lost all CD93 expression. B) Fully-differentiated M0, M1 and M2 macrophages did not express CD93. Cells were imaged at 60X magnification with wide-field immunofluorescence microscopy. All images are representative of a minimum of ten images taken in two experiments (Images courtesy of J. Ellins, 2014).

group XIV members, possess any known sugar-binding capabilities. To date, no ligands for CD93 have been identified. Consistent with other CTLDs, this functional disparity between CD93's CTLD and genuine CRDs is likely caused by structural differences, including different molecular folding and Ca²⁺ interactions, despite their sequence similarity (reviewed in 49). The EGF-like domain contains 5 EGF repeats, with the 3 most membrane-proximal possessing putative calcium binding sites, yet no known direct interactions have been observed to date. However, the EGF domain of the related group XIV protein thrombomodulin is known to act as a ligand binding site, suggesting that the EGF-like domain in CD93 may function in a similar role^{50,51}. Consistent with this, the EGF-like domain acts directly as a potent angiogenic factor, and has been shown to induce proliferation and migration of endothelial cells in mouse models⁵². Furthermore, CD93 expressed on endothelial and myeloid cells is likely involved in regulation of cell adhesion and homing^{41,53,54}. Expression of murine CD93 on hematopoietic stem cell and the vasculature during embryogenesis and angiogenesis suggests that it may function as a homing receptor in intracellular adhesion^{31,42}. CD93 phosphorylation by dystroglycan (a dystrophin associated glycoprotein) has been shown to promote migration and organization of endothelial cells into capillaries⁵⁵. Furthermore, CD93^{-/-} mice show increased leukocyte infiltration in thioglycollate-induced peritonitis models compared to wild type⁴⁷, underscoring its role as a regulatory factor in leukocyte recruitment in addition to its role as an angiogenic factor in embryogenesis and hematopoiesis^{26,42,48}.

CD93 is highly glycosylated, evident by the large discrepancy between its predicted molecular weight of 66 kDa and its observed mobility of 126 kDa on SDS-page gels, with much of the glycosylation predicted to occur within the mucin domain. This predominantly O-linked

glycosylation⁵⁶ has been shown to play a critical role in stabilizing CD93 surface expression⁵⁷. However, beyond this, little is known of any additional functional role played by the mucin domain, with no known ligands or binding interactions observed to date.

Several interactions have been observed in the cytoplasmic region of CD93, including binding with GIPC, a PDZ domain containing protein known to regulate cytoskeletal dynamics and G-protein coupled receptor recycling⁵⁸. Moreover, moesin has been observed to interact with the intracellular tail of CD93⁵⁹. The interactions of these proteins with CD93 may act to anchor CD93 to the cytoskeleton, potentially to localize CD93 to domains which restrict access of the cell surface protease that generates soluble CD93. Alternatively, these interactions may enable CD93-dependent alterations to the cytoskeleton. Indeed, treatment with a cell-permeable peptide encoding the C-terminal of CD93 enhances antibody-mediated (FcR γ -mediated) phagocytosis in human monocytes, indicating that the CD93 intracellular tail may enhance phagocytic signalling or cytoskeletal rearrangements⁵⁸. Additionally, moesin binding to CD93 has been shown to be enhanced in response to addition of PIP₂⁵⁹, suggesting that CD93 may play a role in PIP₂ signalling.

CD93 in Phagocytosis & Efferocytosis

Originally identified as a receptor for C1q^{28,60}, CD93 was believed to enhance phagocytosis in a C1q-dependent manner^{48,60–63}. Guan et al. reported that blocking with R3, a CD93-specific antibody, decreased phagocytic efficiency of monocyte cells plated on a C1q-coated surface⁶¹. Further studies suggested that CD93 acted as a receptor for the structurally related proteins C1q,

MBL and surfactant protein A (SPA), all of which share a similar molecular structure and which recognize PAMPs and apoptotic cells^{48,62,64}. However, it has since been demonstrated that while CD93 does contribute to the removal of apoptotic cells⁴¹, it neither interacts with C1q⁹, nor contributes to the C1q dependent enhancement of phagocytosis⁴¹. Murine studies have shown that CD93^{-/-} mice have significant defects in apoptotic cell clearance compared to strain matched controls⁶⁵, and peritoneal lavage fluid (PLF) containing elevated levels of sCD93 enhances apoptotic cell engulfment compared to PLF from CD93^{-/-} mice³⁰. In humans, CD93 has strong genetic linkages with diseases characterized by impaired apoptotic cell clearance, such as atherosclerosis and SLE, further indicating that that CD93 contributes to efferocytosis either as a efferocytic receptor^{35,66,67}, or as an efferocytosis enhancing opsonin^{25,30}, and moreover, indicating the importance of proper CD93 function in homeostasis and regulation of immune responses in humans. Our data also excluded the membrane-bound CD93 as a phagocytic/efferocytic receptor since ectopic expression of CD93 resulted in no net increase in apoptotic cell efferocytosis (J. Ellins, unpublished data, Figure 5). Associations with diseases characterized by impaired apoptotic cell clearance, such as atherosclerosis and systemic lupus erythematosus, suggest that CD93 may contribute to efferocytosis either as a efferocytic receptor^{35,66,67} or as an efferocytosis-enhancing opsonin^{25,30}. CD93^{-/-} mice have significant defects in apoptotic cell clearance compared to strain matched controls⁶⁵, and PLF containing elevated levels of sCD93 enhances apoptotic cell engulfment compared to PLF from CD93^{-/-} mice³⁰

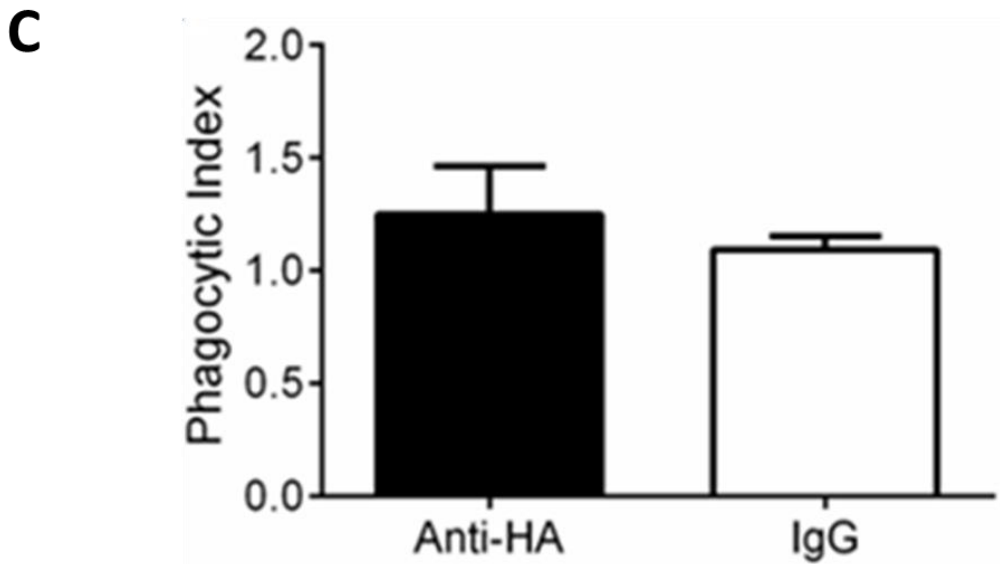
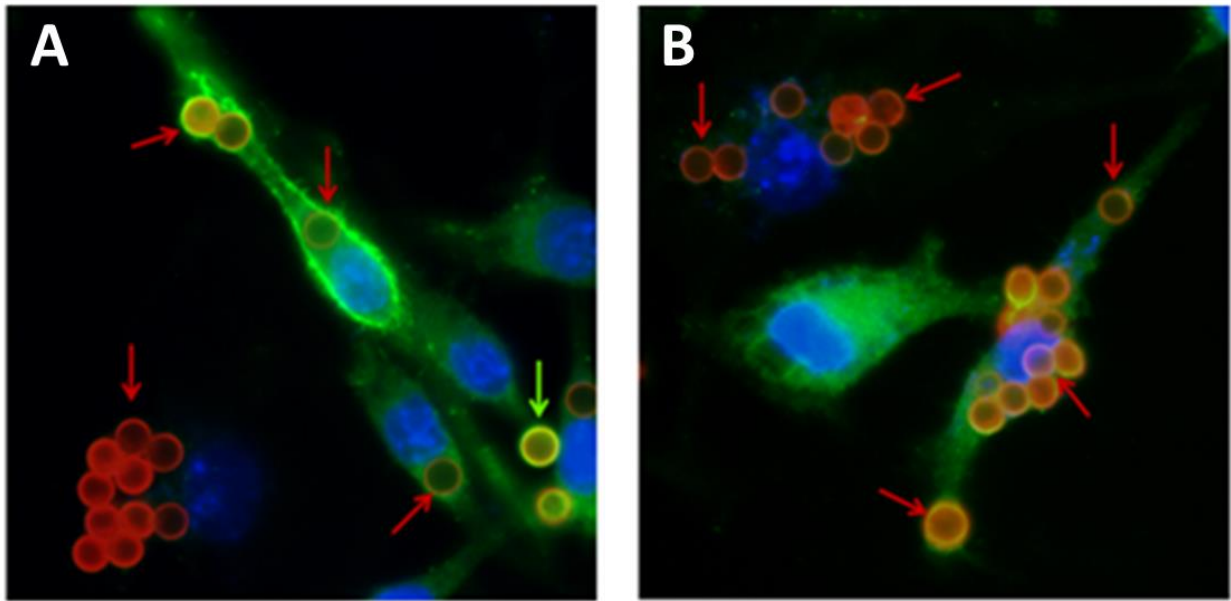


Figure 5: CD93 does not function as a membrane bound phagocytic receptor. HA-CD93-transfected RAW cells were fed A) anti-HA-coated or B) IgG-coated Protein G-conjugated beads. Transfected cells and external beads were stained with anti-HA (green), and internalized beads fluoresced red. Red arrows point to internalized beads, whereas the green arrow points to an external bead. Cells were imaged at 60X magnification with wide-field immunofluorescence microscopy. Each image representative of ten images taken over two experiments (A-B). $p=0.2723$ negative compared to IgG, $n=2$, (Images and data courtesy of J. Ellins, 2014).

1.3 Apoptosis

Apoptosis (programmed cell death) is a tightly regulated cellular process that packages senescent, infected and otherwise damaged or unwanted cells into discrete membrane-bound bodies⁶⁸. In contrast to other forms of cell death such as necrosis, apoptosis is non-inflammatory, and prevents the release of inflammatory and immunogenic intracellular contents into the extracellular milieu. Apoptosis is mediated by a well characterized cascade of intracellular proteases, termed caspases (reviewed in 69–72). Following caspase activation cells become rounded, undergo nuclear condensation, chromatin cleavage⁷³, cytoplasmic contraction, and membrane blebbing → the packaging of cellular contents into discrete, membrane bound apoptotic bodies⁶⁸. During these large scale morphological changes, apoptotic bodies release “find-me” and present “eat-me” signals required for the recognition and uptake by phagocytes.

“Find-me” signals

“Find-me” signals such as lysophosphatidylcholine (LPC)⁷⁴, sphingosine-1-phosphate (S1P)⁷⁵, ATP and UTP⁷⁶, and CXC3CL1⁷⁷ are released by apoptotic cells in order to induce chemotaxis (directional migration) of phagocytes to apoptotic cells. Of the “find-me” signals, CXC3CL1 is currently the only classical chemokine that has been identified as a find-me signal, and promotes phagocyte chemotaxis upon binding to its receptor CXC3R1⁷⁷. The nucleotides ATP and UTP are suggested to be a novel class of “find-me” signals. Bound by the P2Y2 receptor, small amounts of ATP and UTP released by apoptotic cells appear to function as a chemotactic-gradient⁷⁶, allowing for phagocytes to distinguish cells undergoing apoptosis from those undergoing pro-

inflammatory types of cell death (such as necrosis) which release significantly higher levels of nucleotides. Despite the identification of multiple “find-me” signals, their exact role in phagocyte chemotaxis is currently unclear, with many of them serving additional immunomodulatory or phagocytic modifying functions (reviewed in 78). Other find-me signals have been proposed, primarily lysophospholipids such as lysophosphatidylcholine, although the low solubility of these factors has resulted in some controversy about whether they are sufficiently diffusive to act as “find me” signals.

“Eat-me” signals

Specific “Eat-me” signals on the surface of apoptotic cells are crucial for recognition and initiation of efferocytosis, instead of phagocytosis. Numerous “eat-me” signals exist on the surface of apoptotic bodies, including alternatively glycosylated proteins (reviewed in 79), modified sugars, intracellular adhesion molecule 3 (ICAM3), exposure of intercellular proteins such as annexin I⁸⁰ and calreticulin⁸¹, and binding of serum proteins such as C1q to the apoptotic cell surface (reviewed in 82). The best characterized “eat-me” signal is phosphatidylserine (PtdSer)^{83–88}. Usually restricted to the inner leaflet of the plasma membrane by the continuous activity of plasma membrane flippase enzymes, caspase-mediated inactivation of flippases during apoptosis, combined with caspase-mediated activation of a scramblase, leads to PtdSer exposure on the extracellular facet of the plasma membrane^{85,86}. When present on the extracellular leaflet, PtdSer acts as an “eat-me” signal which is recognized by several receptors, binding to them either directly — as with the members of the T cell immunoglobulin mucin (TIM) domain family proteins TIM1, 3, and 4 — or indirectly to opsonins/receptor complexes, such as MFGE8/ $\alpha_v\beta_3$ integrin and

GAS6/TAM family receptors^{82,84,86–90}. Apoptotic cells express multiple “eat-me” signals on their surface, potentially contributing to the ability of phagocytes to distinguish them from their healthy counterparts. For example, PtdSer exposure can occur on healthy cells that do not get engulfed^{91–93}, while colocalization of calreticulin and annexin I with PtdSer on the apoptotic surface enhances phagocytic uptake^{80,81}. Moreover, “don’t eat me” signals such as CD47 (recognized by SIRP1 α) are expressed on healthy cells where they act to prevent efferocytosis^{94–97}. While initial reports suggested that CD93 functioned by directly binding to apoptotic cell eat-me signals, thus initiating the phagocytic uptake of the apoptotic cell, previous research in our lab has demonstrated that membrane-bound CD93 has no role in mediating efferocytosis (Figure 5), indicating that CD93 must function to induce efferocytosis through another mechanism.

1.4 Opsonins

Opsonins are molecules that bind to the surface of a phagocytic or efferocytic target and act as a ‘bridge’ to the cognate phagocytic receptor. Opsonisation dramatically increases uptake efficiency⁹⁸. For example, mannose-binding lectin (MBL), a member of the collectin protein family, binds to a broad range of targets containing numerous sugar groups through its carbohydrate recognition (lectin) domain^{99,100}s. MBL circulates in serum with MASPs (MBL-associated serine proteases) as multimeric units¹⁰¹ and functions as an opsonin by binding directly to pathogens and facilitating phagocytosis mediated by collectin receptors. Indirectly, MBL leads to opsonization by proteolytically cleaving C3 into C3b (the opsonic fragment of C3¹⁰²) through the MBL-MASP pathway, thus triggering phagocytosis through CR3 (reviewed in 103–

105). Additionally, MBL binds to altered cell-surfaces molecules through recognition of modified or oxidized glycolipids and glycoproteins, enabling it to act as an opsonin for both pathogens and apoptotic cells. Enhanced efferocytosis of apoptotic cells have been observed in experiments comparing sCD93-bearing versus sCD93-free serum and PLF³⁰. The enhancement of efferocytosis by sCD93 observed in these experiments is indicative that sCD93 may act as an apoptotic cell opsonin, although this possibility has not been explicitly tested, nor has a receptor for sCD93 been identified.

Hypothesis and Aims

As shown by its associations with numerous inflammatory and auto-immune disease states, CD93 is clearly of clinical importance. However, very little is known of its biological mechanisms or why certain SNPs incur a predisposition for inflammatory and autoimmune diseases. **I hypothesized that biologically important domains in CD93, including ligand-binding and cleavage sites, will be evolutionarily conserved and that soluble CD93 will act as an apoptotic cell opsonin.** To address this hypothesis, bioinformatic and evolutionary analysis of CD93 was performed in order to gain insight into the evolutionary history of CD93 and to identify potential functional domains, including putative cleavage sites, ligand binding sites, and clinically relevant SNPs. This was followed by functional assays to characterize CD93 expression, shedding and opsonic activity towards apoptotic cell mimics. To achieve these ends, I proposed the following aims:

Aim 1: Using bioinformatics and evolutionary approaches, identify putative CD93 cleavage sites, CD93-cleaving proteases, ligand- and receptor-binding, and potential key functional domains of CD93.

Aim 2: Characterize CD93 expression and shedding in monocytes using models of acute stimulation.

Aim 3: Characterize sCD93 opsonic activity.

Materials & Methods

3.1 Cell Culture

Human THP-1 cells (a gift from Dr. Dikeakos, Department of Microbiology and Immunology, Western University) were cultured in suspension at 37°C & 5% CO₂ in RPMI 1640 (Wisent) with 10% fetal bovine serum (Wisent). Cells were passaged 1:5 with fresh media every 2 days. Murine macrophage J774.2 (ATCC), and RAW264.7 cells (ATCC) were cultured at 37°C & 5% CO₂ in DMEM (Wisent) with 10% FBS. CHO-K1 cells were maintained at 37°C & 5% CO₂ in HAM's F12 with 10% FBS. Cells were passaged 1:5 with fresh media when they reached 80-90% confluency.

3.2 Human primary monocyte isolation.

Human primary monocytes were isolated from blood donated from healthy adult donors, and collected in the lab under approval from the Western University Health Science Research Ethic Board (Appendix 1) using methods meeting the guidelines of the Tri-Council Policy Statement on human research. Blood was collected in BD Vacutainer Sodium Heparin collection tubes, and then layered over an equal volume of lympholyte poly (Cedarlane). Tubes were then centrifuged with half acceleration and zero break at 500 x g for 35 minutes at 21°C. The top layer of peripheral blood mononuclear cells was collected, washed in PBS and re-suspended in 300 µL/well of RPMI 1640. Monocytes were then separated from PBMC by adhesion to glass coverslips for 1 h in RPMI 1640 with 10% FBS followed by washing with PBS. Monocytes were used within 1 h of isolation,

with Hoechst staining used to confirm that the isolated cell populations are >95% mononuclear (Figures 11, 13-15).

3.3 Transfection

Cell lines were passaged at 70-80% confluency and seeded 1-2 drops of suspended cells into 1 mL of RPMI 1640 per well onto 10 mm diameter, #1.5 thickness circular glass coverslips placed into the wells of a 12-well plate, 1 day prior to transfection. Cells were then transfected using either Lipofectamine 3000 (J774.2 cells, Invitrogen) or GenJet (all other cell types, Frogga Bio) according to the manufactures instructions. Briefly, for each well to be transfected 0.5-1 µg of DNA was suspended into 38 µL of serum-free media, and 1.5 µL of transfection reagent suspended in 38 µL of serum-free media added. The DNA and reagent mixtures were then mixed and incubated for 15 min at room temperature, and then added drop-wise to the cells. Experiments were performed 18-32 hrs after transfection.

3.4 Immunostaining

Cells on 18 mm, #1.5 thickness coverslips were fixed in 4% PFA in PBS for 20 minutes, washed once with PBS and then blocked in 5% skim milk powder in PBS for 30 mins. For cell surface (non-permabilized) staining, cells were then incubated with primary antibody (goat anti-CD93, BD Bioscience; mouse anti-CD62L, R&D Systems) at a dilution of 1:1000 in 5% skim milk powder in PBS for 30 mins, washed 3x with PBS, and then incubated with fluorescent secondary Fab

antibodies (Cedarlane) diluted 1:500 in 5% skim milk powder in PBS. Cells were then washed 3x 15 min in PBS and mounted on glass slides using Permafluor (Invitrogen) mounting media. For intracellular (permeabilized) staining, 0.1% Triton X-100 was added during the blocking step, and the remainder of the protocol performed as described above. The outlined method was chosen as it retains cytosolic proteins¹⁰⁶, allowing for quantification of loss of surface protein expression while ruling out endocytosis.

3.5 Shedding and Inhibition Assays.

Shedding assays were performed using THP-1 cells and primary human monocytes. Prior to shedding assays, THP-1 cells were cultured in a volume of 2 mL per well of a 12-well plate for 2 days, centrifuged at 250 x g, washed in PBS and re-suspended in 1 mL of serum-free RPMI 1640 per well and spun down onto glass coverslips for 1 min at 250 x g. Adherent monocytes were washed with PBS and placed in serum-free RPMI 1640. To induce shedding cells were incubated in serum-free RPMI 1640 containing PMA (10 ng/mL) for 1 h at room temperature. Shedding Inhibition was performed by incubating cells in serum-free RPMI containing either GM6001 (10 ng/mL, Cayman Chemical) or TAPI-2 (100 ng/mL, Cayman Chemical) for 5 minutes, followed by addition of PMA (10 ng/mL) and incubation for 55 minutes. Shedding was assessed by surface immunostaining for CD93 with shedding of L-selectin used as a positive control for GM6001 and TAPI2 inhibition.

3.6 Synthetic Apoptotic and Opsonized Targets.

Synthetic apoptotic targets were generated using 3 μm silica beads. 10 μL of silica beads were mixed with 145 μL of Phosphatidylcholine alone for control beads or 114 μL of phosphatidylcholine and 84 μL of phosphatidylserine for apoptotic mimics (4:1 mol:mol ratio of PtdChol:PtdSer) in a glass vial. The bead mix was then dried under a steady flow of nitrogen gas, washed 3 x in PBS, and re-suspended in 100 μL of PBS. For each well of a 12 well plate, 3 μL of synthetic apoptotic targets were added to 100 μL of cell-conditioned supernatants containing putative opsonins and rotated for 1 hr at room temperature, centrifuged at 6,000 x g for 1 minute, washed with PBS and then re-suspended in 1 mL of serum-free RPMI 1640.

3.7 Phagocytosis and Efferocytosis assays.

Primary human monocytes, macrophages, or cell lines were seeded onto glass coverslips in 12-well plates one day previously. 1 mL serum-free RPMI 1640 and 3 μL of the synthetic targets added per well, and centrifuged at 250 x g for 1 minute. Plates were then incubated for 10 minutes at 37°C & 5% CO₂, washed with PBS and incubated in serum-free RPMI 1640 for 30 minutes at 37°C & 5% CO₂ and then fixed for 20 minutes with 4% PFA. Cover slips were then washed with PBS and adhered to glass microscopy slides with permafluor and imaged. Phagocytic index for each image was calculated as the number of internalised beads divided by the total number of cells (# internalised beads/ # cells).

3.8 Phylogenetic Analysis.

Mammalian CD93 nucleotide sequences were taken from the NCBI database and imported into MEGA version 6 for analysis, and curated to remove sequences containing pseudogenes, gene fragments, large deletions or large insertions. Coding sequence alignments were generated using *MUSCLE* using default parameters and screened so that major clades were represented. Pairwise amino acid identity and similarity scores were generated from aligned primate sequences. Sequences were then analysed by Maximum Likelihood to determine the nucleotide substitution model of best fit based on Bayesian (BIC) and Akaike information criterion (AIC) scores. Phylogenetic trees were then constructed by maximum likelihood with bootstrapping (10,000 repeats) using the T92 model with Gamma distribution (T92+G) for primate sequences alone, and the Generalized time-reversible model with Gamma distribution and Invariant sites (GTR+G+I) for all mammalian sequences. For each set of sequences, phylogenetic analysis was performed across all open reading frames with an 85% cut off value. Generated phylogenetic trees were then imported into EvolView for annotation.

3.9 Amino acid substitution and selection analysis.

Unaligned mammalian and primate CD93 nucleotide sequences were imported into the Selecton online server (www.selecton.tau.ac.il). For each analysis the *Homo sapiens* sequence was selected as a reference sequence, and previously generated phylogenetic trees used as alignment guides. For both mammalian and primate sequence alignments, selection analysis was then conducted. First, selection analysis was performed using the Mechanistic Empirical Combination Model

(MEC) using 8 distribution categories and the JTT amino-acid matrix. Likelihood and AIC scores for the MEC model were compared against the M8a model as a test of significance, with lower MEC AIC scores indicating significance. Additionally, selection analysis was performed using the M5 model with AIC scores compared to the M7 model as a test of significance, and the M8 model compared against the M8a model. MEC/M8a AIC scores were then compared M5/M7 and M8/M8a to confirm MEC as the model of best fit by maximum-likelihood. Amino acid positions were scored for significance using Ka/Ks values and confidence intervals (CI) generated by Selecton. Ka/Ks scores greater than 1.3 with CI lower bounds greater than 1 were considered strong evidence of positive selection, while those with a CI lower bound of less than 1 were considered a possible indication of positive selection. Similarly, Ka/Ks scores of less than 0.7 with a CI upper bound less than 1 were considered strong evidence for purifying selection, while those with a CI upper bound greater than 1 indicated possible purifying selection. Amino acid positions with Ka/Ks values close to 1.0 or those with large CIs were counted as showing no evidence of selection.

3.10 SNP and cleavage analysis

SNP data were taken from the NCBI SNP, Ensembl, PupaSUITE, UniProKB, OMIM, and 1000 Genome databases and analysed using the Protein Variation Effect Analyser (PROVEAN) web software to characterise deleterious SNPs using PROVEAN and SIFT prediction algorithms. Predicted deleterious SNPs, along with SNPs clinically associated with disease-states taken from the literature, were imposed onto generated selection heat maps. Predicted deleterious SNPs

that aligned to residues with high confidence scores for purifying selection were then selected for further analysis. Putative cleavage sites were detected by PROSPER, and sites found by multiple prediction software programs and that aligned to likely cleavage regions based on reported size of soluble protein fragments reported in the literature.

3.11 Promoter Analysis

The proximal promotor of CD93 was identified by extracting the genomic sequence of the 2000 bp 5' to CD93's start codon from the human genome reference sequence using the UCSC Genome Browser. The promotor region was then further defined by identifying any endogenous retroviral or transposable element sequences using RepeatMasker. RepeatMasker identified L-family ERV at -1006. The proximal promotor region was then re-defined as the sequence between residue -1 and -1006, and the defined promotor sequence analyzed using the ENCODE database, limiting transcription factor binding analysis to primary human monocytes

3.12 Statistical Analysis

Unless otherwise stated, a 1-way ANOVA with Tukey correction was used. All statistics were performed using Graphpad Prism.

Results

4.1 Phylogenetic, amino acid substitution and selection

Despite its importance in inflammatory and autoimmune disease states, little is known of CD93's biology or evolutionary history. Investigations into CD93's recent evolution may provide information regarding its biological role and key functional domains. As such, bioinformatic analysis was performed in order to answer several basic questions. Given that CD93 was found to be present throughout all major mammal clades and appears to serve a conserved function among species (as demonstrated by the similar clinical and disease associations observed between mice and human CD93), it is likely that key functional regions will be evolutionarily conserved (undergone purifying selection), and therefore should be easily identified by evolutionary approaches. Additionally, regions and sites that show either strong evolutionary conservation or evidence of adaptive evolution (positive selection) may contain SNPs of potential clinical importance, further assisting in identifying key functional regions within the human CD93 sequence.

In order to narrow down potential cleavage or functional sites within the coding region of CD93, phylogenetic and selection analysis of available CD93 coding sequences was performed in order to identify highly conserved regions that cross-referenced with SNPs associated with increased disease risk or poorer clinical outcomes, and with sites identified by protease cleavage analysis. Following Maximum Likelihood analysis of unaligned sequences to determine the DNA model of best fit (Table 1 & 2), phylogenetic analysis of available CD93 coding sequences was

Model	Parameters	BIC	AICc	InL	(+I)	(+G)	R
<i>GTR+G+I</i>	83	49820.129	49057.350	-24445.579	0.17	1.57	2.34
<i>GTR+G</i>	82	49862.414	49108.824	-24472.318		0.81	2.35
<i>T92+G+I</i>	77	49866.995	49159.344	-24502.589	0.17	1.58	2.34
<i>TN93+G+I</i>	80	49887.157	49151.943	-24495.882	0.17	1.63	2.35
<i>HKY+G+I</i>	79	49894.480	49168.453	-24505.139	0.17	1.58	2.35
<i>T92+G</i>	76	49907.334	49208.872	-24528.355		0.82	2.36
<i>TN93+G</i>	79	49932.380	49206.354	-24524.090		0.82	2.36
<i>HKY+G</i>	78	49934.425	49217.586	-24530.708		0.82	2.36
<i>K2+G+I</i>	76	49974.804	49276.341	-24562.090	0.15	1.54	2.15
<i>K2+G</i>	75	50000.573	49311.298	-24580.571		0.86	2.16
<i>GTR+I</i>	82	50406.768	49653.178	-24744.495	0.24		2.14
<i>T92+I</i>	76	50445.055	49746.593	-24797.216	0.24		1.89
<i>TN93+I</i>	79	50454.250	49728.223	-24785.024	0.24		1.89
<i>HKY+I</i>	78	50474.104	49757.265	-24800.548	0.24		1.89
<i>K2+I</i>	75	50506.917	49817.643	-24833.743	0.24		2.00
<i>K2</i>	74	51793.517	51113.432	-25482.639			1.88
<i>GTR</i>	81	51869.473	51125.071	-25481.444			1.93
<i>T92</i>	75	51881.271	51191.997	-25520.920			1.93
<i>TN93</i>	78	51904.908	51188.069	-25515.950			1.93
<i>HKY</i>	77	51909.393	51201.742	-25523.788			1.93
<i>JC+G+I</i>	75	52007.790	51318.516	-25584.179	0.15	1.74	
<i>JC+G</i>	74	52038.026	51357.941	-25604.894		0.94	
<i>JC+I</i>	74	52476.217	51796.131	-25823.989	0.24		
<i>JC</i>	73	53695.071	53024.173	-26439.012			

Table 1: Comparison of nucleotide substitution models for mammalian sequences. Available nucleotide substitution models were compared by maximum likelihood with Bayesian (BIC) and Akaike (AICc) Information Criterion scores used to determine the DNA/Protein model of best fit. InL = log Likelihood. (+I) = Invariant sites. (+G) = gamma distribution. R = estimated transition/transversion bias

Model	Parameters	BIC	AICc	lnL	(+I)	(+G)	R
<i>T92+G</i>	20	11791.017	11633.901	-5796.929		0.53	2.52
<i>T92+G+I</i>	21	11800.81	11635.841	-5796.896	0.12	0.68	2.52
<i>HKY+G</i>	22	11811.422	11638.6	-5797.273		0.53	2.52
<i>HKY+I</i>	22	11816.287	11643.464	-5799.706	0.51		2.48
<i>TN93+G</i>	23	11817.447	11636.772	-5795.357		0.53	2.53
<i>HKY+G+I</i>	23	11821.219	11640.544	-5797.243	0.11	0.68	2.52
<i>TN93+I</i>	23	11822.034	11641.358	-5797.65	0.51		2.49
<i>TN93+G+I</i>	24	11827.23	11638.702	-5795.319	0.13	0.71	2.53
<i>T92+I</i>	20	11832.155	11675.04	-5817.498	0.24		2.21
<i>GTR+G</i>	26	11846.727	11642.494	-5795.21		0.52	2.52
<i>GTR+G+I</i>	27	11856.506	11644.42	-5795.17	0.13	0.72	2.53
<i>T92</i>	19	11868.01	11718.748	-5840.354			2.11
<i>HKY</i>	21	11888.23	11723.261	-5840.606			2.11
<i>TN93</i>	22	11894.347	11721.525	-5838.736			2.11
<i>GTR</i>	25	11923.847	11727.466	-5838.699			2.11
<i>K2+G</i>	19	11926.226	11776.965	-5869.462		0.64	2.33
<i>K2+I</i>	19	11930.426	11781.164	-5871.562	0.47		2.31
<i>GTR+I</i>	26	11933.703	11729.469	-5838.698	0		2.11
<i>K2+G+I</i>	20	11936.065	11778.95	-5869.453	0.06	0.74	2.33
<i>K2</i>	18	11985.223	11843.815	-5903.89			2.09
<i>JC+G</i>	18	12225.891	12084.484	-6024.224		0.76	0.5
<i>JC+G+I</i>	19	12235.747	12086.486	-6024.223	0.02	0.79	0.5
<i>JC</i>	17	12273.44	12139.887	-6052.927			0.5
<i>JC+I</i>	18	12283.297	12141.889	-6052.927	0		0.5

Table 2: Comparison of nucleotide substitution models for primate sequences. Available nucleotide substitution models were compared by maximum likelihood with Bayesian (BIC) and Akaike (AICc) Information Criterion scores used to determine the DNA/Protein model of best fit. lnL = log Likelihood. (+I) = Invariant sites. (+G) = gamma distribution. R = estimated transition/transversion bias.

performed in MEGA (version 6.0). Aligned mammalian sequences (Appendix 3 & 5) were analyzed using the GTR+G+I model (Figure 6) and aligned primate sequences (Appendix 2 & 4) using the T92+G (Figure 7), producing phylogenetic trees and amino acid identity and similarity scores (Table 3). Phylogenetic trees followed established evolutionary relationships between the represented phylogenetic clades. Additionally, the relative lengths of internode compared to terminal branches, and internode bootstrap values >50 suggests that the generated trees are stable, lending support to the validity of the phylogenetic trees. Whole gene selection analysis of primate sequences using MEGA7 was then performed. First, to determine whether neutral evolution (genetic drift) accounts for recent CD93 evolution, a Fishers Exact test were performed (Table 4). The Fishers Exact test indicates that neutral evolution is not responsible for the differences between sequence pairs. Following this, Z-tests determined that purifying selection is responsible for the evolutionary CD93 sequences, and not neutral or positive selection (Table 5). Amino acid substitution and selection analysis of CD93 performed using the Selecton web server revealed strong purifying selection across most of the CD93 coding sequence, with several individual amino acids showed evidence of positive selection (Table 7 & Figure 8 & 9). In order to test for significance, Akaike Information Criterion (AIC) scores were calculated for both MEC and M8a (which does not allow for positive selection) outputs and compared. The MEC output had a lower AIC score, and can be considered significant (Table 6). SNPs (Table 9) were then aligned with the selection output data, and those either linked with disease states or falling within evolutionary conserved regions displayed over the selection data along with predicted cleavage sites (Table 8, Figure 10)

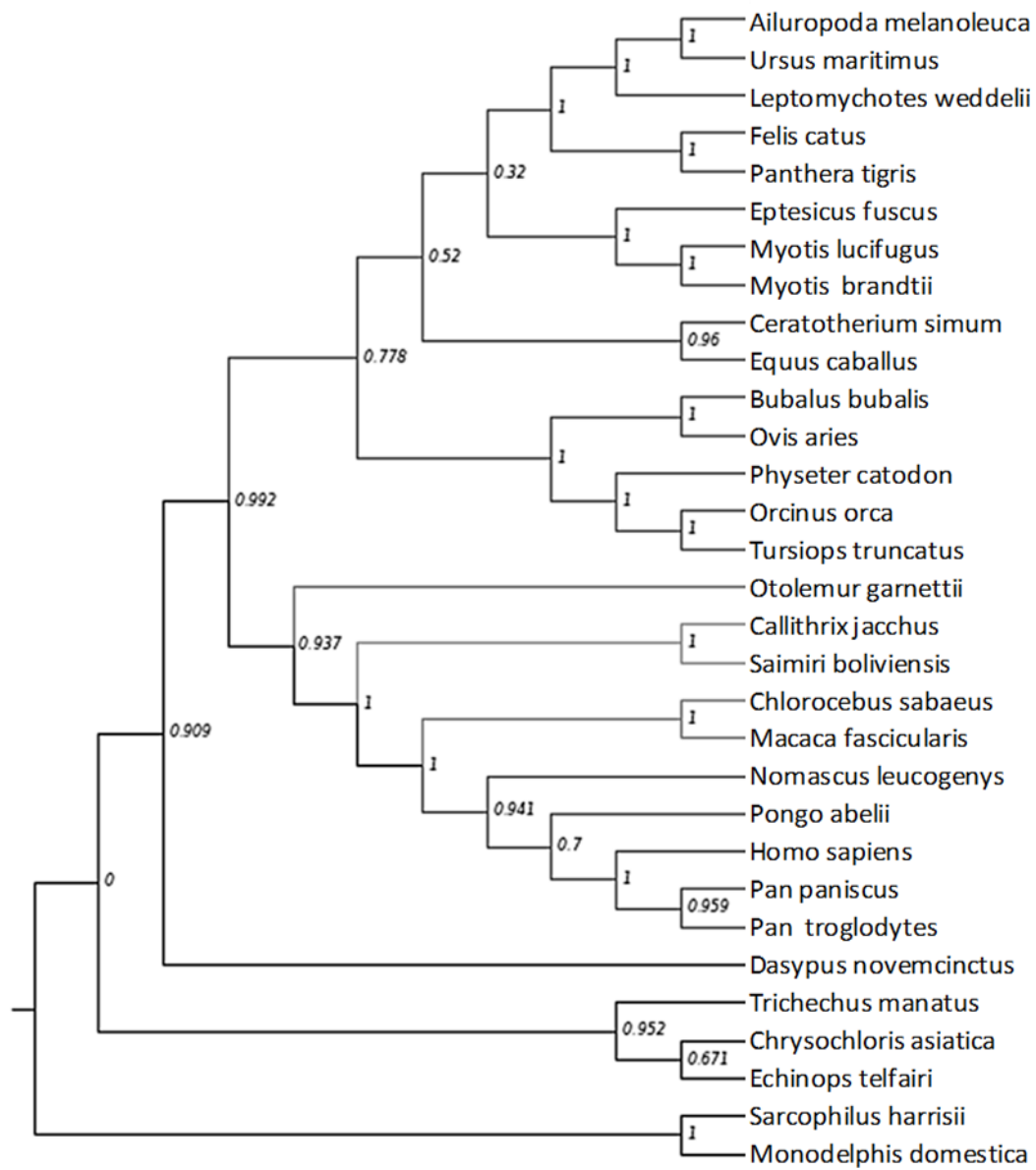


Figure 6: Phylogenetic analysis of CD93 evolution among mammals. Mammals CD93 coding sequences retrieved from the NCBI database and aligned by Muscle. Phylogenetic analysis was performed by maximum-likelihood using the GTR+G+I substitution model with bootstrapping (10,000 repeats, shown as internode values).

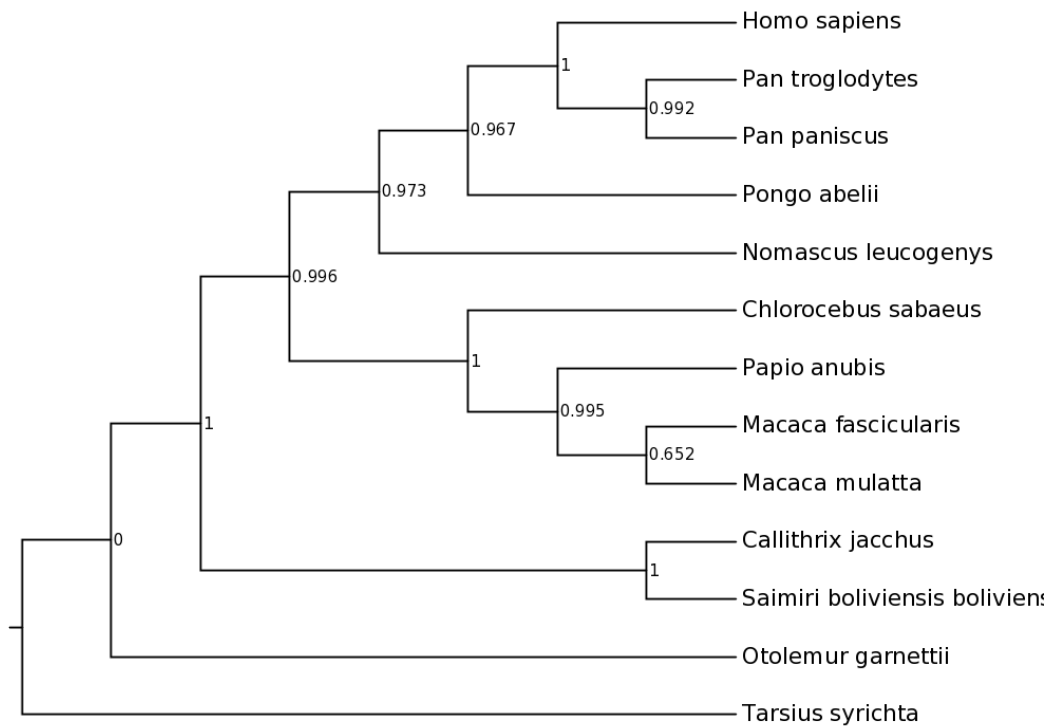


Figure 7: Phylogenetic analysis of CD93 evolution among primates. Primate CD93 coding sequences retrieved from the NCBI database and aligned by Muscle. Phylogenetic analysis was performed by maximum-likelihood using the T92+G substitution model with bootstrapping (10,000 repeats, shown as internode values).

		1	2	3	4	5	6	7	8	9	10	11	12	13
Otolemur garnettii	1		76.05	80.05	80.12	80.14	80.13	80.09	58.3	78.12	79.29	79.69	68.51	79.53
Tarsius syrichta	2	81.88		80.15	80.07	79.97	80.12	79.82	58.46	78.72	79.59	79.95	68.74	79.69
Homo sapiens	3	85.15	85.66		96.43	98.62	98.47	97.09	67.09	90.47	95.1	95.26	81.94	95.1
Nomascus leucogenys	4	85.23	85.69	97.86		96.32	96.22	96.53	67.13	90.35	94.29	94.44	81.24	94.29
Pan paniscus	5	85.32	85.54	99.23	97.85		99.49	97.34	67.21	90.64	94.59	94.74	81.5	94.59
Pan troglodytes	6	85.41	85.59	99.13	97.85	99.64		97.34	67.29	90.74	94.74	94.9	81.67	94.79
Pongo abelii	7	85.26	85.39	98.06	97.6	98.31	98.41		67.44	91.05	94.59	94.85	81.54	94.64
Callithrix jacchus	8	62.36	62.97	69.06	69.06	69.22	69.29	69.33		70.7	66.53	66.72	71.79	66.64
Saimiri boliviensis	9	83.72	84.56	93.05	92.99	93.34	93.54	93.54	71.76		89.64	89.79	78.26	89.74
Chlorocebus sabaeus	10	84.18	84.95	96.53	95.97	96.12	96.22	96.02	68.57	92.48		98.72	84.9	98.57
Macaca fascicularis	11	84.64	85.6	96.79	96.22	96.38	96.48	96.28	68.84	92.74	99.13		85.73	99.44
Macaca mulatta	12	72.76	73.3	83.21	82.73	82.86	82.98	82.73	75.04	80.76	85.21	85.78		85.6
Papio anubis	13	84.53	85.15	96.68	96.12	96.28	96.43	96.12	68.8	99.13	99.03	99.69	85.77	

Similarity

Identity

Table 3: CD93 Primate sequence amino acid identity and similarity. Percent amino acid identity and similarity between analysed CD93 primate sequences. Identity refers to the proportion of amino acid at a given site that are identical between two sequence pairs, while similarity refers to amino acids with similar chemical or physical properties.

	1	2	3	4	5	6	7	8	9	10	11	12
<i>Otolemur garnetti</i>	1											
<i>Tarsius syrichta</i>	2	1.000										
<i>Homo sapiens</i>	3	1.000	1.000									
<i>Nomascus leucogenys</i>	4	1.000	1.000	1.000								
<i>Pan paniscus</i>	5	1.000	1.000	1.000	1.000							
<i>Pan troglodytes</i>	6	1.000	1.000	1.000	1.000	1.000						
<i>Pongo abelii</i>	7	1.000	1.000	1.000	1.000	1.000	1.000					
<i>Callithrix jacchus</i>	8	1.000	1.000	1.000	1.000	1.000	1.000	1.000				
<i>Saimiri boliviensis</i>	9	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000			
<i>Chlorocebus sabaues</i>	10	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000		
<i>Macaca fascicularis</i>	11	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	
<i>Macaca mulatta</i>	12	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
<i>Papio anubis</i>	13	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000

Table 4: Fishers Exact selection tests. Fishers exact test measures if each sequence in a pair is statistically similar to each other, with shown values representing P values. P values less than 0.05 are considered significant at the 95% confidence level.

A

	1	2	3	4	5	6	7	8	9	10	11	12	13	
<i>Otolemur gametti</i>	1		9.970	9.463	9.070	9.640	9.255	8.919	8.470	8.327	9.413	9.158	9.158	9.156
<i>Tarsius syrichta</i>	2	0.000		11.640	11.900	11.998	11.798	12.062	9.823	10.224	11.753	11.738	11.582	11.518
<i>Homo sapiens</i>	3	0.000	0.000		4.006	1.783	1.180	3.497	6.397	6.167	5.571	5.656	5.460	5.425
<i>Nomascus leucogenys</i>	4	0.000	0.000	0.000		4.130	3.697	3.578	5.809	5.865	5.885	5.963	5.775	5.746
<i>Pan paniscus</i>	5	0.000	0.000	0.039	0.000		1.087	3.905	6.558	6.288	5.959	6.042	5.853	5.817
<i>Pan troglodytes</i>	6	0.000	0.000	0.120	0.000	0.140		3.289	6.247	5.930	5.519	5.603	5.406	5.372
<i>Pongo abelii</i>	7	0.000	0.000	0.000	0.000	0.000	0.001		5.791	5.663	5.334	5.217	5.014	4.985
<i>Callithrix jacchus</i>	8	0.000	0.000	0.000	0.000	0.000	0.000	0.000		5.324	6.388	6.569	6.312	6.244
<i>Saimiri boliviensis</i>	9	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000		6.208	6.307	6.046	5.980
<i>Chlorocebus sabaeus</i>	10	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000		2.384	1.774	1.890
<i>Macaca fascicularis</i>	11	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.009			1.737	1.407
<i>Macaca mulatta</i>	12	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.039	0.042			0.191
<i>Papio anubis</i>	13	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.031	0.081	0.424		

B

	1	2	3	4	5	6	7	8	9	10	11	12	13	
<i>Otolemur gametti</i>	1		-9.970	-9.463	-9.070	-9.640	-9.255	-8.919	-8.470	-8.327	-9.413	-9.158	-9.158	-9.156
<i>Tarsius syrichta</i>	2	1.000		-11.640	-11.900	-11.998	-11.798	-12.062	-9.823	-10.224	-11.753	-11.738	-11.582	-11.518
<i>Homo sapiens</i>	3	1.000	1.000		-4.006	-1.783	-1.180	-3.497	-6.397	-6.167	-5.571	-5.656	-5.460	-5.425
<i>Nomascus leucogenys</i>	4	1.000	1.000	1.000		-4.130	-3.697	-3.578	-5.809	-5.865	-5.885	-5.963	-5.775	-5.746
<i>Pan paniscus</i>	5	1.000	1.000	1.000	1.000		-1.087	-3.905	-6.558	-6.288	-5.959	-6.042	-5.853	-5.817
<i>Pan troglodytes</i>	6	1.000	1.000	1.000	1.000	1.000		-3.289	-6.247	-5.930	-5.519	-5.603	-5.406	-5.372
<i>Pongo abelii</i>	7	1.000	1.000	1.000	1.000	1.000	1.000		-5.791	-5.663	-5.334	-5.217	-5.014	-4.985
<i>Callithrix jacchus</i>	8	1.000	1.000	1.000	1.000	1.000	1.000	1.000		-5.324	-6.388	-6.569	-6.312	-6.244
<i>Saimiri boliviensis</i>	9	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000		-6.208	-6.307	-6.046	-5.980
<i>Chlorocebus sabaeus</i>	10	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000		-2.384	-1.774	-1.890
<i>Macaca fascicularis</i>	11	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000		-1.737	-1.407
<i>Macaca mulatta</i>	12	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000		-0.191
<i>Papio anubis</i>	13	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	

C

	1	2	3	4	5	6	7	8	9	10	11	12	13	
<i>Otolemur gametti</i>	1		-9.970	-9.463	-9.070	-9.640	-9.255	-8.919	-8.470	-8.327	-9.413	-9.158	-9.158	-9.156
<i>Tarsius syrichta</i>	2	0.000		-11.640	-11.900	-11.998	-11.798	-12.062	-9.823	-10.224	-11.753	-11.738	-11.582	-11.518
<i>Homo sapiens</i>	3	0.000	0.000		-4.006	-1.783	-1.180	-3.497	-6.397	-6.167	-5.571	-5.656	-5.460	-5.425
<i>Nomascus leucogenys</i>	4	0.000	0.000	0.000		-4.130	-3.697	-3.578	-5.809	-5.865	-5.885	-5.963	-5.775	-5.746
<i>Pan paniscus</i>	5	0.000	0.000	0.077	0.000		-1.087	-3.905	-6.558	-6.288	-5.959	-6.042	-5.853	-5.817
<i>Pan troglodytes</i>	6	0.000	0.000	0.240	0.000	0.279		-3.289	-6.247	-5.930	-5.519	-5.603	-5.406	-5.372
<i>Pongo abelii</i>	7	0.000	0.000	0.001	0.001	0.000	0.001		-5.791	-5.663	-5.334	-5.217	-5.014	-4.985
<i>Callithrix jacchus</i>	8	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-5.324	-6.388	-6.569	-6.312	-6.244
<i>Saimiri boliviensis</i>	9	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-6.208	-6.307	-6.046	-5.980
<i>Chlorocebus sabaeus</i>	10	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000		-2.384	-1.774	-1.890
<i>Macaca fascicularis</i>	11	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.019		-1.737	-1.407	
<i>Macaca mulatta</i>	12	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.079	0.085		-0.191	
<i>Papio anubis</i>	13	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.061	0.162	0.849		

Table 5: Z-tests for selection among CD93 sequence pairs. Z-tests were performed to determine the probability of rejecting neutral evolution (A), and then rejecting neutral evolution in favour of positive (B) or purifying evolution (C). Numbers in the upper half of each table represent the pairwise distance between each sequence pair, while the lower half show the P value. P values lower than 0.05 are significant at the 95% confidence level.

Model	n	K	Log(L)	AIC	AICc	ΔAIC
<i>MEC</i>	13	8	-6703.87	13423.74	43627.155	0
<i>M8</i>	13	8	-6712.44	13440.88	43682.86	17.14
<i>M8a</i>	13	8	-6711.72	13439.44	43678.18	15.7
<i>M5</i>	13	8	-6713.07	13442.14	43686.955	18.4
<i>M7</i>	13	8	-6713.11	13442.22	43687.215	18.48

Table 6: Statistical test for Amino acid substitution and selection analysis of primate CD93 sequences. Selection log likelihood results were used to calculate AIC and AICc scores. Lower AIC and AICc scores were used to infer the model of best fit. n = number of sequences. K = degrees of freedom. Log(L) = log likelihood of each model. AIC = Akaike information criterion. AICc = corrected Akaike information criterion (AIC correct for small sample sizes). ΔAIC = difference between each AIC score and the lowest AIC score.

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
1	M	0.09	0.00017	0.78	51	N	1	0.16	2.3
2	A	0.063	0.00017	0.36	52	H	0.43	0.02	2.3
3	T	0.056	0.00017	0.36	53	C	0.1	0.00017	0.78
4	S	1	1	2.3	54	N	1.5	0.36	2.3
5	M	0.99	0.36	2.3	55	Q	0.77	0.16	2.3
6	G	1.4	0.16	2.3	56	N	0.062	0.00017	0.36
7	L	0.16	0.00017	2.3	57	G	0.11	0.00017	0.78
8	L	0.46	0.00017	2.3	58	G	0.089	0.00017	0.78
9	L	0.26	0.00017	2.3	59	N	0.36	0.02	2.3
10	L	0.16	0.00017	2.3	60	L	0.16	0.00017	2.3
11	L	0.16	0.00017	2.3	61	A	0.42	0.02	2.3
12	L	0.16	0.00017	2.3	62	T	0.13	0.00017	2.3
13	L	0.22	0.00017	2.3	63	V	0.1	0.00017	0.78
14	L	0.11	0.00017	0.78	64	K	0.078	0.00017	0.78
15	L	0.16	0.00017	2.3	65	S	0.05	0.00017	0.36
16	T	1.6	0.36	2.3	66	K	1.1	0.78	2.3
17	Q	0.094	0.00017	2.3	67	E	0.088	0.00017	0.78
18	P	0.7	0.02	2.3	68	E	0.096	0.00017	0.78
19	G	0.72	0.066	2.3	69	A	0.063	0.00017	0.36
20	A	0.53	0.02	2.3	70	Q	0.63	0.02	2.3
21	G	0.76	0.066	2.3	71	H	0.48	0.02	2.3
22	T	0.94	0.16	2.3	72	V	0.39	0.02	2.3
23	G	0.86	0.066	2.3	73	Q	0.094	0.00017	2.3
24	A	1	0.16	2.3	74	R	1.4	0.36	2.3
25	D	0.86	0.16	2.3	75	V	0.97	0.16	2.3
26	T	0.6	0.02	2.3	76	L	0.16	0.00017	2.3
27	E	0.088	0.00017	0.78	77	A	0.063	0.00017	0.36
28	A	0.1	0.00017	2.3	78	Q	0.11	0.00017	2.3
29	V	0.1	0.00017	0.78	79	L	0.11	0.00017	0.78
30	V	0.075	0.00017	0.36	80	L	0.16	0.00017	2.3
31	C	0.11	0.00017	0.78	81	R	0.6	0.066	2.3
32	V	0.9	0.16	2.3	82	R	1.1	0.36	2.3
33	G	1.1	0.36	2.3	83	E	0.42	0.02	2.3
34	T	0.66	0.02	2.3	84	A	0.83	0.066	2.3
35	A	0.064	0.00017	0.36	85	A	0.61	0.066	2.3
36	C	0.1	0.00017	0.78	86	L	0.16	0.00017	2.3
37	Y	0.12	0.00017	0.78	87	T	0.59	0.02	2.3
38	T	0.088	0.00017	0.78	88	A	0.081	0.00017	0.78
39	A	0.063	0.00017	0.36	89	R	0.068	0.00017	0.36
40	H	0.072	0.00017	0.36	90	M	0.82	0.16	2.3
41	S	1	0.16	2.3	91	S	0.44	0.02	2.3
42	G	0.089	0.00017	0.78	92	K	0.078	0.00017	0.78
43	K	0.078	0.00017	0.78	93	F	0.12	0.00017	0.78
44	L	0.16	0.00017	2.3	94	W	0.19	0.00017	2.3
45	S	0.05	0.00017	0.36	95	I	0.15	0.00017	2.3
46	A	0.16	0.00017	2.3	96	G	0.11	0.00017	0.78
47	A	0.59	0.02	2.3	97	L	0.11	0.00017	0.78
48	E	0.4	0.02	2.3	98	Q	0.094	0.00017	2.3
49	A	0.064	0.00017	0.36	99	R	0.33	0.00017	2.3
50	Q	0.094	0.00017	2.3	100	E	0.088	0.00017	0.78

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
101	K	0.087	0.00017	0.78	151	P	0.79	0.066	2.3
102	G	0.09	0.00017	0.78	152	L	0.77	0.066	2.3
103	K	0.087	0.00017	0.78	153	L	1	0.066	2.3
104	C	0.1	0.00017	0.78	154	P	0.86	0.16	2.3
105	L	0.7	0.02	2.3	155	S	0.86	0.16	2.3
106	D	0.086	0.00017	0.78	156	R	0.87	0.16	2.3
107	P	0.1	0.00017	0.78	157	L	0.57	0.02	2.3
108	S	0.4	0.02	2.3	158	P	0.1	0.00017	0.78
109	L	0.16	0.00017	2.3	159	K	0.37	0.02	2.3
110	P	0.11	0.00017	2.3	160	W	0.19	0.00017	2.3
111	L	0.16	0.00017	2.3	161	S	0.11	0.00017	2.3
112	K	0.078	0.00017	0.78	162	E	0.12	0.00017	2.3
113	G	0.089	0.00017	0.78	163	G	0.089	0.00017	0.78
114	F	0.12	0.00017	0.78	164	P	0.093	0.00017	0.78
115	S	0.56	0.066	2.3	165	C	0.22	0.00017	2.3
116	W	0.19	0.00017	2.3	166	G	0.11	0.00017	0.78
117	V	0.1	0.00017	0.78	167	S	0.36	0.02	2.3
118	G	0.13	0.00017	0.78	168	P	0.82	0.066	2.3
119	G	0.092	0.00017	0.78	169	G	1.2	0.78	2.3
120	G	0.11	0.00017	0.78	170	S	0.32	0.02	2.3
121	E	0.088	0.00017	0.78	171	P	0.11	0.00017	0.78
122	D	0.086	0.00017	0.78	172	G	0.29	0.00017	2.3
123	T	0.077	0.00017	0.78	173	S	0.57	0.02	2.3
124	P	1.1	0.36	2.3	174	N	0.32	0.02	2.3
125	Y	0.11	0.00017	0.78	175	I	0.14	0.00017	2.3
126	S	1.1	0.16	2.3	176	E	0.088	0.00017	0.78
127	N	0.061	0.00017	0.36	177	G	0.098	0.00017	0.78
128	W	0.19	0.00017	2.3	178	F	0.12	0.00017	0.78
129	H	0.47	0.02	2.3	179	V	0.1	0.00017	0.78
130	K	0.078	0.00017	0.78	180	C	0.1	0.00017	0.78
131	E	0.088	0.00017	0.78	181	K	0.082	0.00017	0.78
132	L	0.97	0.16	2.3	182	F	0.13	0.00017	0.78
133	R	0.1	0.00017	0.78	183	S	0.05	0.00017	0.36
134	N	0.61	0.066	2.3	184	F	0.12	0.00017	0.78
135	S	0.11	0.00017	2.3	185	K	0.17	0.00017	2.3
136	C	0.1	0.00017	0.78	186	G	0.089	0.00017	0.78
137	I	0.35	0.02	2.3	187	M	0.09	0.00017	0.78
138	S	0.065	0.00017	0.36	188	C	0.1	0.00017	0.78
139	K	0.36	0.02	2.3	189	R	0.14	0.00017	2.3
140	R	0.1	0.00017	0.78	190	P	0.12	0.00017	2.3
141	C	0.22	0.00017	2.3	191	L	0.16	0.00017	2.3
142	V	0.1	0.00017	0.78	192	A	0.074	0.00017	0.78
143	S	0.49	0.02	2.3	193	L	0.16	0.00017	2.3
144	L	0.16	0.00017	2.3	194	G	0.11	0.00017	0.78
145	L	0.16	0.00017	2.3	195	G	0.1	0.00017	0.78
146	L	0.16	0.00017	2.3	196	P	0.24	0.00017	2.3
147	D	0.086	0.00017	0.78	197	G	0.11	0.00017	0.78
148	L	0.16	0.00017	2.3	198	Q	0.49	0.02	2.3
149	S	0.062	0.00017	0.36	199	V	0.1	0.00017	0.78
150	Q	0.57	0.02	2.3	200	T	0.056	0.00017	0.36

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
201	Y	0.12	0.00017	0.78	251	G	0.6	0.02	2.3
202	T	0.52	0.066	2.3	252	S	0.24	0.02	2.3
203	T	0.085	0.00017	2.3	253	S	0.55	0.02	2.3
204	P	0.093	0.00017	0.78	254	G	0.098	0.00017	0.78
205	F	0.13	0.00017	0.78	255	P	0.096	0.00017	0.78
206	Q	0.49	0.02	2.3	256	L	0.61	0.02	2.3
207	T	0.52	0.02	2.3	257	C	0.22	0.00017	2.3
208	T	0.54	0.02	2.3	258	V	0.075	0.00017	0.36
209	S	0.089	0.00017	2.3	259	S	0.68	0.066	2.3
210	S	0.064	0.00017	0.36	260	P	0.1	0.00017	0.78
211	S	0.062	0.00017	0.36	261	K	0.9	0.16	2.3
212	L	0.16	0.00017	2.3	262	Y	1.1	0.066	2.3
213	E	0.41	0.02	2.3	263	G	0.098	0.00017	0.78
214	A	0.14	0.00017	2.3	264	C	0.1	0.00017	0.78
215	V	0.1	0.00017	0.78	265	N	0.79	0.16	2.3
216	P	0.093	0.00017	0.78	266	F	0.12	0.00017	0.78
217	F	0.25	0.00017	2.3	267	N	0.061	0.00017	0.36
218	A	0.07	0.00017	0.36	268	N	0.1	0.00017	2.3
219	S	0.15	0.00017	2.3	269	G	0.12	0.00017	0.78
220	A	0.63	0.02	2.3	270	G	0.089	0.00017	0.78
221	A	0.063	0.00017	0.36	271	C	0.11	0.00017	0.78
222	N	1.5	0.78	2.3	272	H	0.68	0.066	2.3
223	V	0.1	0.00017	0.78	273	Q	0.094	0.00017	2.3
224	A	1.1	0.16	2.3	274	D	0.46	0.02	2.3
225	C	0.22	0.00017	2.3	275	C	0.1	0.00017	0.78
226	G	0.11	0.00017	0.78	276	F	0.17	0.00017	2.3
227	E	0.61	0.02	2.3	277	E	0.13	0.00017	2.3
228	G	0.92	0.16	2.3	278	G	0.13	0.00017	0.78
229	D	0.63	0.02	2.3	279	G	0.65	0.02	2.3
230	K	1	0.16	2.3	280	D	0.14	0.00017	2.3
231	D	0.5	0.02	2.3	281	G	0.089	0.00017	0.78
232	E	1.1	0.78	2.3	282	S	0.062	0.00017	0.36
233	T	0.6	0.02	2.3	283	F	0.12	0.00017	0.78
234	Q	0.8	0.16	2.3	284	L	0.67	0.02	2.3
235	S	0.089	0.00017	2.3	285	C	0.16	0.00017	2.3
236	H	0.14	0.00017	2.3	286	G	0.089	0.00017	0.78
237	Y	1	0.066	2.3	287	C	0.11	0.00017	0.78
238	F	0.66	0.02	2.3	288	R	0.71	0.02	2.3
239	L	0.16	0.00017	2.3	289	P	0.18	0.00017	2.3
240	C	0.11	0.00017	0.78	290	G	0.11	0.00017	0.78
241	K	0.36	0.02	2.3	291	F	0.12	0.00017	0.78
242	E	0.088	0.00017	0.78	292	R	0.13	0.00017	0.78
243	K	0.078	0.00017	0.78	293	L	0.16	0.00017	2.3
244	A	0.88	0.16	2.3	294	L	0.16	0.00017	2.3
245	P	0.13	0.00017	2.3	295	D	0.13	0.00017	1
246	D	1	1	2.3	296	D	0.086	0.00017	0.78
247	V	0.1	0.00017	0.78	297	L	0.16	0.00017	2.3
248	F	0.13	0.00017	0.78	298	V	0.1	0.00017	0.78
249	D	0.46	0.02	2.3	299	T	0.26	0.02	2.3
250	W	0.19	0.00017	2.3	300	C	0.22	0.00017	2.3

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
301	A	0.063	0.00017	0.36	351	D	0.46	0.02	2.3
302	S	0.12	0.00017	2.3	352	S	0.57	0.066	2.3
303	R	0.21	0.00017	2.3	353	P	0.093	0.00017	0.78
304	N	0.061	0.00017	0.36	354	C	0.22	0.00017	2.3
305	P	0.19	0.00017	2.3	355	A	0.51	0.02	2.3
306	C	0.1	0.00017	0.78	356	Q	0.094	0.00017	2.3
307	S	0.05	0.00017	0.36	357	E	0.99	0.16	2.3
308	S	0.065	0.00017	0.36	358	C	0.19	0.00017	2.3
309	S	0.05	0.00017	0.36	359	V	0.072	0.00017	0.36
310	P	0.24	0.00017	2.3	360	N	0.061	0.00017	0.36
311	C	0.12	0.00017	0.78	361	T	0.056	0.00017	0.36
312	R	1.5	0.36	2.3	362	P	0.8	0.066	2.3
313	G	0.12	0.00017	0.78	363	G	0.11	0.00017	0.78
314	G	1	0.36	2.3	364	G	0.75	0.16	2.3
315	A	0.063	0.00017	0.36	365	F	0.12	0.00017	0.78
316	T	0.18	0.00017	2.3	366	R	0.11	0.00017	0.78
317	C	0.14	0.00017	1	367	C	0.14	0.00017	1
318	V	0.66	0.16	2.3	368	E	0.13	0.00017	2.3
319	L	1.3	0.78	2.3	369	C	0.1	0.00017	0.78
320	G	0.93	0.066	2.3	370	W	0.19	0.00017	2.3
321	P	0.51	0.02	2.3	371	V	0.13	0.00017	2.3
322	H	0.56	0.02	2.3	372	G	0.1	0.00017	0.78
323	G	0.53	0.02	2.3	373	Y	0.13	0.00017	0.78
324	K	1.2	0.36	2.3	374	E	0.42	0.02	2.3
325	N	0.4	0.02	2.3	375	P	0.11	0.00017	0.78
326	Y	0.5	0.02	2.3	376	G	0.93	0.16	2.3
327	T	0.75	0.066	2.3	377	G	1	0.16	2.3
328	C	0.1	0.00017	0.78	378	P	0.19	0.00017	2.3
329	R	1	0.36	2.3	379	G	0.19	0.00017	2.3
330	C	0.18	0.00017	2.3	380	E	0.095	0.00017	0.78
331	P	0.093	0.00017	0.78	381	G	1.4	0.78	2.3
332	Q	0.68	0.02	2.3	382	A	1	0.36	2.3
333	G	0.12	0.00017	0.78	383	C	0.2	0.00017	2.3
334	Y	0.51	0.02	2.3	384	Q	1.3	0.36	2.3
335	Q	0.1	0.00017	2.3	385	D	0.14	0.00017	2.3
336	L	0.65	0.02	2.3	386	V	0.11	0.00017	0.78
337	D	0.092	0.00017	0.78	387	D	0.15	0.00017	2.3
338	S	0.69	0.066	2.3	388	E	0.088	0.00017	0.78
339	S	0.12	0.00017	2.3	389	C	0.22	0.00017	2.3
340	Q	0.094	0.00017	2.3	390	A	0.067	0.00017	0.36
341	L	0.16	0.00017	2.3	391	L	1	0.78	2.3
342	D	0.89	0.16	2.3	392	G	1	0.78	2.3
343	C	0.22	0.00017	2.3	393	R	0.52	0.02	2.3
344	V	0.61	0.02	2.3	394	S	0.46	0.02	2.3
345	D	0.13	0.00017	1	395	P	0.12	0.00017	2.3
346	V	0.1	0.00017	0.78	396	C	0.1	0.00017	0.78
347	D	0.15	0.00017	2.3	397	A	0.46	0.02	2.3
348	E	0.13	0.00017	2.3	398	Q	0.095	0.00017	2.3
349	C	0.14	0.00017	1	399	G	0.98	0.16	2.3
350	Q	0.1	0.00017	2.3	400	C	0.11	0.00017	0.78

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
401	T	0.056	0.00017	0.36	451	H	1.8	0.78	2.3
402	N	0.061	0.00017	0.36	452	C	0.22	0.00017	2.3
403	T	0.15	0.00017	2.3	453	G	0.089	0.00017	0.78
404	D	1	0.16	2.3	454	C	0.1	0.00017	0.78
405	G	0.089	0.00017	0.78	455	L	0.16	0.00017	2.3
406	S	0.15	0.00017	2.3	456	P	0.9	0.066	2.3
407	F	0.13	0.00017	0.78	457	G	0.089	0.00017	0.78
408	H	0.51	0.02	2.3	458	W	1	0.066	2.3
409	C	0.11	0.00017	0.78	459	V	0.53	0.02	2.3
410	S	0.062	0.00017	0.36	460	L	0.16	0.00017	2.3
411	C	0.11	0.00017	0.78	461	A	0.07	0.00017	0.36
412	E	1.3	0.36	2.3	462	P	1.3	0.16	2.3
413	E	0.088	0.00017	0.78	463	N	0.81	0.066	2.3
414	G	0.089	0.00017	0.78	464	G	0.11	0.00017	0.78
415	Y	0.18	0.00017	2.3	465	V	0.072	0.00017	0.36
416	V	0.075	0.00017	0.36	466	S	0.063	0.00017	0.36
417	L	0.16	0.00017	2.3	467	C	0.1	0.00017	0.78
418	A	0.097	0.00017	2.3	468	T	0.84	0.16	2.3
419	G	0.66	0.02	2.3	469	M	0.48	0.02	2.3
420	E	0.096	0.00017	0.78	470	G	0.55	0.02	2.3
421	D	0.1	0.00017	0.78	471	P	0.94	0.066	2.3
422	G	0.091	0.00017	0.78	472	V	0.1	0.00017	0.78
423	T	0.12	0.00017	2.3	473	S	0.7	0.02	2.3
424	Q	0.094	0.00017	2.3	474	L	1.2	0.16	2.3
425	C	0.1	0.00017	0.78	475	G	1.4	0.36	2.3
426	Q	0.44	0.02	2.3	476	P	1.3	0.36	2.3
427	D	0.12	0.00017	0.78	477	P	0.95	0.066	2.3
428	V	0.1	0.00017	0.78	478	S	0.97	0.16	2.3
429	D	0.51	0.02	2.3	479	G	0.11	0.00017	0.78
430	E	0.088	0.00017	0.78	480	P	1.2	0.36	2.3
431	C	0.22	0.00017	2.3	481	P	0.095	0.00017	0.78
432	V	1.4	0.36	2.3	482	D	1.2	0.16	2.3
433	G	0.089	0.00017	0.78	483	E	0.088	0.00017	0.78
434	P	1	0.78	2.3	484	E	0.088	0.00017	0.78
435	G	0.67	0.02	2.3	485	D	1	0.36	2.3
436	G	1.1	0.36	2.3	486	K	1.1	0.16	2.3
437	P	1.2	0.16	2.3	487	G	1	0.16	2.3
438	L	1.1	0.78	2.3	488	E	0.98	0.36	2.3
439	C	0.18	0.00017	2.3	489	K	1.2	0.16	2.3
440	D	0.092	0.00017	0.78	490	E	0.089	0.00017	0.78
441	S	0.3	0.02	2.3	491	G	0.59	0.02	2.3
442	L	0.17	0.00017	2.3	492	S	0.59	0.066	2.3
443	C	0.1	0.00017	0.78	493	T	0.43	0.02	2.3
444	F	0.6	0.02	2.3	494	V	1.3	0.36	2.3
445	N	0.061	0.00017	0.36	495	P	0.88	0.16	2.3
446	T	0.21	0.00017	2.3	496	R	0.96	0.16	2.3
447	Q	0.15	0.00017	2.3	497	A	0.74	0.066	2.3
448	G	0.12	0.00017	0.78	498	A	0.82	0.066	2.3
449	S	0.062	0.00017	0.36	499	T	1.1	0.36	2.3
450	F	0.12	0.00017	0.78	500	A	0.78	0.16	2.3

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
501	S	0.14	0.00017	2.3	551	H	0.36	0.02	2.3
502	P	0.1	0.00017	0.78	552	A	1.9	0.78	2.3
503	T	0.067	0.00017	0.36	553	T	0.81	0.066	2.3
504	R	0.46	0.02	2.3	554	A	0.16	0.00017	2.3
505	G	0.09	0.00017	0.78	555	A	0.5	0.02	2.3
506	P	1	0.16	2.3	556	S	0.61	0.02	2.3
507	E	0.64	0.02	2.3	557	G	0.098	0.00017	0.78
508	G	0.5	0.02	2.3	558	P	0.82	0.16	2.3
509	T	0.27	0.02	2.3	559	Q	0.97	0.36	2.3
510	P	1.1	0.36	2.3	560	E	0.39	0.02	2.3
511	K	1.1	0.36	2.3	561	P	0.86	0.066	2.3
512	A	0.85	0.16	2.3	562	A	0.74	0.066	2.3
513	T	1.2	0.36	2.3	563	G	0.82	0.066	2.3
514	P	0.51	0.02	2.3	564	G	0.54	0.02	2.3
515	T	0.42	0.02	2.3	565	D	0.56	0.02	2.3
516	T	1.8	0.36	2.3	566	S	0.19	0.00017	2.3
517	S	0.75	0.066	2.3	567	S	0.077	0.00017	2.3
518	R	0.9	0.16	2.3	568	V	0.095	0.00017	0.78
519	P	0.91	0.066	2.3	569	A	0.86	0.16	2.3
520	S	0.95	0.16	2.3	570	T	1.4	0.78	2.3
521	L	0.95	0.16	2.3	571	Q	0.7	0.02	2.3
522	S	1.8	0.36	2.3	572	N	0.66	0.066	2.3
523	S	1.5	0.36	2.3	573	N	0.99	0.16	2.3
524	D	1	0.066	2.3	574	D	0.72	0.066	2.3
525	A	0.88	0.16	2.3	575	G	0.45	0.02	2.3
526	P	0.11	0.00017	0.78	576	T	0.14	0.00017	2.3
527	I	0.34	0.02	2.3	577	D	0.088	0.00017	0.78
528	T	0.068	0.00017	0.36	578	G	0.12	0.00017	0.78
529	S	0.18	0.00017	2.3	579	Q	0.15	0.00017	2.3
530	A	1	0.36	2.3	580	K	0.078	0.00017	0.78
531	P	0.98	0.16	2.3	581	L	0.16	0.00017	2.3
532	L	1.1	0.78	2.3	582	L	0.21	0.00017	2.3
533	K	0.72	0.02	2.3	583	L	0.19	0.00017	2.3
534	M	0.9	0.16	2.3	584	F	0.12	0.00017	0.78
535	L	0.16	0.00017	2.3	585	Y	0.11	0.00017	0.78
536	A	0.4	0.02	2.3	586	I	0.066	0.00017	0.36
537	P	0.55	0.02	2.3	587	L	0.19	0.00017	2.3
538	S	0.14	0.00017	2.3	588	G	0.089	0.00017	0.78
539	G	0.58	0.02	2.3	589	T	0.063	0.00017	0.36
540	S	0.58	0.066	2.3	590	V	0.1	0.00017	0.78
541	P	0.21	0.00017	2.3	591	V	0.1	0.00017	0.78
542	G	1.4	0.36	2.3	592	A	0.34	0.02	2.3
543	V	1.1	0.16	2.3	593	I	0.066	0.00017	0.36
544	W	0.91	0.066	2.3	594	L	0.19	0.00017	2.3
545	R	1.2	0.36	2.3	595	L	0.11	0.00017	0.78
546	E	0.53	0.02	2.3	596	L	0.16	0.00017	2.3
547	P	0.5	0.02	2.3	597	L	0.16	0.00017	2.3
548	S	0.67	0.066	2.3	598	A	0.07	0.00017	0.36
549	I	0.59	0.02	2.3	599	L	0.16	0.00017	2.3
550	H	0.14	0.00017	2.3	600	A	0.15	0.00017	2.3

Position	Amino Acid	Ka/Ks	Confidence Interval		Position	Amino Acid	Ka/Ks	Confidence Interval	
			Lower	Upper				Lower	Upper
601	L	0.19	0.00017	2.3	627	S	0.71	0.066	2.3
602	G	0.11	0.00017	0.78	628	Y	0.11	0.00017	0.78
603	L	0.22	0.00017	2.3	629	S	0.07	0.00017	0.78
604	L	0.16	0.00017	2.3	630	W	0.19	0.00017	2.3
605	V	0.072	0.00017	0.36	631	V	0.77	0.066	2.3
606	Y	0.95	0.066	2.3	632	P	0.95	0.066	2.3
607	R	0.095	0.00017	0.78	633	E	0.088	0.00017	0.78
608	K	0.36	0.02	2.3	634	R	0.22	0.00017	2.3
609	R	0.12	0.00017	0.78	635	A	0.72	0.066	2.3
610	R	0.2	0.00017	2.3	636	E	0.088	0.00017	0.78
611	A	0.096	0.00017	2.3	637	S	0.34	0.02	2.3
612	K	0.078	0.00017	0.78	638	R	0.08	0.00017	0.78
613	R	0.68	0.066	2.3	639	A	0.067	0.00017	0.36
614	E	0.77	0.16	2.3	640	M	1	0.16	2.3
615	E	0.58	0.02	2.3	641	E	0.088	0.00017	0.78
616	K	0.078	0.00017	0.78	642	N	0.067	0.00017	0.36
617	K	0.69	0.02	2.3	643	Q	1.3	0.36	2.3
618	E	0.72	0.16	2.3	644	Y	0.11	0.00017	0.78
619	K	0.39	0.02	2.3	645	S	0.55	0.02	2.3
620	K	2	0.78	2.3	646	P	0.14	0.00017	2.3
621	P	0.099	0.00017	0.78	647	T	0.26	0.00017	2.3
622	Q	0.37	0.02	2.3	648	P	0.26	0.00017	2.3
623	N	0.59	0.02	2.3	649	G	0.15	0.00017	2.3
624	A	0.13	0.00017	2.3	650	T	0.91	0.066	2.3
625	A	0.2	0.00017	2.3	651	D	0.11	0.00017	0.78
626	D	0.086	0.00017	0.78	652	C	0.13	0.00017	0.78

Table 7: Amino acid substitution and selection analysis. Unaligned primate CD93 sequences were imported into the Selecton server, and selection analysis performed using the MEC model with statistical significance assessed against the M8a model. Ka/Ks scores greater than 1 are evidence of positive selection, and score less than 1 are evidence of purifying selection, with 95% Confidence intervals used as a measure of significance.

Amino Acid (P1)	Sequence
468	SCT M PG
473	PV S LGP
497	PRA A TA
531	SAP L KM
533	PL K MLA

Table 8: Predicted matrix metalloproteinase cleavage sites. Location of the P1 amino acid residue within the CD93 sequence is shown, along with the 6 amino acids flanking the cut site (P1 position highlighted shown in bold)

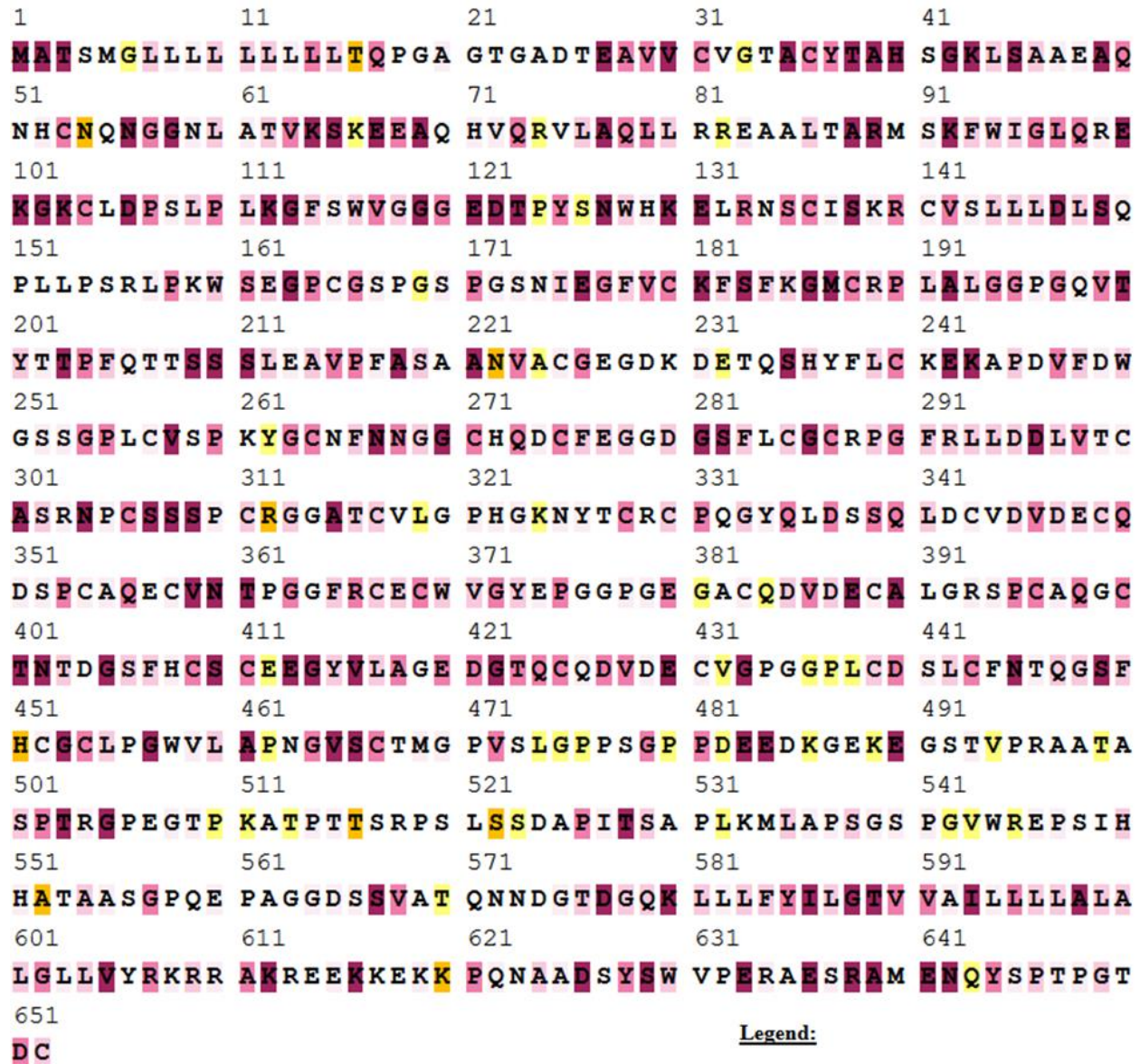


Figure 8: Selecton output for selection in CD93 among primates overlaid onto the human CD93 sequence. Unaligned sequences retrieved from NCBI were entered into the Selecton web server, and Ka/Ks values inferred using the Mechanistic Empirical Combination (MEC) model with the previously generated evolutionary tree used as a guide. Ka/Ks > 1 (represented on the selecton scale as <4) suggest positive selection, while Ka/Ks < 1 (>4 on the selecton scale) suggest purifying selection. In order to test for significance, Akaike Information Content (AIC) scores were calculated for both MEC and M8a (which does not allow for positive selection) outputs, and compared. The MEC output had a lower AIC score, and can be considered significant.

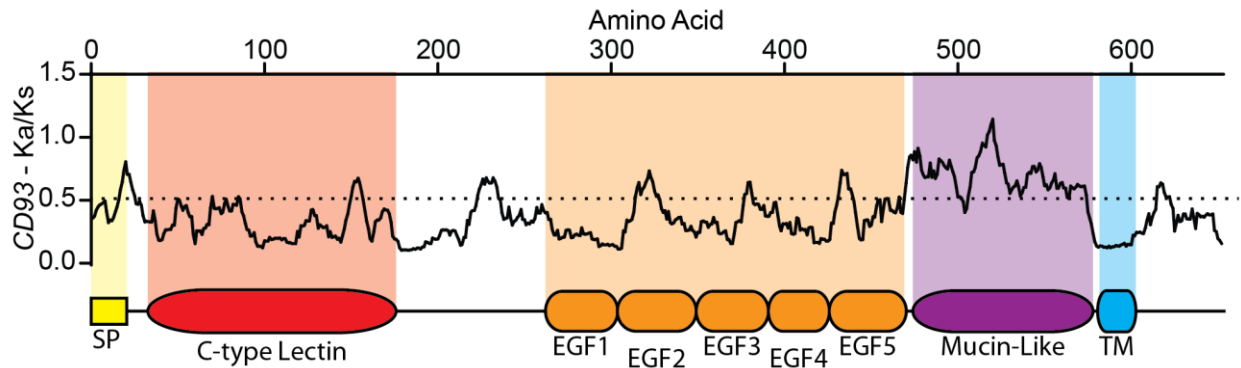


Figure 9 : Selection in CD93 among primates. Ka/Ks values obtained from selection were averaged over 10 amino acids and aligned with CD93 domains. Ka/Ks values of 1 represent neutral evolution (genetic drift), where as Ka/Ks greater or less than 1 are evidence of possible positive or purifying selection respectively. Ka/Ks values of 0.5 or less are strong evidence of purifying selection.

Position	Amino Acid	Ka/Ks	Confidence Interval		Mutation		Pop.	Valid.	Prediction
			Lower	Upper	Change	Type			
28	A	0.1	0.00017	2.3	A>V	missense		N/A	SIFT
62	T	0.13	0.00017	2.3	T>S	missense	EU	1000G, Frequency	PROVEAN
78	Q	0.11	0.00017	2.3	Q>H	missense	NA	1000G, Cluster, Frequency	SIFT
119	G	0.092	0.00017	0.78	G>R	missense	NA	Cluster	SIFT
155	S	0.86	0.16	2.3	S>I	missense	NS, EA, NA	Cluster, Frequency	SIFT
169	G	1.2	0.78	2.3	G>C	missense		N/A	SIFT/FUNCPRED
186	G	0.089	0.00017	0.78	G>S	missense		N/A	SIFT/PROVEAN
187	M	0.09	0.00017	0.78	M>I	missense		N/A	SIFT/PROVEAN
209	S	0.089	0.00017	2.3	S>R	missense	NA	N/A	SIFT/PROVEAN
219	S	0.15	0.00017	2.3	A>D	missense	NS, EA, NA	Cluster, Frequency	SIFT/PROVEAN
264	C	0.1	0.00017	0.78					SIFT/PROVEAN
278	G	0.13	0.00017	0.78	G>R/E	missense	NA	1000G	SIFT/PROVEAN
293	L	0.16	0.00017	2.3	L>M	missense		N/A	SIFT
313	G	0.12	0.00017	0.78	G>R/A	missense		1000G, Cluster, Frequency	SIFT/PROVEAN
333	G	0.12	0.00017	0.78	G>E	missense	NA	N/A	SIFT/PROVEAN
375	P	0.11	0.00017	0.78	P>L	missense	NA	N/A	SIFT
419	G	0.66	0.02	2.3	G>R	missense		1000G	SIFT/PROVEAN
422	G	0.091	0.00017	0.78	G>R	missense	NA	Frequency	PROVEAN
502	P	0.1	0.00017	0.78	P>L	missense		N/A	SIFT/PROVEAN
541	P	0.21	0.00017	2.3	P>S	missense		Van der Net <i>et al</i>	Clinical
624	A	0.13	0.00017	2.3	A>E	missense		1000G, Frequency	SIFT/PROVEAN
641	E	0.088	0.00017	0.78	E>Ter/G	STOP/missense	EU	Cluster	SIFT/PROVEAN
646	P	0.14	0.00017	2.3	P>R	missense	NA	1000G, Frequency	SIFT

Table 9: Predicted deleterious and disease associated CD93 SNPs. Disease related SNPs along with SNPs predicted as potentially deleterious compiled with CD93 selection data. Ka/Ks values show the ratio of the synonymous mutation rate to non-synonymous mutation rate at each codon site. Ka/Ks values greater than 1 are evidence of positive selection, while Ka/Ks values less than 1 are evidence of purifying selection. Confidence Intervals are used as a measure of significance. Population groups information and validation methods shown when available, along with prediction method.

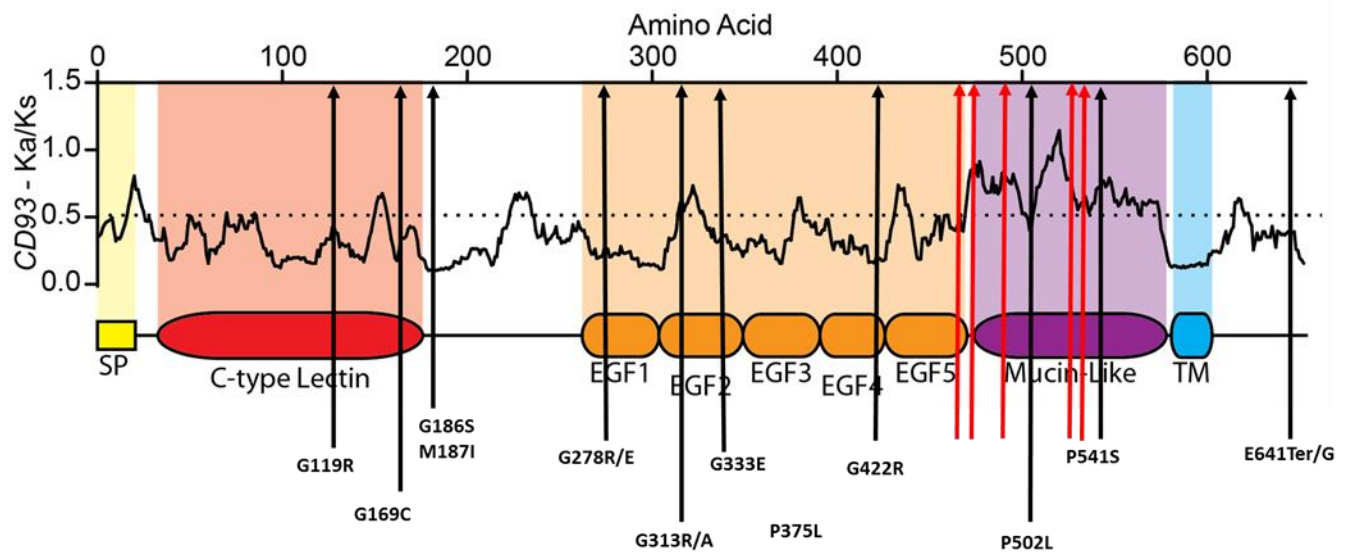


Figure 10: Predicted SNPs of interest and predicted matrix metalloproteinase cleavage sites. Validated SNPs and predicted protease cleavage sites aligned with CD93 selection heat map output. SNPs are shown by black arrows, with their amino acid changes indicated below. Predicted matrix metalloproteinase cleavage sites are shown by red arrows.

4.1 Promotor Analysis

While CD93 expression patterns have been well classified in the literature, no published promoter analysis is currently available. Promoter analysis was performed in order to determine if transcription factors identified by chromatin immunoprecipitation (ChIP) and limited to human monocytic and macrophage cell lines within the ENCODE dataset could provide information regarding CD93's biological function in inflammatory and autoimmune diseases. The ENCODE data set was chosen for this analysis over computational models, as ENCODE ChIP data for primary human monocytes and macrophages was available, thereby directly assessing transcription factor binding to the promoter. Promoter analysis generated a small list of transcription factors and binding sites (Table 10), but notably, the myeloid developmental transcription factors GATA2 and PU.1, the AP-1 transcription factor subunits c-Jun and c-Fos, and the cell cycle transcription factor Max were found to associate with CD93's proximal promoter. Max, GATA2 and PU.1 expression are consistent with CD93 expression during hematopoiesis when myeloid cells are undergoing cell division and differentiation, while the presence of AP-1 binding suggests that CD93 may also be upregulated following pro-inflammatory stimuli.

Name	Chromosome Position		Start ATG	End ATG
	Start	End		
Pol2	23066844	23067124	15	295
c-Fos	23066866	23067210	37	381
GATA-2	23066867	23067247	38	418
c-Jun	23066883	23067159	54	330
Pol2(b)	23066920	23067240	91	411
Pol2-4H8	23066937	23067213	108	384
Max	23067617	23067827	788	998
PU.1	23067841	23068006	1012	1177
3' UTR			148	1

Table 10: CD93 Promotor Analysis Output. Table shows transcription factors and binding sites identified using the ENCODE dataset.

4.1 In Vitro Shedding Assay Optimization and Results

While sCD93 has been well documented in the literature, and various clinical associations identified, the exact mechanisms of its shedding are currently unknown. Investigations involving CD93 shedding in mice suggest that shedding occurs through an MMP, and bioinformatic analysis revealed 5 putative MMP cleavage sites within the mucin domain of CD93. To this end, shedding and inhibition assays were performed to determine whether an MMP is responsible for CD93 shedding in humans.

Previous studies have shown that PDBu (Phorbol 12,13-dibutyrate), an activator of protein kinase C, stimulates shedding of CD93 *in vitro*^{29,30}. Isolated primary human monocytes were tested for CD93 expression and shedding in responses to PMA (phorbol 12-myristate 13-acetate) which is a more potent analog of PDBu. As shown in Figure 11, loss of CD93 expression was observed in response to PMA. Importantly, the timeframe of these experiments (1 hr) is insufficient to downregulate CD93 through transcriptional changes and degradation through multi-vesicular bodies, and moreover, permeabilized PMA-stimulated cells did not reveal significant internal CD93 staining, further indicating that CD93 was likely shed, rather than internalized or degraded (Figure 11). Moreover, results from our lab have detected ~60 kDa cleavage fragment, reactive to anti-CD93 antibodies, following PMA stimulation that is consistent with the previously reported size of sCD93 (M. Goiko, manuscript in preparation, Appendix 6). CHO-K1, J774.2, RAW264.7 cells were then selected for *in vitro* shedding assays. Cells were cultured and

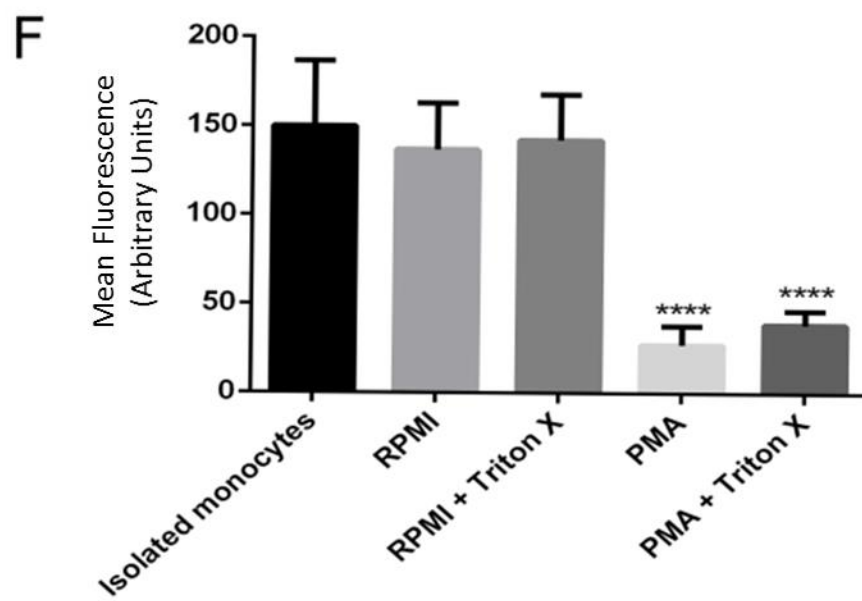
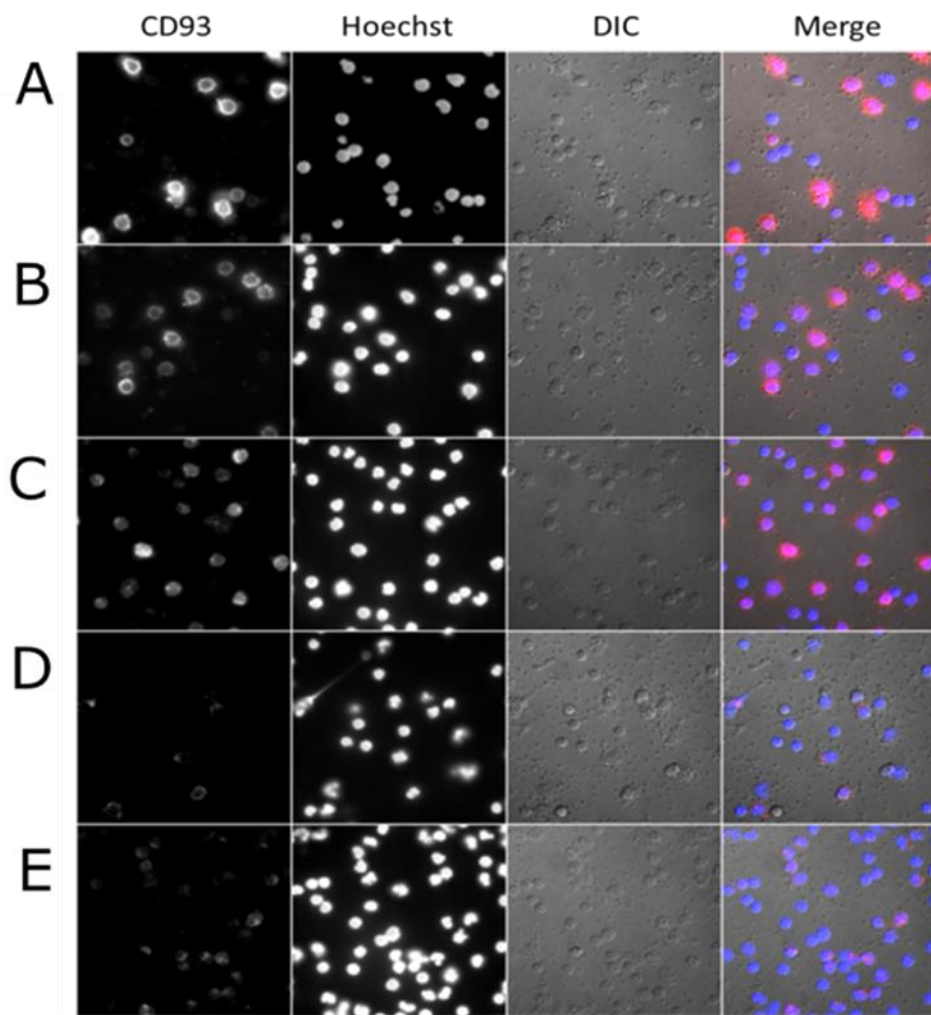


Figure 11: Primary human monocytes shed CD93 in response to PMA stimulation. Primary human monocytes isolated from human blood stained for CD93 expression after adhering for 1hr **(A)** or adhering for 1hr followed by 1hr incubation in serum free media (SFM) **(B)**; 1hr incubation in SFM and then permeabilized with 0.1% Triton-X **(C)**; 1hr incubation in SFM with PMA (100ng/mL) **(D)**; 1hr incubation in SFM with PMA and then permeabilized with 0.1% Triton-X **(E)**. For 3 separate experiments, two coverslips for each condition were imaged, with a minimum of 6 fields of view taken for each condition and a minimum of 6 cells per field. Representative images shown. Mean fluorescence for each field of view was measured using Image J software, and then used to calculate overall mean fluorescence for each condition. **(F)**.

transfected with a CD93-GFP plasmid. Sixteen hours post transfection cells were imaged for GFP expression to confirm successful transfection. Transfected cells were then incubated with 10 ng/mL PMA in serum-free media and immunostained for cell-surface CD93. As none of the cells showed a loss of CD93 expression in response to PMA (data not shown), I then assessed primary cells and myeloid cell lines for endogenous CD93 expression. Among them, THP-1 cells, a human monocytic cell line, expressed high levels of CD93 and displayed shedding in response to PMA stimulation (Figure 12). Previous studies demonstrated that murine CD93 was shed by an unidentified GM6001-sensitive protease that is not TACE (ADAM17)²⁹. I attempted to recapitulate this result in human cells by performing shedding assays in the presence of GM6001. Unexpectedly, GM6001 appeared to not inhibit PMA induced CD93 shedding in human cells. GM6001 treatment alone reduced CD93 staining by ~2.5 fold, while treatment with both GM6001 and PMA reduced CD93 staining by ~6 fold (Figure 13); whereas, the shedding of L-selectin, which occurs via the GM6001-sensitive protease TACE/ADAM17, was inhibited by GM6001 (Figure 14). As GM6001 inhibits only a subset of ADAMs, TAPI-2 [which inhibits TACE, ADAMs, ACE secretases and other MMPs] was used in the shedding inhibition assays. As shown in Figure 15, TAPI-2 inhibited PMA induced CD93 shedding. Incubation with TAPI-2 and PMA, and TAPI-2 alone showed no difference in MFI compared to control treatment. These results suggest that, as with murine CD93, human CD93 is not shed by TACE/ADAM17. However, humans may have evolved to shed CD93 by another, as yet to be identified, protease. Consistent with literature demonstrating differential CD93 expression across monocyte subsets we observed variable CD93 expression in both primary human monocytes and THP-1, with both low- and high-expressers appearing to undergo PMA-induced cleavage with similar efficacy (Figures 11-15).

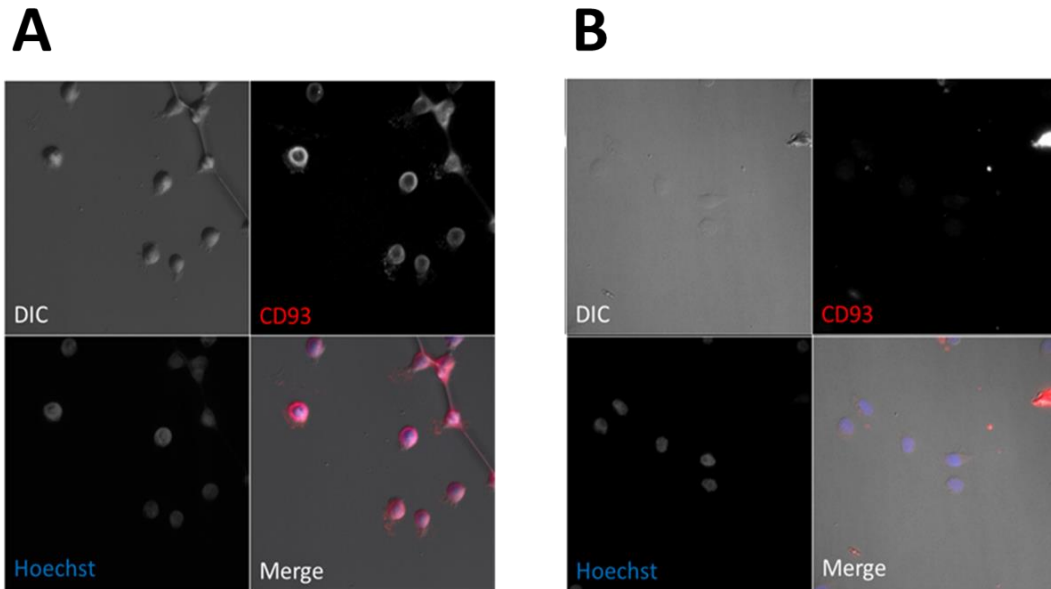


Figure 12: CD93 is shed from THP-1 cells in response to PMA. THP-1 cells were placed into 12-well plates containing 8 mm glass coverslips and incubated in serum-free RPMI (**A**) or serum-free RPMI + PMA (**B**) for 1 h. Plates were then spun in a centrifuge for 1 minute at 250x g. Cells were then fixed, stained for CD93 and imaged.

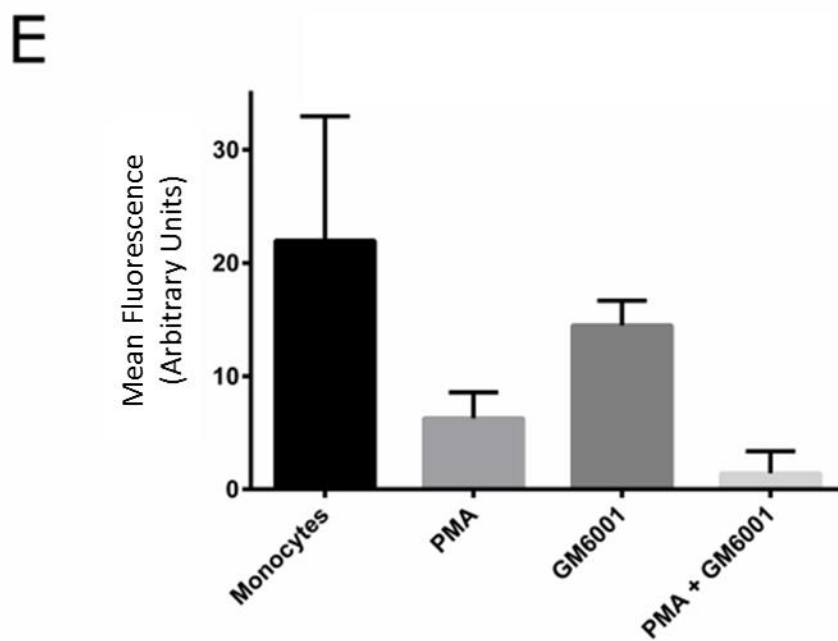
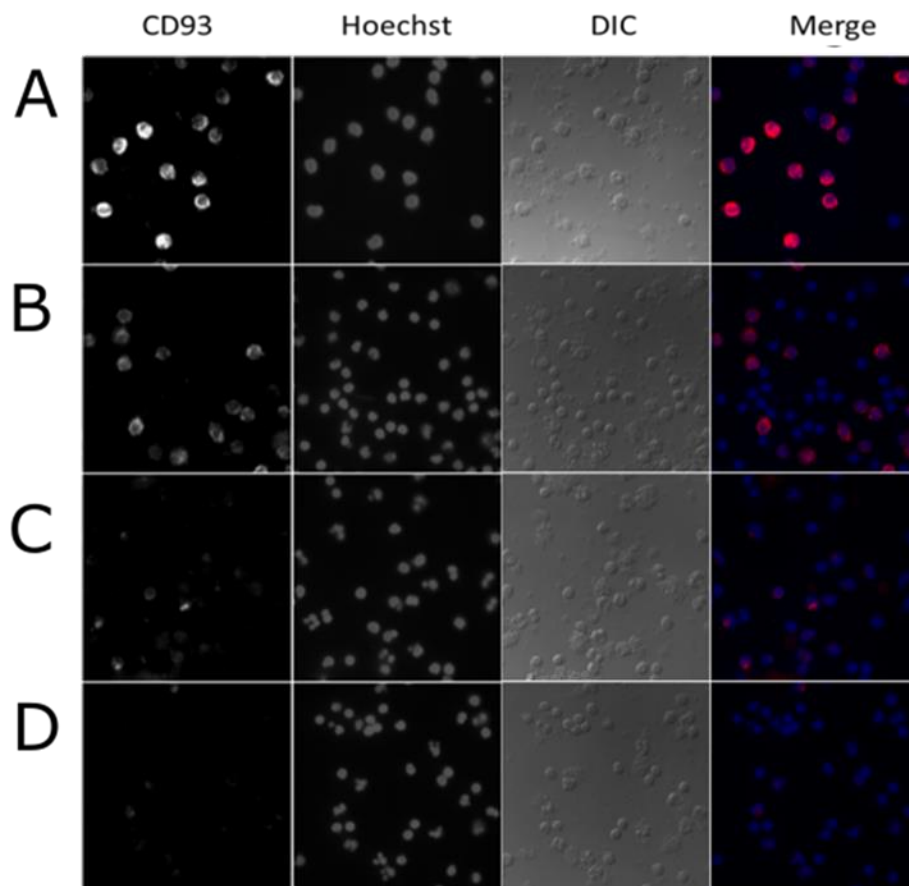


Figure 13: PMA induced shedding of CD93 from primary human monocytes is not inhibited by GM6001. Primary human monocytes isolated from human blood were allowed to adhere to glass coverslips for 1 h in serum-free RPMI. Monocytes were then washed with PBS and incubated with (C, D) or without (A, B) GM6001 for 5 min. Monocytes were then incubated with (B, D) or without (A, C) PMA for 55 min. Monocytes were then permeabilized with 0.1% Triton-X, and stained for CD93 expression. For 2 separate experiments, two coverslips for each condition were imaged, with a minimum of 6 fields of view taken for each condition and a minimum of 6 cells per field. (E) Mean fluorescence for each field of view was measured using Image J software, and then used to calculate overall mean fluorescence for each condition.

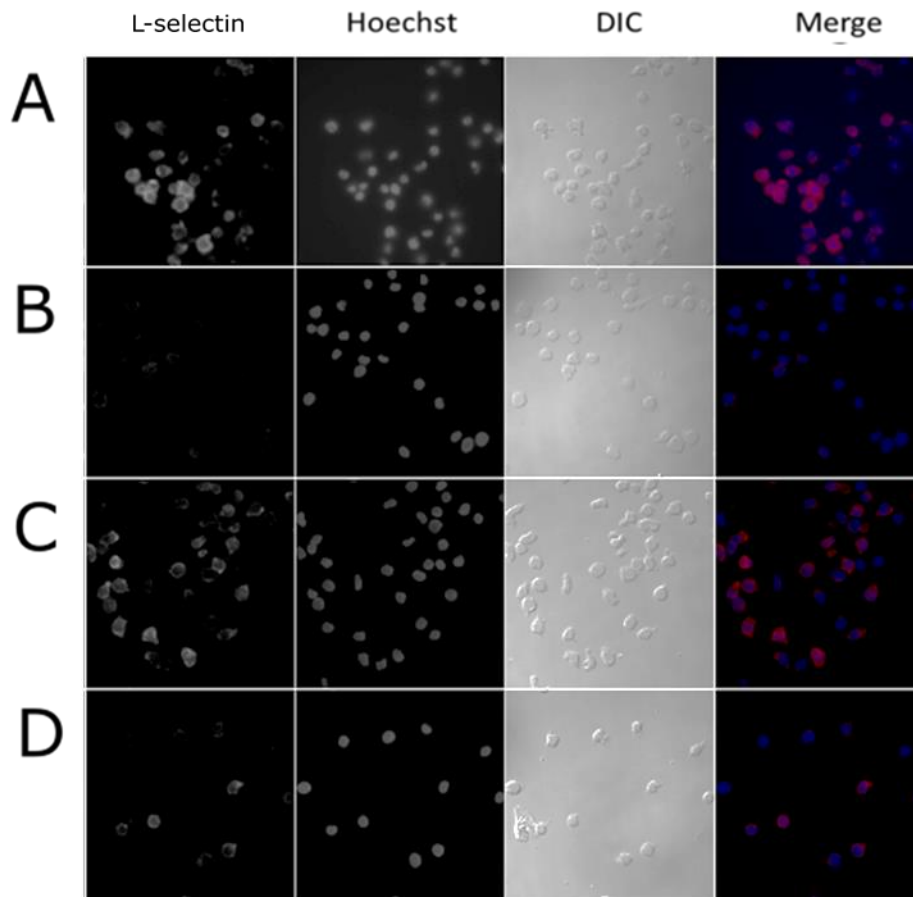


Figure 14: L-selectin shedding control. Primary human monocytes isolated from human blood were allowed to adhere to glass coverslips for 1 h in serum-free RPMI. Monocytes were then washed with PBS and incubated with (C, D) or without (A, B) GM6001 for 5 min. Monocytes were then incubated with (B, D) or without (A, C) PMA for 55 min. Monocytes were then permeabilized with 0.1% Triton-X, and stained for L-selectin (CD62L) expression. For 2 separate experiments, two coverslips for each condition were imaged, with a minimum of 6 fields of view taken for each condition and a minimum of 6 cells per field. Representative images shown

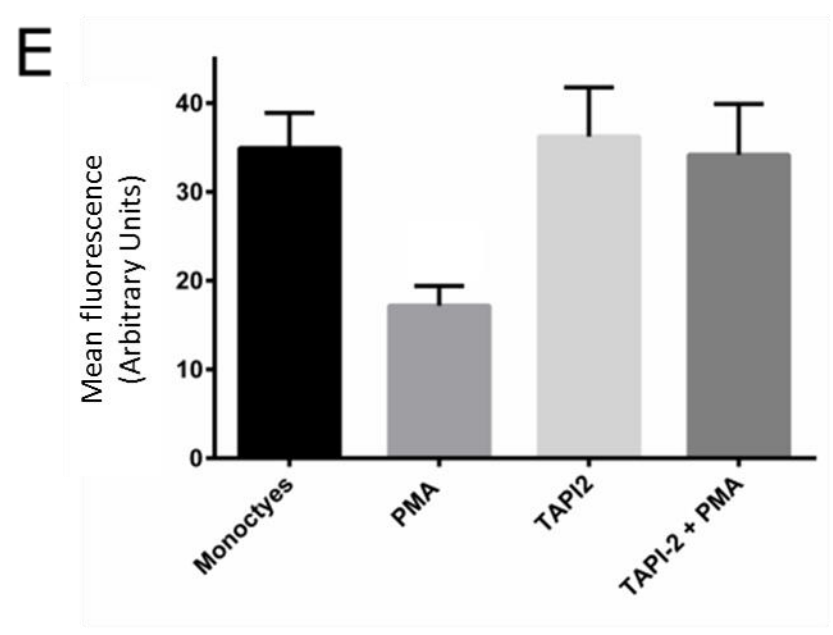
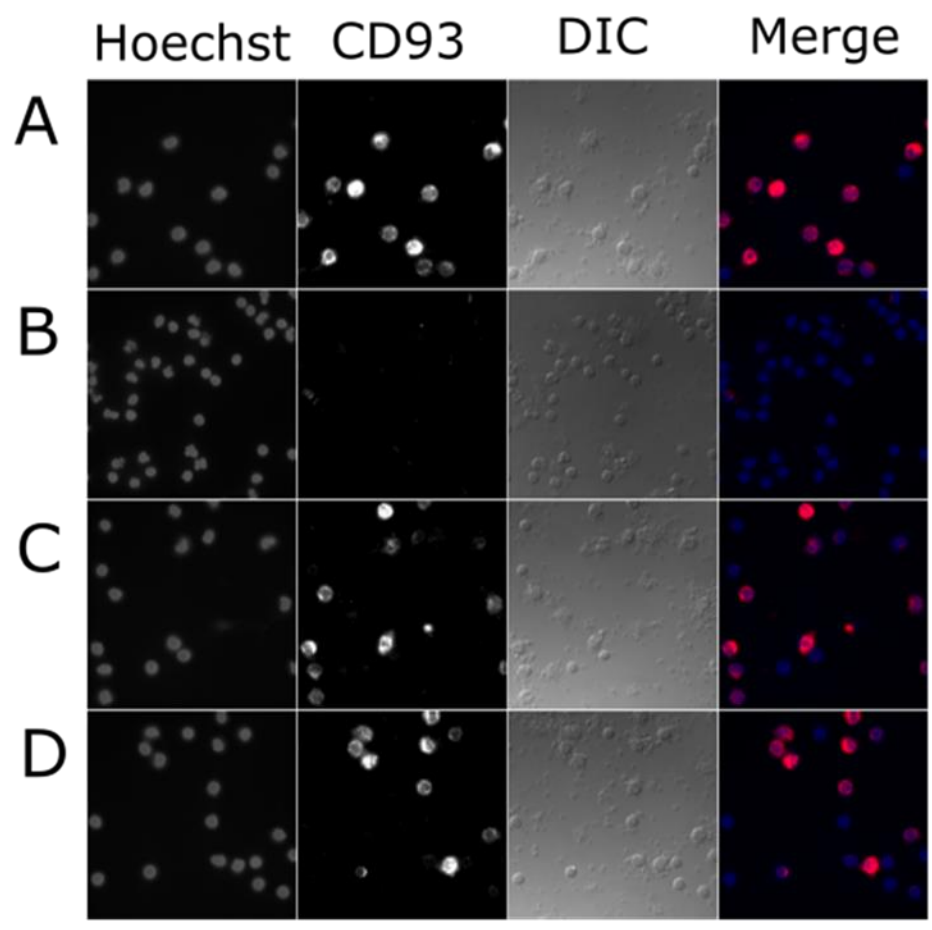


Figure 15: PMA induced shedding of CD93 from primary human monocytes is inhibited by TAPI-2. Primary human monocytes isolated from human blood were allowed to adhere to glass coverslips for 1 h in serum-free RPMI. Monocytes were then washed with PBS and incubated with (C, D) or without (A, B) TAPI-2 for 5 min. Monocytes were then incubated with (B, D) or without (A, C) PMA for 55 min. Monocytes were then permeabilized with 0.1% Triton-X, and stained for CD93 expression. For 2 separate experiments, two coverslips for each condition were imaged, with a minimum of 6 fields of view taken for each condition and a minimum of 6 cells per field. (E) Mean fluorescence for each field of view was measured using Image J software, and then used to calculate overall mean fluorescence for each condition.

4.1 Opsonization and Phagocytosis Assays

While CD93 has been shown not to function as a phagocytic receptor (Figure 5), there is evidence from the literature that it functions as an efferocytic opsonin. CD93^{-/-} mice show significant defects in apoptotic cell clearance compared to strain matched controls⁶⁵, and PLF containing elevated levels of sCD93 enhances apoptotic cell engulfment compared to PLF from CD93^{-/-} mice³⁰. Coupled with my observations that CD93 expression is lost from the surface of primary human monocytes and THP-1 cells in response to PMA stimulation (Figures 11 and 12), supernatants from PMA incubated THP-1 cells were used initially to investigate if CD93 acts as an efferocytic enhancing opsonin. As shown in Figure 16, J774.2 cells were fed either PS beads alone (PS), PS bead incubated in RPMI (RPMI), PS beads incubated with PMA (PMA), PS beads incubated with non-PMA treated supernatants (Non-shed), or PS beads incubated with PMA-treated supernatants (Shed), stained for external beads (Figure 17), and phagocytic index calculated. J774.2s showed no significant difference in phagocytic index among the PS, RPMI, PMA and Non-shed treatment groups, indicating that neither the cell culture media, PMA itself, or something secreted by monocytes was causing any differences in phagocytosis. The Shed treatment showed significant increase in phagocytic index compared to the Non-shed, PMA, RPMI treatments and the PS beads alone. These results indicate that a factor shed from THP-1 cells following PMA treatment opsonizes apoptotic cell mimics, and that J774.2 macrophages express the cognate receptor. However, these results do not directly indicate that this PMA-released opsonin is sCD93. At the time of writing, we have developed a sCD93 ectopic expression system which will be used to directly test the role of sCD93 in apoptotic cell opsonisation.

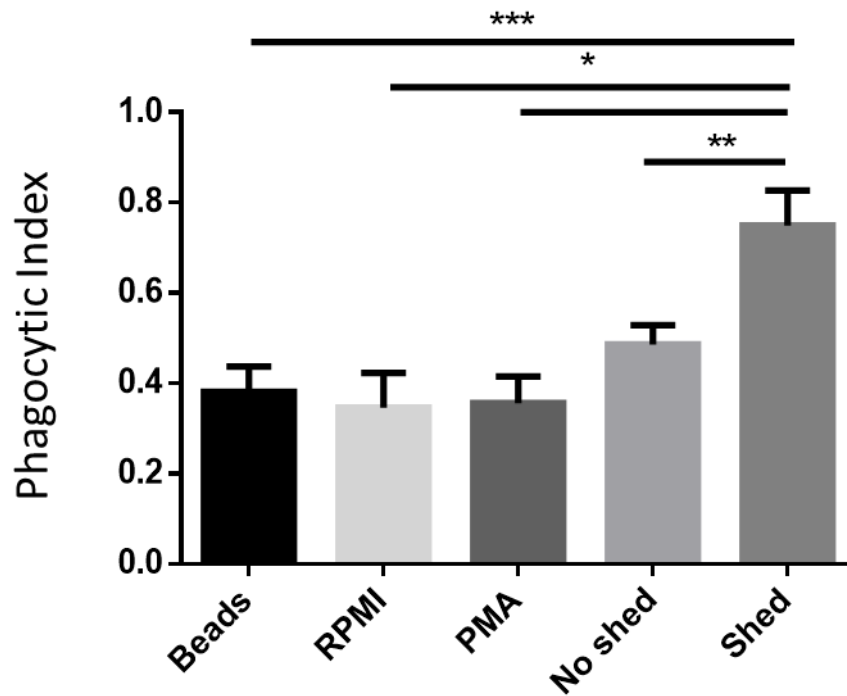


Figure 16: Silica beads opsonized with supernatants from PMA treated monocytes show increased phagocytic uptake. Primary human monocytes were collected from human blood and allowed to adhere for 1 h in serum-free RPMI. Monocytes were then washed with PBS, and incubated for 30 min in serum-free RPMI with or without PMA. Supernatants were then collected, and along with serum-free RPMI with and without PMA, were incubated with silica beads for 2 h. Silica beads were then fed to J774.2 cells in efferocytosis assays, and external beads labelled with. Total number of internal and external beads were then counted for 3 separate experiments, with 10 fields of view counted for each condition in each experiment. Phagocytic index was then calculated ($PI = \# \text{ internalized beads} / \# \text{ of cells counted}$). Error bars represent standard error of the mean (***) = $P < 0.001$, ** = $P < 0.005$, * = $P < 0.05$).

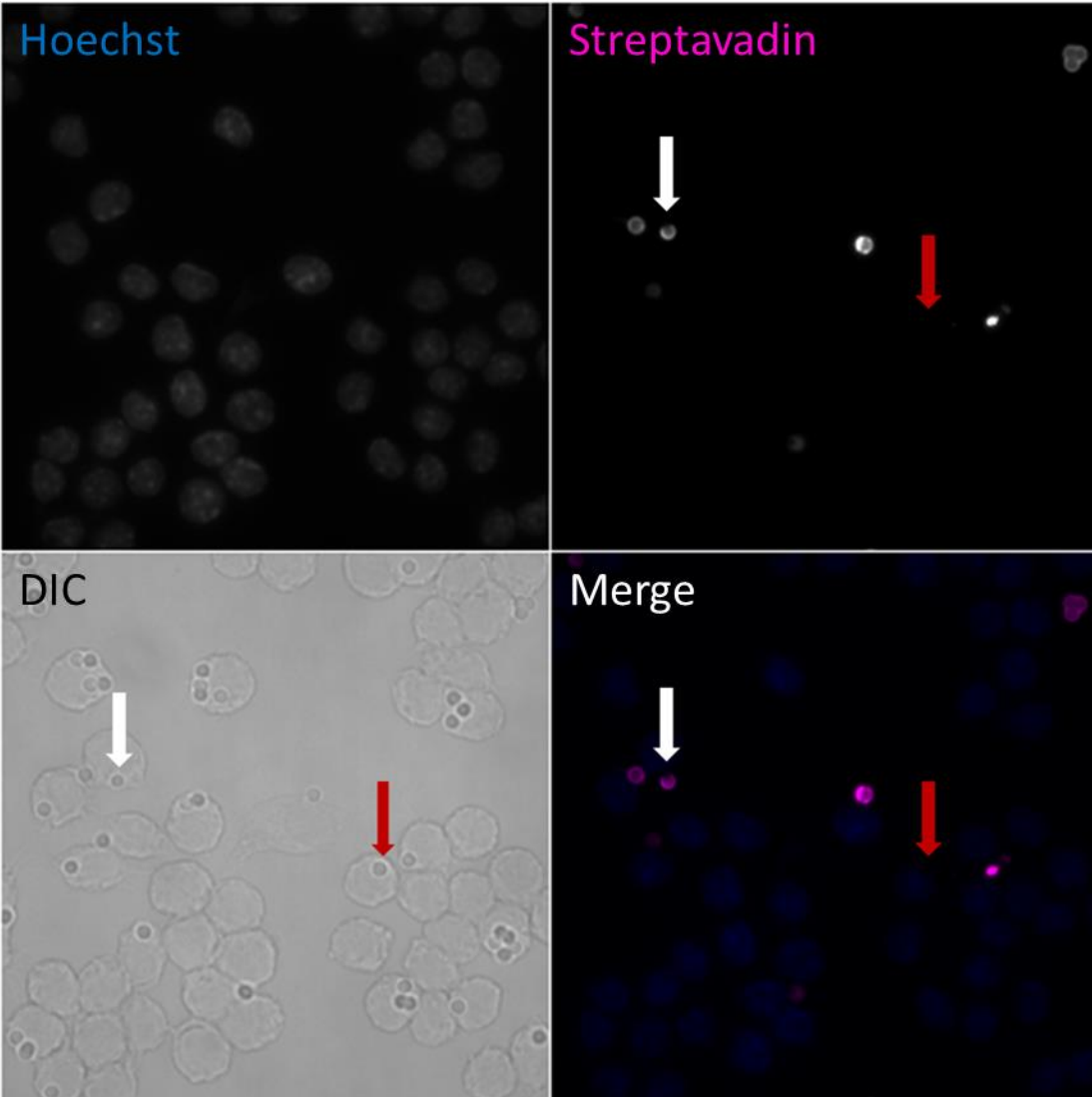


Figure 17: Example of internal and external beads in J774.2 phagocytosis and opsonisation assays. Shown is a sample image used in quantification of J774.2 phagocytosis assays. White arrows point to an external bead, while red arrows point to an internalised bead.

Discussion

5.1 Rationale and Summary of Results

While CD93 contributes to the removal of apoptotic cells⁴¹, it does not function as a membrane bound phagocytic/efferocytic receptor, with ectopic expression of CD93 resulting in no net increase in apoptotic cell efferocytosis (J. Ellins, unpublished data, Figures 4 & 5). Associations with diseases characterized by impaired apoptotic cell clearance, such as atherosclerosis and systemic lupus erythematosus, suggest that CD93 may contribute to efferocytosis as an efferocytosis enhancing opsonin^{25,30}. Indeed, CD93^{-/-} mice have significant defects in apoptotic cell clearance compared to strain matched controls⁶⁵, and PLF containing sCD93 enhances efferocytic uptake compared to PLF from CD93^{-/-} mice³⁰. Additionally, while sCD93 has been shown to be shed from the surface of monocytes in a protease dependent manner the exact protease is still unknown, with current literature showing that TACE is not responsible and suggesting that an MMP as the likely protease^{25,30}. Given this, the hypothesis of my thesis was that **biologically important domains in CD93, including ligand-binding and cleavage sites, will be evolutionarily conserved and that soluble CD93 will act as an apoptotic cell opsonin**. Support for this hypothesis comes mainly from the fact that CD93 was observed to be shed from murine cells in a MMP-dependent fashion, and serum from CD93 knockout mice shows a reduced opsonic activity towards apoptotic cells compared to wild type serum. In order to investigate this hypothesis three aims were generated. 1) Analysis of recent CD93 evolution among primates, coupled with computational prediction of protease cleavage sites the locations of validated SNPs, in order to identify putative functional domains and cleavage sites. 2) Shedding and inhibition

assays using primary human monocytes and shedding competent cell lines in order to confirm protease activated shedding, and to identify the protease responsible by inhibiting its function through pharmacological inhibition. 3) quantification of CD93 opsonic activity using sCD93-containing supernatants to opsonized apoptotic mimics.

5.2 Bioinformatic and SNP Analysis

As shown by the CD93 selection analysis among primates (Table 7, Figure 8), CD93 is highly conserved among humans and primates. This high degree of conservation was expected, given the apparent importance of CD93 in development, embryogenesis, apoptosis, and other critical conserved processes. The areas of high evolutionary conservation presented an opportunity to narrow down the potential search for cleavage sites or functional domains. Putative cleavage site analysis revealed several potential MMP cleavage sites within regions of CD93's mucin domain (Figure 10), which has previously been identified as the most likely site of cleavage based on fragment size and investigations into domains retained by the soluble form^{29,30}. However, the shedding-inhibition results (Figure 13-15) suggest that human CD93 is not shed by an MMP as mouse CD93. Given that shedding likely occurs within the mucin domain, the apparent lack of GM6001 inhibition of human CD93 shedding observed in this thesis (Figure 13), compared to GM6001-inhibited shedding in mice, may be a consequence of evolutionary drift within the MMP cleavage site. The majority of sites within the mucin domain (along with all predicted cleavage sites) are characterised by neutral evolution, with several sites showing some evidence of weak purifying selection, and a few sites showing evidence of strong purifying or positive selection At

the same time, validated SNPs from numerous databases that aligned to these conserved regions may be linked to altered cleavage patterns³⁰, altered opsonin functionality, altered mRNA expression or even ablated cleavage activity. While these SNPs represent potential targets for future studies, their limitations must be addressed. As shown in Figure 8, the most important and well characterised CD93 SNP, the P541Q missense linked to a 24% increased risk of CAD/MI, falls within a region of the mucin domain undergoing neutral evolution. This suggests that either the mutation falls within a region that may have only recently evolved to be of functional significance, or that the SNP may be in linkage disequilibrium with a second SNP that incurs the increased risk of CAD/MI. Indeed, this mutation is known to be in linkage disequilibrium with a mutation within the 3' UTR linked to altered sCD93 levels, altered CD93 mRNA stability, and which also associates with increased rates of CAD/MI³⁵. However, it is unclear if a causal relationship exists between these two mutations and their associated increased risk of CAD/MI. This result further highlights both the limits of using known SNPs to identify functional components of a protein, and moreover, indicates that future studies should expand the search for SNPs to include those found in the promotor, 5' UTR, introns and 3' UTR. In this thesis these regions were not investigated due to the focus on the mechanism for producing sCD93, and sCD93's potential function as an efferocytic opsonin, which necessitated a coding-region centric approach. As the two identified cleavage³⁰ forms contain most of the external domains, minus potentially a fragment of the mucin domain, comparing the efferocytic ability of these identified SNPs to the wild type could reveal regions of functional importance to the soluble form, and provide greater understanding into the associations between soluble CD93 and inflammatory diseases. While the 3' UTR – as shown by the aforementioned mutation associated with CAD/MI – likely has impacts on the

regulation of CD93 expression and thus implications for inflammatory disease states, introns provide a more challenging target for bioinformatic analysis. Indeed, no alternative splice forms of CD93 have been discovered to date, nor have any validated SNPs been identified within CD93's introns, thus limiting options for future analysis. While non-coding regions may provide an additional regulatory layer to CD93 expression – their potential to function as independent RNAs, or as cis- or trans-acting elements – elucidating these roles using bioinformatics or evolutionary approaches is extremely difficult, and there is no evidence at this time to indicate that these sorts of processes impact on aspects of CD93 biology that are of relevance to our work. If CD93 introns form functional RNA molecules, or act as regulatory gene elements independent of CD93 function, then it is possible that they are subject to different selective pressures, which may obfuscate evolutionary processes which impact on CD93 function. Unfortunately, none of the predicted protease cleavage sites fell within conserved regions within the mucin domain, indicating that alternative approaches to identifying the protease responsible for CD93 cleavage – e.g. an siRNA screen of all cell surface proteases – will be required to identify the responsible protease.

Finally, despite being characterised primarily by conserved sites, several positively selected sites were found by the selection analysis. This positive selection provides an opportunity to investigate recent changes in CD93 evolution that may be critical to its biological function. For example, one of the identified positively selected amino acid sites is also the location of one of the identified potentially deleterious mutations (G169C). This mutation falls within the CTLD domain, suggesting that it may interfere with ligand binding and therefore is of interest for future opsonisation and efferocytosis studies. While no other sites undergoing

positive selection contained potentially deleterious mutations, they still represent sites of interest for further investigation, as they may fall within Ω and thus assist in identifying Ω regions of functional importance within the human CD93 sequence

5.3 Promoter Analysis

Promoter analysis (Table 10) of CD93 found factors consist with expression during myeloid development and macrophage differentiation (PU.1 and GATA-2), and following inflammatory stimuli (the AP-1 subunits c-Jun and C-Fos). Identification of PU.1, a transcription factor known to be critical for development and differentiation of hematopoietic stem cells, B-cells, and monocytes/macrophages¹⁰⁷⁻¹¹¹, is consistent with CD93 expression on hematopoietic stem cells, early B cells, and changes in expression during macrophage differentiation. PU.1 is needed for development of B cells and several hematopoietic cell lineages^{108-110,112}. Indeed, mice lacking PU.1 and Spi-B in the B cell lineage have reduced numbers and impaired differentiation of B-cells¹¹³, while PU.1 mutant embryos die during later gestational stages, seemingly from defects in the development of multiple hematopoietic lineages¹⁰⁸. CD93 expression is a marker of B cell immaturity, with down-regulation of CD93 noted as a sign of B cell transition and maturation¹¹⁴. PU.1 deficient B cells failed to transition from CD93⁺ to CD93⁻¹¹², indicating that Ω at least in the context of B cell development Ω CD93 is negatively regulated by PU.1. CD93 is likely negatively regulated by PU.1 during macrophage differentiation. While high levels of PU.1 are involved in commitment of early myeloid cells towards the monocyte/macrophage lineage, suggesting that

CD93 is not exclusively negatively regulated by PU.1, during final differentiation to macrophages PU.1 expression is further elevated^{110,111} and accompanied by apparent loss of CD93 expression (Figure 4). This maintenance of CD93 expression may be mediated by GATA-2, which we found associated with the CD93 promotor in monocytes (Table 10). GATA-2 and PU.1 have been shown to act antagonistically during macrophage differentiation, which increased expression of one shown to transcriptionally repress the other¹¹⁵. GATA-2 expression has been shown to be important for myeloid differentiation to monocytes¹¹⁶, with GATA-2 mutations linked to composite mononuclear cell deficiencies¹¹⁷. Moreover, GATA-2 and PU.1 reciprocally suppress each others expression¹¹⁸. Combined, these studies support a PU.1 mediated transcriptional repression model of CD93 expression. The high PU.1 expression present during hematopoietic stem cell proliferation and early stages of B cell & myeloid maturation suppresses both GATA2 and CD93 expression. Upregulation of GATA-2 during the later stages of B cell development and myleopoiesis downregulates PU.1, reducing transcriptional inhibition of the CD93 promotor, thereby allowing CD93 expression on mature B cells, neutrophils and monocytes. In monocytes, a second wave of PU.1 expression is induced upon induction of monocyte-to-macrophage differentiation. This increased PU.1 expression counteracts GATA-2 mediated transcriptional activation, thus re-repressing CD93 expression during macrophage differentiation. To assess the roles of these transcription factors, future studies will use siRNA against PU.1 and GATA-2 to investigate their role in mediating CD93 expression in THP-1 cells, using a CD93 promotor-driven luciferase reporter.

In line with the upregulation of CD93 in inflammatory disease states and apoptosis, AP-1 (comprised of a heterodimer of c-Jun and c-Fos) was also identified in our promoter analysis. AP-1 is involved in numerous cellular processes, including inflammatory responses and apoptosis^{119–122}. Inflammatory cytokines, including those of the TNF family, as well as Toll-like receptors (TLRs), have been shown to induce AP-1 activation through mitogen-activated protein kinase subfamilies, such as stress-activated protein kinases (SAPKs, or JNKs, reviewed in 121 and 123). Furthermore, AP-1 is known to be induced by SAPKs upon UV damage (reviewed in 120) , a hallmark precursor to induction of apoptosis. The binding of AP-1 to the CD93 promoter highlights the importance of CD93 in inflammatory disease states and apoptosis and efferocytosis. However, because AP-1 can cause induce and repress transcription – depending on the specific cofactors bound to the promoter region – it is not possible to determine at this point if inflammation-induced AP-1 signaling would cause upregulation of CD93 expression. However, observations demonstrating increased CD93 expression during inflammation, along with a concordant increase in plasma sCD93, suggest that AP-1 signaling induces the expression of CD93 in competent cells. Future studies will address this, using the CD93 promoter assay described previously.

5.4 CD93 Shedding and Inhibition

In order to investigate the protease responsible for CD93 cleavage, a shedding model was designed using PMA and either primary human monocytes or THP-1 cells, a monocyte-like cell line with endogenous CD93 expression. Both monocytes and THP-1 cells showed shedding

competence in response to PMA, with the loss of CD93 that was caused by shedding, not endocytosis, based on staining of permeabilized cells (Figure 11). Consistent with this observation, our lab has identified sCD93 in the supernatants of PMA-stimulated monocytes, confirming that upon PMA stimulation human monocytes shed CD93 from the cell surface (M. Goiko, manuscript in preparation, Appendix 6). Moesin binds to the intracellular tail of CD93, where it most likely acts to cross-link CD93 to the cytoskeleton; a process which immobilizes the molecules on the cell surface. PMA induces moesin to release bound proteins, which may then expose CD93 to the protease responsible for its cleavage. Indeed, CX3CL1 shedding is regulated in this fashion, where release from the cytoskeleton enables it to interact with TACE, which subsequently cleaves CX3CL1 in a fashion reminiscent of CD93 shedding¹²⁴. Murine models suggest that CD93 is cleaved by an MMP other than TACE. We were not able to recapitulate this response, as CD93 shedding was not inhibited by the pan-MMP inhibitor GM6001, and instead we observed inhibition of shedding in response to TAPI2, which inhibits a range of proteases including ADAM's, ACE secretases, and a subset of MMPs¹²⁴⁻¹³⁵. Previous studies on human CD93 shedding were not coupled with inhibition studies, meaning that the identification of an MPP as the likely protease was driven only by the observation of shedding in response to PdBu stimulation. Although we were not able to identify the specific protease involved in the formation of sCD93 in humans, the lack of inhibition by GM6001 and the absence of highly conserved predicted MMP cleavage sites in the mucin domain, are consistent with humans having evolved to shed CD93 by a non-MMP mechanism. Given the sensitivity of human CD93 shedding induced by PMA to TAPI2, we believe that CD93 is most likely cleaved by an ADAM protease, as ACE secretases tend to cleave proteins in the transmembrane domain; an observation inconsistent

with the known sizes of sCD93^{29,30}. The results obtained through my investigation into CD93 shedding have provided a clear direction for future work. Based on the observations that an ADAM is most likely responsible for CD93 shedding, shedding assays using cleavage resistant forms of CD93 generated through mutations in putative ADAM binding sites, in combination with siRNA knockdowns of ADAM members, will identify the ADAM responsible for forming sCD93.

5.5 CD93 Opsonisation and Regulation of Phagocytosis

My phagocytosis and opsonisation assays demonstrated that opsonisation of silica beads with supernatants recovered from PMA incubated THP-1 cells lead to an increase in phagocytic uptake by J774.2 cells (Figure 16), indicating that something released from the cell surface in response to PMA stimulation is responsible for the increased rate of phagocytic uptake, and not due to residual PMA. While it is possible that something aside from CD93 is shed from the cell surface and responsible for the observed increase in phagocytosis, evidence from the literature that serum from CD93 knockout mice show reduced apoptotic clearance compared to serum from wild type mice indicates that sCD93 is a likely candidate in the observed increase in efferocytosis in my model system. The role of sCD93 in efferocytosis, and whether it does indeed act as an opsonin, will be confirmed by future experiments using a recombinant sCD93. Indeed, these constructs have already been generated, but there was insufficient time to generate the sCD93 prior to submission of this thesis. Apoptotic mimics will be opsonized with recombinant sCD93 and used in efferocytosis assays in order to determine if sCD93 alone is sufficient to either

initiate or enhance efferocytosis. In addition to this, if the recombinant sCD93 assays show that sCD93 is sufficient to initiate efferocytosis, efferocytosis assays using PMA-incubated supernatants will be repeated using CD93 depleted supernatants in order to determine if sCD93 acts as an opsonin in a more biologically relevant system than the assays using pure recombinant sCD93.

While my results are consistent with sCD93 or other PMA-released factors acting as an opsonin, we must also consider other possibilities. For example, membrane-bound CD93 may enhance efferocytosis through other efferocytic receptors through tethering apoptotic cells to the phagocyte. Consistent with this model, membrane-bound CD93 can mediate cell adhesion through an uncharacterized mechanism. Moreover, tethering would be independent of intracellular signaling, consistent with the minimal signaling motifs found in CD93 and with the minimal number of intracellular proteins CD93 is known to interact with. Thus, through its adhesive capabilities, CD93 may act to tether efferocytic targets to phagocytes, thus enhancing interactions between other efferocytic receptors and the target. While this possibility remains unexplored, it is inconsistent with the observation that serum from CD93 mice is more opsonic than serum from CD93 knockouts, an observation which suggests that the soluble form of CD93 is required for efferocytosis. Another possibility is that CD93 acts to enhance phagocytosis through signaling via its intracellular domain. Indeed, studies showing binding between the cytoplasmic tail of CD93 and various proteins (such as PDZ domains, G coupled proteins, and moesin) indicate that CD93 may be capable of a limited degree of signaling⁵⁸. The last 11 residues within the CD93 cytoplasmic tail (C11) have been shown to regulate protein interactions, and

also enhance phagocytic uptake. Moreover, a cell-permeable form of CD93's intracellular domain enhances phagocytosis⁵⁸, indicating that the role of cleavage may not be to release a functional extracellular fragment, but rather to release a functional intracellular/membrane bound fragment that modulates signaling through other receptors. In this model, adhesion of CD93 to extracellular ligands would immobilize the intracellular domain, with CD93 cleavage producing a freely-diffusive intracellular tail which could then interact with other signalling molecules or phagocytic receptors. But again, this model is inconsistent with the enhanced opsonic activity of serum from CD93 wild-type versus CD93^{-/-} mice¹³⁶.

While my studies illustrated the successful use of PMA to induce CD93 shedding, PMA remains a non-physiological stimulus. Future work should investigate the role of inflammatory versus find-me/eat-me signals in inducing the release of CD93 from its moesin anchor and subsequent shedding. Evidence in the literature may indicate that inflammatory signals alone will induce shedding; indeed, the majority of CD93 clinical interactions and disease associations are with inflammatory diseases (reviewed in 137), sCD93 levels tend to be elevated in inflammatory conditions, and lastly, sCD93 levels are inversely correlated with prednisone (an apoptosis-inducing glucocorticosteroid) dose in patients with SLE⁶⁷.

While the exact mechanism by which CD93 functions to enhance efferocytosis remains to be elucidated, the links between CD93, defective efferocytosis, and inflammation indicate that future studies remain important. At a minimum, the association of sCD93 with inflammatory diseases highlights its potential as a diagnostic or prognostic biomarker^{138,139}. Its established

roles in cell adhesion and angiogenesis indicate an important role for CD93 in inflammatory conditions. It may be possible that release of CD93 from bound moesin upon exposure to the inflammatory milieu allows for phagocytic enhancing interactions. While there are several alternate hypotheses as to how CD93 could function to modulate efferocytosis and inflammation, my results, as well as data from CD93 knockout mice demonstrating reduced clearance of apoptotic cells and decreased opsonic activity of CD93-deficient serum, are consistent with a role for CD93 as a soluble apoptotic-cell targeting opsonin. However, it is important to consider that none of these models of CD93 activity are mutually exclusive, and that CD93 may impact on efferocytosis and inflammation via several different mechanisms.

In conclusion, I have demonstrated that CD93 has been strongly conserved by evolution, shown that putative protease cleavage sites do not align with conserved regions suggesting that recent evolution of CD93 has caused the shedding mechanisms in humans to deviate from that documented in mice and provided further evidence supporting an opsonic role for soluble CD93. These findings provide additional insight into the evolutionary history and biological role of CD93, and will form an important foundation for future studies into CD93 function.

References

1. Stuart, L. M. & Ezekowitz, R. A. B. Phagocytosis: Elegant complexity. *Immunity* **22**, 539–550 (2005).
2. Brown, E. J. Phagocytosis. *BioEssays* **17**, 109–117 (1994).
3. Botelho, R. J. & Grinstein, S. Phagocytosis. *Curr. Biol.* **21**, R533–8 (2011).
4. Rabinovitch, M. *et al.* Professional and non-professional phagocytes: an introduction. *Trends Cell Biol.* **5**, 85–7 (1995).
5. Flannagan, R. S., Jaumouillé, V. & Grinstein, S. The cell biology of phagocytosis. *Annu. Rev. Pathol.* **7**, 61–98 (2012).
6. Castellano, F., Chavrier, P. & Caron, E. Actin dynamics during phagocytosis. *Semin. Immunol.* **13**, 347–55 (2001).
7. Caron, E. & Hall, A. Identification of two distinct mechanisms of phagocytosis controlled by different Rho GTPases. *Science* **282**, 1717–21 (1998).
8. Massol, P., Montcourrier, P., Guillemot, J. C. & Chavrier, P. Fc receptor-mediated phagocytosis requires CDC42 and Rac1. *EMBO J.* **17**, 6219–6229 (1998).
9. Ridley, A. J. & Hall, A. The small GTP-binding protein rho regulates the assembly of focal adhesions and actin stress fibers in response to growth factors. *Cell* **70**, 389–399 (1992).
10. Nobes, C. D. & Hall, A. Rho, Rac, and Cdc42 GTPases regulate the assembly of multimolecular focal complexes associated with actin stress fibers, lamellipodia, and filopodia. *Cell* **81**, 53–62 (1995).
11. Duclos, S. *et al.* Rab5 regulates the kiss and run fusion between phagosomes and endosomes and the acquisition of phagosome leishmanicidal properties in RAW 264.7 macrophages. *J. Cell Sci.* **113 Pt 19**, 3531–3541 (2000).
12. Boulais, J. *et al.* Molecular characterization of the evolution of phagosomes. *Mol. Syst. Biol.* **6**, 423 (2010).
13. Vieira, O. V *et al.* Acquisition of Hrs, an essential component of phagosomal maturation, is impaired by mycobacteria. *Mol. Cell. Biol.* **24**, 4593–4604 (2004).
14. Vieira, O. V *et al.* Modulation of Rab5 and Rab7 recruitment to phagosomes by phosphatidylinositol 3-kinase. *Mol. Cell. Biol.* **23**, 2501–14 (2003).
15. Vieira, O. V. *et al.* Distinct roles of class I and class III phosphatidylinositol 3-kinases in phagosome formation and maturation. *J. Cell Biol.* **155**, 19–25 (2001).
16. Araki, N., Johnson, M. T. & Swanson, J. A. A role for phosphoinositide 3-kinase in the completion of macropinocytosis and phagocytosis by macrophages. *J. Cell Biol.* **135**, 1249–1260 (1996).
17. Simonsen, A. *et al.* EEA1 links PI(3)K function to Rab5 regulation of endosome fusion. *Nature*. **394**, 494–498 (1998).
18. Fairn, G. D. & Grinstein, S. How nascent phagosomes mature to become phagolysosomes. *Trends Immunol.* **33**, 397–405 (2012).

19. Harrison, R. E., Bucci, C., Vieira, O. V, Schroer, T. A. & Grinstein, S. Phagosomes fuse with late endosomes and/or lysosomes by extension of membrane protrusions along microtubules: role of Rab7 and RILP. *Mol. Cell. Biol.* **23**, 6494–506 (2003).
20. Johansson, M. *et al.* Activation of endosomal dynein motors by stepwise assembly of Rab7-RILP-p150Glued, ORP1L, and the receptor β III spectrin. *J. Cell Biol.* **176**, 459–471 (2007).
21. Kinchen, J. M. & Ravichandran, K. S. Identification of two evolutionarily conserved genes regulating processing of engulfed apoptotic cells. *Nature* **464**, 778–82 (2010).
22. Nepomuceno, R. R. & Tenner, a J. C1qRP, the C1q receptor that enhances phagocytosis, is detected specifically in human cells of myeloid lineage, endothelial cells, and platelets. *J. Immunol.* **160**, 1929–1935 (1998).
23. Dean, Y. D., McGreal, E. P., Akatsu, H. & Gasque, P. Molecular and cellular properties of the rat AA4 antigen, a C-type lectin-like receptor with structural homology to thrombomodulin. *J. Biol. Chem.* **275**, 34382–34392 (2000).
24. Fonseca, M. I. *et al.* C1qR(P), a myeloid cell receptor in blood, is predominantly expressed on endothelial cells in human tissue. *J. Leukoc. Biol.* **70**, 793–800 (2001).
25. Bohlson, S. S., Silva, R., Fonseca, M. I. & Tenner, a J. CD93 Is Rapidly Shed from the Surface of Human Myeloid Cells and the Soluble Form Is Detected in Human Plasma. *J. Immunol.* **175**, 1239–1247 (2005).
26. Beyer, M. *et al.* High-Resolution Transcriptome of Human Macrophages. *PLoS One* **7**, e45466 (2012).
27. Ikewaki, N., Sonoda, T. & Inoko, H. Unique properties of cluster of differentiation 93 in the umbilical cord blood of neonates. *Microbiol. Immunol.* **57**, 822–32 (2013).
28. Nepomuceno, R. R., Henschen-Edman, a H., Burgess, W. H. & Tenner, a J. cDNA cloning and primary structure analysis of C1qR(P), the human C1q/MBL/SPA receptor that mediates enhanced phagocytosis in vitro. *Immunity* **6**, 119–29 (1997).
30. Greenlee, M. C., Sullivan, S. a. & Bohlson, S. S. Detection and characterization of soluble CD93 released during inflammation. *Inflamm. Res.* **58**, 909–919 (2009).
31. Norsworthy, P. J., Taylor, P. R., Walport, M. J. & Botto, M. Cloning of the mouse homolog of the 126-kDa human C1q/MBL/SP-A receptor, C1qR(p). *Mamm. Genome* **10**, 789–793 (1999).
32. Suk, T. *et al.* Characterization of the murine homolog of C1qR P : identical cellular expression pattern , chromosomal location and functional activity of the human and murine C1qR P. *Mol. Immunol.* **37**, 377–389 (2000).
33. Bäckman-Petersson, E., Miller, J. R., Hollyoake, M., Aguado, B. & Butcher, G. W. Molecular characterization of the novel rat NK receptor 1C7. *Eur. J. Immunol.* **33**, 342–351 (2003).
34. Wang, J.-S. & Liu, H.-C. Systemic hypoxia enhances bactericidal activities of human polymorphonuclear leucocytes. *Clin. Sci.* **116**, 805–817 (2009).
35. Mälärstig, a *et al.* Plasma CD93 concentration is a potential novel biomarker for coronary artery disease. *J. Intern. Med.* **270**, 229–36 (2011).

36. van der Net, J. B. *et al.* Replication study of 10 genetic polymorphisms associated with coronary heart disease in a specific high-risk population with familial hypercholesterolemia. *Eur. Heart J.* **29**, 2195–201 (2008).
37. Jeon, J.-W. *et al.* Soluble CD93 induces differentiation of monocytes and enhances TLR responses. *J. Immunol.* **185**, 4921–4927 (2010).
38. Huang, H. & Auerbach, R. Identification and characterization of hematopoietic stem cells from the yolk sac of the early mouse embryo. *Proc. Natl. Acad. Sci. U. S. A.* **90**, 10110–4 (1993).
39. Yamane, T., Hosen, N., Yamazaki, H. & Weissman, I. L. Expression of AA4.1 marks lymphohematopoietic progenitors in early mouse development. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 8953–8 (2009).
40. Jordan, C. T., McKearn, J. P. & Lemischka, I. R. Cellular and developmental properties of fetal hematopoietic stem cells. *Cell* **61**, 953–963 (1990).
41. McGreal, E. P., Ikewaki, N., Akatsu, H., Morgan, B. P. & Gasque, P. Human C1qRp is identical with CD93 and the mNI-11 antigen but does not bind C1q. *J. Immunol.* **168**, 5222–5232 (2002).
42. Petrenko, O. *et al.* The molecular characterization of the fetal stem cell marker AA4. *Immunity* **10**, 691–700 (1999).
43. McKearn, J. P. & Baum, C. Cell surface antigens expressed by subsets of pre-B cells and B cells. *J. Immunol.* **132**, 332-339 (2016).
44. Allman, D. *et al.* Resolution of three nonproliferative immature splenic B cell subsets reveals multiple selection points during peripheral B cell maturation. *J. Immunol.* **167**, 6834–6840 (2001).
45. Chevrier, S. *et al.* CD93 is required for maintenance of antibody secretion and persistence of plasma cells in the bone marrow niche. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 3895–3900 (2009).
46. Gren, S. T. *et al.* A Single-Cell Gene-Expression Profile Reveals Inter-Cellular Heterogeneity within Human Monocyte Subsets. *PLoS One* **10**, e0144351 (2015).
47. Greenlee-Wacker, M. C. *et al.* Membrane-Associated CD93 Regulates Leukocyte Migration and C1q-Hemolytic Activity during Murine Peritonitis. *J. Immunol.* **187**, 3353–3361 (2011).
48. Nepomuceno, R. R., Ruiz, S., Park, M. & Tenner, a J. C1qRP is a heavily O-glycosylated cell surface protein involved in the regulation of phagocytic activity. *J. Immunol.* **162**, 3583–9 (1999).
49. Drickamer, K. C-type lectin-like domains. *Curr. Opin. Struct. Biol.* **9**, 585–590 (1999).
50. Schenk-Braat, E. A. M., Morser, J. & Rijken, D. C. Identification of the epidermal growth factor-like domains of thrombomodulin essential for the acceleration of thrombin-mediated inactivation of single-chain urokinase-type plasminogen activator. *Eur. J. Biochem.* **268**, 5562–5569 (2001).
51. Tsiang, M., Lentz, S. R. & Sadler, J. E. Functional domains of membrane-bound human thrombomodulin: EGF-like domains four to six and the serine/threonine-rich domain are required for cofactor activity. *J. Biol. Chem.* **267**, 6164–6170 (1992).
52. Kao, Y.-C. *et al.* The epidermal growth factor-like domain of CD93 is a potent angiogenic factor. *PLoS One* **7**, e51647 (2012).
53. Fonseca, M. I. *et al.* C1qR P , a myeloid cell receptor in blood , is predominantly expressed on

- endothelial cells in human tissue Abstract : C1qR P is a type I cell surface glycoprotein that has been shown to enhance ingestion of suboptimally opsonized targets by phagocytes . **70**, 793–800 (2001).
54. Dean, Y. D., McGreal, E. P. & Gasque, P. Endothelial cells, megakaryoblasts, platelets and alveolar epithelial cells express abundant levels of the mouse AA4 antigen, a C-type lectin-like receptor involved in homing activities and innate immune host defense. *Eur. J. Immunol.* **31**, 1370–1381 (2001).
 55. Galvagni, F. *et al.* CD93 and dystroglycan cooperation in human endothelial cell adhesion and migration. **7**, (2016).
 56. Nepomuceno, R. R., Ruiz, S., Park, M., Tenner, A. J. & Alerts, E. C1qR P Is a Heavily O -Glycosylated Cell Surface Protein Involved in the Regulation of Phagocytic Activity. (2013).
 57. Park, M. & Tenner, A. J. Cell surface expression of C1qRP/CD93 is stabilized by O-glycosylation. *J. Cell. Physiol.* **196**, 512–22 (2003).
 58. Bohlsion, S. S., Zhang, M., Ortiz, C. E. & Tenner, A. J. CD93 interacts with the PDZ domain-containing adaptor protein GIPC: implications in the modulation of phagocytosis. *J. Leukoc. Biol.* **77**, 80–89 (2005).
 59. Zhang, M., Bohlsion, S. S., Dy, M. & Tenner, A. J. Modulated interaction of the ERM protein, moesin, with CD93. *Immunology* **115**, 63–73 (2005).
 60. Guan, E. N. *et al.* Phagocytic cell molecules that bind the collagen-like region of C1q. Involvement in the C1q-mediated enhancement of phagocytosis. *J. Biol. Chem.* **266**, 20345–55 (1991).
 61. Guan, E., Robinson, S. L., Goodman, E. B. & Tenner, A. J. Cell-surface protein identified on phagocytic cells modulates the C1q-mediated enhancement of phagocytosis. *J. Immunol.* **152**, 4005–16 (1994).
 62. Tenner, A. J., Robinson, S. L. & Ezekowitz, R. A. Mannose binding protein (MBP) enhances mononuclear phagocyte function via a receptor that contains the 126,000 M(r) component of the C1q receptor. *Immunity* **3**, 485–93 (1995).
 63. Tenner, A. J. C1q receptors: regulating specific functions of phagocytic cells. *Immunobiology* **199**, 250–64 (1998).
 64. Bohlsion, S. S., Fraser, D. a. & Tenner, A. J. Complement proteins C1q and MBL are pattern recognition molecules that signal immediate and long-term protective immune functions. *Mol. Immunol.* **44**, 33–43 (2007).
 65. Norsworthy, P. J. *et al.* Murine CD93 (C1qRp) contributes to the removal of apoptotic cells in vivo but is not required for C1q-mediated enhancement of phagocytosis. *J. Immunol.* **172**, 3406–3414 (2004).
 66. Zekavat, G. *et al.* A novel CD93 polymorphism in non-obese diabetic (NOD) and NZB/W F1 mice is linked to a CD4+ iNKT cell deficient state. *Immunogenetics* **62**, 397–407 (2010).
 67. Moosig, F. *et al.* C1qRP (CD93) expression on peripheral blood monocytes in patients with systemic lupus erythematosus. *Rheumatol. Int.* **26**, 1109–12 (2006).
 68. Kerr, J. F. R., Wyllie, A. H., & Currie, A. R. Apoptosis: a Basic Biological Phenomenon With

- Wideranging Implications in Tissue Kinetics. *Br. J. Cancer* **26**, 239–257 (1972).
69. Cryns, V. & Yuan, J. Proteases to die for. *Genes Dev.* **12**, 1551–1570 (1998).
 70. Degterev, A., Boyce, M. & Yuan, J. A decade of caspases. *Oncogene* **22**, 8543–8567 (2003).
 71. Martin, S. J. & Green, D. R. Protease activation during apoptosis: Death by a thousand cuts? *Cell* **82**, 349–352 (1995).
 72. Nicholson, D. W. Caspase structure, proteolytic substrates, and function during apoptotic cell death. *Cell Death Differ.* **6**, 1028–1042 (1999).
 73. Wyllie, A. H., Morris, R. G., Smith, A. L. & Dunlop, D. Chromatin Cleavage in Apoptosis - Association With Condensed Chromatin Morphology and Dependence on Macromolecular-Synthesis. *J. Pathol.* **142**, 67–77 (1984).
 74. Lauber, K. *et al.* 1-s2.0-S0092867403004227-main. **113**, 717–730 (2003).
 75. Gude, D. R. *et al.* Apoptosis induces expression of sphingosine kinase 1 to release sphingosine-1-phosphate as a 'come-and-get-me' signal. *FASEB J.* **22**, 2629–2638 (2008).
 76. Elliott, M. R. *et al.* Nucleotides released by apoptotic cells act as a find-me signal to promote phagocytic clearance. *Nature* **461**, 282–6 (2009).
 77. Truman, L., Ford, C., Pasikowska, M. & Jd. CX3CL1/fractalkine is released from apoptotic lymphocytes to stimulate macrophage chemotaxis. *Blood* **112**, 5026–5036 (2008).
 78. Peter, C., Wesselborg, S., Herrmann, M. & Lauber, K. Dangerous attraction: Phagocyte recruitment and danger signals of apoptotic and necrotic cells. *Apoptosis* **15**, 1007–1028 (2010).
 79. Kinchen, J. M. & Ravichandran, K. S. Journey to the grave: signaling events regulating removal of apoptotic cells. *J. Cell Sci.* **120**, 2143–2149 (2007).
 80. Arur, S. *et al.* Annexin I is an endogenous ligand that mediates apoptotic cell engulfment. *Dev. Cell* **4**, 587–598 (2003).
 81. Gardai, S. J. *et al.* Cell-surface calreticulin initiates clearance of viable or apoptotic cells through trans-activation of LRP on the phagocyte. *Cell* **123**, 321–334 (2005).
 82. Ravichandran, K. S. & Lorenz, U. Engulfment of apoptotic cells: signals for a good meal. *Nat. Rev. Immunol.* **7**, 964–974 (2007).
 83. Fadok, V. A. *et al.* Exposure of phosphatidylserine on the surface of apoptotic lymphocytes triggers specific recognition and removal by macrophages. *J. Immunol.* **148**, 2207–16 (1992).
 84. Fadok, V. a, Bratton, D. L., Frasch, S. C., Warner, M. L. & Henson, P. M. The role of phosphatidylserine in recognition of apoptotic cells by phagocytes. *Cell Death Differ.* **5**, 551–562 (1998).
 85. Fadok, V. A., De Cathelineau, A., Daleke, D. L., Henson, P. M. & Bratton, D. L. Loss of phospholipid asymmetry and surface exposure of phosphatidylserine is required for phagocytosis of apoptotic cells by macrophages and fibroblasts. *J. Biol. Chem.* **276**, 1071–1077 (2001).
 86. Balasubramanian, K. & Schroit, A. J. A Matter of Life and Death. *Rev. Lit. Arts Am.* (2003). doi:10.1146/annurev.physiol.65.092101.142459

87. Borisenko, G. G. *et al.* Macrophage recognition of externalized phosphatidylserine and phagocytosis of apoptotic Jurkat cells - Existence of a threshold. *Arch. Biochem. Biophys.* **413**, 41–52 (2003).
88. Ravichandran, K. S. Find-me and eat-me signals in apoptotic cell clearance: progress and conundrums. *J. Exp. Med.* **207**, 1807–17 (2010).
89. Tsou, W.-I. *et al.* Receptor tyrosine kinases, TYRO3, AXL, and MER, demonstrate distinct patterns and complex regulation of ligand-induced activation. *J. Biol. Chem.* **289**, 25750–63 (2014).
90. Nandrot, E. F. *et al.* Essential role for MFG-E8 as ligand for alphavbeta5 integrin in diurnal retinal phagocytosis. *Proc. Natl. Acad. Sci. U. S. A.* **104**, 12005–12010 (2007).
91. van den Eijnde, S. M. *et al.* Transient expression of phosphatidylserine at cell-cell contact areas is required for myotube formation. *J. Cell Sci.* **114**, 3631–3642 (2001).
92. Huppertz, B., Bartz, C. & Kokozidou, M. Trophoblast fusion: Fusogenic proteins, syncytins and ADAMs, and other prerequisites for syncytial fusion. *Micron* **37**, 509–517 (2006).
93. Helming, L. & Gordon, S. Molecular mediators of macrophage fusion. *Trends Cell Biol.* **19**, 514–522 (2009).
94. Brown, S. *et al.* Apoptosis disables CD31-mediated cell detachment from phagocytes promoting binding and engulfment. *Nature* **418**, 200–203 (2002).
95. Games, E. Repulsive encounters. *Nature* **418**, 139–141(2002).
96. Jaiswal, S. *et al.* CD47 Is Upregulated on Circulating Hematopoietic Stem Cells and Leukemia Cells to Avoid Phagocytosis. *Cell* **138**, 271–285 (2009).
97. Oldenborg, P. A., Gresham, H. D. & Lindberg, F. P. Cd47-Signal Regulatory Protein α (Sirp α) Regulates Fc γ and Complement Receptor–Mediated Phagocytosis. *J. Exp. Med.* **193**, 855–862 (2001).
98. Ezekowitz, B. Y. R. A. B., Sim, R. B., Hill, M. & Gordon, S. Local opsonization by secreted complement role of receptors for complement in uptake of zymosan. **159**, 244–260 (1984).
99. Huang, K., Merkle, T. & Beck, C. F. Isolation and characterization of a Mannan-binding protein. **94**, 613–622 (2002).
100. Burley, S. K., Kim, J. L. Human mannan-binding protein carbohydrate recognition domain trimerizes through a triple α -helical coiled-coil. *Nature* **1**, 638–653 (1994).
101. Matsushita, M. & Fujita, T. Activation of the classical complement pathway by mannan-binding protein in association with a novel C1s-like serine protease. *J. Exp. Med.* **176**, 1497–1502 (1992).
102. Ehlenberger, A. G. & Nussenzweig, V. The role of membrane receptors for c3b and c3d in phagocytosis. *J. Exp. Med.* **145**, 357–371 (1977).
103. Matsushita, M., Endo, Y. & Fujita, T. Structural and functional overview of the lectin complement pathway: Its molecular basis and physiological implication. *Arch. Immunol. Ther. Exp. (Warsz)*. **61**, 273–283 (2013).
104. Jack, D. L., Klein, N. J. & Turner, M. W. Mannose-binding lectin: targeting the microbial world for complement attack and opsonophagocytosis. *Immunol. Rev.* **180**, 86–99 (2001).

105. Turner, M. W. The role of mannose-binding lectin in health and disease. *Neth. J. Med.* **62**, 4–9 (2004).
106. Heit, B. *et al.* Multimolecular signaling complexes enable sky-mediated signaling of CD36 internalization. **24**, 372–383 (2014).
107. DeKoter, R. P. & Singh, H. Regulation of B lymphocyte and macrophage development by graded expression of PU.1. *Science* **288**, 1439–1441 (2000).
108. Scott, E. W. *et al.* Requirement of Transcription Factor PU . 1 in the Development of Multiple Hematopoietic Lineages. **265**, 1573–1577 (2016).
109. Iwasaki, H. *et al.* Distinctive and indispensable roles of PU. 1 in maintenance of hematopoietic stem cells and their differentiation. *Blood* **106**, 1590–1600 (2005).
110. Dahl, R. & Simon, M. C. The importance of PU.1 concentration in hematopoietic lineage commitment and maturation. *Blood Cells, Mol. Dis.* **31**, 229–233 (2003).
111. Henkel, G. W. *et al.* PU.1 but not ets-2 is essential for macrophage development from embryonic stem cells. *Blood* **88**, 2917–2926 (1996).
112. Sokalski, K. M. *et al.* Deletion of genes encoding PU . 1 and Spi-B in B cells impairs differentiation and induces pre-B cell acute lymphoblastic leukemia. *Lymphoid Neoplasia* **118**, 2801–2808 (2011).
113. McKercher, S. R. *et al.* Targeted disruption of the PU.1 gene results in multiple hematopoietic abnormalities. *EMBO J.* **15**, 5647–5658 (1996).
114. Allman, D. *et al.* Resolution of three nonproliferative immature splenic B cell subsets reveals multiple selection points during peripheral B cell maturation. *J. Immunology* **167**, 6834–6840 (2001).
115. Walsh, J. C. *et al.* Cooperative and antagonistic interplay between PU.1 and GATA-2 in the specification of myeloid cell fates. *Immunity* **17**, 665–676 (2002).
116. Nagai, T. *et al.* Transcription factor GATA-2 is expressed in erythroid, early myeloid, and CD34+ human leukemia-derived cell lines. *Blood* **84**, 1074–1084 (1994).
117. Bigley, V. & Collin, M. Dendritic cell, monocyte, B and NK lymphoid deficiency defines the lost lineages of a new GATA-2 dependent myelodysplastic syndrome. *Haematologica* **96**, 1081–1083 (2011).
118. Zhang, P. *et al.* Negative cross-talk between hematopoietic regulators: GATA proteins repress PU.1. *Proc. Natl. Acad. Sci. U. S. A.* **96**, 8705–10 (1999).
119. Shaulian, E. & Karin, M. AP-1 as a regulator of cell life and death. *Nat Cell Biol* **4**, E131–6 (2002).
120. Wisdom, R. AP-1: one switch for many signals. *Exp. Cell Res.* **253**, 180–185 (1999).
121. Kyriakis, J. M. Activation of the AP-1 transcription factor by inflammatory cytokines of the TNF family. *Gene Expr.* **7**, 217–31 (1999).
122. Yang-Yen, H. F. *et al.* Antagonism between retinoic acid receptors and AP-1: implications for tumor promotion and inflammation. *New Biol.* **3**, 1206–19 (1991).
123. Takeda, K. & Akira, S. TLR signaling pathways. *Semin. Immunol.* **16**, 3–9 (2004).

124. Wong, H. S. *et al.* Cytoskeletal confinement of CX 3 CL1 limits its susceptibility to proteolytic cleavage by ADAM10. *Mol. Biol. Cell* **25**, 3884–99 (2014).
125. Arribas, J. *et al.* Diverse cell surface protein ectodomains are shed by a system sensitive to metalloprotease inhibitors. *J. Biol. Chem.* **271**, 11376–11382 (1996).
126. Parvathy, S. *et al.* Angiotensin-converting enzyme secretase is inhibited by zinc metalloprotease inhibitors and requires its substrate to be inserted in a lipid bilayer. *Biochem. J.* **327 (Pt 1)**, 37–43 (1997).
127. Maskos, K. *et al.* Crystal structure of the catalytic domain of human tumor necrosis factor-alpha-converting enzyme. *Proc. Natl. Acad. Sci. U. S. A.* **95**, 3408–3412 (1998).
128. Fiorucci, S. *et al.* TNFalpha processing enzyme inhibitors prevent aspirin-induced TNFalpha release and protect against gastric mucosal injury in rats. *Aliment. Pharmacol. Ther.* **12**, 1139–1153 (1998).
129. Buxbaum, J. D. *et al.* Evidence that tumor necrosis factor alpha converting enzyme is involved in regulated alpha-secretase cleavage of the Alzheimer amyloid protein precursor. *J. Biol. Chem.* **273**, 27765–27767 (1998).
130. Codony-Servat, J., Albanell, J., Lopez-Talavera, J. C., Arribas, J. & Baselga, J. Cleavage of the HER2 ectodomain is a pervanadate-activable process that is inhibited by the tissue inhibitor of metalloproteases-1 in breast cancer cells. *Cancer Res.* **59**, 1196–1201 (1999).
131. Sadhukhan, R. *et al.* Unaltered cleavage and secretion of angiotensin-converting enzyme in tumor necrosis factor-??-converting enzyme-deficient mice. *J. Biol. Chem.* **274**, 10511–10516 (1999).
132. Galko, M. J. & Tessier-Lavigne, M. Function of an axonal chemoattractant modulated by metalloprotease activity. *Science (80-.)*. **289**, 1365–1367 (2000).
133. Brou, C. *et al.* A Novel Proteolytic Cleavage Involved in Notch Signaling. *Mol. Cell* **5**, 207–216 (2000).
134. Franzke, C. W. *et al.* Transmembrane collagen XVII, an epithelial adhesion protein, is shed from the cell surface by ADAMS. *EMBO J.* **21**, 5026–5035 (2002).
135. Moss, M. L. & Rasmussen, F. H. Fluorescent substrates for the proteinases ADAM17, ADAM10, ADAM8, and ADAM12 useful for high-throughput inhibitor screening. *Anal. Biochem.* **366**, 144–148 (2007).
136. Norsworthy, P. J. *et al.* Murine CD93 (C1qRp) Contributes to the Removal of Apoptotic Cells In Vivo but Is Not Required for C1q-Mediated Enhancement of Phagocytosis. *J. Immunol.* **172**, 3406–3414 (2004).
137. C. Greenlee-Wacker, M., D. Galvan, M. & S. Bohlsion, S. CD93: Recent Advances and Implications in Disease. *Curr. Drug Targets* **13**, 411–420 (2012).
138. Youn, J.-C. *et al.* Soluble CD93 levels in patients with acute myocardial infarction and its implication on clinical outcome. *PLoS One* **9**, e96538 (2014).
139. M??larstig, a. *et al.* Plasma CD93 concentration is a potential novel biomarker for coronary artery disease. *J. Intern. Med.* **270**, 229–236 (2011).

Appendices



Use of Human Participants - Initial Ethics Approval Notice

Principal Investigator: Prof. Bryan Heit
 File Number: 104010
 Review Level: Delegated
 Protocol Title: Venipuncture for Immune Cell Purification
 Department & Institution: Schulich School of Medicine and Dentistry/Microbiology & Immunology, Western University
 Sponsor:
 Ethics Approval Date: October 09, 2013 Expiry Date: July 31, 2016
 Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Protocol	Microscopy & analysis protocols	2013/07/02
Letter of Information & Consent	Consent Statement	2013/07/02
Protocol	Preparation of phagocytic/efferoctytic targets	2013/07/02
Protocol	Western blotting protocol	2013/07/02
Protocol	Mass spectometry protocols	2013/07/02
Protocol	Macrophage & neutrophil isolation and differntiation methods.	2013/07/02
Western University Protocol		2013/07/03
Other	Reply to Reviewer Request #4 - attach data collection forms.	2013/08/13
Letter of Information & Consent	Consent form	2013/08/22
Advertisement	Advertisement poster	2013/08/22




This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRR 00000940

Ethics Officer to Contact for Further Information

 Erka Basile (ebasile@uwo.ca)	 Grace Kelly (grace.kelly@uwo.ca)	 Vikki Tran (vikki.tran@uwo.ca)
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 London, ON, Canada N6A 3K7 t. 519.661.3036 f. 519.850.2466 www.uwo.ca/research/services/ethics

Appendix 1 : Ethics approval for performing venipuncture on human participants

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus C C C A G T G C C C T T C C A C C C A C C C T A G T G T C C T T C C A C C T C C C C A G T G C C
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta - - - - -
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus C T T C C A C C C A C C C T A G T G T C C T T C C A C C T C C C C A G T G C C C T T C C A C C C
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta - - - - - T G C T G T T G C C A G G
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus A C C C T A G T G T C C T T C C A C C T C T C C A G T G C C C T T C C A C A C A C C C C A A A G
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta T T C A C A G G T G T T C C C T G T G T T C T C C A C C G T G G C G C G T C C C C T G G G G C C
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus C T C C T G T C C C C G T C G T C C C T G C T G G G T T T C T C A C C T C C C G C C G A G G G G
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta T T C A C A A A G C T A C T G T C G C T G C T G G G C T T C T C G C C T C C T G C C G A G G G G
Papio anubis - - - - -

Otolemur garnettii - - - - - A T G G C C A C C T C C A C C C A C - - - - - C T G C T G C T G
Tarsius syrichta - - - - - A T G G C C A C C T C C A C A G G C - - - - - C T G C T G C T G C T G
Homo sapiens - - - - - A T G G C C A C C T C C A T G G G C C T G C T G C T G C T G C T G
Nomascus leucogenys - - - - - A T G G C C A C C C C C A T G G G C - - - - - C T G C T G C T G C T G
Pan paniscus - - - - - A T G G C C A C C T C C A T G G G C - - - - - C T G C T G C T G
Pan troglodytes - - - - - A T G G C C A C C T C C A T G G G C - - - - - C T G C T G C T G
Pongo abelii - - - - - A T G G C C A C C T T C A T G G G C - - - - - C T G C T G C T G
Callithrix jacchus C A C A T G G A G A C C G G G A T G G C C A C C T T C A C A C C - - - - - C T G C T G C T G
Saimiri boliviensis - - - - - A T G G A G A C C G G G A T G G C C A C C T T C A C C G G C - - - - - C T G C T G C T G
Chlorocebus sabaues - - - - - A T G G C C A C C T C T A T G G G C C T G C T G C T G C T G C T G
Macaca fascicularis - - - - - A T G G C C A C C T C T G T G G G C C T G C T G C T G C T G C T G
Macaca mulatta C A C A C G G A G A C C G G G A T G G C C A C C T C T G T G G G C C T G C T G C T G C T G
Papio anubis - - - - - A T G G C C A C C T C T G T G G G C C T G C T G C T G C T G C T G

Otolemur garnettii C T G C T G C T G C T G G G T C A G C C C T G G G C C A C A G C T G G G G C C G C C A T G G A G
Tarsius syrichta C T G C T A C T C C T G G G C C A G C C C T G G G T C G G G A C C A G C G T G G A C A C G G A G
Homo sapiens C T G C T G C T C C T G A C C C A G C C C G G G G C G G G A C G G G A G C T G A C A C G G A G
Nomascus leucogenys C T G C T G C T C C T G A G C C A G C C C G G G G C C G G G A C G G G A G C T A A C A C G G A G
Pan paniscus C T G C T G C T C C T G A C C C A G C C C G G G G C G G G G A C G G G A G C T G A C A C G G A G
Pan troglodytes C T G C T G C T C C T G A C C C A G C C C G G G G C G G G G A C G G G A G C T G A C A C G G A G
Pongo abelii C T G C T G C T C C T G A G C C A G C C C G G G G C C G G G A C G G G A G C T G A C A C A G A G
Callithrix jacchus C T G C T T C T C C T G G T C C A G C C A G G G G C T G G A C G G G A G G T G A C A C G G A G
Saimiri boliviensis C T G C T A C T C C T G G G C C A G C C A G G G G C T G G C A T G G G A G G T G A C A C G G A G
Chlorocebus sabaues C T G C T G C T C C T G A G G C A G C T C G G G G C C G G G A C A G G A G C T G A C A C G G A G
Macaca fascicularis C T G C T G C T C C T G A G G C A G C T C G G G G C C G G G A C A G G A G C T G A C A C A G A G
Macaca mulatta C T G C T G C T C C T G A G G C A G C T C G G G G C C G G G A C A G G A G C T G A C A C A G A G
Papio anubis C T G C T G C T C C T G A G G C A G C T C G G G G C C G G G A C A G G A G C T G A C A C A G A G

Otolemur garnettii G C T G T G G T G T G C G C A G A C A C C G C C T G C T A C A C A G C C C A C T G G G G C A A G
Tarsius syrichta G C T G T G G T C T G T G G C G G C A C T G C C T G C T A C A C G G C C C A C T G G G G C A A G
Homo sapiens G C G G T G G T C T G C G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G
Nomascus leucogenys G C G G T G G T C T G C G C G G G G A C T G C T T G C T A C A C T G C C C A C T C G G G C A A G
Pan paniscus G C G G T G G T C T G C G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G
Pan troglodytes G C G G T G G T C T G C G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G
Pongo abelii G C G G T G G T C T G C G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G
Callithrix jacchus G C G G T G G T C T G C G C G G G G A T G G C C T G C T A C A C G G C C C A C T G G G G C A A G
Saimiri boliviensis G C G G T G G T C T G C G C G G G A T G G C C T G C T A C A C G G C C C A C T G G G G C A A G
Chlorocebus sabaues G C G G T G G T C T G C G C G G G G A C C G C C T G C T A T A C G G C C C A C T C G G G C A A G
Macaca fascicularis G C G G T G G T C T G C G C G G G G A C C G C C T G C T A T A C G G C C C A C T G G G G C A A G
Macaca mulatta G C G G T G G T C T G C G C G G G G A C C G C C T G C T A T A C G G C C C A C T G G G G C A A G
Papio anubis G C G G T G G T C T G C G C G G G G A C C G C C T G C T A T A C G G C C C A C T G G G G C A A G

Otolemur garnettii C T G A G C G C A G A T G A G G C C A G C A G C A C T G C A G C A A G A A C G G G G G C A A G
Tarsius syrichta C T G A G C G C T G C T G A G G C C C A G G A C C A C T G C C A G T C C A A C G G G G G C A A C
Homo sapiens C T G A G C G C T G C C G A G G C C A G A A C C A C T G C A C C A G A A C G G G G G C A A C
Nomascus leucogenys C T G A G C G C T G C C G A G G C A C A G A A C C A C T G C A G C C A G A A C G G G G C A A C
Pan paniscus C T G A G C G C T G C C G A G G C T C A G A A C C A C T G C A A C C A G A A C G G G G G C A A C
Pan troglodytes C T G A G C G C T G C C G A G G C C A G A A C C A C T G C A A C C A G A A C G G G G G C A A C
Pongo abelii C T G A G C G C T G C C G A G G C C A G A A C C A C T G C A G C C A G A A C G G C G G C A A C
Callithrix jacchus C T G A G C G C C G C T G A T G C C C A G A A C C A C T G C A G C C A G A A C G G G G G C A A C
Saimiri boliviensis C T G A G C G C T G C C G A G G C C C A G A G C C A C T G C A G C C A G A A T G G G G G C A A C
Chlorocebus sabaues C T G A G C G C T G C C G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C
Macaca fascicularis C T G A G C G C T G C C G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C
Macaca mulatta C T G A G C G C T G C C G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C
Papio anubis C T G A G C G C T G C C G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C

Otolemur garnettii C T G A C C A C A G T G A A G A G C G A G G A G G A G G C C G G G C A T G T T C A G C G A A C C
Tarsius syrichta C T G G C C A C C G T G A A G A G C G A A G A G G A A G C C C A G C A C G T C C A G C A A G C C
Homo sapiens C T G G C C A C T G T G A A G A G C A A G G A G G A G G C C C A G C A C G T C C A G C G A G T A
Nomascus leucogenys C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A
Pan paniscus C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A
Pan troglodytes C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A
Pongo abelii C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G G A T G T C C A G C G A G T A
Callithrix jacchus C T G G C C A C T G T G A A G A G C A A G G A G G A G G C C C A G C A C A T C C A G C G A G C C
Saimiri boliviensis C T G G C C A C T G T G A A G A G C C G G G A G G A G G C C C A G C A C A T C C A G C G A G C C
Chlorocebus sabaues C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A
Macaca fascicularis C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C A A G T A
Macaca mulatta C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C A A G T A
Papio anubis C T G G C C A C T G T G A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C A A G T A

Otolemur garnettii C T G G C C C A G C T C C T G A G C C T G C A G G C A T C C C T G G C T G C G A G G A T G G G C
Tarsius syrichta C T G G C C C A A C T C C T G A C G C C A G A G A A G G C C C T G G C A G C G A G G T T C G G C
Homo sapiens C T G G C C C A G C T C C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G A G C
Nomascus leucogenys C T G G C C C A G C T C C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C
Pan paniscus C T G G C C C A G C T C C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C
Pan troglodytes C T G G C C C A G C T C C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T A G G C
Pongo abelii C T G G C C C A G C T C C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C
Callithrix jacchus C T G G C C C A G C T C C T G A G G C T G G A G G C A A A C C T G A C G G C G A G G A T G G G C
Saimiri boliviensis C T G G C C C A G C T C C T G A G G C T G G A G G C G A A C C T G A C G G C G A G G A T G G G C
Chlorocebus sabaues C T G G C C C A A C T C C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C
Macaca fascicularis C T G G C C C A A C T C C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C
Macaca mulatta C T G G C C C A A C T C C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C
Papio anubis C T G G C C C A A C T C C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C

<i>Otolemur garnettii</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A A T G C C A G G A C C C C
<i>Tarsius syrichta</i>	A A G T T C T G G A T C G G C C T C C A G C G A G A G A A A G G C A A G T G C C T G G A C C C C
<i>Homo sapiens</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T
<i>Nomascus leucogenys</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T
<i>Pan paniscus</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T
<i>Pan troglodytes</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T
<i>Pongo abelii</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T
<i>Callithrix jacchus</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Saimiri boliviensis</i>	A A G T T C T G G A T C G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Chlorocebus sabaues</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Macaca fascicularis</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Macaca mulatta</i>	A A G T T C T G G A T T G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Papio anubis</i>	A A G T T C T G G A T T G G G C T T C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C
<i>Otolemur garnettii</i>	A G G C T G C C G C T G A A G G G C T T C A G C T G G G T G G G T G G C G G G G A G G A C A C G
<i>Tarsius syrichta</i>	A G C C T G C C G C T G A A G G G C T T C G C C T G G G T G G G T G G C G G G G A G G A C A C G
<i>Homo sapiens</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G G G G G A G G A C A C G
<i>Nomascus leucogenys</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G G G G G A G G A C A C G
<i>Pan paniscus</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G G G G G A G G A C A C G
<i>Pan troglodytes</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G G G G G A G G A C A C G
<i>Pongo abelii</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G G G G G A G G A C A C G
<i>Callithrix jacchus</i>	A G C C T G C C A C T G A A G G G C T T C A G C T G G G T G G G T G G C G G T G A G G A C A C G
<i>Saimiri boliviensis</i>	A G C C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G C G G G A G G A C A C G
<i>Chlorocebus sabaues</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G C G G G A G G A C A C G
<i>Macaca fascicularis</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G T G G G A G G A C A C G
<i>Macaca mulatta</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G C G G G A G G A C A C G
<i>Papio anubis</i>	A G T C T G C C G C T G A A G G G C T T C A G C T G G G T G G G C G G C G G G G A G G A C A C G
<i>Otolemur garnettii</i>	C T C T A C A C C A A C T G G C A C A A G G A G G C C C G C A A C T C A T G C A T C T C C A A G
<i>Tarsius syrichta</i>	G C C T A C A C C A A C T G G C A C A A G G A G G T C C G C A G C T C T T G C A T C T C G A G G
<i>Homo sapiens</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Nomascus leucogenys</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Pan paniscus</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Pan troglodytes</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Pongo abelii</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Callithrix jacchus</i>	C C T T A C A C T A A C T G G T A C A A G G A G C T C C G C A A C T C G T G C A T C T C C A A G
<i>Saimiri boliviensis</i>	C C T T A C G C G A A C T G G T A C A A G G A G C T C C G C A G C T C G T G C G T C T C C A A G
<i>Chlorocebus sabaues</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Macaca fascicularis</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Macaca mulatta</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Papio anubis</i>	C C T T A C T C T A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G
<i>Otolemur garnettii</i>	C G C T G T G T G T C C C T G C T G C T G G A C C T G T C C C T G A C A C C C A C C A C C A G C
<i>Tarsius syrichta</i>	C G T T G T G T G G C A C T G C T G C T G G A C C T G T C C C A G C C A C C C C T G C C T G G C
<i>Homo sapiens</i>	C G C T G T G T G T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G C
<i>Nomascus leucogenys</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G C
<i>Pan paniscus</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G C
<i>Pan troglodytes</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G C
<i>Pongo abelii</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G C
<i>Callithrix jacchus</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C T C T T T T C C A G C
<i>Saimiri boliviensis</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C T C T C C T T T C C A G C
<i>Chlorocebus sabaues</i>	C G C T G T G T T T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G G
<i>Macaca fascicularis</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C G G G
<i>Macaca mulatta</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C G G G
<i>Papio anubis</i>	C G C T G T G T G T C T C T G C T G C T G G A C C T G T C C C A G C C G C T C C T T C C A G G
<i>Otolemur garnettii</i>	C G C C T C C C T A A G T G G T C T G A A G G C C C C T G T G G G A A C C C T G T C T C T C C C
<i>Tarsius syrichta</i>	C G C T T C C C C A A G T G G T C C G A G G G C C C C T G T G G G A A C C C C A G C A C C C C A
<i>Homo sapiens</i>	C G C C T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Nomascus leucogenys</i>	C G C C T C C C C A A G T G G T C T G A G G G C C C C T G C G G G A G C C C A G G C T C C C C T
<i>Pan paniscus</i>	C G C C T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Pan troglodytes</i>	C G C C T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Pongo abelii</i>	C G C C T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A A G C T C C C C C
<i>Callithrix jacchus</i>	T A C C T C C C C A G G T G G T C C G A G G G C C C C T G T G G G A G C C C A G A C T C C C C T
<i>Saimiri boliviensis</i>	C A C C T C C C C A G G T G G T C C G A A G G C C C C T G T G G G A G C T C A G A C T C C C C C
<i>Chlorocebus sabaues</i>	C G C C T C C C G A A G T G G T C G G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Macaca fascicularis</i>	C G C C T C C C G A A G T G G T C C G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Macaca mulatta</i>	C G C C T C C C G A A G T G G T C C G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C
<i>Papio anubis</i>	C G C C T C C C G A A G T G G T C C G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C

Otolemur garnettii G G A A G T A A C A T C G A G G G T T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Tarsius syrichta G G A A G C A G C A T T G A G G G C T T C G T G T G C A A G T T T A G C T T C A A G G G C A T G
Homo sapiens G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Nomascus leucogenys G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Pan paniscus G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Pan troglodytes G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Pongo abelii G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Callithrix jacchus G G A A T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Saimiri boliviensis G G A A T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
Chlorocebus sabaues G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G
Macaca fascicularis G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G
Macaca mulatta G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G
Papio anubis G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G

Otolemur garnettii T G C C G A C C C C T G G C T C T G G G G G G C C C A G G C A A G G T G A C C T A T T C C A C T
Tarsius syrichta T G C C G G C C C C T G G C G C T G G G C G G A C C G G G C C A G G T G A C C T A C A C A C A C T
Homo sapiens T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Nomascus leucogenys T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Pan paniscus T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Pan troglodytes T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Pongo abelii T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Callithrix jacchus T G C C G G C C C C T G G C C C T G G G G G G T C C A G G C C A G G T G A C C T A C A C C A C C
Saimiri boliviensis T G C C G G C C C C T G G C C C T G G G G G G C C C A G G C C A G G T G A C C T A C A C C A C C
Chlorocebus sabaues T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Macaca fascicularis T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Macaca mulatta T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
Papio anubis T G C C G G C C T C T G G C C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C

Otolemur garnettii C C C T T T C A G G C C A C C A G C T C C T C C C T G G A C G C T G T G C C C T T T G C C T C T
Tarsius syrichta C C C T T C A A G G C C A T A A G C T C C T C C C T G G A G G C C G T G C C C T T T G C T T C C
Homo sapiens C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Nomascus leucogenys C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Pan paniscus C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Pan troglodytes C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Pongo abelii C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Callithrix jacchus C C C T T C C A G A C C A C C A G T T C T T C C T T G G A G G C C G T G C C C T T T G C C T C T
Saimiri boliviensis C C C T T C C A G A C C A C C A G T T C C T C C T T G G A A G C T G T G C C C T T T G C C T C T
Chlorocebus sabaues C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Macaca fascicularis C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Macaca mulatta C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T
Papio anubis C C C T T C C A G A C C A C C A G T T C C T C C T T G G A G G C T G T G C C C T T T G C C T C T

Otolemur garnettii A T G G C C A G T G T G G C C T G T G G G G A C G G - - - - - G A A T G A G A G T A C C A G C
Tarsius syrichta A T G G C C T A T G T G T C C T G T G G G G A C A G G G C C A C G G A C A A G A G C C A C A - -
Homo sapiens G C G G C C A A T G T A G C C T G T G G G G A A G G T G A C A A G G A C G A G A C T C A G A G T
Nomascus leucogenys G C G G C C G A T G T G G C C T G T G G G G A A G G G G A C A A G G A C A A G A G T C A G A G T
Pan paniscus G C G G C C A A T G T A G C C T G T G G G G A A G G C G A C A A G G A C G A G A G T C A G A G T
Pan troglodytes G C G G C C A A T G T A G G C T G T G G G G A A G G C G A C A A G G A C G A G A G T C A G A G T
Pongo abelii G C G G C C A C T G T G G C C T G T G G G G A A G G G G A C A A G G A C G A G A G T C A G A G T
Callithrix jacchus G A G C C A A T G T G G C C T G T G G G G A C A G G G A C C A G G A C A A G A G T C A G A G T
Saimiri boliviensis G C G G C C A A C G T G A T C T G T G G G G A T G G G G A C C A G G A C A A G A G T C A G A G T
Chlorocebus sabaues G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T
Macaca fascicularis G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T
Macaca mulatta G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T
Papio anubis G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T

Otolemur garnettii C A T T A T T T C C T G T G C A A G G A G A A G G A G C C C A A C G T G T T T G A G T G G A A C
Tarsius syrichta - - - A C A T C C T G T G C A G G G A G A A G G G C C C T G G T G T G T T C G A G T G G G G C
Homo sapiens C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Nomascus leucogenys C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Pan paniscus C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Pan troglodytes C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Pongo abelii C A T T A T T T C C T A T G C A A G G A G A A G G C C C C G G T G T G T T C G A C T G G G G C
Callithrix jacchus C A T T A T T T C C T G T G T A A G G A G A A G G C C C C T G A T G T G T T C G A T T G G G G C
Saimiri boliviensis C A T T A T T T C C T G T G C A A G G A G A A G G C C C C T G A T G T G T T C G A C T G G G G C
Chlorocebus sabaues C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Macaca fascicularis C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Macaca mulatta C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
Papio anubis C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C

Otolemur garnettii A G C T C G G G C C C C T T T G T G T C A G C C C C G A C T A T G G C T G C A A C T T C A A C
Tarsius syrichta A C C C C G G G C C C C T T C T G T G T G A A C C C T G A A C T C G G T T G C A G C T T C A A C
Homo sapiens A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Nomascus leucogenys A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Pan paniscus A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Pan troglodytes A G C T C G G G C C C C T C T G T G T C A T C C C C A A G T A T G G C T G C A G C T T C A A C
Pongo abelii A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Callithrix jacchus A G C T C G G G C C C C T C T G T G T C A G C C C G A A G T A C G G C T G C A G C T T C A A C
Saimiri boliviensis A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Chlorocebus sabaues A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Macaca fascicularis A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Macaca mulatta A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
Papio anubis A G C T C G G G C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C

Otolemur garnettii A A C G G G G G C T G C C A G C A G G C C T G C T T C G A G G G C G G G G A C G G C T C C T T C
Tarsius syrichta A A C G G T G G C T G T G A G C A G G A C T G C T T C G A G G G G G C G A T G G C T C C T T C
Homo sapiens A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G A T G G C T C C T T C
Nomascus leucogenys A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G A C G G C T C C T T C
Pan paniscus A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G A G G A T G G C T C C T T C
Pan troglodytes A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G A G G A T G G C T C C T T C
Pongo abelii A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G A T G G C T C C T T C
Callithrix jacchus A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G A G G C G A T G G C T C C T T C
Saimiri boliviensis A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G A G G G A T G G C T C C T T C
Chlorocebus sabaues A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G A T G G C T C C T T C
Macaca fascicularis A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G A T G G C T C C T T C
Macaca mulatta A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G A T G G C T C C T T C
Papio anubis A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G A T G G C T C C T T C

Otolemur garnettii C G C T G T G G C T G C C T G C C G G G C T T C C G G C T G C T G G A T G A C C T G G T G A C C
Tarsius syrichta C G C T G T G G C T G C C G C C C G G G C T T C C G G C T G C T G G A C G A C C T G G T G A G C
Homo sapiens C T C T G C G G C T G C C A C C A G G A C T T C C G G C T G C T G G A T G A C C T G G T G A C C
Nomascus leucogenys C T C T G T G G C T G T C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
Pan paniscus C T C T G C G G C T G C C G G C C A G G A T T C C G G C T G C T G G A T G A C C T G G T G A C C
Pan troglodytes C T C T G C G G C T G C C G G C C A G G A T T C C G G C T G C T G G A T G A C C T G G T G A C C
Pongo abelii C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
Callithrix jacchus C T T T G T G G C T G C C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
Saimiri boliviensis C T T T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
Chlorocebus sabaues C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
Macaca fascicularis C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
Macaca mulatta C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
Papio anubis C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C

Otolemur garnettii T G T G C C T C T C G G A A C C C T T G C A G C T C C A G C C C A T G C A T C G G A G A G G C C
Tarsius syrichta T G T G C C T C C C G G A A C C C C T T G C A G C T C C A G C C C G T G C A G C G G G G A G G C C
Homo sapiens T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
Nomascus leucogenys T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
Pan paniscus T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
Pan troglodytes T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
Pongo abelii T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
Callithrix jacchus T G T G C C T C C C G A A A C C C T T G C A G C T C C A G C C C A T G C C G T G G G G G G C C
Saimiri boliviensis T G T G C C T C C C G T A A C C C T T G C A G C T C C A G C C C A T G C C G T G G G G G G C C
Chlorocebus sabaues T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C
Macaca fascicularis T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C
Macaca mulatta T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C
Papio anubis T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C

Otolemur garnettii A C A T G T G T C T C T G C A C C T C A T G G G A C A A A C T A C A C A T G C C A C T G T C C C
Tarsius syrichta A C G T G T G T C C C C G G G C C C A C A G G G A G G A C T T C A T G T G C C G C T G T C C C
Homo sapiens A C G T G C G T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
Nomascus leucogenys A C A T G T A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
Pan paniscus A C G T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C T
Pan troglodytes A C G T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C T
Pongo abelii A C A T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
Callithrix jacchus A C A T G C A T C C A G G G A T C C C A G G G A A A A A C T A C A C A T G C C A C T G T C C C
Saimiri boliviensis A C A T G C A T C C A G G G T T C C A T G G G A A A A A C T A C A C A T G C C A C T G T C C C
Chlorocebus sabaues A C A T G C A T C C C G G G A C C C C A T G G G A A A A A C T A C A C G T G C G G C T G C C C C
Macaca fascicularis A C A T G C A T C C C A G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
Macaca mulatta A C A T G C A T C C C G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
Papio anubis A C A T G C A T C C C G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C

<i>Otolemur garnettii</i>	C A A G G T T T C C A A G T G G A C G A G A G T C A G T T G G G C T G T G T G G A T G T G G A T
<i>Tarsius syrichta</i>	A G C G G C T A C C A G C T G G A T G C A A G C C A G C T G A G C T G T G A G G A C G T G G A T
<i>Homo sapiens</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
<i>Nomascus leucogenys</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G T T G G A C T G T G T G G A T G T G G A T
<i>Pan paniscus</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
<i>Pan troglodytes</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
<i>Pongo abelii</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A T G T G G A T
<i>Callithrix jacchus</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A T G T G G A T
<i>Saimiri boliviensis</i>	C A A G G G T A C C A G C T G G A C T C A A G T C A G C T G G A C T G T G T G G A T G T G G A T
<i>Chlorocebus sabaues</i>	C A A G G G T A T C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
<i>Macaca fascicularis</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
<i>Macaca mulatta</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
<i>Papio anubis</i>	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
<i>Otolemur garnettii</i>	G A G T G T C A A G A C A G C C C C T G T G T C C A G G C C T G T G T C A A C A C C C A T G G G
<i>Tarsius syrichta</i>	G A G T G T C A G G C C T C A C C C T G T G C A C A G C A G T G C G T C A A C A C C C C C G G G
<i>Homo sapiens</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Nomascus leucogenys</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Pan paniscus</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Pan troglodytes</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Pongo abelii</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G A
<i>Callithrix jacchus</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Saimiri boliviensis</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Chlorocebus sabaues</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Macaca fascicularis</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Macaca mulatta</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Papio anubis</i>	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
<i>Otolemur garnettii</i>	A G C T T C C G A T G T G A G T G C T G G G T G G G C T A C G A G C C C A G C A G C C C T G G G
<i>Tarsius syrichta</i>	G G C T T C C G C T G T G A G T G C T G G G T G G G C T A C G A G C C G G G T G G C C C G G G
<i>Homo sapiens</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Nomascus leucogenys</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Pan paniscus</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C A G T C C T G G A
<i>Pan troglodytes</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Pongo abelii</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Callithrix jacchus</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G T A C C A G C C G G A C G G T C C T G G A
<i>Saimiri boliviensis</i>	G G C T T C C G C T G C G A A T G C T G G G T T G G T A C G A A C C G G G T G G T C C T G G A
<i>Chlorocebus sabaues</i>	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Macaca fascicularis</i>	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Macaca mulatta</i>	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Papio anubis</i>	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G C G G T C C T G G A
<i>Otolemur garnettii</i>	G A A G G T G C C T G C C A G G A T G T G G A T G A G T G T G C C C T T G G C C G T T C A C C C
<i>Tarsius syrichta</i>	G A G G C A G C C T G T C G T G A C G T T G A T G A G T G T G C C C T A G C C G C A C A C C C
<i>Homo sapiens</i>	G A G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C G C C T
<i>Nomascus leucogenys</i>	G A G A G G A C C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A T C G C T C G C C T
<i>Pan paniscus</i>	G A G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C A C C T
<i>Pan troglodytes</i>	G A G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C A C C T
<i>Pongo abelii</i>	G A G G G G C C T G T C G G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C G C C T
<i>Callithrix jacchus</i>	G A G G G T G C C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A C C C C T C G C C C
<i>Saimiri boliviensis</i>	G A G G G T G T C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A C C C C T C G C C C
<i>Chlorocebus sabaues</i>	G A G G G G T C T G T C A G G A T G T G G A T G A G T G T G C C C C G G G C C G C T C G C C T
<i>Macaca fascicularis</i>	G A G G G G C C T G T C A G G A T G T G G A T G A G T G T G C C C T G G G C C G C T C G C C T
<i>Macaca mulatta</i>	G A G G G G C C T G T C A G G A T G T G G A T G A G T G T G C C C T G G G C C G C T C G C C T
<i>Papio anubis</i>	G A G G A G G C C T G T C A G G A T G T G G A T G A G T G T G C C C T G G G C C G C T C G C C T
<i>Otolemur garnettii</i>	T G C A C T C A G C G C T G T A C C A A C A C T G A T G G C T C G T T C C A T T G C T C C T G T
<i>Tarsius syrichta</i>	T G C G C C C A G A A C T G C A C C A A C A C C G A C G G C T C G T T C C A C T G C T C C T G C
<i>Homo sapiens</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A T G G C T C A T T T C A C T G C T C C T G T
<i>Nomascus leucogenys</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G C T C C T G C
<i>Pan paniscus</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A T G G C T C A T T T C A C T G C T C C T G T
<i>Pan troglodytes</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A T G G C T C A T T T C A C T G C T C C T G T
<i>Pongo abelii</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A C G G C T C A T T T C A C T G C T C C T G C
<i>Callithrix jacchus</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A C G G C T C A T T T C A C T G C T C C T G C
<i>Saimiri boliviensis</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G C T C C T G C
<i>Chlorocebus sabaues</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G T T C C T G C
<i>Macaca fascicularis</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G T T C C T G C
<i>Macaca mulatta</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G T T C C T G C
<i>Papio anubis</i>	T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G T T C C T G C

Otolemur garnettii G A G G A G G G C T A T G T G C T G G C T G G G G A G G A T G G C A C G C A G T G C C A G G A T
Tarsius syrichta C G T G A G G G C T A T G T C C T G G C C G G C G A A G A T G G C A C C C A G T G C C A G G A T
Homo sapiens G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G G A C
Nomascus leucogenys G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G G A C
Pan paniscus A A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G G A C
Pan troglodytes A A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G G A C
Pongo abelii G A G G A G G G C T A C G T C C T G G C T G G G G A G G A C G G G A C T C A G T G C C A G G A C
Callithrix jacchus C A G G A G G G C T A T G T C C T G G C T G A G G A G G A C G G C A C T C A G T G C C A G G A C
Saimiri boliviensis C A G G A G G G C T A C G T C C T G G C T G A G G A G G A C G G C A C T C A G T G C C A G G A T
Chlorocebus sabaues G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G G A C
Macaca fascicularis G A G G A G G G C T A T G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G G A C
Macaca mulatta G A G G A G G G C T A T G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G G A C
Papio anubis G A G G A G G G C T A T G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A C G A C

Otolemur garnettii G T G G A C G A G T G T G C C G G C C C T G G G G A C A G C C T C T G T G A C A A C C T C T G C
Tarsius syrichta G T G A A T G A G T G T G A G G G C C T G G G C A G C A G C C C C T G T G A T A G C C T G T G C
Homo sapiens G T G G A T G A G T G T G T G G G C C C G G G G G C C C C C T C T G C G A C A G C T T G T G C
Nomascus leucogenys G T G G A C G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C C T G T G C
Pan paniscus G T A G A C G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G T G C
Pan troglodytes G T A G A C G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G T G C
Pongo abelii G T G G A C G A G T G T T T G G G C C T G G G G G G C C C C T C T G T G A C A G C T T G T G C
Callithrix jacchus G T G G A C G A G T G T G C A G G C C C C G G A G T C T C C C C C T G T G A C A G C T T G T G C
Saimiri boliviensis G T G G A C G A G T G T G C A G G C C C T G G G G T C T C C C C T G T G A C A G C T T G T G C
Chlorocebus sabaues G T G G A T G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G T G C
Macaca fascicularis G T G G A T G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G T G C
Macaca mulatta G T G G A T G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G T G C
Papio anubis G T G G A T G A G T G T G T G G G C C C G G A G G G C C C C C T C T G C G A C A G C T T G T G C

Otolemur garnettii T T C A A C A C A C A G G G C T C C T T C A G C T G T G G C T G C C T G C C A G G C A T G G A G
Tarsius syrichta C T C A A C A C T C A G G G T T C C T T C C T T T G T G G C T G C C T G C C G G G C T G G G A G
Homo sapiens T T C A A C A C A C A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G G T G
Nomascus leucogenys T T C A A C A C A C A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G T G
Pan paniscus T T C A A C A C A C A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G G T G
Pan troglodytes T T C A A C A C A C A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G G T G
Pongo abelii T T C A A C A C A C A A G G G T C C T T C C A C T G T G G C T G C C T T G C C A G G C T G G T G
Callithrix jacchus T T C A A C A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G A C A G G C T G G G A G
Saimiri boliviensis T T C A A C A C A C A A G G G T C C T T C C T C T G T G G C T G C C T G A C A G G C T G G G A G
Chlorocebus sabaues T T C A A C A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G G T G
Macaca fascicularis T T C A A C A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G T G
Macaca mulatta T T C A A C A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G G T G
Papio anubis T T C A A C A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G G T G

Otolemur garnettii C T G G C C C C C G A T G G G G T C T C C T G C A T C A T A G C C C C T G T G T C T C T G G T C
Tarsius syrichta C T G G C T G C T G A T G G G G T C T C C T G C A C C A T G G G T C C T G T G C C C C C A G A
Homo sapiens C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G G G A
Nomascus leucogenys C T A G C C C C A A A T G G G G T C T C C T G C A C C A T G G G G C C T G T G T C T C T G G G A
Pan paniscus C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G G G A
Pan troglodytes C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G G G A
Pongo abelii C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G G G A
Callithrix jacchus C T G G C C C C A A A T G G G G T C T C C T G C A C C A T G G G G C T T G T G T C T C T G G G A
Saimiri boliviensis C T G G C C C C A A A T G G G G T C T C C T G C A C C A T G G G G C T T G T G T C T G T G G G A
Chlorocebus sabaues C T G G C C T C C A A T G G G G T C T C C T G C G C C A T G G G G C C T G T G T C T C T G G G A
Macaca fascicularis C T G G C C C C A A T G G G G T C T C C T G C G C C A T G G G G C C T G T G T C T C T G G G A
Macaca mulatta C T G G C C C C A A T G G G G T C T C C T G C G C C A T G G G G C C T G T G T C T C T G G G A
Papio anubis C T G G C C C C A A T G G G G T C T C C T G C G C C A T G G G G C C T G T G T C T C T G G G A

Otolemur garnettii C C A C T G G C T G G G G C T C C C C A A G A G G A G G A C A A T G G A A A G A G A G A G C G G
Tarsius syrichta T C C C C T A C T G G G C T C C C C A G G A G G A G G A C C A G G A A G A G A G A G A G G G G
Homo sapiens C C A C C A T C T G G G C C C C C G A T G A G G A G G A C A A A G G A G A G A A A G A A G G G
Nomascus leucogenys C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A G G A G A G A A A G A G G G G
Pan paniscus C C A C C A T C T G G G C C C C C G A T G A G G A G G A C A A A G G A G A G A A A G A A G G G
Pan troglodytes C C A C C A T C T G G G C C C C C G A T G A G G A G G A C A A A G G A G A G A A A G A A G G G
Pongo abelii C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A A G G A G A G A A A G A G G G G
Callithrix jacchus C G A C C A T C T G G G T C C C C T - - - G A G G A G T A C A A A G G A A G A A A G A G G G G
Saimiri boliviensis C C A C C A T C T G G G C C C C C G A G G A G G A G T A C A A A G G A A G A A A G A G G G G
Chlorocebus sabaues C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A G G A G A G A G A G A G G G G
Macaca fascicularis C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A G G A G A G A G A G A G G G G
Macaca mulatta C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A G G A G A G A G A G A G G G G
Papio anubis C C A C C A T C T G G G C C C C C G A T G A G G A G T A C A A G G A G A G A G A G A G A G G G G

Otolemur garnettii A G A C C C A T G C C C T C T G C T A C T A C A C T C A G T C C C A C C A G G G G C C C T G A G
Tarsius syrichta A G C A C C A T T C C C C C T G C T G C A G C G T C C A G T C C T A C C G G G G G C T C T G A G
Homo sapiens A G C A C C G T G C C C G T G C T G C A A C A G C C A G T C C C A C A A G G G G C C C G A G
Nomascus leucogenys A A C A C C A T A C T C C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C T C C G A G
Pan paniscus A G C A C C G T G C C C C G G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G
Pan troglodytes A G C A C C G T G C C C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G
Pongo abelii A G C A C C G T G C C C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G
Callithrix jacchus A G C A C T G T G G C C C C A C T G C A A C A G C C A G T C C C A C G A G G G G C C C A A G
Saimiri boliviensis A G C A C C G T G G C C C C G C T G C A G C A G C C A G T C C C A C G A G G G G C C T G A G
Chlorocebus sabaues A G C A C T G T G C C T C C C G C T G C A A C A G C C A G T C C C A C G A G G G G T C C C G A G
Macaca fascicularis A G C A C T G T G C C T C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G
Macaca mulatta A G C A C T G T G C C T C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G
Papio anubis A G C A C T G T G C C T C C C G C T G C A A C A G C C A G T C C C A C G A G G G G C C C G A G

Otolemur garnettii A C A A G C T T T G A A G C A G T G C C T G C C T C C A G G A A - - - - G C C C C C A T C C
Tarsius syrichta G G C A C C T C C C A A G G T G G C A C C C A C T T C T G G G A G A C C T T C G C T C T T G T T C
Homo sapiens G G C A C C C C C A A G G C T A C A C C C A C C A C C A C A A G T A G A C C T T C G C T G T C A T C T
Nomascus leucogenys G G C A C C C C C A A G G C T A C A C C C A C C G C A A G G A G A C C T T C G C T G T C A T C T
Pan paniscus G G C A C C C C C A A G G C T A C A C C C A C C A C C A C A A G T A G A C C T T C G C T G T C A T C T
Pan troglodytes G G C A C C C C C A A G G C T A C A C C C A C C A C C A C A A G T A G A C C T T C G C T G T C A T C T
Pongo abelii G G C A C C C C C A A G G C T A C A T C C A C C G C A A G G A G A C C T T C G C T G T C A T C T
Callithrix jacchus G G C A C T C C C A G G G C C A C A C C C A C C A C A A G G A G A C T T T C A C T C T C A C C T
Saimiri boliviensis G G C A C C C C C A G G G C C A C A C C C A C C A C A A G A G A C C T T T C A C T C T C A C C T
Chlorocebus sabaues G G C A C C G C C A A G T C T A C A C C C A C C A C A A G A G A C C C T T C G C T C T C A T C T
Macaca fascicularis G G C A C C C C C A A G T C T A C A C C C A C C A C A A G G A G A C C T T T G C T C T C A T C T
Macaca mulatta G G C A C C C C C A A G T C T A C A C C C A C C A C A A G G A G A C C T T T G C T C T C A T C T
Papio anubis G G C A C C C C C A A G T C T A C A C C C A C C A C A A G G A G A C C T T T G C T C T C A T C T

Otolemur garnettii A G C A C G C C C A T C A C C T C T G C C C T G C C T G A G A C G C T G G C C C C C A G T G G G
Tarsius syrichta C G G G T C C C C A T C A C T T C T G C C C C A C C T G A G A T G C T G A C C C A C A G T G G G
Homo sapiens G A C G C C C C A T C A C A T C T G C C C C A C T C A A G A T G C T G G C C C C A G T G G G
Nomascus leucogenys G A C A C C C C A T C A C G T C T G C C C C A C T G G A G A T G C T G G C C C C A G T T G G
Pan paniscus G A C G C C C C A T C A C A T C T G C C C C A C T C A A G A T G C T G G C C C C A G T G G G
Pan troglodytes G A C G C C C C A T C A C A T C T G C C C C A C T C A A G A T G C T G G C C C C A G T G G G
Pongo abelii G A T G C C C C A T C A C G T C T G A C C C A C T C A A G A T G C T G G C C C C A G T G G G
Callithrix jacchus G A C G C C C C A G T C A C C T C T G A C C C A T T T G A A A T G C T G G C C C T A G T G G G
Saimiri boliviensis G A C G C C C C A G T C A C C T C T G A C C C A C T G G A A A T G C T G G C C C T A G T G G G
Chlorocebus sabaues G A T G C C C C A T C A C C T C T G T C C C A C T T G A G G T G C T G G C C C C A G T G G G
Macaca fascicularis G A T G C C C C A T C A C C T C T G T C C C A C T T G A G G T G C T G G C C C C A G T G G G
Macaca mulatta G A T G C C C C A T C A C C T C T G T C C C A C T T G A G G T G C T G G C C C C A G T G G G
Papio anubis G A T G C C C C A T C A C C T C T G T C C C A C T T G A G G T G C T G G C C C C A G T G G G

Otolemur garnettii G C C C C T G A G G T C C G A G T G A A T C C T G G C A C C C A C C A G C C C A C A G C T G C C
Tarsius syrichta C C C C C G G G C A T C C G G A C A G A G T C C C G C A C C C A T C A C C C C A T G G C T G C C
Homo sapiens T C C C C A G G C G T C T G G A G G G A G C C A G C A T C C A T C A C G C C A C A G C T G C C
Nomascus leucogenys T C C C C A G G C G T C T G G A G G G A G C C A G C A T C C A T C A C G C C A C A G C T G C C
Pan paniscus T C C C C A G G C G T C T G G A G G G A G C C A G C A T C C A T C A C G C C A C A G C T G C C
Pan troglodytes T C C C C A G G C G T C T G G A G G G A G C C A G C A T C C A T C A C A C C A C A G C T G C C
Pongo abelii T C C C C A G G C G T C T G G A G G G A G C C A G C A T C C A T C A C G C C A C A G C T G C C
Callithrix jacchus T C C C C A A G C G T C T G G A A G G A G C C A G C A T C C A T C A C A A C A C G G C T G C C
Saimiri boliviensis T C C C C A C G C A T C T G G A A G G A G C C A G C A T C C A T C A T G T C A C G G C C A T C
Chlorocebus sabaues T C C C C A G G C C T C T G G A G G G A G C C A G C A T C C A T C A C A C C A C A G C T G C C
Macaca fascicularis T C C C C A G G C C T C T G G A G G G A G C C A G C A T C C A T C A C A C C A C A G C T G C C
Macaca mulatta T C C C C A G G C C T C T G G A G G G A G C C A G C A T C C A T C A C A C C A C A G C T G C C
Papio anubis T C C C C A G G C C T C T G G A G G G A G C C A G C A T C C A T C A C A C T A C A G C T G C C

Otolemur garnettii A C T G G T C A C C G T G A G T C T G C A G G T A G G G A - - - T T C G G T G G C C A C A C A A
Tarsius syrichta A C T G G C C A C T G G G A C T C T G C C G C G G G G G - - - C T C T G T G G A C A C A A A G
Homo sapiens T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A A
Nomascus leucogenys T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A A
Pan paniscus T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C G C A C A A
Pan troglodytes T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C G C A C A A
Pongo abelii T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C G C A C A A
Callithrix jacchus T C T G G C C C C A G G A G C C T G C A G G T G G G G A - - - C T C C G T C G C C A A A C A A
Saimiri boliviensis T C T G G C C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G C A C A A C A A
Chlorocebus sabaues T C T G G C G C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A G
Macaca fascicularis T C T G G T G C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A A
Macaca mulatta T C T G G C G C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A A
Papio anubis T C T G G C G C C C A G G A G C C T G C A G G T G G G G A C T C C T C C G T G G C C A C A C A A

<i>Otolemur garnettii</i>	A G T G A T G A T G G C A C T G A C G G A C A G A A G C T G C T T T T G T T C T A C A T C C T G
<i>Tarsius syrichta</i>	A G G G A T G A T G G C A C C G A C G G G C A G A A G T T G C T C C T G T T C T A C A T C C T G
<i>Homo sapiens</i>	A A C A A C G A T G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Nomascus leucogenys</i>	A A T G A C G A T G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Pan paniscus</i>	A A C A A C G A T G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Pan troglodytes</i>	A A C A A C G A T G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Pongo abelii</i>	A A C A A C G A T G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Callithrix jacchus</i>	A A C G A C A T G G C A C T G A T G G G C A A A A G T T G C T T T T G T T C T A C A T C C T G
<i>Saimiri boliviensis</i>	A A C A A C G A T G G C A C T G A C G G G C A A A A G T T G C T T T T G T T C T A C A T C C T G
<i>Chlorocebus sabaues</i>	A A C G A C G A C A G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Macaca fascicularis</i>	A A C G A C G A C G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Macaca mulatta</i>	A A C G A C G A C G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Papio anubis</i>	A A C G A C G A C G G C A C T G A C G G G C A A A A G C T G C T T T T A T T C T A C A T C C T A
<i>Otolemur garnettii</i>	G G C A C T G T G G T G G C C A T C C T G C T C C T G C T G G C T C T G G C G C T A G G G C T T
<i>Tarsius syrichta</i>	G G C A C C G T G G T G G C C A T C C T G C T C C T G C T G G C C C T G G C T C T T G G G C T G
<i>Homo sapiens</i>	G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C C C T G G C T C T G G G G C T A
<i>Nomascus leucogenys</i>	G G C A C C G T G G T G G C C A T C T T A C T C C T G C T G G C C C T G G C T C T G G G G C T A
<i>Pan paniscus</i>	G G C A C C G T G G T G G C T A T C C T A C T C C T G C T G G C C C T G G C T C T G G G G C T A
<i>Pan troglodytes</i>	G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C C C T G G C T C T G G G G C T A
<i>Pongo abelii</i>	G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C C C T G G C T C T G G G G C T A
<i>Callithrix jacchus</i>	G G C A C C G T G G T G G C C A T C C T C C T C C T G C T G G C C C T G G C T C T G G G G C T G
<i>Saimiri boliviensis</i>	G G C A C C G T G G T G G C C A T C C T C C T C C T G C T G G C C C T G G C T C T G G G G C T C
<i>Chlorocebus sabaues</i>	G G C A C C G T G G T A G G C A T C C T A C T T C T G C T G G C C C T G G C T C T G G G G C T A
<i>Macaca fascicularis</i>	G G C A C C G T G G T G G G C A T C C T A C T T C T G C T G G C C C T G G C T C T G G G G C T A
<i>Macaca mulatta</i>	G G C A C C G T G G T G G G C A T C C T A C T T C T G C T G G C C C T G G C T C T G G G G C T A
<i>Papio anubis</i>	G G C A C C G T G G T G G G C A T C C T A C T T C T G C T G G C C C T G G C T C T G G G G C T A
<i>Otolemur garnettii</i>	C T G G T C T G T C G C A G G C G G A G A G C T A A G C A G G C G G A G A A G A A G G A G A A G
<i>Tarsius syrichta</i>	C T G G T C T A C C G C A A G C G C C G A G C A A A G C A G G A G G G G A A G A A G G A G A G A
<i>Homo sapiens</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G A G A G A G A A G A G A G A G A G
<i>Nomascus leucogenys</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G C A G G A G A A G A A G A G A G A G
<i>Pan paniscus</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A A G
<i>Pan troglodytes</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A A G
<i>Pongo abelii</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G C A G A A G
<i>Callithrix jacchus</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G G A G G A T A - -
<i>Saimiri boliviensis</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G G A G G A G A - -
<i>Chlorocebus sabaues</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A - -
<i>Macaca fascicularis</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A - -
<i>Macaca mulatta</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A - -
<i>Papio anubis</i>	C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A G G A G A A G A A G G A G A - -
<i>Otolemur garnettii</i>	A T G C C C T C A A A C G C A G C A G A C A G T T A C T C C T G G G C T T C A G A G C G G G C A
<i>Tarsius syrichta</i>	C C A C C G C A G A G T G C A G C T G A C A C C T A C T C T T G G G T C C C T G A G C G G G C A
<i>Homo sapiens</i>	A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G G G T T C C A G A C G A G C T
<i>Nomascus leucogenys</i>	A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G T G
<i>Pan paniscus</i>	C A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C T
<i>Pan troglodytes</i>	C A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C A
<i>Pongo abelii</i>	A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C G
<i>Callithrix jacchus</i>	- A G C C C C A G A A T G C G G C A G A C A G G T A C T C C T G G G T T C C A G A G C G A G C G
<i>Saimiri boliviensis</i>	- A G C C T C A G A A T G C G G C A G A C A G G T A C T C C T G G G T T C C A G A G C G A G C G
<i>Chlorocebus sabaues</i>	- A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C A
<i>Macaca fascicularis</i>	- A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C A
<i>Macaca mulatta</i>	- A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C A
<i>Papio anubis</i>	- A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G G G T T C C A G A G C G A G C A
<i>Otolemur garnettii</i>	G A G A G C A G G G C C A C A G A G A A C C A G T A C A G G T A A A - - - - - - - - - - - - - -
<i>Tarsius syrichta</i>	G A G A G C C G G G C C T C A G A G A A T C C C T A C A G T C C G A C A C C T G G G A C A G A C
<i>Homo sapiens</i>	G A G A G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Nomascus leucogenys</i>	G A G A G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Pan paniscus</i>	G A G A G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Pan troglodytes</i>	G A G A G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Pongo abelii</i>	G A G A G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C C G G G A C A G A C
<i>Callithrix jacchus</i>	G A G G G C A G G G C C A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Saimiri boliviensis</i>	G A G G G C A G G G C C A T G G A G A A C C G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Chlorocebus sabaues</i>	G A G A G C A G G G C A A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Macaca fascicularis</i>	G A G A G C A G G G C A A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Macaca mulatta</i>	G A G A G C A G G G C A A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G A C A G A C
<i>Papio anubis</i>	G A G A G C A G G G C A A T G G A G A A C C A G T A C A G T C C G A C A C C T G G G G C A G A C

<i>Otolemur garnettii</i>	- - - - -
<i>Tarsius syrichta</i>	T G C T G A T
<i>Homo sapiens</i>	T G C T G A C
<i>Nomascus leucogenys</i>	T G C T G A C
<i>Pan paniscus</i>	T G C T G A C
<i>Pan troglodytes</i>	T G C T G A -
<i>Pongo abelii</i>	T G C T G A T
<i>Callithrix jacchus</i>	T G C T G A G
<i>Saimiri boliviensis</i>	T G C T G A -
<i>Chlorocebus sabaeus</i>	T G C T G A T
<i>Macaca fascicularis</i>	T G C T G A T
<i>Macaca mulatta</i>	T G C T G A -
<i>Papio anubis</i>	T G C T G A -

Appendix 2 : Nucleotide alignment for primate CD93 sequences.

AiluropodaMelanoleuca	- - - - - T G G C C A C C T C T G C T G G G - - - - - C T G - - - C C G
UrsusMaritimus	- - - - - T G A T G G C C A C C T C T G C C G G G - - - - - C T G - - - C C G
FelisCatus	- - - - - T G G C C A C C T C T G C C G G C - - - - - C T G - - - C T G
LeptonychotesWeddellii	- - - - - T G A T G G C C A C C T G C G C T G G G - - - - - C T G - - - C C G
PantheraTigris	- - - - - T G G C C A C C T C T G C C G G C - - - - - C T G - - - C T G
EptesicusFuscus	- - - - - T G G C C A C C T C C G C C A G C - - - - - C T G - - - C T G
MyotisLucifugus	G A C A C G G A G A C C G C G A T G G C C A C C T C - G C C A G C C T G C T G C T G - - - C T G
MyotisBrandtii	- - - - - T G G C C A C C T C C G C C A G C - - - - - C T G - - - C T G
CeratheriumSimum	- - - - - T G G C C A C C T C C A C C A G G - - - - - - - - - - - C T G
EquusCaballus	- - - - - T G G C C A C C T C C G C C G G C - - - - - C T G - - - C T G
OrcinusOrca	- - - - - T G A T G G C C G G C T C C A C C G G C - - - - - C T G - - - C T G
PhyseterCatodon	- - - - - T G A T G G C T G G T C C C G C C G T - - - - - - - - - - - - -
TursiopsTruncatus	- - - - - T G A T G G C C G G C T C C A C C G G C - - - - - - - - - - - C T G
BubalusBubalis	- - - - - T G G C C A G T T C C G C T G G C - - - - - C T G - - - C T G
OvisAries	- - - - - T G G C C A G T T C C G C T G G C - - - - - C T G - - - C T G
OtolemurGarrettii	- - - - - T G G C C A C C T C C A C C A C - - - - - - - - - - - C T G
CallithrixJacchus	C A C A T G G A G A C C G G G A T G G C C A C C T T C A C C A C C - - - - - - - - - C T G
SaimiriBoliviensis	- - - - T G G A G A C C G G G A T G G C C A C C T T C A C C G G C - - - - - - - - - C T G
ChlorocebusSabaeus	- - - - - T G G C C A C C T C T A T G G G C - - - - - C T G C T G C T G
MacacaFascicularis	- - - - - T G G C C A C C T C T G T G G G C - - - - - C T G C T G C T G
HomoSapiens	- - - - - T G G C C A C C T C C A T G G G C - - - - - C T G C T G C T G
NomascusLeucogenys	- - - - - T G G C C A C C C C C A T G G G C - - - - - C T G - - - C T G
PanPaniscus	- - - - - T G G C C A C C T C C A T G G G C - - - - - - - - - - - C T G
PanTrogodytes	- - - - - T G G C C A C C T C C A T G G G C - - - - - - - - - - - C T G
PongoAbelii	- - - - - T G G C C A C C T T C A T G G G C - - - - - - - - - - - C T G
ChrysochlorisAsiatica	- - - - - T G G C C A T C C C A C T G G G C A T G T C T T T G A T C C T G
EchinopsTelfairi	- - - - - T G G C C T C T C C C G G G C T G G T T A T T G C T G C T G
DasypusNovemcinctus	- - - - - T G G C C A C C T C C A G C T G C C A G C T G C C G - - - C T G
TrichechusManatus	- - - - - T G G C C A C C T C C A C T G G C A T G T C C T T G C T C C T G
SarcophilusHarrisii	- - - - - T G G G G A C A G C C T T G C T C C C - - - - - A C T G A T C C T A
MonodelphisDomestica	- - - - - T G G G G A C A G C C T T G C T C C C - - - - - A C T G A T C C T G
AiluropodaMelanoleuca	C T G C T G C T G C C G C T G C T G C T G C T G C T G C T A C T G C T G G G C C - - - A G C C C
UrsusMaritimus	C T G C T G C T G C C - - - - - G C T G C T G C T G C C A C T G C T G G G C C - - - A G C C C
FelisCatus	C T G C C G C T - - - - - - - - - - - - - - - G C T G C T C C T G G G C C - - - A G C C C
LeptonychotesWeddellii	C T G C T G C T G C C G C T G C T G C T G C T G A G G C T G C T T C T G G G C C - - - A G C C C
PantheraTigris	C T G C C G C T - - - - - - - - - - - - - - - G C T G C T C C T G G G C C - - - A G C C C
EptesicusFuscus	C T G C T G C T - - - - - - - - - - - - - - - G C C G C T G C T G A G C C - - - A G C C C
MyotisLucifugus	C T G C T G C T - - - - - - - - - - - - - - - G C C G C T G C T G A G C C - - - A G C C C
MyotisBrandtii	C T G C T G C T - - - - - - - - - - - - - - - G C C G C T G C T G A G C C - - - A G C C C
CeratheriumSimum	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G G G C C - - - A G C G G
EquusCaballus	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G C T G G G C C - - - A A C C G
OrcinusOrca	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G G T G G T A C - - - A G C C C
PhyseterCatodon	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G C T G G T C C - - - A G C C C
TursiopsTruncatus	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G G T G G T A C - - - A G C C C
BubalusBubalis	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G T C G A T C C - - - A G T C C
OvisAries	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G T C G A T C C - - - A G T C C
OtolemurGarrettii	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T G C T G G G T C - - - A G C C C
CallithrixJacchus	C T G C T G C T - - - - - - - - - - - - - - - G C T T C T C C T G G T C C - - - A G C C A
SaimiriBoliviensis	C T G C T G C T - - - - - - - - - - - - - - - G C T A C T C C T G G G C C - - - A G C C A
ChlorocebusSabaeus	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A G G C - - - A G C T C
MacacaFascicularis	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A G G C - - - A G C T C
HomoSapiens	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A C C C - - - A G C C C
NomascusLeucogenys	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A G C C - - - A G C C C
PanPaniscus	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A C C C - - - A G C C C
PanTrogodytes	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A C C C - - - A G C C C
PongoAbelii	C T G C T G C T - - - - - - - - - - - - - - - G C T G C T C C T G A G C C - - - A G C C C
ChrysochlorisAsiatica	C T A C C G C T - - - - - - - - - - - - - - - G C T G C T C C T G G G T C - - - G G C C T
EchinopsTelfairi	C T G C C G C T - - - - - - - - - - - - - - - G C C C T C C T G G C C C - - - G G C C G
DasypusNovemcinctus	C T G C T G C T - - - - - - - - - - - - - - - G C T G T T C C T G G G C C - - - A G G C T
TrichechusManatus	C T G C C G C T - - - - - - - - - - - - - - - G C T G C T T C T G G G C T - - - - - - -
SarcophilusHarrisii	C T G C T G C T C A G C C A - - - - - - - - - - - - - - - G A T G C T G T T C A G C C C C A A G G C C
MonodelphisDomestica	C T G C T A C T C A A C C A - - - - - - - - - - - - - - - G A T G C T C T T C A G C A C G A G G A G C

AiluropodaMelanoleuca	C A G G C G G G G C C G G C G C T C A C A G - - - - - G G A A G C C G T G - - - G T G T G C
UrsusMaritimus	C G G G C G G G G C C G G C G C T C A C A G - - - - - G G A A G C C G T G - - - G T G T G C
FelisCatus	T G G G C G G G G C T G G A G C T C C C G G - - - - - G G A A G C T G T G - - - G T G T G C
LeptonychotesWeddellii	T G G G C G G G G C C G G C G C T C A C A G - - - - - G G A A G C C G C G - - - G T G T G C
PantheraTigris	T G G G C G G G G C T G G A G C T C C C G G - - - - - G G A A G C T G T G - - - G T G T G C
EptesicusFuscus	T G G C T G G G G C T G G T G C T G A C A C - - - - - A C A G G C C G T G - - - G T G T G C
MyotisLucifugus	T G G C T G G G G C T G G C G C T G A C A C - - - - - A C A G G C A G T G - - - G T G T G C
MyotisBrandtii	T G G C T G G G G C T G G T G C T G A C A C - - - - - A C A G G C C G T G - - - G T G T G C
CeratotheriumSimum	T G G C T G G G G C C G G C G C T G A G A G - - - - - G G A G G C T G C G - - - G T C T G C
EquusCaballus	A G G G T G G G T G C C G G G G C T G A G A G - - - - - G A A G G C T G T G - - - G T C T G T
OrcinusOrca	T G G G C C G G G C T G T C G C T G C C A - - - - - G G A G G C C G T G - - - G T C T G C
PhyseterCatodon	T G C G C G G G G C T G C C G C T G C C C G - - - - - T G A G G C C G T G - - - G T C T G C
TursiopsTruncatus	T G G G C G G G G C T G C C G C T G C C A - - - - - G G A G G C C G T G - - - G T C T G C
BubalusBubalis	T G G G C A G A G A C A C C A C T G A C T G - - - - - G G A G G C T G T G - - - G T C T G C
OvisAries	C G G G C G G T G A A C A C C A T T G A C C A - - - - - G G A G G C T G T G - - - G T C T G C
OtolemurGarnettii	T G G G C C A C A G C T G G G G C C G C A T - - - - - G G A G G C T G T G - - - G T G T G C
CallithrixJacchus	G G G G C T G G A A C G G G A G C T G A C A C - - - - - G G A G G C G T G - - - G T C T G C
SaimiriBoliviensis	G G G G C T G G C A T G G G A G G T G A C A C - - - - - G G A G G C G G T G - - - G T C T G C
ChlorocebusSabaeus	G G G G C C G G G A C A G G A G C T G A C A C - - - - - G G A G G C G G T G - - - G T C T G C
MacacaFascicularis	G G G G C C G G G A C A G G A G C T G A C A C - - - - - A G A G G C G G T G - - - G T C T G C
HomoSapiens	G G G G C G G G G A C G G G A G C T G A C A C - - - - - G G A G G C G G T G - - - G T C T G C
NomascusLeucogenys	G G G G C C G G G A C G G G A G C T A A C A C - - - - - G G A G G C G G T G - - - G T C T G C
PanPaniscus	G G G G C G G G G A C G G G A G C T G A C A C - - - - - G G A G G C G G T G - - - G T C T G C
PanTrogodytes	G G G G C G G G G A C G G G A G C T G A C A C - - - - - G G A G G C G G T G - - - G T C T G C
PongoAbelii	G G G G C C G G G A C G G G A G C T G A C A C - - - - - A G A G G C G G T G - - - G T C T G C
ChrysochlorisAsiatica	G G A A C T G G G C C A G G C A G A G A G A G A C T T T A G G T G A G G C T G T G - - - G T G T G T
EchinopsTelfairi	G G A G T C C G G G C G G A C A G C - - - - - - - - - - - C G A G G C G G T G - - - G T G T G C
DasypusNovemcinctus	G G G G C C A A G G C G G C A G G - - - - - - - - - - - A G A G G C T G T G - - - G T C T G T
TrichechusManatus	- G G G C T G G C A C T G G T G C C G T G G C - - - - - - - - - - - C G A G G C C G T G - - - G T G T G T
SarcophilusHarrisii	T G G G C C A G G G C C A G C A A T G A G G A G G A G G A G G A G G C A G C C G C T G T G T G T
MonodelphisDomestica	T G G G C G G A G G C C A G C A A T G A G G A G G A G G A G G A G G C C G C G C T G T G T G T
AiluropodaMelanoleuca	G C G G G G A A C G C C T G C T A C A C G G C C C A C T G G G G C A G G C T G A G C G C T G C C
UrsusMaritimus	G C G G G G A A C G C C T G C T A C A C G G C C C A C T G G G G C A G G C T G A G C G C T G C C
FelisCatus	G C G G G G A A T G C C T G C T A C A C A G C C C A C T G G G G C A A G C T G A G T G C G G C C
LeptonychotesWeddellii	G C G G G C A G G G C C T G C T A C A C T G C G C A C T G G G G C A A G C T G A G T G C G G C C
PantheraTigris	G C G G G G A A T G C C T G C T A C A C A G C C C A C T G G G G C A A G C T G A G T G C G G C C
EptesicusFuscus	G C G G G C A C T G C C T G C T A C T C A G C C C A C T G G G G C A A G C T G C C T G C G G C C
MyotisLucifugus	G C G G G C A C T G C C T G C T A C T C G G C C C A C T G G G G C A A G C T T T C T G C C G C C
MyotisBrandtii	G C G G G C A C T G C C T G C T A C T C G G C C C A C T G G G G C A A G C T T T C T G C C G C C
CeratotheriumSimum	G C A G G G A C T G C C T G C T A C A C G G C C C A C T G G A A C A A G C T G A G T G C G G G C
EquusCaballus	G C G G G G A C C G C C T G C T A C A C G G C C C A C T G G G A C A A G C T G A C T G C G G C C
OrcinusOrca	G C G G G G G C T G C C T G C T A C A C A G C C C A C A G G G T C A A G C T G A G T G C G G A C
PhyseterCatodon	G C G G G G G C T G C C T G C T A C A C A G C C C A C A G G G T C A A G C T G A G T G C G G A C
TursiopsTruncatus	G C G G G G G C T G C C T G C T A C A C A G C C C A C A G G G T C A A G C T G A G T G C G G A C
BubalusBubalis	G C G G G G C T G C C T G C T A C A C G G C C C A C A G G C A C A A G C T G A G T G C G G A G
OvisAries	G C G G G G G C T G C C T G C T A C A C G G C C C A C A G G C G C A A G C T G A A T G C G G A G
OtolemurGarnettii	G C A G A C A C C G C C T G C T A C A C A G C C C A C T G G G G C A A G C T G A G C G C A G A T
CallithrixJacchus	G C G G G A T G G C C T G C T A C A C G G C C C A C T G G G G C A A G C T G A G C G C G C T
SaimiriBoliviensis	G C G G A G A T G G C C T G C T A C A C G G C C C A C T G G G G C A A G C T G A G C G C T G C C
ChlorocebusSabaeus	G C G G G G A C C G C C T G C T A T A C G G C C C A C T C G G G C A A G C T G A G C G C T G C C
MacacaFascicularis	G C G G G G A C C G C C T G C T A T A C G G C C C A C T G G G G C A A G C T G A G C G C T G C C
HomoSapiens	G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G C T G A G C G C T G C C
NomascusLeucogenys	G C G G G G A C T G C T T G C T A C A C T G C C C A C T C G G G C A A G C T G A G C G C T G C C
PanPaniscus	G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G C T G A G C G C T G C C
PanTrogodytes	G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G C T G A G C G C T G C C
PongoAbelii	G T G G G G A C C G C C T G C T A C A C G G C C C A C T C G G G C A A G C T G A G C G C T G C C
ChrysochlorisAsiatica	G C T G G G G A T G C C T G T T A T A C A G C T T A C T G G G G C A A G C T G A G T G C G G A T
EchinopsTelfairi	G C G G G C G C T G C C T G C T T A C G G C C C A C T G G G G C A A G C T G A G C G C C G A A
DasypusNovemcinctus	G C C G G G A A C G C C T G C T A C A C G G C C C A C T G G G G C A A G C T G A G T G C G G C C
TrichechusManatus	G C G G G G A C T G C C T G C T A C A C G G C C C A C T G G G G C A A G C T G A G T G C G G A C
SarcophilusHarrisii	G C T G G G A C T G C C T G C T A T A C T G C C C A C T G G G G C A A G A T C A G T G C C G C C
MonodelphisDomestica	G C T G G G A C T G C C T G C T A C A C G G C C C A C T G G G A C A A G C T C A G T G C C T C C

AiluropodaMelanoleuca	G A G G C C C A G C T T C A C T G C A G C A A G A A C G G G G C A A C C T G G C C A C G G T G
UrsusMaritimus	G A G G C C C A G C T T C A C T G C A G C A A G A A C G G G G C A A C C T G G C C A C G G T G
FelisCatus	G A G G C C C A G A G T C A C T G C A G C A A G A A T G G G G G C A A C C T G G C C A C C G T G
LeptonychotesWeddellii	G A G G C C C A G C T T C A C T G C A G C A G G A A C G G C G G C A A C C T G G C C A C G G T G
PantheraTigris	G A G G C C C A G A G T C A C T G C A G C A A G A A T G G G G G A A A C C T G G C C A C T G T G
EptesicusFuscus	G A G G C C C A G C T T C T C T G C A A C A A G A A T G G G G G C A A C C T G G C C A C A G T G
MyotisLucifugus	G A G G C C C A G C A T C T C T G C A G C A A G G A C G G G G G C A A C C T G G C C A C G G T G
MyotisBrandtii	G A G G C C C A G C T T C T C T G C A G C A A G G A C G G G G G C A A C C T G G C C A C A G T G
CeratheriumSimum	G A G G C C C A G A A T C A T T G C A G C A G G A A C G G G G G C A A C C T G G C C A C G G T G
EquusCaballus	G A G G C C C A A T C T C A C T G C A G C A A G A A C G G G G G T A A C C T G G C C A C G G T G
OrcinusOrca	G A C G C C C A G C T C C G C T G C A G C A A G A A A G G G G G C A A C C T G G C C A C G G T G
PhyseterCatodon	G A T G C C C A G C T C C A G T G C A G C A A G A A A G G G G G T G A C C T G G C C A C A G T G
TursiopsTruncatus	G A C G C C C A G C T C C G C T G C A G C A A G A A A G G G G G C A A C C T G G C C A C G G T G
BubalusBubalis	G A T G C C C A G C T C C A T T G C A G C A A G A A A G G G G G C A A T C T G G C C A C G G T A
OvisAries	G A T G C C C A G C T C C A T T G C A G C A A G A A A G G G G G C A A T C T G G C C A C G G T G
OtolemurGarnettii	G A G G C C C A G C A G C A C T G C A G C A A G A A C G G G G G C A A G C T G A C C A C A G T G
CallithrixJacchus	G A T G C C C A G A A C C A C T G C A G C A A G A A C G G G G G C A A C C T G G C C A C G T G
SaimiriBoliviensis	G A G G C C C A G A G C C A C T G C A G C C A G A A T G G G G G C A A C C T G G C C A C T G T G
ChlorocebusSabaeus	G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C C T G G C C A C T G T G
MacacaFascicularis	G A G G C C C A G A A C C T C T G C C T C C A G A A C G G G G G C A A C C T G G C C A C T G T G
HomoSapiens	G A G G C C C A G A A C C A C T G C A A C C A G A A C G G G G G C A A C C T G G C C A C T G T G
NomascusLeucogenys	G A G G C C C A G A A C C A C T G C A G C C A G A A C G G G G G C A A C C T G G C C A C T G T G
PanPaniscus	G A G G C T C A G A A C C A C T G C A A C C A G A A C G G G G G C A A C C T G G C C A C T G T G
PanTrogodytes	G A G G C C C A G A A C C A C T G C A A C C A G A A C G G G G G C A A C C T G G C C A C T G T G
PongoAbelii	G A G G C C C A G A A C C A C T G C A G C C A G A A C G G C G G C A A C C T G G C C A C T G T G
ChrysochlorisAsiatica	G A G G C C C A G C T C A A C T G C A G T G C T A A T G G A G G C A A C C T G G C C A C A G T G
EchinopsTelfairi	G A G G C C C A A C T C A C T G C A G C A C C A A C G G G G G A A C C T G G C C A C C G T G
DasypusNovemcinctus	C A G G C C C A G C A G A G C T G C A G C C A A T G G G G G C A A C C T G G C C A C G G T G
TrichechusManatus	C A G G C C C A G G T T A A C T G C A G C A C C A A C G G A G G C A A C C T G G C C A C A G T G
SarcophilusHarrisii	G A G G C C C A G C T C A A C T G C A G T A C C A A T G G G G G A A A C C T G G C C A C A G T A
MonodelphisDomestica	G A G G C C C A G C T C A G C T G C A G T A C C A A T G G G G G A A A C C T G G C C A C C G T A
AiluropodaMelanoleuca	A G G A G T G A G G A G G A G G C C T G G C A C A T C C A G C A A G C T C T C A C C C A A C T C
UrsusMaritimus	A G G A G T G A G G A G G A G G C C T G G C A C A T C C A G C A G C C C T C A C C C A A C T C
FelisCatus	A A G A G T G A A G A G G A G G C T T G G C A C A T C C A G C G A G C C C T G G C C A C G C T C
LeptonychotesWeddellii	A G G A G T G A G G A G G A G G C C C G G C A C A C C C A G C G A G C C C T C A C C C A G C T C
PantheraTigris	A A G A G T G A A G A G G A G G C C T G G A A C A T C C A G C G A G C C C T G G C C A G C T C
EptesicusFuscus	A G G A C T G A G G A G G A G G C C C A G C A C A T C C A G C G A G C A C T G G C C A C G C T C
MyotisLucifugus	A G G A C C G A G G A G G A G G C C C G G C A C A T C C A C C G A G C A C T G G C C C A G C T C
MyotisBrandtii	A G G A C T G A G G A G G A G G C C C G G C A C A T C C A G C G A G C A C T G G C C C A G C T C
CeratheriumSimum	A A G A C T G A G G A G G A G G C C C G G C A C G T C C A G C G A G C C C T G G C C C A G C T C
EquusCaballus	A A G A C T G A G G A G G A G G C C C G G C T C A T C C A G C G A G C C C T G G C C C A G C T C
OrcinusOrca	A A G A G C G A G G A G G A G G C C C T G C A C G T C C A G G G T G C C C T G G C C C A G C T C
PhyseterCatodon	A A G A G C G A G G A G G A G G C C C T G T A C G T C C A G C G C G C C C T G G C C C A G C T C
TursiopsTruncatus	A A G A G C G A G G A G G A G G C C C T G C A C G T C C A G G G C G C C C T G G C C C A G C T C
BubalusBubalis	A A G A G T G A G G A G G A G G C C C G G C A C A T C C A G G G T G C C C T G A G C A G C T C
OvisAries	A A G A G T G A G G A G G A G G C C C G G C A C A T C C A G G G C G C C C T G A C C C A G C T C
OtolemurGarnettii	A A G A G C G A G G A G G A G G C C C G G C A T G T T C A G C G A A C C C T G G C C C A G C T C
CallithrixJacchus	A A G A G C A A G G A G G A G G C C C A G C A C A T C C A G C G A G C C C T G G C C C A G C T C
SaimiriBoliviensis	A A G A G C C G G G A G G A G G C C C A G C A C A T C C A G C G A G C C C T G G C C C A G C T C
ChlorocebusSabaeus	A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A C T G G C C C A A C T C
MacacaFascicularis	A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C A G T A C T G G C C C A A C T C
HomoSapiens	A A G A G C A A G G A G G A G G C C C A G C A C G T C C A G C G A G T A C T G G C C C A G C T C
NomascusLeucogenys	A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A C T G G C C C A G C T C
PanPaniscus	A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A C T G G C C C A G C T C
PanTrogodytes	A A G A G C G A G G A G G A G G C C C A G C A C G T C C A G C G A G T A C T G G C C C A G C T C
PongoAbelii	A A G A G C G A G G A G G A G G C C C A G G A T G T C C A G C G A G T A C T G G C C C A G C T C
ChrysochlorisAsiatica	A G A A A T G C A G A G G A G G C A C G G T A C A T C C A G G A G G T C C T A G T C C A G C T T
EchinopsTelfairi	C G G A G C G C C G A G G A G G C C C G A T A C A T T C A G G A G G C C C T A G C C C A A C T G
DasypusNovemcinctus	A A G T C G G A G G A G G A G G C T C G G C A C A T C C A G G A A G C C C T G G C C C A G C T G
TrichechusManatus	A G G A G C G C T G A G G A G G C C C A G C G T G T C C A G C A G G C C C T A G C C C A G C T T
SarcophilusHarrisii	A A A A G C G A A G A A G A A G C C C A G C A T A T C C A A G A A G T C C T G A C C C A G C T G
MonodelphisDomestica	A A G A A T G A A G A A G A G G C C C A G C A C A T C C A A G A A G C C C T G G C C C A G C T G

AiluropodaMelanoleuca C T G G A G T C A G A G G T G A C C A T G G C A G G T T G G G T G G G C A A G T T C T G G A T C
 UrsusMaritimus C T G G A G T C A G A G G T G A C C C T G G C A A C T T G G G T G G G C A A G T T C T G G A T C
 FelisCatus T T G G A G T T G G A G G A G G C C C T A G A A G C T C G G A T G G G C A A G T T C T G G A T C
 LeptonychotesWeddellii C T G G A G T C G G A G G C G C C C T G G C A G C T C G G A T G G G C A A G T T C T G G A T C
 PantheraTigris T T G G A G T T G G A G G A G G C C C T A G A A G C T C G G A T G G G C A A G T T C T G G A T C
 EptesicusFuscus C T A C A G C C T G G G G C G C C - - - - - T G G A C A G G C A A G T T C T G G A T A
 MyotisLucifugus C T A C A G C C T G G G G C G C C - - - - - T G G A C A G G C A A G T T C T G G A T A
 MyotisBrandtii C T A C A G C C T G G G G C G C C - - - - - T G G A C A G G C A A G T T C T G G A T A
 CeratotheriumSimum C T A C A G C T G G A G G C A C C C C A G C A G C T C G G A C A G G C A A G T T C T G G A T C
 EquusCaballus C T C C A G C T G G A G G C G C C C C T G G T A A C T C G G A T G G G C A A G T T C T G G A T G
 OrcinusOrca C T G C C A C C G G G G G C G C C C T G A C A G A G C G C A T G G G C A G G T T C T G G A T T
 PhyseterCatodon C T G C C A C C A G G G G C G C C C C T G G C A G A G C G C A T G G G C A G G T T C T G G A T T
 TursiopsTruncatus C T G C C A C C G G G G G C G C C C C T G A C G G A G C G C A T G G G C A G G T T C T G G A T T
 BubalusBubalis C T G C T G C T G G G G G C G C C C C T G C A A G A A C G C C G - - - A A A T T C T G G A T T
 OvisAries C T G C T G C T G G G G G C G C C C C T G C C A G A A C G C C A G A A C A A A T T C T G G A T T
 OotemurGarnettii C T G A G C C T G C A G G C A T C C C T G G C T G C G A G G A T G G G C A A G T T C T G G A T T
 CallithrixJacchus C T G A G C C T G A G G C A A A C C T G A C G G C G A G G A T G G G C A A G T T C T G G A T T
 SaimiriBoliviensis C T G A G G C T G G A G G C G A A C C T G A C G G C G A G G A T G G G C A A G T T C T G G A T C
 ChlorocebusSabaeus C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C A A G T T C T G G A T T
 MacacaFascicularis C T G A G G C G G G A G G C A G C C C T G A C G G C A A G G A T G G G C A A G T T C T G G A T T
 HomoSapiens C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G A G C A A G T T C T G G A T T
 NomascusLeucogenys C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C A A G T T C T G G A T T
 PanPaniscus C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C A A G T T C T G G A T T
 PanTroglodytes C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T A G G C A A G T T C T G G A T T
 PongoAbelii C T G A G G C G G G A G G C A G C C C T G A C G G C G A G G A T G G G C A A G T T C T G G A T T
 ChrysochlorisAsiatica C T G C A G C C G A G G T A C A G C T A A C T G C G C G C A T G G G C A A G T T C T G G A T T
 EchinopsTelfairi C T T C T G C C G G A G G C C G C G C T G A C T G C C C G C A T G G G C A A G T T C T G G A T C
 DasypusNovemcinctus C T G C G G C C C A G G A C C C A C A G C T G C C C G G A T G G G C A A G T T C T G G A T C
 TrichechusManatus C T T C G A C C C G A G G C A C C A C T G A C T A C A C G C A C A G G C A A G T T C T G G A T T
 SarcophilusHarrisii C C T G A G A A G G G G G C C T C - - - - - A G C C C G G A C A G T C A A A T T C T G G A T T
 MonodelphisDomestica C C T G A C A G G G A G G C C C - - - - - A G G C C G G A C G G T C A A A T T C T G G A T T

AiluropodaMelanoleuca G G G C T C C A G C G C G A G A A G G G C A A G T G C T T A G A C C C C A G C T T G C C G C T G
 UrsusMaritimus G G G C T C C A G C G T G A G A A G G G C A A G T G C T T A G A C C C C A G C T T G C C G C T G
 FelisCatus G G G C T C A G C G C G A A A A G G G C A A A G T G C T T A G A C T C C A G C T T G C C G C T G
 LeptonychotesWeddellii G G G C T C C A G C G C G A G A A G G C C A A G T G C T T G G A C C C C A G C C T G C C G C T G
 PantheraTigris G G G C T C C A G C G C G A A A A G G C A A A G T G C T T A G A C T C C A G C T T G C C G C T G
 EptesicusFuscus G G A C T C C A G C G A G A A A G A G C A A G T G C T T G G A C C C C A G T T C T G C C T C G
 MyotisLucifugus G G A C T C C A G C G A G A A A G G G C A A G T G C T T G G A C C C C A G G C T G C C C C T G
 MyotisBrandtii G G A C T C C A G C G A G A A A G G G C A A G T G C T T G G A C C C C A G G C T G C C C C T G
 CeratotheriumSimum G G G C T C C A G C G A G A G A A G G G C A A G T G C T T G G A C C C C A G C C T G C C G C T G
 EquusCaballus G G G C T C C A G C G A G A G A A G G G C A A G T G C T T G G A C A G C A C C C T G C C G C T G
 OrcinusOrca G G G C T C C A G A G A G A C A A G G G C A A G T G C C T G G A C A G C A G C C T G C C C C T G
 PhyseterCatodon G G G C T C C A G C G A G A C A A G G G C A A G T G C C T G G A C A G C A A C C T G C C C C T G
 TursiopsTruncatus G G G C T C C A G C G A G A C A A G G G C A A G T G C C T G G A C A G C A G C C T G C C C C T G
 BubalusBubalis G G G C T C C A G C G A G A G A A A G G C A C T T G C T C G G A C A G C A G C C T A C C C C T G
 OvisAries G G G C T C C A G C G A G A G A A G G G C A A T T G C T C G G A C A G C A G C C T A C C C C T G
 OotemurGarnettii G G G C T C C A G C G A G A G A A G G G C A A T G C C A G G A C C C C A G G C T G C C G C T G
 CallithrixJacchus G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C A G C C T G C C A C T G
 SaimiriBoliviensis G G G C T C C A G C G A G A G A A G G G G A A G T G C C T G G A C C C C A G C C T G C C G C T G
 ChlorocebusSabaeus G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C A G T C T G C C G C T G
 MacacaFascicularis G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C A G T C T G C C G C T G
 HomoSapiens G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C C T A G T C T G C C G C T G
 NomascusLeucogenys G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T A G T C T G C C G C T G
 PanPaniscus G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T A G T C T G C C G C T G
 PanTroglodytes G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T A G T C T G C C G C T G
 PongoAbelii G G G C T C C A G C G A G A G A A G G G C A A G T G C C T G G A C C C T A G T C T G C C G C T G
 ChrysochlorisAsiatica G G G T T G C A G C G C G A G A A G A G C A A G T G C C T G G A T C C C A G C C T G C C C C T G
 EchinopsTelfairi G G T T T G C A G C G G A A A A G G C A A G T G C C T G G A C G C C A C C T G C C C C T G
 DasypusNovemcinctus G G G C T G C A G C G T G A G A A G G G C A A G T G C T T G G A C C C C A A C C T G C C G C T G
 TrichechusManatus G G G C T C C A G C G G G A C A A G G G C A A G T G C C T G G A C A G C A A C C T G C C G C T G
 SarcophilusHarrisii G G G C T T C A A C G G G A A A G A G T A A G T G C A T G G A C C G T G A T G A C C C A C T G
 MonodelphisDomestica G G G C T T C A G A G G G A A A A G G G C A A G T G T A T G A A C C C T G A T G A A G C G C T G

AiluropodaMelanoleuca	A A A G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G C T T T A C A C C
UrsusMaritimus	A A A G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G C T T T A C A C C
FelisCatus	A A A G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C A C T T T A C A C C
LeptonychotesWeddellii	A A A G G C T T C A G C T G G G T - - - G G G C G G T G G G G A G G A C A C G C T T T A C A C C
PantheraTigris	A A A G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C A C T T T A C A C C
EptesicusFuscus	A A G G G C T T C A G C T G G G T - - - G G G C G G T G G G G A G G A C A C G C T T T A T T C C
MyotisLucifugus	A A G G G C T T C A G C T G G G T - - - G G G C G G T G G G G A G G A C A C A C T G T A T T C C
MyotisBrandtii	A A G G G C T T C A G C T G G G T - - - G G G C G G T G G G G A G G A C A C A C T G T A T T C C
CeratotheriumSimum	A A G G G C T T C A G C T G G A T - - - G G G C G G T G G G G A G A C A C G T C T T A C G C C
EquusCaballus	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G A A C A C G T C C T A T G C C
OrcinusOrca	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G T C G T A T A C C
PhyseterCatodon	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G T C G T A T A C C
TursiopsTruncatus	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G T C G T A T A C C
BubalusBubalis	A A G G G C T T C A G C T G G C T - - - G G G C G A T G G G G A G G A C T C G C A G T A C A A C
OvisAries	A A A G G C T T C A G C T G G C T - - - G G G C G A T G G G G A G G C C T C G C A G T A C A A C
OtolemurGarrettii	A A G G G C T T C A G C T G G G T - - - G G G T G G C G G G G A G G A C A C G C T C T A C A C C
CallithrixJacchus	A A G G G C T T C A G C T G G G T - - - G G G T G G C G G T G A G G A C A C G C C T T A C A C T
SaimiriBoliviensis	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G C C T T A C G C G
ChlorocebusSabaeus	A A G G G C T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G C C T T A C T C T
MacacaFascicularis	A A G G G C T T C A G C T G G G T - - - G G G C G G T G G G G A G G A C A C G C C T T A C T C T
HomoSapiens	A A G G G C T T C A G C T G G G T - - - G G G C G G G G G G G A G G A C A C G C C T T A C T C T
NomascusLeucogenys	A A G G G C T T C A G C T G G G T - - - G G G C G G G G G G G A G G A C A C G C C T T A C T C T
PanPaniscus	A A G G G C T T C A G C T G G G T - - - G G G C G G G G G G G A G G A C A C G C C T T A C T C T
PanTrogodytes	A A G G G C T T C A G C T G G G T - - - G G G C G G G G G G G A G G A C A C G C C T T A C T C T
PongoAbelii	A A G G G C T T C A G C T G G G T - - - G G G C G G G G G G G A G G A C A C G C C T T A C T C T
ChrysochlorisAsiatica	A A G G G C T T C A G C T G G A T T G G T G G T G G C G G G G G A G G A C A C A C A C A C T A C T C T
EchinopsTelfairi	A A G G G T T T C A G C T G G A T - - - C G G T G G C G G G G A G A C A C A C G T C G T A C A C C
DasypusNovemcinctus	A A G G G T T T C A G C T G G G T - - - G G G C G G C G G G G A G G A C A C G C T G T A C T C A
TrichechusManatus	A A G G G C T T C A G C T G G A T - - - T G G T G G T G G G G G C G A C A C A C C G T A C A C C
SarcophilusHarrisii	A A G G G C T T C A G C T G G G T - - - G G G A G G T G G T G A G A A C A C T T T C T T A C T C C
MonodelphisDomestica	A A G G G C T T C A G C T G G G T - - - G G G A G G T G C T G A G A A T A C A T C T T A C T C C
AiluropodaMelanoleuca	A A C T G G A A C A A G G A G G T C A G G A G C T C T T G T A T C T C C A G G C G C T G C G T G
UrsusMaritimus	A A C T G G A A C A A G G A G G T C A G G A G C T C T T G T A T C T C C A G G C G C T G C G T G
FelisCatus	A A C T G G A A C A G G A G G T C A G G A G C T C C T G C A T C T C T A G G C G C T G C G T A
LeptonychotesWeddellii	A A C T G G A A C A A G G A G G T C A G G A G C T C T T G C A T C T C C A G G C G C T G T G T G
PantheraTigris	A A C T G G A A C A G G A G G T C A G G A G C T C C T G C G T C T C T A G G C G C T G T G T A
EptesicusFuscus	A A T T G G T A C A A G G A G C C A G G A C A C A C T T G C A T C T C C A A G C G C T G T G C G
MyotisLucifugus	A A C T G G T A C A A G G A G G C A G G C A C A C T T G C A T C T C C A A G C G C T G T G T G
MyotisBrandtii	A A C T G G T A C A A G G A G G C A G G C A C A C T T G C A T C T C C A A G C G C T G T G T G
CeratotheriumSimum	A A C T G G T A C A A G G A G C T C A A G C A C T C G T G C A T C T C C A A G C G C T G T G T G
EquusCaballus	A A C T G G T A C A A G G A G C C A A G A A C A G C T G C A C C T T C A G G C G C T G T G T G
OrcinusOrca	A A C T G G C A C A A G G A G G C A A A G A A C T C T T G C A C C T C C A A G C G C T G C G T G
PhyseterCatodon	A A C T G G C A C A A G G A A G C A A G A A C T C T T G C A C C T C C A A G C G C T G C G T G
TursiopsTruncatus	A A C T G G C A C A A G G A G C C A A G A A C T C T T G C A C C T C C A A G C G C T G C G T G
BubalusBubalis	A A C T G G T A C A A A G A A G T T A G G A A C A C C T G T A C C C A A G G C G C T G C G T G
OvisAries	A A C T G G T A C A A A G A G G T T A A G A A C A C C T G C A T T C A G A G G C G C T G C G T G
OtolemurGarrettii	A A C T G G C A C A A G G A G G C C C G C A A C T C A T G C A T C T C C A A G C G C T G T G T G
CallithrixJacchus	A A C T G G T A C A A G G A G C T C C G C A A C T C G T G C A T C T C C A A G C G C T G T G T G
SaimiriBoliviensis	A A C T G G T A C A A G G A G C T C C G C A G C T C G T G C G T C T C C A A G C G C T G T G T G
ChlorocebusSabaeus	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
MacacaFascicularis	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
HomoSapiens	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
NomascusLeucogenys	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
PanPaniscus	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
PanTrogodytes	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
PongoAbelii	A A C T G G C A C A A G G A G C T C C G G A A C T C G T G C A T C T C C A A G C G C T G T G T G
ChrysochlorisAsiatica	A A C T G G C A C A A A G A G C T C A A G A A C A C G T G C G T C T C C A A G C G A T G T G T C
EchinopsTelfairi	A A C T G G T A C A A G G A G C C A A G G G C A C C T G C A T C T C C A A G C G C T G C G T G
DasypusNovemcinctus	A A C T G G T A C A A G G A G G C A A G G G C A C G T G C A T C T C C A A G C G C T G C G T G
TrichechusManatus	A A C T G G C A A A A G G A G C C A A G A A C A C G T G C A T C T C C A A A C G C T G C G T G
SarcophilusHarrisii	A A T T G G C A C A A G G A G C C A T G A G C A C A T G T C T C T T C A A G C G C T G T G C C
MonodelphisDomestica	A A C T G G C A G A A G G A G C C A T G A G C A C G T G C A T C T C C A A G C G C T G C G C T

AiluropodaMelanoleuca	T C C C T G C T G C T G T A T C T G T C C C A G C C G T C - - - C C A A G C C - - - A G C C A T
UrsusMaritimus	T C C C T G C T G C T G T A T C T G T C C C A G C C A T C - - - C C A T G C C - - - A G C C A T
FelisCatus	T C C C T G C T G C T C T A T C T G T C T C T G C C G T C - - - T C A T G C C - - - A G C C A C
LeptonychotesWeddellii	T C C C T G C T G C T C T A T C T G T C C C A G C C G T C - - - C C A T G C C - - - A G C C A C
PantheraTigris	T C C C T G C T G C T C T A T C T G T C T C T G C C G T C - - - T C A T G C C - - - A G C C A C
EptesicusFuscus	T C C C T G A T G C T G G A C C C G T C C C T C T C T T C - - - C C T C T C C - - - A G C C A C
MyotisLucifugus	T C C C T G A T G C T G G A C C C G T C C G T C T C T T C - - - C C T C T C C - - - A G C C A C
MyotisBrandtii	T C C C T G A T G C T G G A C C C G T C C G T C T C T T C - - - C C T C T C C - - - A G C C A C
CeratotheriumSimum	T C C C T G G T G C T G G A C C T G T C C C T G A C A C C - - - T C T C A C C - - - G G C C A C
EquusCaballus	T C G C T G G T G C T G G A C C T G T C C C T G C C T C C - - - C C T C G C C - - - A G C C A C
OrcinusOrca	T C T C T G A T G C T G G A C C T G T C C G C G C G C G G C - - - C C T G G C T - - - A G C C G C
PhyseterCatodon	T C C C T G A T G C T G G A C C T G T C C C T G C C G C G G C - - - C C T G G C C - - - A A C C G C
TursiopsTruncatus	T C T C T G A T G C T G G A C C T G T C C C A G C C G G C - - - C C T G G C T - - - A G C C G C
BubalusBubalis	T C C C T G A T T C T G G A C C T G T C T G T G C C G G G - - - C C T G G C C - - - A G C A G C
OvisAries	T C C C T G A T T C T G G A C C T G T C T G T G C C G G G - - - C C T G G C C - - - A G C A G C
OtolemurGarnettii	T C C C T G C T G C T G G A C C T G T C C C T G A C A C C - - - C A C A C C - - - A G C C G C
CallithrixJacchus	T C T C T G C T G C T G G A C C T G T C C C A G C C T C T - - - T C T T T C C - - - A G C T A C
SaimiriBoliviensis	T C T C T G C T G C T G G A C C T G T C C C A G C C T C T - - - C C T T T C C - - - A G C C A C
ChlorocebusSabaeus	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G G C G C
MacacaFascicularis	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - G G G C G C
HomoSapiens	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G C C G C
NomascusLeucogenys	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G C C G C
PanPaniscus	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G C C G C
PanTrogodytes	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G C C G C
PongoAbelii	T C T C T G C T G C T G G A C C T G T C C C A G C C G C T - - - C C T T C C C - - - A G C C G C
ChrysochlorisAsiatica	T C C C T G A T G C T T G A C C T G T C C T T G C C A C A - - - C C T C A C C - - - A A C C A G
EchinopsTelfairi	T C C C T G G C G C T T G A C C T T T C C C T C C T G C C A A G C C G C A C C - - - A G C C A C
DasypusNovemcinctus	G C C C T C T T G C T C G A C C T G T C C T T G C A G T C - - - C C T C C C C - - - A G C C A C
TrichechusManatus	T C C C T G C T G C T T G A C C T G T C C C T G T C G C C - - - C C C C A C C - - - G G C C G C
SarcophilusHarrisii	T C C C T C C T T T T G G A T C T T T C T T C T C C T G C - - - T T C T G C C - - - - - C A C
MonodelphisDomestica	T C G C T C T C C G T G G A T C T T T C T G C A T C C T C - - - T C T T G C C G C G G C C C A C
AiluropodaMelanoleuca	C - - - T G C C C A A G T G G T C T G A G A G C C C C T G C G G G A G C C C G A C C T C T C C G
UrsusMaritimus	C - - - T G C C C A A G T G G T C T G A G A G C C C C T G C G G G A G C C C G A C C T C T C C G
FelisCatus	C - - - T C C -
LeptonychotesWeddellii	C - - - T C C C C A A G T G G T C C G A G G G C C C C T G C G G G A G C C C G G G C T C T C C G
PantheraTigris	C - - - T C T C C A A A T G G T C T G A G G G C C C C T G T G G G A C C C C A A A C T C T C C T
EptesicusFuscus	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G A A A C C C A G G C T C T C C T
MyotisLucifugus	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C G G G C G C T C C T
MyotisBrandtii	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C T G G G C G C T C C T
CeratotheriumSimum	C - - - T C C C A A A G T G G G C T G A G G G C C C C T G T G G G A G C C C A G C T C T C C T
EquusCaballus	C - - - T C C C C A A G T G G G C C G A G G G C C C C T G T G G G A A C C C C G G C T T T T C T
OrcinusOrca	C - - - T T T C C A A G T G G A C C G A G G G T C C G T G T G G G A G C T C C A A G T T T T C T
PhyseterCatodon	C - - - T T T C C A A G T G G A C C G A G G G T C C G T G T G G G A A C T C C A G G T T T T C T
TursiopsTruncatus	C - - - T T T C C A A G T G G A C C G A G G G T C C G T G T G G G A G C T C C A A G T T T T C T
BubalusBubalis	C - - - T C T C C A A G T G G T C G A T G G T C C T T G T G G G C A C T C C G G T T T T C C T
OvisAries	C - - - T C T C C A A G T G G G T C G A T G G T C C T T G T G G G C A A T C C G G G T T T C C T
OtolemurGarnettii	C - - - T C C C T A A G T G G T C T G A A G G C C C C T G T G G G A A C C C T G T C T C T C C C
CallithrixJacchus	C - - - T C C C C A G G T G G T C C G A G G G C C C C T G T G G G A G C T C A G A C T C C C C T
SaimiriBoliviensis	C - - - T C C C C A A G T G G T C C G A A G G C C C C T G T G G G A G C T C A G A C T C C C C C
ChlorocebusSabaeus	C - - - T C C C G A A G T G G T C G G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C
MacacaFascicularis	C - - - T C C C G A A G T G G T C C G A A G G C C C C T G T G G G A G C C C A G G C T C C C C C
HomoSapiens	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
NomascusLeucogenys	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G C G G G A G C C C A G G C T C C C C T
PanPaniscus	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
PanTrogodytes	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A G G C T C C C C C
PongoAbelii	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G T G G G A G C C C A A G C T C C C C C
ChrysochlorisAsiatica	C - - - T C C C C A A G T G G T C T G A G G G C C C C T G C G G A A G C C A T G G C T C C C C A
EchinopsTelfairi	C - - - T C C C C A C T T G G T C T G A G G G C C C C T G C G G G A A C T C T G G C T C C C C G
DasypusNovemcinctus	C - - - T C C C C A A G T G G T C C G A G G G C C C C T G T G G G A G T C C C A A C T C C C C A
TrichechusManatus	C - - - T C T C C A A G T G G G C T G A G G G C C C C T G C G G G A G C C C T A A C T C C C C G
SarcophilusHarrisii	T C A G T C C C C A A A T G G T C A G A A A G T C C C T G T G G C A C C C C A G G C T C A C C A
MonodelphisDomestica	T C G G T C C C C A A G T G G A C A G A A A G C C C G T G C G G C A C A A C A G A T T C G C C A

AiluropodaMelanoleuca G G A A G C A A A A T C G A G G G C T T C G T G T G C A A G T T C A G T T T C A A A G G C A T G
 UrsusMaritimus G G A A G C A A A A T C G A G G G C T T C G T G T G C A A G T T C A G T T T C A A A G G C A T G
 FelisCatus - - - - - G C A T G
 LeptonychotesWeddellii G G A A G C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G T T T C A A A G G C A T G
 PantheraTigris G G A A G C A A C A T C G A G G G C T T T G T G T G C A A G T T C A G T T T C A A A G G C A T G
 EptesicusFuscus G T A A G C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 MyotisLucifugus G T A A A C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 MyotisBrandtii G T A A A C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 CeratotheriumSimum G G A A G C A A C A T C G A G G G C T T T G T G T G C A A G T T C A G C T T C A A A G G C A T G
 EquusCaballus G T A A A C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 OrcinusOrca G G G A G C A G C A T C G A G G G C T T T G T G T G C A A G T T C A G C T T C A A A G G C A T G
 PhylseterCatodon G G G A G C A A T A T C G A G G G C T T T G T G T G C A A G T T C A G C T T C A A A G G C A T G
 TursiopsTruncatus G G G A G C A G C A T C G A G G G C T T T G T G T G C A A G T T C A G C T T C A A A G G C A T G
 BubalusBubalis G G G A T G A A C A T C G A G G G C T T T G T G T G C A A G T T C A G T T T C A A A G G C A T G
 OvisAries G A G A G C A A C A T C G A G G G C T T T G T G T G C A A G T T C A G C T T C A A A G G C A T G
 OtlemurGarneittii G G A A G T A A C A T C G A G G G C T T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 CallithrixJacchus G G A A A T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 SaimiriBoliviensis G G A A A T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 ChlorocebusSabaenus G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G
 MacacaFascicularis G G A A G T A A C A T C G A G G G C T T C G T G T G C A A A T T C A G C T T C A A A G G C A T G
 HomoSapiens G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 NomascusLeucogenys G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 PanPaniscus G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 PanTrogodytes G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 PongoAbelii G G A A G T A A C A T T G A G G G C T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 ChrysochlorisAsiatica G G A A G C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G T T C A A A G G C A T G
 EchinopsTelfairii G G A A G C A A C A T C G A G G G C T T C G T G T G T A A A T T C A G C T T T C G A G G T A T G
 DasyplusNovemcinctus G G G A G C A A C G T G G A G G G T T T C G T G T G C A A G T T C A G C T T C A A A G G C A T G
 TrichechusManatus G G A A G C A A C A T C G A G G G C T T C G T G T G C A A G T T C A G C T T C G A A G G C A T G
 SarcophilusHarrisii G T G A G G A A C A T T G A G G G T A T G T G T G C A A G T T C A G T T T C A A A G G T A T G
 MonodelphisDomestica G G C A G G A A C A T T G A G G G C T A C G T G T G C A A G T T C A G T T T C A A A G G T A T G

AiluropodaMelanoleuca T G C C A G C C T C T G G C T C T G G G G G G C C C A G G C T G G G T G A A C T A C A C G A C C
 UrsusMaritimus T G C C A G C C T C T G G C T C T G G G G G G C C C A G G C T G G G T G A A C T A C A C G A C C
 FelisCatus T G C C A G C C T C T G G C T C T G G G G G G C C C A G G C C G G T G G A A C T A C A G G A C C
 LeptonychotesWeddellii T G C C A G C C T C T G G C T C T G G G G G G C C C A G G C C G G T G A A C T A C A C G A C C
 PantheraTigris T G C C A G C C T C T G G C T C T G G G G G G C C C A G G C C G G T G G A A C T A C A G G A C C
 EptesicusFuscus T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A A C T A C C A C C
 MyotisLucifugus T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A A C T A C A C C A C T
 MyotisBrandtii T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A A C T A C A C C A C T
 CeratotheriumSimum T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A T G T G A A C T A T A C C A C C
 EquusCaballus T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A A C T A T A C C A C C
 OrcinusOrca T G C T G G C C G C T G A C C C T G G G G G G C C C G G G C C A G G T G A A T T A C A C C A C T
 PhylseterCatodon T G C C G G C C G C T G A C C C T G G G G G G C C C G G G C C A G G T G A A T T A C A C C A C C
 TursiopsTruncatus T G C T G G C C G T G A C C C T G G G G G G C C C G G G C C A G G T G A A T T A C A C C A C C
 BubalusBubalis T G C C G G C C G C T G A C C C T G G G G G G C C C G G G T C A G G T G A A C T A C A C G A C C
 OvisAries T G C C G G C C G C T G A C C C T G A G G G G C C C G G G T C A G G T G A A C T A C A C G A C C
 OtlemurGarneittii T G C C G A C C C T G G C T C T G G G G G G C C C A G G C A A G G T G A C C T A T T C C A C T
 CallithrixJacchus T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A C C T A C A C C A C C
 SaimiriBoliviensis T G C C G G C C C T G G C C T G G G G G G C C C A G G C C A G G T G A C C T A C A C C A C C
 ChlorocebusSabaenus T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 MacacaFascicularis T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 HomoSapiens T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 NomascusLeucogenys T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 PanPaniscus T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 PanTrogodytes T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 PongoAbelii T G C C G G C C T C T G G C C T G G G G G G C C C A G G T C A G G T G A C C T A C A C C A C C
 ChrysochlorisAsiatica T G C C A G C C C T T A G C C T G G G A G G T C C A G G C C A G G T T A C C T A C A C C A C T
 EchinopsTelfairii T G C C G G C C C T G G C T C T A G G A G G G C C A G G C C A G A T T A G C T A C A C C A C C
 DasyplusNovemcinctus T G T C G G C C C T G G T C T G G G G G G C C C A G G T C A G G T G A C C T A T A C C A C C
 TrichechusManatus T G C C G G C C C T T G C C T G G G G G G T C C A G G C C A G G T T A C C T A C A C C A C C
 SarcophilusHarrisii T G C C A C C C T G T G G C T C T T G G G G G G C C A G G T G A G G T G A C T T A C A C A A C G
 MonodelphisDomestica T G C C A C C C T G T G G C T C T C G G G G G T C C A G G T G A G G T G A C C T A C A C A C A

AiluropodaMelanoleuca C C G T T C A A T G C C A C C A G C T C T T C C C T G G A G G C C G T G C C C T T C G C C T C T
 UrsusMaritimus C C G T T C A A T G C C A C C A G C T C T T C C C T G G A G G C C G T A C C C T T C G C C T C T
 FelisCatus C C G T T C A A G G C C A C C A G C T C T T C C C T G G A C A C T G T G C C C T T T G C C T C T
 LeptonychotesWeddellii C C G T T C A A T G C C A C C A G C T C T T C C C T G G A G G C C G T G C C C T T C G G C T C T
 PantheraTigris C C G T T C A A G G C C A C C A G C T C T T C C C T G G A C A C T G T G C C C T T C G C C T C T
 EptesicusFuscus C C T T T C A A G G C C A C C A G C T C T T C C C T G G A G G C T G T G C C C T T C G C C T C G
 MyotisLucifugus C C T T T C A A G G C C A C C A G C T C T T C C C T G G A G G C T G T G C C C T T C G C C T C G
 MyotisBrandtii C C T T T C A A G G C C A C C A G C T C T T C C C T G G A G G C T G T G C C C T T C G C C T C G
 CeratotheriumSimum C C C T T C A A G G C C A C C A G C T C T T C C C T G G A G G C C G T G C C C T T C G C C T C C
 EquusCaballus C C C T T C A A G G C C A C C A G C T C T T C C C T G G A G G C C G T G C C G T T C G C C T C C
 OrcinusOrca C C C T T C A A G G C C A C C A G C T C T T C C C T G C A G G C C G T G C C C T T C G C T T C C
 PhyseterCatodon C C C T T C A A G G C C A C C A G C T C T T C C C T G C A G G C C G T G C C C T T T G C C T T C C
 TursiopsTruncatus C C C T T C A A G G C C A C C A G C T C T T C C C T G C A G G C C G T G C C C T T C G C T T C C
 BubalusBubalis C C T T T C A A G G C T A C C A G C T C T T C C C T G C A G G C C G T G C C C T T T G C C T C G
 OvisAries C C T T T C A A G G C C A C C A G C T C T T C C C T G C A G G C C G T G C C C T T T G C C T C G
 OtlemurGarnettii C C C T T T C A G G C C A C C A G C T C T T C C C T G G A C G C T G T G C C C T T T G C C T C T
 CallithrixJacchus C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C C G T G C C C T T T G C C T C T
 SaimiriBoliviensis C C C T T C A A G A C C A C C A G T T C T T C C T T G G A A G C T G T G C C C T T T G C C T C T
 ChlorocebusSabaeus C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 MacacaFascicularis C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 HomoSapiens C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 NomascusLeucogenys C C C T T C A A G A C T A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 PanPaniscus C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 PanTrogodytes C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 PongoAbelii C C C T T C A A G A C C A C C A G T T C T T C C T T G G A G G C T G T G C C C T T T G C C T C T
 ChrysochlorisAsiatica C C C T T C G G G C C A C C A G T T C T T C C C T G G A G G C C G T G C C C T T T G C C T C A
 EchinopsTelfairi C C C T T T G G G C C A G C A G C T C T T C T A G A T G C T G T G C C C T T C G C C T C T
 DasypusNovemcinctus C C G T T T C T G G C C A C C A G C T C T T C C C T G G G A C C G T G C C C T T T G C C T C T
 TrichechusManatus C C C T T C A A G G C T A C C A G C T C T T C C C T G G A G G C C G T G C C C T T T G C C T C G
 SarcophilusHarrisii C C C T T C G G G G C A C T A G C A C C T C C C T G G C T G C T G T G C C C T T T G C T T C A
 MonodelphisDomestica C C C T T T G G G G C T A C T A G C A C C T C C C T G G C T G C T G T G C C T T T C G C C T C A

AiluropodaMelanoleuca G C G G C T A C T G T G G C C T G T G G G G C C A G - - - - - G G A A G A T G G T C A G G A G
 UrsusMaritimus G C G G C T A C C G T G T C C T G T G G G G A C A G - - - - - G G A A G A T G G T C A G G A G
 FelisCatus G T G G C T A A C G T G G C C T G T G G G G A T G G - - - - - G G A C G A G G T C G G G A G
 LeptonychotesWeddellii G C G G C T A C T G T G G T C T G T G G G G C C G G - - - - - G G A A G C C G G T C A G G A G
 PantheraTigris G T G G C T A A C G T G G C C T G T G G G G A T G G - - - - - G G A C G A G G T C G G G A G
 EptesicusFuscus G T G G C C A A C G T G G C C T G T G G G G T T G G - - - - - G G T G A G A G T G G A C A G
 MyotisLucifugus G T G G C C A A C G T G G C C T G T A G G A A T G G - - - - - G G A T A G A G T A A G C A G
 MyotisBrandtii G T G G C C A A T G T G G C C T G T A G - - - - - - - - - - - G G A T G A G A T T A G G C A G
 CeratotheriumSimum G T G G C C A A C G T G G C C T G T G G G G A C G G - - - - - G C G C G A A A G T G G G C A T
 EquusCaballus A T G G C C A A C G T G G C C T G T G G G G A C A G - - - - - G A C G A G A G T G A G T G G
 OrcinusOrca A T G G C C A A C G T G G C C T G T G G G G A C G G - - - - - G G A C G A G A G C T G G C A G
 PhyseterCatodon A T G G C C A A C G T G G C C T G T G G G G A C G G - - - - - G G A C G A G A G C T G G C A G
 TursiopsTruncatus A T G G C C A A C G T G G C C T G T G G G A C G G - - - - - G G A C G A G A G C T G G C A G
 BubalusBubalis A T G G C C A C C G T G G C C T G T G A G G A C G G - - - - - G G A C G A G G C A G G C A G
 OvisAries A T G G C C A G T G T G G T C T G T G A G G A C G G - - - - - G G A C G A G G G C A C G C C G
 OtlemurGarnettii A T G G C C A G T G T G G C C T G T G G G G A C G G - - - - - G A A T G A G A T A C C A G C
 CallithrixJacchus G C A G C C A A T G T G G C C T G T G G G G A C A G G G A C C A G G A C A A G A G T C A G A G T
 SaimiriBoliviensis G C G G C C A A C G T G A T C T G T G G G G A T G G G G A C C A G G A C A A G A G T C A G A G T
 ChlorocebusSabaeus G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T
 MacacaFascicularis G C C G C C A A T G T G G C C T G T G G G G A A G G G G A C A A A G A C G A C A G T C A G A G T
 HomoSapiens G C G G C C A A T G T A G C C T G T G G G G A A G G T G A C A A G G A C G A G A C T C A G A G T
 NomascusLeucogenys G C G G C C G A T G T G G C C T G T G G G G A A G G G G A C A A G G A C A A G A G T C A G A G T
 PanPaniscus G C G G C C A A T G T A G C C T G T G G G G A A G G C G A C A A G G A C G A G T C A G A G T
 PanTrogodytes G C G G C C A A T G T A G G C T G T G G G G A A G G C G A C A A G G A C G A G A G T C A G A G T
 PongoAbelii G C G G C C A C T G T G G C C T G T G G G G A A G G G G A C A A G G A C G A G A G T C A G A G T
 ChrysochlorisAsiatica G T G G C C T C C G T G G T G T G T G A C G A T A T - - - - - G G A T A C A C A G A G A G T
 EchinopsTelfairi A T A G C C A C T G T G G C C T G T G G G G A G G A - - - - - G G G C A G A A T G G G A G C
 DasypusNovemcinctus T C G G C T G A T G T G A C T T G T G G G G A G G A - - - - - G G A A A T G G A G G A G A C A
 TrichechusManatus A T G G C C A A C G T G G C C T G T G G G G A C G A - - - - - G G G C A A G G A G G G A G C
 SarcophilusHarrisii G T A G C C A A T G T G A A C T G T A G G G A T G G - - - - - A G G T G A A A A A A G A A T
 MonodelphisDomestica G C A G C C A G T G T G A A C T G T G G G T A T G G - - - - - A G A T G A A A G A A A A A G T

AiluropodaMelanoleuca	C A T T A C C T C A T G T G C A G G G A G A A G G C C C C T G A T G T G T T C G A C T G G G G C
UrsusMaritimus	C A T T A C T T C A T G T G C A G G G A G A A G G C C C C T G A T G T G T T C G A C T G G G G C
FelisCatus	C A T T A C T T C C T G T G T A A G G A G A A G G C C T C A G A T G T G T T C G A C T G G G G C
LeptonychotesWeddellii	G A T T A C T T C A T G T G C A G G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
PantheraTigris	C A T T A C T T C C T G T G T A A G G A G A A G G C C T C A G A T G T G T T C G A C T G G G G C
EptesicusFuscus	C A T T T C T T C C T G T G C A A G G A G A A G G C C A C C G A T G T G T T C G A C T G G G G C
MyotisLucifugus	C A T T T C T T C C T G T G C A A G G A G A A G G C C A C T G A T G T G T T C G A C T G G G G C
MyotisBrandtii	C A T T T C T T C C T G T G C A A G G A G A A G G C C A C T G A T G T G T T C G A C T G G G G C
CeratotheriumSimum	C A T T A C T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
EquusCaballus	C A T T A C T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G A C
OrcinusOrca	C A T T A C T T C C T G T G C A A G G A G A A G A C C C C G G T G T G T T T G A C T G G G A C
PhyseterCatodon	C A T T A C T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T T G A C T G G G A C
TursiopsTruncatus	C A T T A C T T C C T G T G C A A G G A G A A G G C C C C G G T G T G T T T G A C T G G G A C
BubalusBubalis	C A C T A C T T T C T G T G C A A G G A G A A G G C C C C A G C G A G T T T G A C T G G G A C
OvisAries	C A C T A C T T C C T G T G T T T G G A G A A G G C C C C A G C G T G T T T G A C T G G G A C
OtolemurGarnettii	C A T T A T T T C C T G T G C A A G G A G A A G G A G C C C A A C G T G T T T G A G T G G A A C
CallithrixJacchus	C A T T A T T T C C T G T G T A A G G A G A A G G C C C C G A T G T G T T C G A T T G G G G C
SaimiriBoliviensis	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C T G A T G T G T T C G A C T G G G G C
ChlorocebusSabaeus	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
MacacaFascicularis	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
HomoSapiens	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
NomascusLeucogenys	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
PanPaniscus	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
PanTrogodytes	C A T T A T T T C C T G T G C A A G G A G A A G G C C C C G A T G T G T T C G A C T G G G G C
PongoAbelii	C A T T A T T T C C T A T G C A A G G A G A A G G C C C C G G T G T G T T C G A C T G G G G C
ChrysochlorisAsiatica	C A T T A T T T C T G T G C A A G G A G A A A G G T G C T G A T G T T C A A C T G G G G C
EchinopsTelfairi	A A T T A T T T C A G T G C A G G G A G A A A G G G A G T A A G C T G T T T G A C T G G G A T
DasypusNovemcinctus	C A C T A T T T C T T G T G C A A G G A G A A A G A C C C G G C G T G T T T G A C T G G G A C
TrichechusManatus	C A T T A T T T C T T G T G C A A G A A G A A A G G C G C C G A T G T G T T T G A C T G G G G C
SarcophilusHarrisii	C A C T A C C T C T T G T G C A A G G A G C G A A G C T C C A A C C T G T T T G A C T G G G G C
MonodelphisDomestica	C A C T A C C T T G T G T G C A A G G A A A G A A A C C C C A A C C A G T T T G A C T G G G G C
AiluropodaMelanoleuca	A A C T T G G G C C C C C T C T G T G T C A G C G C C C A G T A T G G C T G C A G C T T C A A C
UrsusMaritimus	A A C T C G G G C C C C C T C T G C A T C A G C G C C C A G T A T G G C T G C A G C T T C A A C
FelisCatus	A G C T C A G G C C C C C T C T G T T A G C C C C A A G T A C G G C T G C A G C T T C A A C
LeptonychotesWeddellii	A G C T C G G G C C C C C T C T G C G T C A G C C C C A G T A T G G G T G C A G C T T C A A C
PantheraTigris	A G C T C A G G C C C C C T C T G T G T A G C C C C A A G T A C G G C T G C A G C T T C A A C
EptesicusFuscus	A T C T C G G G A C C C C T C T G T G C A G C G C T G A G T A C A A T G C A G C T T C A A T
MyotisLucifugus	A T C T C G G G A C C C C T C T G T G C A G C G C T G A G T A C G G A T G C A G C T T C A G T
MyotisBrandtii	A T C T C G G G A C C C C T C T G T G C A G C G C T G A G T A C G G A T G C A G C T T C G G T
CeratotheriumSimum	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A A T A C G G C T G C G A C T T C A A C
EquusCaballus	A G C T C G G G C C C C C T C T G T G T C A A C C C C A A G T A C G G C T G C G A C T T C A A C
OrcinusOrca	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T T C A G C T G C G A C T T C A A C
PhyseterCatodon	A G C T C G G G C C C C C T C T G C G T C A G C C C C A A G T T C A G C T G C G A C T T C A A C
TursiopsTruncatus	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T T C A G C T G C G A C T T C A A C
BubalusBubalis	A G C T C A G G G C C C C T C T G T G T G A G C C C C A A G T T C G G C T G C G A C T T C A A C
OvisAries	T G C T C A C G G C C C C T C T G T G T G A G C T C C A A G T T C A G C T G T G A C T T C A A C
OtolemurGarnettii	A G C T C G G G T C C C C T T T G T G T C A G C C C C G A C T A T G G C T G C A A C T T C A A C
CallithrixJacchus	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A C G G C T G C A G C T T C A A C
SaimiriBoliviensis	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
ChlorocebusSabaeus	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
MacacaFascicularis	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
HomoSapiens	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
NomascusLeucogenys	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
PanPaniscus	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A G C T T C A A C
PanTrogodytes	A G C T C G G G C C C C C T C T G T G T C A T C C C C A A G T A T G G C T G C A G C T T C A A C
PongoAbelii	A G C T C G G G C C C C C T C T G T G T C A G C C C C A A G T A T G G C T G C A A C T T C A A C
ChrysochlorisAsiatica	A C C T C G G G T C C C C T C T G T G T C A G C T C C A A G C T G G G C T G T A G C T T C A A C
EchinopsTelfairi	A C C T C A G G A C C A C T C T G T G T C A A C T C C A A A C T T G G C T G C A G C T T C A A C
DasypusNovemcinctus	A G C T C A G G C C C C T T T G T G C A G C C C C A A G T A C A G C T G C A G T T T C A A C
TrichechusManatus	A C C T C T G G C C C C C T C T G C G T C A G C T C C A A G C T A A G C T G C A G C T T C A A C
SarcophilusHarrisii	A C C C C A G G C C C T T T C T G T G C T C C C C A A A C C A T G G C T G T G C T T T C A A T
MonodelphisDomestica	A C C T C G G G C C C T A T C T G T G C A T C C C C A A A T C A T G G C T G T G C T T C A A T

AiluropodaMelanoleuca	A A C G G G G G C T G C C A G C A G G A C T G C T T T G A G G G G G G C A A T G G C T C C T T C
UrsusMaritimus	A A C G G G G G C T G C C A G C A G G A C T G C T T T G A G G G G G G C A C G G C T C C T T -
FelisCatus	A A C G G G G G C T G C C A G C A A G A C T G T T T C G A G G G T G G T G A T G G C T C C T T C
LeptonychotesWeddellii	A A T G G G G G C T G C C A G C A G G A C T G C T T C G A G G G G G G C G A C G G T T C C T T C
PantheraTigris	A A C G G G G G C T G C C A G C A A G A C T G T T T C G A G G G T G G T G A T G G C T C C T T C
EptesicusFuscus	A A C G G G G G C T G C C A G C A G G A A T G C T T G G A G G G G G A G G A T G G C T C C T T C
MyotisLucifugus	A A C G G G G G C T G C C A G C A G G A A T G C T T G G A G G G G G A G G G T G G C T C C T T C
MyotisBrandtii	A A C G G G G G C T G C C A G C A G G A A T G C T T G G A G G G G G A G G G T G G C T C C T T C
CeratotheriumSimum	A A C G G G G G C T G C C A G C A G G A C T G C T T T G A G G G G G G G A C G G C T C C T T C
EquusCaballus	A A T G G G G G C T G C C A G C A G G A C T G C T T C G A G G G G G G A G A T G G C T C C T T C
OrcinusOrca	A A C G G A G G C T G C C A G C A G G A C T G C T T C G A G G G T G G G G A A G G C T C C T T C
PhyseterCatodon	A A C G G A G G C T G C C A G C A G G A C T G C T T C G A G G G T G G G G A A G G T T C C T T C
TursiopsTruncatus	A A C G G A G G C T G C C A G C A G G A C T G C T T C G A G G G T G G G G A A G G C T C C T T C
BubalusBubalis	A A T G G A G G C T G C C A G C A G G A C T G C T T C G A G G G C G G G G A T G G C T C C T T C
OvisAries	A A T G G A C G C T G C C A A C A G G A C T G C T T C G A G G G A A A A A T G T C T C C T T C
OtolemurGarnettii	A A C G G G G G C T G C C A G C A G G C C T G C T T C G A G G G C G G G A C G G C T C C T T C
CallithrixJacchus	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G A G G C G A T G G C T C C T T C
SaimiriBoliviensis	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G A G G G G A T G G C T C C T T C
ChlorocebusSabaeus	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G G A T G G C T C C T T C
MacacaFascicularis	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G C G G G G A T G G C T C C T T C
HomoSapiens	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G G A T G G C T C C T T C
NomascusLeucogenys	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G G A C G G C T C C T T C
PanPaniscus	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G A G G A T G G C T C C T T C
PanTrogodytes	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G A G G A T G G C T C C T T C
PongoAbelii	A A T G G G G G C T G C C A C C A G G A C T G C T T T G A A G G G G G G G A T G G C T C C T T C
ChrysochlorisAsiatica	A A T G G A G G C T G C C A C A G G A C T G C T T C G A G G G G G G T G A T G G T T C C T T C
EchinopsTelfairi	A A T G G A G G C T G C C A C A G G A A T G C T T T G A G G G A C T G A T G G T T C C T T T
DasypusNovemcinctus	A A C G G G G G C T G C C A G C A G G A G T G C T T T G A G G G G G G G A C G G C T C C T T C
TrichechusManatus	A A T G G G G G C T G C C A G C A G T A C T G C T T T G A T G G G G G T G A G G G T T C C T T C
SarcophilusHarrisii	A A T G G T G G C T G T C A G C A A G A A T G C T T G G A G G G G G G A G A T G G T T C A T T C
MonodelphisDomestica	A A T G G C G G C T G C C A G C A G G A G T G C T T A G A G G G A G G G G A C G G T T C A T T C
AiluropodaMelanoleuca	C G C T G C G G C T G C C G T C C G G G C T T C C G G C T G C T C G A T G A C C T G G T G A C C
UrsusMaritimus	- - - - - C T G C C G G C C G G G C T T C C G G C T G C T C G A C G A C C T G G T G A C C
FelisCatus	C G C T G T G G C T G T C G G C C G G G A T T C C G G C T G C T G A T G A C C T G G T G A C C
LeptonychotesWeddellii	C G C T G C G G C T G C C G G C C G G G C T T C C G G C T G C T C G A C G A C C T G G T G A C C
PantheraTigris	C G C T G T G G C T G T C G G C C G G A T T C A G G C T G C T G G A T G A C C T A G T G A C C
EptesicusFuscus	C G C T G C G G C T G C C G G C C G G G T T C A G G C T G C T G G A T G A C C T G G T G A C C
MyotisLucifugus	C G C T G C G G C T G C C G C C C G G G T T C A G G C T G C T G G A T G A C C T G G T G A C C
MyotisBrandtii	C G C T G C G G C T G C C G C C C G G G T T C A G G C T G C T G G A T G A C C T G G T G A C C
CeratotheriumSimum	C G C T G C G G C T G C C G G C C G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
EquusCaballus	C G C T G C G G C T G C C G G C C A G G T T C C G G C T G C T G G A C G A C C T G G T G A C T
OrcinusOrca	C G C T G T G G C T G C C G G C C G G G T T C C G G C T G C T G G A C G A C C T G G T C A C C
PhyseterCatodon	C G C T G T G G C T G C C G G C C G G G T T C C G G C T G C T G G A C G A C C T G G T C A C C
TursiopsTruncatus	C G C T G C G G C T G C C G G C C G G G T T C C G G C T G C T G G A C G A C C T G G T C A C C
BubalusBubalis	C G A T G C G G C T G C C G G C C G G G T T C A G G C T G C T G G A C G A C C T G G T C A G T
OvisAries	C G A T G C T G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T C A G T
OtolemurGarnettii	C G C T G T G G C T G C C T G C C G G G C T T C C G G C T G C T G G A T G A C C T G G T G A C C
CallithrixJacchus	C T T T G T G G C T G C C G G C C A G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
SaimiriBoliviensis	C T T T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
ChlorocebusSabaeus	C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
MacacaFascicularis	C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
HomoSapiens	C T C T G C G G C T G C C G A C C A G G A T T C C G G C T G C T G G A T G A C C T G G T G A C C
NomascusLeucogenys	C T C T G T G G C T G T C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
PanPaniscus	C T C T G C G G C T G C C G G C C A G G A T T C C G G C T G C T G G A T G A C C T G G T G A C C
PanTrogodytes	C T C T G C G G C T G C C G G C C A G G A T T C C G G C T G C T G G A T G A C C T G G T G A C C
PongoAbelii	C T C T G C G G C T G C C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
ChrysochlorisAsiatica	C G C T G T G G C T G C C G G C C G G G T T C C G G C T G C T G G A C G A C C T G G T G A C C
EchinopsTelfairi	A A C T G T G G C T G C C T A C C A G G G T A C C A G C T G C T A G A G G A C A T G G T G A C T
DasypusNovemcinctus	C G C T G T G G C T G C C G G C C A G G G T T C C G G C T G C T G G A T G A C C T G G T G A C C
TrichechusManatus	C G C T G C G G T T G C C A G C C A G G G T T C C G G C T G A T G G A C G A C C T G G T G A C C
SarcophilusHarrisii	C T C T G T G G C T G C C G T C C A G G A T A C C G C C T T C T A G A T G A C T T G G T G A C C
MonodelphisDomestica	C T C T G T G G C T G C C G T C C G G G A T A T C G C C T C C T C G A T G A C T T G G T G T C C

AiluropodaMelanoleuca	T G T G C C T C C C G G A A C C C T T G C A G C T C C A A C C C A T G C G G A G G G C C A G C C
UrsusMaritimus	T G T G C C T C C C G G A A C C C T T G C A G C T C C A A C C C A T G C A G A G G G G C A G C C
FelisCatus	T G T G C C T C C C G G A A C C C T T G C A G C T C C A G T C C C T G C A A A G G G G C A G C C
LeptonychotesWeddellii	T G T G C C T C C C G G A C C C T T G C A G C T C C A G C C C G T G C C G G G G G C A G C C
PantheraTigris	T G T G C C T C C C G G A A C C C T T G C A G C T C C A G T C C C T G C A A A G G G G C A G C C
EptesicusFuscus	T G T A T C T C C C G G A C C C T T G T A G C T C C A G C C C G T G C A G A G G A G T G G C C
MyotisLucifugus	T G T A T C T C C C G G A C C C T T G T A G C T C C A G C C C T T G C A G A G G A G T G G C C
MyotisBrandtii	T G T A T C T C C C G G A C C C T T G T A G C T C C A G C C C G T G C A G A G G A G T G G C C
CeratotheriumSimum	T G C G C C T C C C G G A A C C C T T G C A G C T C C A G C C C G T G C G G A G G G G C A G C C
EquusCaballus	T G C G C C T C C C G G A A C C C T T G C A G C T C C A G C C C G T G C A G A G G G G T G G C T
OrcinusOrca	T G C G C C T C T C G G A A C C C T T G C A G C T C C A G C C C A T G T G G A G G G G G T C C
PhyseterCatodon	T G T G C C C C T C G G A A C C C T T G C A G C T C C A G C C C G T G T G G A G G G G G T C C
TursiopsTruncatus	T G C G C C T C T C G G A A C C C T T G C A G C T C C A G C C C A T G T G G A G G G G G T C C
BubalusBubalis	T G C G C C T C T C G G A A C C C T T G C A G C T C C A G C C C G T G C A G A G G G G A G G C C
OvisAries	T G C G C C T C T C G G A A C C C T T G C A G C T C C A G C C C G T G C G G A G G G G A G G C C
OtolemurGarnettii	T G T G C C T C T C G G A A C C C T T G C A G C T C C A G C C C A T G C A T C G G A G A G G C C
CallithrixJacchus	T G T G C C T C C C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
SaimiriBoliviensis	T G T G C C T C C C G T A A C C C T T G C A G C T C C A G C C C A T G C C G T G G G G G G C C
ChlorocebusSabaeus	T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C
MacacaFascicularis	T G T G C C T C A C G A A A C C C T T G C A G C T C T A G C C C A T G T C G T G G G G G G C C
HomoSapiens	T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
NomascusLeucogenys	T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G A G G C C
PanPaniscus	T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
PanTroglodytes	T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
PongoAbelii	T G T G C C T C T C G A A A C C C T T G C A G C T C C A G C C C A T G T C G T G G G G G G C C
ChrysochlorisAsiatica	T G T A C C T C C C G A A A C C C T T G C A G C T C C A A C C C C T G C A A A G G G G T G G C C
EchinopsTelfairi	T G T G C C T C T C G A A A C C C T T G T A G C T C C A A C C C A T G C A G A G G G A T A G C C
DasypusNovemcinctus	T G C G C T T C T C G G A A C C C C T G T A G C T C C A G C C C G T G C G A G G G A T G G C C
TrichechusManatus	T G C A C C T C C C G A A A C C C C T G C A G C T C C A A T C C C T G C A G A G G G T G G C C
SarcophilusHarrisii	T G T A T C C C C G A G A C C C T T G C C A T C C T A A C C C A T G C A G G G G A A A G G C A
MonodelphisDomestica	T G T G T C C C C G A G A C C C T T G C C A T C C T A A C C C A T G C A G G G G A A A G G C A
AiluropodaMelanoleuca	A C C T G T G A G C A G G G A C C C C A T G G G A A G A G C T A C A C G T G C C A C T G C C C C
UrsusMaritimus	A C C T G T G A G C A G G G A C C C C A T G G G A A G A G C T A C A C G T G C C A C T G C C C C
FelisCatus	A C C T G T G T C C T G G G A C C T C A C A G G A A G A A C T A C A C G T G C C A C T G C C C C
LeptonychotesWeddellii	A C C T G T G T C C C G G C A C C C C A C G G G A A G A A T T A C A C A T G C C G C T G C C C C
PantheraTigris	A C C T G T G T C C T G G G A C C C C A C A G G A A G A A C T A C A C G T G T C T C T G C C C C
EptesicusFuscus	A C A T G C G T C C C G G A C C C C T C T G G A G A A A A C T A C A C G T G C C A G T G C C C A
MyotisLucifugus	A C A T G C G T C C C G A G T C C C T C T G G A A A A A C T A C A C G T G C C A G T G C C C C
MyotisBrandtii	A C A T G C G T C C C G A G T C C C T C T G G A A A A A C T A C A C G T G C C A G T G C C C C
CeratotheriumSimum	A C A T G C G T T C C T G G A C C C C T T G G G A A A A A C T A C A T G T G C C G C T G C C C C
EquusCaballus	A C A T G C G T C C C T G A G A C C C T C G G G A A A A G C T A C C T G T G C C G C T G C C C C
OrcinusOrca	A C G T G C G T C C C T G G G C C C C T C G G G A A G G A C T T C A C G T G C C A C T G C C C C
PhyseterCatodon	A C G T G C G T C C C T G G G C C C C T C G G G A A G G A C T T C A C G T G C A G C T G C C C C
TursiopsTruncatus	A C G T G C G T C C C T G G G C C C C T C G G G A A G A G A C T T C A C G T G C C A C T G C C C C
BubalusBubalis	A C G T G C T T C C C C G G G T C C C T C G G A A C A G A C T T T A C G T G C C A C T G T C C C
OvisAries	A C G T G C T T C C C C G G G T C C C T C G G A A C A G A C T T C A C A T G C C A C T G T C C C
OtolemurGarnettii	A C A T G T G T C T C T G C A C C T C A T G G G A C A A A C T A C A C A T G C C A C T G T C C C
CallithrixJacchus	A C A T G C A T C C A G G G A T C C C A G G G G A A A A C T A C A C A T G C C A C T G T C C C
SaimiriBoliviensis	A C A T G C A T C C A G G G T T C C C A T G G G A A A A A C T A C A C A T G C C A C T G T C C C
ChlorocebusSabaeus	A C A T G C A T C C C G G G A C C C C A T G G G A A A A A C T A C A C G T G C G G C T G C C C C
MacacaFascicularis	A C A T G C A T C C C G G G A C C C C A T G G G A A A A A C T A C A C G T G C G C T G C C C C
HomoSapiens	A C G T G C G T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
NomascusLeucogenys	A C A T G T A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
PanPaniscus	A C G T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C T
PanTroglodytes	A C G T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C T
PongoAbelii	A C A T G C A T C C T G G G A C C C C A T G G G A A A A A C T A C A C G T G C C G C T G C C C C
ChrysochlorisAsiatica	A C A T G C G A G C C C G G G T C T C T G G G A G A A A G T T A T A A A T G C C G C T G C C C A
EchinopsTelfairi	A C A T G T G A G C C C A G C C C A C T T G G G A A A G T T A C G G T T G C T C C T G C C C A
DasypusNovemcinctus	A C G T G T G T C C C C G G G A C C C A C G G G A A G A G T T A C A C T T G C C G C T G C C C T
TrichechusManatus	A C A T G C A A G C C C G A T T C C C T C G G G A A A A G T T A T A G G T G C C A C T G C C C C
SarcophilusHarrisii	A A G T G C A G C C C T G G G A C T C A T G G A C A G C A C T A T G A G T G T C A A T G C C C T
MonodelphisDomestica	A A G T G C A G C C C T G G A G G G C A C G G A A A A C A C T A T G A G T G C C T G T G T C C T

AiluropodaMelanoleuca	C A A G G C T A C C A G C T G G A C T C A A G T C A G C G G G A C T G T C T G G A C G T G G A C
UrsusMaritimus	C G A G G C T A C C A G C T G G A C T C A A G T C A G C G G G A C T G T C T G G A C G T G G A C
FelisCatus	C A A G G C T A C C A G C T G G A C T C A A G T C A G C A G G A C T G T G T G G A T G T G G A C
LeptonychotesWeddellii	C A G G G C T A C C A G C T G G A C T C A A G T C A G C G G G A C T G C G T G G A C A T G G A C
PantheraTigris	C A A G G C T A C C A G C T G G A C T C A A G T C A G C A G G A C T G T G T G G A T G T G G A C
EptesicusFuscus	G A A G G C T A C C A G C T G A A C G C G A C T C A G C G G G A C T G T G T G G A T G T G G A C
MyotisLucifugus	G A A G G C T A C C A G C T G A A C A C G A C T C A G C A G G A C T G T G T A G A T G T G G A C
MyotisBrandtii	G A A G G C T A C C A G C T G A A C G C G A C T C A G C A G G A C T G T G T A G A T G T G G A C
CeratheriumSimum	C C A G G C T A C C A G C T A G A C T C G A C T C A G C A G G A C T G T G T G G A T G T G G A C
EquusCaballus	C A A G G C T A C C A G C T G G A C T C C A C T C A G C G G G A C T G C G T G G A C G T A G A T
OrcinusOrca	C C A G G C T A C C G G C T A G A C T C G A C T C A G C A G G A C T G C G T G G A C A T G G A C
PhyseterCatodon	C C A G G C T A C C G G C T A G A C T C G A C T C A G C A G G A C T G T G T G G A C A C G G A C
TursiopsTruncatus	C C A G G C T A C C G G C T A G A C T C G A C T C A G C A G G A T T G T G T G G A C A T G G A C
BubalusBubalis	C C A G G C T A C C A G C T G G A C T C G A C T C A G C G G G A C T G C G T G G A C G T G G A T
OvisAries	C C A G G C T A C C A G C T G G A C T C G A C T C A G C G A G A C T G C G T G G A T G T G G A C
OtolemurGarrettii	C A A G G T T T C C A A G T G G A C G A G A G T C A G T T G G G C T G T G T G G A T G T G G A T
CallithrixJacchus	C A A G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A T G T G G A T
SaimiriBoliviensis	C A A G G G T A C C A G C T G G A C T C A A G T C A G C T G G A C T G T G T G G A T G T G G A T
ChlorocebusSabaeus	C A A G G G T A T C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
MacacaFascicularis	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A C
HomoSapiens	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
NomascusLeucogenys	C A A G G G T A C C A G C T G G A C T C G A G T C A G T T G G A C T G T G T G G A T G T G G A T
PanPaniscus	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
PanTrogodytes	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A C G T G G A T
PongoAbelii	C A A G G G T A C C A G C T G G A C T C G A G T C A G C T G G A C T G T G T G G A T G T G G A T
ChrysochlorisAsiatica	C T A G G T T A C C A G T T G G A C C T G A G T G A G C T G G A C T G A T G A T G T G G A T
EchinopsTelfairi	C T G G G C T A C C A G C T G G A C C C G A G T A A G C T G G G T T G C A G T G A T A T A G A T
DasypusNovemcinctus	C C A G G C T A C C A G C T G G A C C C G A G C C A G A T G G A C T G T G A G G A C G T G G A T
TrichechusManatus	C C A G G C T A C C A G C T A G A C C C G A G T G A G C T G G A C T G C A G G G A C G T G G A T
SarcophilusHarrisii	G C A G G C T T C A A A T C G A C T C C A A A T C G A C T A G A T T G T G A A G A T G T G G A T
MonodelphisDomestica	G C A G G T T T C A A G C C C A C T C C A A A T A G A C T A G A T T G C G A T G A T G T G G A C
AiluropodaMelanoleuca	G A G T G C C A G G A A T C C C C C T G C C C A C A G G A G T G T G T C A A C A C C C C T G G G
UrsusMaritimus	G A G T G C C A G G A C T C C C C C T G C C C A C A G G A G T G T G T C A A C A C C C C T G G G
FelisCatus	G A G T G C C A G G A C T C C C C C T G C C C A C A G A G T G T G T C A A C A C C C T G G G
LeptonychotesWeddellii	G A G T G C C A G G A C T C C C C C T G C C G G C A G G C C T G T G T C A A C G T C C C T G G G
PantheraTigris	G A G T G C C A G G A C T C C C C C T G C C C A C A G A G T G T G T C A A C A C C C C T G G G
EptesicusFuscus	G A G T G C C A G G C C T C C C C C T G T G A A C A G G A G T G T G T C A A C A C C C C G G G
MyotisLucifugus	G A A T G C C A G G C C T C C C C C T G T G A A C A G G A G T G T G T C A A C A C C C C T G G G
MyotisBrandtii	G A G T G C C A G G C C T C C C C C T G T G A A C A G G A G T G T G T C A A C A C C C C T G G G
CeratheriumSimum	G A G T G C C A G G A C T C C C C C T G C G C C A G G A A T G T G T C A A C A C C C C T G G G
EquusCaballus	G A G T G C C A G G G C T C A C C C T G T G C C C A G G A G T G T G T C A A C A C C C C G G G
OrcinusOrca	G A G T G C C A G G A C G C T C C C T G C G C C C A G G A G T G T G T C A A C A C T C T C G G G
PhyseterCatodon	G A G T G C C A G G A C A C T C C C T G T G C C C A G G A G T G T G T C A A C A C C C T C G G G
TursiopsTruncatus	G A G T G C C A G G A C G C T C C C T G T G C C C A G G A G T G T G T C A A C A C A C T C G G G
BubalusBubalis	G A G T G C C G G A C A A C C C C T G T G C C C A G G A C T G T G T C A A C A C C C C T G G A
OvisAries	G A G T G C C A G G A C A A C C C C T G T G C C C A G G A C T G T G T C A A C A C C C C T G G G
OtolemurGarrettii	G A G T G T C A A G A C A G C C C C T G T G T C C A G G C C T G T G T C A A C A C C C A T G G G
CallithrixJacchus	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
SaimiriBoliviensis	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
ChlorocebusSabaeus	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
MacacaFascicularis	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
HomoSapiens	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
NomascusLeucogenys	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
PanPaniscus	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
PanTrogodytes	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G G
PongoAbelii	G A A T G C C A G G A C T C C C C C T G T G C C C A G G A G T G T G T C A A C A C C C C T G G A
ChrysochlorisAsiatica	G A G T G C C A G G C C T C A C C T T G T G C C C A G G A G T G C A T C A A C A C C C T T G G G
EchinopsTelfairi	G A G T G C C A G G C C T C C C C C T G T C C C C A G G T G T G C A T C A A C A C C C C T G G G
DasypusNovemcinctus	G A G T G C C T G C C C T C C C C C T G C C C C A G G A G T G T G T C A A C A C C C C G G G
TrichechusManatus	G A A T G T C A G G C C T C C C C C T G C G C C C A G G A G T G C A T C A A C A C C C C T G G G
SarcophilusHarrisii	G A G T G C A G T A G A T T C C C A T G T A C T C A C A A G T G T G T C A A C A C T C C T G G T
MonodelphisDomestica	G A G T G T G A T A G G A T A C C G T G T G C C C A G G A T T G T G T C A A C A C T C C T G G G

AiluropodaMelanoleuca	A G C T T C C G C T G T G A G T G C T G G G T G G G C T A T G A G C C C G G - - - C G G C C C T
UrsusMaritimus	A G C T T C C G C T G T G A G T G C T G G G T G G G C T A T G A G C C C G G - - - C G G C C C T
FelisCatus	G G C T T C C A C T G T G A G T G C T G G G T G G G C T A C G A G C T C C G - - - T G G C C C T
LeptonychotesWeddellii	G G C T T C C G C T G T G A G T G C T G G G T G G G C T A C G A G C C C A G - - - C G G C C C C
PantheraTigris	G G C T T C C A C T G T G A G T G C T G G G T G G G C T A C G A G C C C C G - - - T G G C C C T
EptesicusFuscus	A G C T T C C A C T G C C A G T G C T G G G T G G G C T A C G A G C C T G G - - - C G G C C C C
MyotisLucifugus	A G C T T C C A C T G C C A G T G C T G G G T G G G C T A C G A G C C C A G - - - C A G C C C C
MyotisBrandtii	A G C T T C C A C T G C C A G T G C T G G G T G G G C T A C G A G C C C A G - - - C A G C C C C
CeratheriumSimum	G G C T T C C A C T G C C A G T G C T G G G T G G G C T A C G A G C C C G G - - - G G G C C C C
EquusCaballus	G G C T T C C A C T G C C A G T G C T G G G T G G G C T A C G A G C C T A G - - - C G G C C C C
OrcinusOrca	G G C T T C C G C T G C G A G T G C T G G G T G G G C T A C G A G C C T G G - - - T G G C C C C
PhyseterCatodon	G G C T T C C G C T G C G A G T G C T G G G T G G G T A C G A G C C T G G - - - T G G C C C C
TursiopsTruncatus	G G C T T C C G C T G C G A G T G C T G G G T G G G C T A C G A G C C T G G - - - T G G C C C C
BubalusBubalis	A G C T T C C G C T G T G A G T G C T G G G T G G G C T T T G A G C C T G G - - - C G G C C C T
OvisAries	A G C T T C C G C T G T G A G T G C T G G G T G G G C T T T G A G C C T G G - - - T G G C C C C
OtolemurGarrettii	A G C T T C C G A T G T G A G T G C T G G G T G G G C T A C G A G C C C A G - - - C A G C C C T
CallithrixJacchus	G G C T T C C G C T G C G A A T G C T G G G T T G G T T A C C A G C C G G A - - - C G G T C C T
SaimiriBoliviensis	G G C T T C C G C T G C G A A T G C T G G G T T G G T T A C G A A C C G G G - - - T G G T C C T
ChlorocebusSabaeus	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
MacacaFascicularis	A G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
HomoSapiens	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
NomascusLeucogenys	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
PanPaniscus	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C A G T C C T
PanTrogodytes	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
PongoAbelii	G G C T T C C G C T G C G A A T G C T G G G T T G G C T A T G A G C C G G G - - - C G G T C C T
ChrysochlorisAsiatica	A G C T T C C A C T G T G T C T G C T G G G T G G G C T A T G A G C C T G A - - - - - - - - - -
EchinopsTelfairi	A G C T T C C A C T G T G C T G C T G G G T G G G C T A T G A G C C T G G - - - - - - - - - -
DasypusNovemcinctus	G G C T T C C T C T G T G A G T G C T G G G T G G G C T A C C A G C T C G G C C C C G G A G A G
TrichechusManatus	A G C T T C C G C T G C A C C T G C T G G G T G G G C T A T G A A C C T G A - - - - - - - - - -
SarcophilusHarrisii	A G C T T C C A T T G C A C C T G C C A T C T A G G T T A T G A G A C C C A - - - G G G C C A C
MonodelphisDomestica	A G C T T C C A T T G C A C C T G C C G C C C A G G T T A T G A G C C C C A - - - A G G C C A C
AiluropodaMelanoleuca	G G G G A G G G G G T C T G T C A A G A T G T G G A C G A G T G T G C G C C T G G C C G G C T C G
UrsusMaritimus	G G A G A G G G G G C C T G T C A A G A T G T G G A C G A G T G T G C G C C T G G C C G C T C G
FelisCatus	G G G G A G G A G G C C T G T C A G G A T G T G G A C G A G T G T G C C C T G G C C A C T C A
LeptonychotesWeddellii	G G G G A G G G G C C C T G T C G G G A T G T G G A C G A A T G T G T C C C G G G C C G C T C G
PantheraTigris	G G G G A G G A G G C C T G T C A G G A T G T G G A C G A G T G T G C C C T G G T C A C T C G
EptesicusFuscus	C G A G G G A G G C C T G T C G G G A T G T G G A T G A G T G T A C - - - - - - - - - -
MyotisLucifugus	G G A G G G C A G G C C T G T C A G G A T G T G G A T G A G T G T A T - - - - - - - - - -
MyotisBrandtii	G G A G G G C A G G C C T G T C A G G A T G T G G A T G A G T G T A C - - - - - - - - - -
CeratheriumSimum	G G A G A A G G G G C C T G T C G G G A C A T G G A C G A G T G T G C C C A G G C C G C T C A
EquusCaballus	G G A G A A G A A A C C T G T C G G G A C G T G G A C G A G T G T G C C C A G G C C G C T C G
OrcinusOrca	G G A G A G G G G G C C T G T G T G G A T G T G G A C G A G T G T G C C C C A G C C A C T C G
PhyseterCatodon	G G A G A G G G G G C C T G T G T G G A C G T G G A C G A G T G T G C C C C A G C C A C T C G
TursiopsTruncatus	G G A G A G G G G G C C T G T G T G G A T G T G G A C G A G T G T G C C C C A G C C A C T C G
BubalusBubalis	G A A G A G G G G C C T G C G T G G A T G T A G A T G A G T G T G C C C T G G C C A C T C G
OvisAries	G A A G A G G G G G C C T G T G T G G A T G T G G A T G A G T G T G C C C T G G C C A C T C A
OtolemurGarrettii	G G G G A A G G T G C C T G C C A G G A T G T G G A T G A G T G T G C C C T G G C C G T T C A
CallithrixJacchus	G G A G A G G T G C C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A C C C C T C G
SaimiriBoliviensis	G G A G A G G G T G T C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A C C C C T C G
ChlorocebusSabaeus	G G A G A G G G G G T C T G T C A G G A T G T G G A T G A G T G T G C C C G G G C C G C T C G
MacacaFascicularis	G G A G A G G G G G C C T G T C A G G A T G T G G A T G A G T G T G C C C T G G G C C G C T C G
HomoSapiens	G G A G A G G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C G
NomascusLeucogenys	G G A G A G A G G A C C T G T C G G G A T G T G G A T G A G T G T G C C C T G G A T C G C T C G
PanPaniscus	G G A G A G G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C A
PanTrogodytes	G G A G A G G G G G C C T G T C A G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C A
PongoAbelii	G G A G A G G G G G C C T G T C G G G A T G T G G A T G A G T G T G C T C T G G G T C G C T C G
ChrysochlorisAsiatica	- - G G A G G G G A C C T G T C G G G A C T T G G A T G A G T G T G C C C A G A C C G A A A C
EchinopsTelfairi	- - G G A G G G G A C C T G T C A G G A C A T A G A T G A G T G T G T C C C T G G C C A G A A C
DasypusNovemcinctus	G G A G A G G G A G C C T G T C T G G A C G T G G A C G A G T G T G C C C A G G G C C T G G C
TrichechusManatus	- - T G A G G G G A C C T G C C G G G A C T T G G A T G A G T G T G C C C A G G C C G A A A C
SarcophilusHarrisii	A A T G G A A T G G A A T G C T G G G A T G T G G A T G A A T G T G C T G G G G A C C A T T C C
MonodelphisDomestica	A A T G G A A T G G A A T G C T G G G A C G T G G A T G A A T G T G C C G A G G G C C G C T C A

AiluropodaMelanoleuca	C C C T G C T C C C A G G A G T G C A C C A A C A C C G A C G G G C T C C T T C T A C T G C T C C
UrsusMaritimus	C C C T G C G C C C A G G A G T G C A C C A A C A C C G A C G G G C T C C T T C T A C T G C T C C
FelisCatus	C C C T G C G C C C A G G G C T G C A C T A A C A C A G A T G G G C T C G T T C T A C T G C T C C
LeptonychotesWeddellii	C C C T G C G C C C A G G A G T G C A C C A A C A C C G A C G G G C T C C T T C T A C T G C T C C
PantheraTigris	C C C T G C T C C C A G G A C T G C A C T A A C A C G G A T G G G C T C A T T C C A C T G C T T C
EptesiscusFuscus	- - - - -
MyotisLucifugus	- - - - -
MyotisBrandtii	- - - - -
CeratheriumSimum	C C C T G T G C C C A G G G C T G C A C C A A C A C C G A T G G C T C G T T C T T C T G C T C C
EquusCaballus	C C C T G T G C C C A G G A C T G C A C C A A T A C C G A C G G G C T C G T T C T A C T G C T C C
OrcinusOrca	C C C T G T G C C C A G G G C T G C A C C A A C A C A G A C G G G T C T T T C T A C T G C T C C
PhyseterCatodon	C C C T G T G C C C A G G G C T G C A C C A A C A C A G A T G G G T C T T T C T A C T G C C C C
TursiopsTruncatus	C C C T G T G C C C A G G G C T G C A C C A A C A C A G A C G G G T C T T T C T A C T G C T C C
BubalusBubalis	C C C T G C G C C C A G A G C T G C A C C A A C A C C G A G G G C T C C T T C T A T T G C T C C
OvisAries	C C C T G C G C C C A G A G C T G C A C C A A C A C C G A G G G C T C C T T C T A T T G C T C C
OtolemurGarnettii	C C C T G C A C T C A G C G C T G T A C C A A C A C T A T G G G C T C G T T C C A T T G C T C C
CallithrixJacchus	C C C T G C G C C C A G G G C T G C A C C A A C A C A G A T G G G C T C A T T C C A C T G C T C C
SaimiriBoliviensis	C C C T G C G C C C A G G G C T G C A C C A A C A C A G A C G G G C T C A T T C T A C T G C T C C
ChlorocebusSabaeus	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A G G G C T C A T T C C A C T G T T C C
MacacaFascicularis	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A T G G G C T C A T T T C A C T G T T C C
HomoSapiens	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A T G G G C T C A T T T C A C T G C T C C
NomascusLeucogenys	C C T T G C G C C C A A G G C T G C A C C A A C A C A G A G G G C T C A T T T C A C T G C T C C
PanPaniscus	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A T G G G C T C A T T T C A C T G C T C C
PanTrogodytes	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A T G G G C T C A T T T C A C T G C T C C
PongoAbelii	C C T T G C G C C C A G G G C T G C A C C A A C A C A G A C G G G C T C A T T T C A C T G C T C C
ChrysochlorisAsiatica	C C C T G C G C A C A G G C C T G C A C C A A C A C C G A T G G G C T C C T T C C A C T G C T C C
EchinopsTelfairi	C C C T G T G A T C A G A C T G C A C C A A C A C C T A C G G C T C C T T T C A C T G C T C C
DasypusNovemcinctus	C C C T G C G C C C A A G C C T G T T C C A A C A C C C T C G G G C T C C T T C A C T G C T C C
TrichechusManatus	C C C T G T G C C C A G G C C T G T A C C A A C A C C G A T G G G C T C C T T C C A C T G C T C C
SarcophilusHarrisii	C C C T G T G C A C A G C T T T G C A T C A A C A C C G T A G G G C T C T T T T C A A T G T G C C
MonodelphisDomestica	C C C T G T G C C C A G C T T T G T A A C A A C A C G G A A G G G C T C C T T T C A A T G T A C C
AiluropodaMelanoleuca	T G T G A G A A G G G C T A T G T T C T G G C C G G T G A G G A C A G C A C C C A G T G C C A G
UrsusMaritimus	T G T G A G A A G G G C T A T G T T C T G G C T G G T G A G G A C A G C A C C C A G T G C C A G
FelisCatus	T G C A A G A A G G G C T A T G T C C T G G C T A A G G A G G A T G G C A C C C A G T G C C T G
LeptonychotesWeddellii	T G T G A G A A G G G C T A T G T T C T G G C C G G G G C G G A A G G C A C C G A G T G C C A G
PantheraTigris	T G C A A G A A G G G C T A T G T C C T G G C T G G G G A G G A T G G C A C C C A G T G C C T G
EptesiscusFuscus	- - - - -
MyotisLucifugus	- - - - -
MyotisBrandtii	- - - - -
CeratheriumSimum	T G C G A G G A G G G C T A T G T C C T G G C T G G G G A C G A C G G C A C C C A G T G C A A G
EquusCaballus	T G C A A G G A G G G C T T T G T C C T G G C A G G T G A G G A T G A C A C C C A G T G C C A G
OrcinusOrca	T G C G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C C C G G T G C G T G
PhyseterCatodon	T G C G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C C C A G T G C G T G
TursiopsTruncatus	T G C G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C C C G G T G C G T G
BubalusBubalis	T G C G A G G A G G G C T A C G A G C T G G C C G A G G A G G A T G G C A C C C A G T G C C T G
OvisAries	T G C G A G G A G G G C T A C G A G C T G G C T G G G G A G G A T G G C A C C C A G T G C C T G
OtolemurGarnettii	T G T G A G G A G G G C T A T G T G C T G G C T G G G G A G G A T G G C A C C C A G T G C C A G
CallithrixJacchus	T G C C A G G A G G G C T A T G T C C T G G C T G A G G A G G A C G G C A C T C A G T G C C A G
SaimiriBoliviensis	T G C C A G G A G G G C T A C G T C C T G G C T G A G G A G G A C G G C A C T C A G T G C C A G
ChlorocebusSabaeus	T G C G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G
MacacaFascicularis	T G C G A G G A G G G C T A T G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G
HomoSapiens	T G T G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G
NomascusLeucogenys	T G C G A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G C A C T C A G T G C C A G
PanPaniscus	T G T A A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G
PanTrogodytes	T G T A A G G A G G G C T A C G T C C T G G C C G G G G A G G A C G G G A C T C A G T G C C A G
PongoAbelii	T G C G A G G A G G G C T A C G T C C T G G C T G G G G A G G A C G G G A C T C A G T G C C A G
ChrysochlorisAsiatica	T G C G A G A A G G G C T A C G T A T T G G C T G G A G A G G A T G G C A C C C A G T G C C A G
EchinopsTelfairi	T G C G A G G A G G G C T A C G T G C T G C T G G T G A G G A T G G C A C C C A G T G C C A G
DasypusNovemcinctus	T G T G A C A C A G G C T A C G A A G T G G C A G G G A G G A C A C A C C C A A T G T C A G
TrichechusManatus	T G T G A G G A G G G C T A C A A G G T G G C T G G T G A G G A T G G C A C C C A G T G C C A G
SarcophilusHarrisii	T G C C A A A A G G G C T A C C A G A C A A C T G G G G A A G A T G G G A C C C A A T G C C A A
MonodelphisDomestica	T G C C A C A A G G G C T A T G T G G C T A C T G G G G A G G A T G G G A C C C A G T G C C A G

AiluropodaMelanoleuca	G A C G T G G A C G A G T G T G C G G A C A T G G A G A A T G G C C T T T G T G A C A G C T T G
UrsusMaritimus	G A C G T G G A C G A G T G T G C G G A C A T G G A G A A C G G C C T T T G T G A C A G C T T G
FelisCatus	G A T G T G G A T G A G T G T G A G G G C C C G G A G C A T G G C C T T T G T G A G G G C T T G
LeptonychotesWeddellii	G A C G T G G A C G A G T G T G C G G A C A C G G A G A A C A G C C T T T G T G A T A G C T T G
PantheraTigris	G A T G T G G A T G A G T G T G A G G G C C C G G A G C A T G G C C T T T G T G A G G G C T T G
EptesicusFuscus	- -
MyotisLucifugus	- -
MyotisBrandtii	- -
CeratheriumSimum	G A C G T G G A C G A G T G T G A G G G C C -
EquusCaballus	G A T G T G G A C G A G T G T G A G G A C T C G G A G G G C C A C C T C T G C G A C A G C T T G
OrcinusOrca	G A C G T G G A C G A G T G T G C G G G C C C G C A G G G C G G C C T C T G T G A C A G C C T G
PhyseterCatodon	G A C G T G G A C G A G T G T G C G G G C C C G C A G G G C G G C C T C T G T G G C G G C C T G
TursiopsTruncatus	G A C G T G G A C G A G T G T G C G G G C C C A C A G G G C G G C C T C T G T G A C A G C C T G
BubalusBubalis	G A C G T G G A T G A G T G T G A G G T C C A G C A G G G T G G C C T C T G C G A C A G C C T G
OvisAries	G A C G T G G A C G A G T G T G A G G T C C A G C A G G G T G G C C T C T G C G A C A G C C T G
OtolemurGarrettii	G A T G T G G A C G A G T G T G C G G C C C T G G G G A C A G C C T C T G T G A C A A C C T C
CallithrixJacchus	G A C G T G G A C G A G T G T G C A G G C C C C G G A G T C T C C C C C T G T G A C A G C T T G
SaimiriBoliviensis	G A T G T G G A C G A G T G T G C A G G C C C T G G G G T C T C C C C C T G T G A C A G C T T G
ChlorocebusSabaeus	G A C G T G G A T G A G T G T G T G G G C C C G G G G G C C C C T C T G C G A C A G C T T G
MacacaFascicularis	G A C G T G G A T G A G T G T G T G G G C C C G G G G G C C C C T C T G C G A C A G C T T G
HomoSapiens	G A C G T G G A T G A G T G T G T G G G C C C G G G G G C C C C C T C T G C G A C A G C T T G
NomascusLeucogenys	G A C G T G G A C G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C C T G
PanPaniscus	G A C G T A G A C G A G T G T G T G G G C C C G G G G G G C C C C T C T G C G A C A G C T T G
PanTroglodytes	G A C G T A G A C G A G T G T G T G G G C C C G G G G G G C C C C C T C T G C G A C A G C T T G
PongoAbelii	G A C G T G G A C G A G T G T T T G G G C C T G G G G G G C C C C T T C T G T G A C A G C T T G
ChrysochlorisAsiatica	G A T G T G G A T G A G T G C A C A G G C C C A G A G G C C A G T C C T T G T G A A G G C C T G
EchinopsTelfairi	G A C A T A G A C G A A T G C A C A A G C C C A G G A G C T G A G C A T T G C G G G A A C A G
DasypusNovemcinctus	G A C G T G G A C G A G T G C A C A G G C T G G A G A G C A G C C C T T G T G A C A G C T T G
TrichechusManatus	G A T G T G G A C G A G T G C A C A G G C C A G G G G G C C G G C C C T G C A G G G A C C T G
SarcophilusHarrisii	G A T G T G A A T G A G T G T G A G G A - - - - - G G A G A G A A A C C C C T G T G A A G G C T T C
MonodelphisDomestica	G A C G T G A A T G A G T G T G A T G A T - - - - - G A G G G C A A C C C A T G T G A A A G C C T C
AiluropodaMelanoleuca	T G C C T C A A C A C A C A G G G G T C C T T C C G C T G C G G C T G C C T G C C G G G C T G G
UrsusMaritimus	T G C C T C A A C A C A C A G G G G T C C T T C C G C T G C G G C T G C C T G C C G G G C T G G
FelisCatus	T G C C T C A A T A C G C A G G G T C C T T C C G C T G C A G C T G C C T G C C G G G C T G G
LeptonychotesWeddellii	T G C C T C A A C A C G C A G G G T C C T T C C G C T G C G G C T G C C T G C C G G G C T G G
PantheraTigris	T G C C T C A A T A C G C A G G G T C C T T C C G C T G C A G C T G C C T G C C G G G C T G G
EptesicusFuscus	T G C C T C A A C A C G C A G G G T C C T T C C G C T G C A C C T G C T G C C A G G C A G G
MyotisLucifugus	T G C C T C A A C A C G C A A G G T C C T T C C G C T G C A C C T G C T T G C C A G G T A T G
MyotisBrandtii	T G C C T C A A C A C G C A A G G T C C T T C C G C T G C A C C T G C T T G C C A G G C A T G
CeratheriumSimum	T G C T T C A A C G T G C A G G G T C C T T C C G C T G C G G C T G C C T G C C A G G C T G G
EquusCaballus	T G C T T C A A C A T G C A G G G T C C T T C C G C T G C G G C T G C C T G C C A G G C T G G
OrcinusOrca	T G C T T C A A C A C G G A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
PhyseterCatodon	T G C T T C A A C A C G G A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
TursiopsTruncatus	T G C T T C A A C A C G G A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
BubalusBubalis	T G C T T C A A C A C A G A G G G T C C T T C C G C T G T G G C T G C C T G C C G G G C T G G
OvisAries	T G C T T C A A C A C A G A G G G T C C T T C C G C T G T G G C T G C C T G C C G G G C T G G
OtolemurGarrettii	T G C T T C A A C A C A G G G T C C T T C A G C T G T G G C T G C C T G C C A G G C A T G
CallithrixJacchus	T G C T T C A A C A C A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
SaimiriBoliviensis	T G C T T C A A C A C A A A G G G T C C T T C C T C T G T G G C T G C C T G A C A G G C T G G
ChlorocebusSabaeus	T G C T T C A A C A C A A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
MacacaFascicularis	T G C T T C A A C A C A A A G G G T C C T T C C G C T G T G G C T G C C T G C C A G G C T G G
HomoSapiens	T G C T T C A A C A C A A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G
NomascusLeucogenys	T G C T T C A A C A C A A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G
PanPaniscus	T G C T T C A A C A C A A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G
PanTroglodytes	T G C T T C A A C A C A A A G G G T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G
PongoAbelii	T G C T T C A A C A C A A A G G G T C C T T C C A C T G T G G C T G C T T G C C A G G C T G G
ChrysochlorisAsiatica	T G C T T C A A T A T C C C A G G C T C C T T C C A C T G C G G A T G C C T A C C A G G C T G G
EchinopsTelfairi	T G T T T C A A T G T G C C A G G C T C C T T C C A C T G T G G C T G C C T G C C A G G C T G G
DasypusNovemcinctus	T G C T T C A A C A C G C C A G G C T C T T T C T A C T G C G A C T G C C T G C C G G G C T G G
TrichechusManatus	T G C T T C A A T G T G C C G G G C T C C T T C C G C T G T G G C T G C T T G C C A G G C T G G
SarcophilusHarrisii	T G C T A C A A T A T A C C A G G T T C T T T C C A G T G T G G C T G C C T G C C A G G A T G G
MonodelphisDomestica	T G C T T C A A T A T A C A A G G T T C C T T C C G C T G T G G C T G C C T G C C A G G A T G G

AiluropodaMelanoleuca	G A G C T G G G C C T G G A C G G G G T C T C G T G C A C C C C T G G C C C A C G T C C C T G
UrsusMaritimus	G A G C T G G G C C C G G A C G G G G T C T C G T G C A C C C C T G G C C C A T G T C T C T G
FelisCatus	G A G C T G G G C C C G G A T G G G G T C T C G T G T A C C A C A G G G T C C A C G T C T C T G
LeptonychotesWeddellii	G A G C T G G G C C T G G A C G G G G T C T C G T G C A C C C C G G G C C C A C G T C C C T G
PantheraTigris	G A G C T G G G C C C G G A T G G G G T C T C A T G T A C C G C A G G G T C C A C G T C T C T G
EptesicusFuscus	G A G C T G G C C C C G A C G G G T C T C T G T A T C A C A G G C C C A C G T C C C T G
MyotisLucifugus	G A G C T G G C C C C G A C G G G T C T C T G T A T C A C A G G C A C C A C A T C C C T G
MyotisBrandtii	G A G C T G G C T C C G A C G G G T C T C T G T A T C A C A G G C C C A C G T T C C T G
CeratotheriumSimum	G A A C T G G C T C C T G A T G G A G T C T C T G C A C C A T G G G C G C T A C G A C C C T G
EquusCaballus	G A G C T G G C T C C C A A T G G G G T C T C T G C A T C A T G G G C A C C A C A A C C C T G
OrcinusOrca	G A G C T G T C C C C G A T G G G G T C T C T G C A C T G G G G G C C T C A C A T C C C T A
PhyseterCatodon	G A G C T G T C C C C G A T G G G G T C T C T G C A C T G G G G G C C T C A C A T C C C T A
TursiopsTruncatus	G A G C T G T C C C C G A T G G G G T C T C T G C A C T G G G G G C C T C A C A T C C C T A
BubalusBubalis	G A G C T G G A C C C C A A T G G C G T C T C T G C A C T G G G G G C C C A C A T C A T T G
OvisAries	G A G C T G G A C A C C A A C G G C G T C T C T G C A C T G G G G G C C C A C A T C G T T G
OtolemurGarrettii	G A G C T G G C C C C G A T G G G G T C T C T G C A T C A T A G C C C C T G T G T C T C T G
CallithrixJacchus	G A G C T G G C C C C A A A T G G G G T C T C T G C A C C A T G G G C C T G T G T C T C T G
SaimiriBoliviensis	G A G C T G G C C C C A A A T G G G G T C T C T G C A C C A T G G G G C T T G T G T C T G T G
ChlorocebusSabaeus	G T G C T G G C C T C C A A T G G G G T C T C T G C G C C A T G G G G C C T G T G T C T C T G
MacacaFascicularis	G T G C T G G C C C C A A A T G G G G T C T C T G C G C C A T G G G G C C T G T G T C T C T G
HomoSapiens	G T G C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G
NomascusLeucogenys	G T G C T A G C C C C A A A T G G G G T C T C T G C A C C A T G G G G C C T G T G T C T C T G
PanPaniscus	G T G C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G
PanTrogodytes	G T G C T G G C C C C A A A T G G G G T C T C T T G C A C C A T G G G G C C T G T G T C T C T G
PongoAbelii	G T G C T G G C C C C A A A T G G G G T C T C T G C A C C A T G G G G C C T G T G T C T C T G
ChrysochlorisAsiatica	G A G C T G T C C C C G A T G G T A T C T G T A C C C T C A A T C A T A C A T C C T C T
EchinopsTelfairi	G A G C G G T C T C C C G A T G G G G T C T C T G C A C C C T T A G C C A C G A T C C C C T
DasypusNovemcinctus	G A G C T G G C C C C A A T G G G G T C T C T G C A C C T T C C G C A A C G T G T C T C C A
TrichechusManatus	G A G C T G G C C C C A A T G G G G T C T C T G C A T C C T C G G C C A C A C G T C C C C T
SarcophilusHarrisii	A A T T T A G C C C C C A A T G G G G T C T C T G C A T T G C C A A C C - - - - -
MonodelphisDomestica	A A T T T A G C G C C C A A A T G G T G T C T C T G C A T T G C C A A C C A C A C C A T G T C A
AiluropodaMelanoleuca	G C A C C A C C T T T C - - T G G G - - - - - C C T C C C C A G G G G G A G G - - - - - G T G C
UrsusMaritimus	G C A C C A C G G T C - - T G G G - - - - - T C T C C C C A G G G G G A G G - - - - - A T G C
FelisCatus	G C A C C A C A G A C - - T G G G - - - - - C C T C C C C A G G G A G A G G - - - - - A T A T
LeptonychotesWeddellii	A C C C T G T T G T C - - T G G G - - - - - C C T C C C C A G G G G G A G G - - - - - A T G C
PantheraTigris	G C A C C A C A G A C - - T G G G - - - - - C C T C C C C A G G G A G A G G - - - - - A T A T
EptesicusFuscus	G G A C C A T C T A C - - C G A G - - - - - A C C T C C C A G G G G C A G G - - - - - A C A C
MyotisLucifugus	G G A C C A T C T G C - - T G A G - - - - - A C C C C C A G G A G C A G A - - - - - A C A C
MyotisBrandtii	G G A C C A T C T G C - - T G A G - - - - - A C C C C C A G G A G C A G A - - - - - A C A C
CeratotheriumSimum	G G A C C A C C A G C - - T G G G - - - - - C C T C C T C A G G G G G A T G - - - - - G C A C
EquusCaballus	G G G C C A C C A G C - - T G G G - - - - - C C T C A C C A G G G G G A T G - - - - - A C A T
OrcinusOrca	G G A C C A A C A G C - - T G G G - - - - - C C T C C C C A A G G G G A G G - - - - - A C A C
PhyseterCatodon	G G A C C A C C A G C - - T G G G - - - - - C C T C C C C A A G G G G A G G - - - - - A C A C
TursiopsTruncatus	G G A C C A A C A G C - - T G G G - - - - - C C T C C C C A A G G G G A G G - - - - - A C A C
BubalusBubalis	G G A C C A C T G A C - - C A G G - - - - - T C T C C C C T T G G G G A A G - - - - - A C A C
OvisAries	G G G C C A C C G A G - - C A G G - - - - - T C T C C C C T T G G G G A A G - - - - - A C A C
OtolemurGarrettii	G T C C C A C T G G C - - T G G G - - - - - G C T C C C C A A G A G G A G G - - - - - A C A A
CallithrixJacchus	G G A C G A C C A T C - - T G G G - - - - - T C C C C T - - G A G G A G T - - - - - A C A A
SaimiriBoliviensis	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A G G A G G A G T - - - - - A C A A
ChlorocebusSabaeus	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G T - - - - - A C A A
MacacaFascicularis	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G T - - - - - A C A A
HomoSapiens	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G G - - - - - A C A A
NomascusLeucogenys	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G T - - - - - A C A A
PanPaniscus	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G G - - - - - A C A A
PanTrogodytes	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G G - - - - - A C A A
PongoAbelii	G G A C C A C C A T C - - T G G G - - - - - C C C C C G A T G A G G A G T - - - - - A C A A
ChrysochlorisAsiatica	G G A T C A A G G T C - - A A G G G G G C C T G C A C T G C A G G A G A G A G - - - - - A C C -
EchinopsTelfairi	G A A C C A C C T G T - - A G G A G G A C C T A C A T C C C A G G G A G A G - - - - - A C C -
DasypusNovemcinctus	G G A A C C C A G C - - G G G G - - - - - C C T C G C C A G G G G A A G - - - - - T C G A
TrichechusManatus	G G A C C T C C C A C A G A G G G A C C T G C G C C C C C A C A G A C A G A C C T G C A C C C
SarcophilusHarrisii	- - A C A A C A A A T - - C G G G - - - - - G C T T C A G A A G A C A A G - - - - - G A A A
MonodelphisDomestica	G T T C T T C C A A G - - T G A C - - - - - G A T C A A G A G A G G A T G - - - - - A G A A

AiluropodaMelanoleuca	C C T G G C C G C A C C T G A C G T G C T G G C T C C C A G T G G G C C C C C T G G T G T T T G
UrsusMaritimus	C C T G G C C G C A C C T G A C A T G C T G G C T C C C A G T G G G C C C C C T G G T G T T T G
FelisCatus	C C T G A C T G T G C C T G A C A T G C T G G C T C A C A G T G G G C C C C C T G G C G A A T G
LeptonychotesWeddellii	C C T G G C C G C A C C C C A C A T G C C G G C T C C C A G T G G G C C C C C T G A T G T C T G
PantheraTigris	C C T G A C T G C G C C T G A C A T G C T G G C T C C C A G T G G G C C C C C T G G T G A A T G
EptesicusFuscus	C C C T A C G T C A C C C C A G T C T C T G G C C A C C A G T G G G T C C C C A G G A A T C T G
MyotisLucifugus	C C C T A C G T C A C C C C A G T C T C T G G C C A C C A C T G G G T C C C C T G G A A T C T G
MyotisBrandtii	C C C T A C G T C A C C C C A G T C T C T G G C C A C C A C T G G G T C C C C T G G A A T C T G
CeratotheriumSimum	T C C T G C T C C A C C C A A G A C G C T G G C C C C A G T G G G C C C C C T G G C G T C T G
EquusCaballus	C C C A A C C C A C C C A A G A C G A T G T C C C A G T G G G C C C C C T G G C G T C T G
OrcinusOrca	C C T T G T C C C A C C T G A C A T G C T G G C C C C C A G T G G G T C C C C T G G T G T C T G
PhyseterCatodon	C C T T G C C C C A C C C G A C A T G C T G G C C C C C A G T G G G T C C C C T G G T G T C T G
TursiopsTruncatus	C C T T G C C C C A C C T G A C A T G C T G G C C C C A G T G G G T C C C C T G G T G T C T G
BubalusBubalis	C C T G C C C C A T C G G A G A T G C T G G C C C C C A G T G C G A C G C C T G G G G T C T G
OvisAries	C C T G C C T C C A C C G G A G A T G C T G G C C C C C A G T G A G A C G C C G G G G T C T G
OtolemurGarnettii	C T C T G C C C T G C C T G A G A C G C T G G C C C C A G T G G G G C C C C T G A G G T C C G
CallithrixJacchus	C T C T G A C C C A T T T G A A A T G C T G G C C C C A G T G G G T C C C C A A G C G T C T G
SaimiriBoliviensis	C T C T G A C C C A C T G G A A A T G C T G G C C C C T A G T G G G T C C C C A C G C A T C T G
ChlorocebusSabaeus	C T C T G T C C C A C T T G A G G T G C T G G C C C C C A G T G G G T C C C C A G G C C T C T G
MacacaFascicularis	C T C T G T C C C A C T T G A G G T G C T G G C C C C C A G T G G G T C C C C A G G C C T C T G
HomoSapiens	A T C T G C C C C A C T C A A G A T G C T G G C C C C C A G T G G G T C C C C A G G C G T C T G
NomascusLeucogenys	G T C T G C C C C A C T G G A G A T G C T G G C C C C C A G T T G G T C C C C A G G C G T C T G
PanPaniscus	A T C T G C C C C A C T C A A G A T G C T G G C C C C C A G T G G G T C C C C A G G C G T C T G
PanTrogodytes	A T C T G C C C C A C T C A A G A T G C T G G C C C C C A G T G G G T C C C C A G G C G T C T G
PongoAbelii	G T C T G A C C C A C T C A A G A T G C T G G C C C C C A G T G G G T C C C C A G G C G T C T G
ChrysochlorisAsiatica	C C A T G C T C C A A C C A A G C C C T G A C C T C C A G T G G G C C C C T G A C A T C A G
EchinopsTelfairi	T C A T G T C C C A C C C A A G A C C A T G G C C T C C A G T G G G T C C C C A T C A T C A G
DasypusNovemcinctus	C C T C A C C C T G C C C C A G A C C C T G G A G C C T A G T G G G A C C C C A G C A T C A G
TrichechusManatus	C C A T G C C C C A C C C A A G C T C C T G G C C T C C A G T G G G C C C C C A G C A A C A A
SarcophilusHarrisii	T C A A G A T C C T T C T A G G C C T C C T A C A T A C A G T A C G C A A C C A A G A A T T C A
MonodelphisDomestica	T C A A A G C C T T C C C A G G C C T C C T A C A T T C A G T A G G A A A C C A A A A C T T C A
AiluropodaMelanoleuca	G A T G G A G C C C A G C A C C C A T C A C G C C A - - - T G G C C A C C A C T G G C A G A G T
UrsusMaritimus	G A T G G A G C C C A G C A C C C A T C A A G C C C A - - - T G G C C A C C A C T G G C A G A G C
FelisCatus	G A T G G A G C C C A G C A C C C A T C A C C C C A - - - A G G C T A C C A C A G A T G G T G G
LeptonychotesWeddellii	G A T G G A G C C C A G C A C C C A T C A C C C C A - - - T G G T C A C C C C T G G C C G T G G
PantheraTigris	G A T G G A G C C C A T C A C C C A T C A C C C C A - - - A G G C T A C C A C A G A T C G T G G
EptesicusFuscus	G A T G G A G C C A G C A G C C A T C A C C C C A - - - C G G C C A C C A C T G G T C A C G A
MyotisLucifugus	G A T G G A G T A C A G C A G C C A T C A C C C C A - - - C A G C C A C C A C T G A T C A C G A
MyotisBrandtii	G A T G G A G T A C A G C A G C C A T C A C C C C A - - - C A G C C A C C A C T G G T C A C G A
CeratotheriumSimum	G A T G G A G C C C A G C A C C C A T C A C C C C T - - - C A G C C A C C A C T G G C C A T A G
EquusCaballus	G A T G G A G C C C A G C A C C C A T C A C C C C A - - - C G G C C A G C A C T G G C C A T A G
OrcinusOrca	G A T G G A G G C C A G C A C C C A T C A C C C C A - - - C G G C C A C C A C T G G C C G T G A
PhyseterCatodon	G A T G G A G G C C A G C A C C C A T C A G C C C A - - - C G G C C A C C A C C G G C C G T G A
TursiopsTruncatus	G A T G G A G G C C A G C A C C C A T C A C C C C A - - - C G G C C A C C A C T G G C C G T G A
BubalusBubalis	G A T G G A G C C C A G C A C C C A T T A C C C C A - - - C A G C C A C C A C G G C C A C A G
OvisAries	G A T G G A G C C C A G C A C C C A T C A C C C C A - - - C A G C C A C C A C G G G C C A C A G
OtolemurGarnettii	A G T G A A T C C T G G C A C C C A C C A G C C C A - - - C A G C T G C C A C T G G T C A C C G
CallithrixJacchus	G A A G G A G C C C A G C A T C C A T C A C A A C A - - - C G G C T G C C T C T G G C C C C C A
SaimiriBoliviensis	G A A G G A G C C C A G C A T C C A T C A T G T C A - - - C G G C C A T C T C T G G C C C C C A
ChlorocebusSabaeus	G A G G G A G C C C A G C A T C C A T C A C A C C A - - - C A G C T G C C T C T G G C G C C C A
MacacaFascicularis	G A G G G A G C C C A G C A T C C A T C A C A C C A - - - C A G C T G C C T C T G G T G C C C A
HomoSapiens	G A G G G A G C C C A G C A T C C A T C A C G C C A - - - C A G C T G C C T C T G G C C C C C A
NomascusLeucogenys	G A G G G A G C C C A G C A T C C A T C A C G C C A - - - C A G C T G C C T C T G G C C C C C A
PanPaniscus	G A G G G A G C C C A G C A T C C A T C A C G C C A - - - C A G C T G C C T C T G G C C C C C A
PanTrogodytes	G A G G G A G C C C A G C A T C C A T C A C A C C A - - - C A G C T G C C T C T G G C C C C C A
PongoAbelii	G A G G G A G C C C A G C A T C C A T C A C G C C A - - - C A G C T G C C T C T G G C C C C C A
ChrysochlorisAsiatica	G G T G G A G T C C A G C A C C A G C C A C C C C A - - - - - C C G C C A C T G G C C A T G C
EchinopsTelfairi	G G T A G A G C C T A G C A T G A G C T A C C C C A - - - T T A C C G T T G C T G G C C A T G C
DasypusNovemcinctus	G A T G G A G C C A A G C A C T A G T T A C C T C A - - - T G G C C A C A G C C G G C T G G G G
TrichechusManatus	G G T G G A G C C C A G C A C C A G C C G C C C C A - - - C G G C T G C T G C T G G C C A T G C
SarcophilusHarrisii	G A T G G T A T C C A G C A T C A C C C A C C C C A C A T C A A T G A T C A C C C C T G A T G G
MonodelphisDomestica	G C T G A T C T C C A G C A C T G T C T A C C C C A C A G A G A T C A C C A C T G A T G G A G G

AiluropodaMelanoleuca	G T T G T T C T A T A T C C T G G G C A C C G T G G T G G C C A T C T T A C T C T T A C T G G C
UrsusMaritimus	G T T G T T C T A T A T C C T G G G C A C A G T G G T G G C C A T C T T A C T C T T A C T G G C
FelisCatus	T T T G T T C T A T A T C C T G G G C A C A G T G G T A G C C A T C T T A C T C T T A C T G G C
LeptonychotesWeddellii	G T T G T T C T A C A T C C T G G G C A C C G T G G T G G C C A T C T T A C T C T T A C T G G C
PantheraTigris	T T T G T T C T A T A T C C T G G G C A C A G T G G T A G C C A T C T T A C T C T T A C T A G C
EptesicusFuscus	T T T G T T C T A C A T C C T C G G C A C C G T G G C G G C C A T C T T A T T C C T G C T G G C
MyotisLucifugus	T T T G T T C T A T A T C C T C G G C A C T G T G G C G G C C A T C T T A C T C C T G C T G G C
MyotisBrandtii	T T T G T T C T A T A T C C T C G G C A C T G T G G C G G C C A T C T T A C T C C T G C T G G C
CeratheriumSimum	C T T G T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C C T A C T C T T G C T G G C
EquusCaballus	C T T A T T C T A C A T C C T G G G C A C C G T G G T G G C C A T C C T G C T C T T G C T G G C
OrcinusOrca	C C T G T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C C T A T T C C T G C T G G C
PhyseterCatodon	C C T G T T C T A C A T C C T G G G C A C A G T G G T G G C C A T C C T G C T C C T G C T G G C
TursiopsTruncatus	C C T G T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C C T G T T C C T G C T G G C
BubalusBubalis	C T T A T T T T A C A T T C T T G G C A C C G T G G T G G C C A T C C T G C T C C T G C T A G C
OvisAries	C T T A T T C T A C A T T C T T G G C A C C G T C G T G G C C A T C C T G C T C C T G C T A G C
OtolemurGarrettii	T T T G T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C C T G C T C C T G C T G G C
CallithrixJacchus	T T T A T T C T A C A T C C T G G G C A C C G T G G T G G C C A T C C T C C T C C T G C T G G C
SaimiriBoliviensis	T T T G T T C T A C A T C C T G G G C A C C G T G G T G G C C A T C C T C C T C C T G C T G G C
ChlorocebusSabaeus	T T T A T T C T A C A T C C T A G G C A C C G T G G T A G G C A T C C T A C T T C T G C T G G C
MacacaFascicularis	T T T A T T C T A C A T C C T A G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C
HomoSapiens	T T T A T T C T A C A T C C T A G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C
NomascusLeucogenys	T T T A T T C T A C A T C C T A G G C A C C G T G G T G G C C A T C T T A C T C C T G C T G G C
PanPaniscus	T T T A T T C T A C A T C C T A G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C
PanTrogodytes	T T T A T T C T A C A T C C T A G G C A C C G T G G T G G C C A T C C T A C T C C T G C T G G C
PongoAbelii	T T T A T T C T A C A T C C T A G G C A C T G T G G T G G C C A T C C T A C T C C T G C T G G C
ChrysochlorisAsiatica	T C T A T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C T T A C T C C T T C T G G C
EchinopsTelfairi	T C T G T A C T A C A T T C T G G G C A C T G T G G T G G C C A T C T T A C T A C T G C T G G C
DasypusNovemcinctus	T T T G T T C T A T A T C C T G G G C A C G G T G G T G G C A T T C C T A C T C A T G C T G G C
TrichechusManatus	T C T A T T C T A C A T C C T G G G C A C T G T G G T G G C C A T C T T A C T A C T G C T G G C
SarcophilusHarrisii	C C T G T T T T A T A T T T T G G G A C A G T A G C A G C T A C C T T G C T G C T T T T G G C
MonodelphisDomestica	C C T A T T T T A T A T C C T T G G G A G C A G T A G C A G C T G T C T T G C T T C T T C T G G C
AiluropodaMelanoleuca	T C T G G C T C T G G G G C T G C T G G T C T A T C G C A A G C G G A G A G C A A A G A G G G A
UrsusMaritimus	T C T G G C T C T G G G G C T G C T G G T C T A T C G G A A G C G G A G A G C A A A G A G G G A
FelisCatus	T C T G G C T C T T G G A C T T C T G T C T A T C G C A A G C G G A A A G C A A A G A G G G A
LeptonychotesWeddellii	T C T G G C T C T A G G G C T A C T G G T C T A C C G C A A G C G G A G A G C A A A G A G A G A
PantheraTigris	T C T G G C T C T T G G A C T T C T G T C T A T C G C A A G C G G A A A G C A A A G A G G G A
EptesicusFuscus	T C T G G C C C T G G G G C T G C T G G T C T A T C G C A A G C G G A G A G C A A A G A G G G A
MyotisLucifugus	T C T G G C C C T G G G G C T G C T G G T C T A C C G C A A G C G G A G A G C A A A G A G G G A
MyotisBrandtii	T C T G G C C C T G G G G C T G C T G G T C T A C C G C A A G C G G A G A G C A A A G A G G G A
CeratheriumSimum	T C T G G C T C T C G G G C T C C T G G T C T A T C G C A A A C G G A G A G C A A A G A G G G A
EquusCaballus	T C T G G C T C T A G G G C T C C T G G T T A T C G C A A G C G G A G A G C A A A G C G G G A
OrcinusOrca	T C T G G C T C T G G G G C T C C T G G T C T A T C G C A A G C G C A G A G C A A A G A G G G A
PhyseterCatodon	T C T G G C T C T G G G G C T C C T G G T C T A T C G C A A G C G C A G A G C A A A G A G G G A
TursiopsTruncatus	T C T G G C T C T G G G G C T C C T G G T C T A T C G C A A G C G C A G A G C A A A G A G G G A
BubalusBubalis	T C T G G C C T T A G G G C T G C T G G T C T G T C G C A A G C G C A G G G C A A A G A G G G A
OvisAries	T C T G G C C C T A G G G C T G C T G G T C T G T C G C A A G C G C A G G G C A A A G A G G G A
OtolemurGarrettii	T C T G G C G C T A G G G C T T C T G T C T G T C G C A A G C G G A G A G C T A A G C A G G C
CallithrixJacchus	C C T G G C T C T G G G G C T G C T G G T C T A T C G C A A G C G G A G A G C A A A G A G G G A
SaimiriBoliviensis	C C T G G C T C T G G G G C T C C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
ChlorocebusSabaeus	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
MacacaFascicularis	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
HomoSapiens	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
NomascusLeucogenys	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G C A
PanPaniscus	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
PanTrogodytes	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
PongoAbelii	C C T G G C T C T G G G G C T A C T G G T C T A T C G C A A G C G G A G A G C G A A G A G G G A
ChrysochlorisAsiatica	T T T A G C C C T A G T G C T A C T A G T C T A T C G C A A G C G G A A A G C A A A A A G G C
EchinopsTelfairi	T C T A G C T C T A G G G C T A C T G A T C T A T C G C A A G C G G A A A G C A A G T C G G G C
DasypusNovemcinctus	C C T T G C T C T T G G G C T G C T G G T C T A C C G C A A G C A G A A A G C A A A G A G G G A
TrichechusManatus	T C T C G C C C T G G G G C T A C T G G T C T A C C G C A A G C G G A A A G C A A A G A G G G C
SarcophilusHarrisii	T A T G A C C C T G G G G T T A G T G T T C T A T C G C A A G A A A A A G C A A A A A G G G C
MonodelphisDomestica	T A T G G C C C T G G G G T T A G T G T T C T A T C G C A A G A A G A A A A C A A A A A G G C

AiluropodaMelanoleuca	A G A G G A G A A G G A G A A A A G C C C C A G A A C G C G G C T G A C A G C T A C T C C T G
UrsusMaritimus	A G A G G A G A A G G A G A A A A G C C C C A G A A C G C G G C T G A C A G C T A C T C C T G
FelisCatus	G G A G G A G A A G G A G A A A A G C C C C A G A A C G C T G C T G A C A G C T A C T C C T G
LeptonychotesWeddellii	G A A G G A G A A G G A G A A A A G C C C C A G A A C G C A G C T G A C A G C T A C T C C T G
PantheraTigris	G G A G G A G A A G G A G A A A A G C C C C A G A A C G C T G C T G A C A G C T A C T C C T G
EptesicusFuscus	G G A G - - A A G G A G A A G A A G C C T C A G A G C G C G C A G A C A G C T A C T C C T G
MyotisLucifugus	G G A G - - - A A G G A G A A G A A G C C C C A G A G C G C G C A G A C A G C T A C T C C T G
MyotisBrandtii	G G A G - - - A A G G A G A A G A A G C C C C A G A G C G C G C A G A C A G C T A C T C C T G
CeratheriumSimum	G G A G A T A A A G G A G A A A A G C C C C A G A G T G C G A C C G A C A G C T A C G C C T G
EquusCaballus	G G A G A G A A G G A G A A A A A G C C C C A G A G T G C A A C A G A C A G C T A C T C C T G
OrcinusOrca	G G A G - - - A A G G A G A A G A A G C C G C A G A G C G C A G C A G A C A G C T A C G C C T G
PhyseterCatodon	G G A G - - - A A G G A G A A G A A G C C G C A G A G C G C A G C A G A C A G C T A C G C C T G
TursiopsTruncatus	G G A G - - - A A G G A G A A G A A G C C C C A G A G C G C A G C A G A C A G C T A C G C C T G
BubalusBubalis	G G A G - - - A A G A A G C A G C A G C C G C A G A G C G C A G C G G A C A G C T A T G C C T G
OvisAries	G G A G - - - A A G A A G C A G C A G C C G C A G A G T G C C G C G G A C A G C T A C G C C T G
OtolemurGarnettii	G G A G A G A A G A G G A G A A G A T G C C C T C A A A C G C A G C A G A C A G T T A C T C C T G
CallithrixJacchus	G G A G - - - A A G G A G G A T A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
SaimiriBoliviensis	G G A G - - - A A G G A G G A G A A G C C T C A G A A T G C G G C A G A C A G G T A C T C C T G
ChlorocebusSabaeus	G G A G - - - A A G A A G G A G A A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G
MacacaFascicularis	G G A G - - - A A G A A G G A G A A G C C C C A G A A T G C A G C A G A C A G T T A C T C C T G
HomoSapiens	G G A G A G A A G A G G A G A A G A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
NomascusLeucogenys	G G A G A G A A G A G G A G A A G A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
PanPaniscus	G G A G A G A A G A G G A G A A G C A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
PanTroglodytes	G G A G A G A A G A G G A G A A G C A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
PongoAbelii	G G A G A G A A G C A G A A G A A G C C C C A G A A T G C G G C A G A C A G T T A C T C C T G
ChrysochlorisAsiatica	T C T G A A A A A G G A G A A A A A A C C C C A A T G C A G C T G A C A G T T A C T C T T G
EchinopsTelfairi	A G A G A G A A G G A G A A C A A A G T C C C A A G T G C A A C C G A C A G T T A T G C C T G
DasypusNovemcinctus	G G A G A G A A G A G G A G A A A A C C C C A G A G C G C A G C T G A C A G T T A C T C C T G
TrichechusManatus	A G A G A G A G G G A G A A A A C A C C C C A A G C G C A G C T G A C A G T T A C T C C T G
SarcophilusHarrisii	A G A G - - - - - A A G A A A T C C C C T C A A A A T G C A G C T G A C A G C T A C T C C T G
MonodelphisDomestica	A A T G - - - A A G A A G A A G T C C C C T A A G A A T G C A G C T G A C A G C T A T T C C T G
AiluropodaMelanoleuca	G G C T C C A G A G C G A G C A G A G A G C A G G G C T T T G G A G A A T C A G T A C A - - - -
UrsusMaritimus	G G C T C C A G A G C G A G C A G A G A G C A G G G C T T T G G A G A A T C A G T A C A - - - -
FelisCatus	G G C T C C A G A G C G G G C T G A G A A C A G G G C C T T G G A G A A T C A G T A C A - - - -
LeptonychotesWeddellii	G G C T C C A G A G C G A G C T G A G A G C A G G G C T T T G G A G A A T C A G T A C A - - - -
PantheraTigris	G G C T C C A G A G C G G G C T G A G A A C A G G G C C T T G G A G A A T C A G T A C A - - - -
EptesicusFuscus	G G T T C C G A G A G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
MyotisLucifugus	G G T T C C G G A G A G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
MyotisBrandtii	G G T T C C G G A G A G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
CeratheriumSimum	G G T T C C C G A G C G A G C C G A G A G C A G G G C C A T G G A G A A T C A G T A C A - - - -
EquusCaballus	G G C C C C A G A G C G A G C T G A G A G C A G G G C C A C A G A G A A C C A G T A C A - - - -
OrcinusOrca	G G T C C C T G A G C G A G C C G A G A G C A G G G C A A C G G A G A A C C C C T A C A - - - -
PhyseterCatodon	G G T C C C T G A G C G A G C C G A G A G C A G G G C A A C G G A G A A C C C C T A C A - - - -
TursiopsTruncatus	G G T C C C T G A G C G A G C C G A G A G C A G G G C A A C G G A G A A C C C C T A C A - - - -
BubalusBubalis	G G T C C C G A G C G G G C T G A G A G C A G A G C C A T G G A G A A C C C C T A C A - - - -
OvisAries	G G T C C C G A G C G G G C T G A G A G C A G A G C C A C G G A G A A C C C C T A C A - - - -
OtolemurGarnettii	G G C T T C A G A G C G G G C A G A G A G C A G G G C C A C A G A G A A C C A G T A C A - - - -
CallithrixJacchus	G G T T C C A G A G C G A G C G G A G G G C A G G G C C A T G G A G A A C G A G T A C A - - - -
SaimiriBoliviensis	G G T T C C A G A G C G A G C G G A G G G C A G G G C C A T G G A G A A C G C G T A C A - - - -
ChlorocebusSabaeus	G G T T C C A G A G C G A G C A G A G A G C A G G G C A A T G G A G A A C C A G T A C A - - - -
MacacaFascicularis	G G T T C C A G A G C G A G C A G A G A G C A G G G C A A T G G A G A A C C A G T A C A - - - -
HomoSapiens	G G T T C C A G A G C G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
NomascusLeucogenys	G G T T C C A G A G C G A G T G G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
PanPaniscus	G G T T C C A G A G C G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
PanTroglodytes	G G T T C C A G A G C G A G C T G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
PongoAbelii	G G T T C C A G A G C G A G C G G A G A G C A G G G C C A T G G A G A A C C A G T A C A - - - -
ChrysochlorisAsiatica	G G T T C C T G A G C G A G G A G A G T G C A G G G C C G T G G A G A A T C A A T A C A - - - -
EchinopsTelfairi	G G T T G C C G A G C G A G C T G A G C C A G G G C C A C G A G A A T C A G T A C A - - - -
DasypusNovemcinctus	G G T T C C A G A G C G A A G T G A G A A C A G G G C C A T G G A G A A T C A G T A C A - - - -
TrichechusManatus	G G T T C C C G A G C G A G C T G A G A G C A G G G C T A A G A A G A A T G A G T A C A - - - -
SarcophilusHarrisii	G G T C C C T G A G C A G G C T G A G A A C A G G G C A G T A G A A A A T G A G T A C A G C G T
MonodelphisDomestica	G G T C C C T G A G C A G G T T G A G A A C A G G G C A A T A G A A A A T G A G T A C A - - - -


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AiluropodaMelanoleuca - - - - -
UrsusMaritimus - - - - -
FelisCatus - - - - -
LeptonychotesWeddellii - - - - -
PantheraTigris - - - - -
EptesicusFuscus - - - - -
MyotisLucifugus - - - - -
MyotisBrandtii - - - - -
CeratotheriumSimum - - - - -
EquusCaballus - - - - -
OrcinusOrca - - - - -
PhyseterCatodon - - - - -
TursiopsTruncatus - - - - -
BubalusBubalis - - - - -
OvisAries - - - - -
OtolemurGarnettii - - - - -
CallithrixJacchus - - - - -
SaimiriBoliviensis - - - - -
ChlorocebusSabaeus - - - - -
MacacaFascicularis - - - - -
HomoSapiens - - - - -
NomascusLeucogenys - - - - -
PanPaniscus - - - - -
PanTroglodytes - - - - -
PongoAbelii - - - - -
ChrysochlorisAsiatica - - - - -
EchinopsTelfairi - - - - -
DasypusNovemcinctus - - - - -
TrichechusManatus - - - - -
SarcophilusHarrisii G G G A G A T G G A G A C C G T T A T T T G T T T A C T T T G T A A A C T C C T C G G T G T A
MonodelphisDomestica - - - - -

AiluropodaMelanoleuca - G T C C G A C G C C A G G G A C G G A - - - - -
UrsusMaritimus - G T C C G A C G C C A G G G A C G G A - - - - -
FelisCatus - G T C C A A C G C C A G G G A C G G A - - - - -
LeptonychotesWeddellii - G T C C G A C G C C A G G G A C G G A - - - - -
PantheraTigris - G C T G T G T G C A T T T A T C T G C - - - - -
EptesicusFuscus - G T C C A A C A C C T G G G A C A G A - - - - -
MyotisLucifugus - G T C C A A C A C C T G G G A C A G A - - - - -
MyotisBrandtii - G T C C A A C A C C T G G G A C A G A - - - - -
CeratotheriumSimum - G T C C A A C A C C A G G G A C A G A - - - - -
EquusCaballus - G T C C G A C G C C G G G T C A G A - - - - -
OrcinusOrca - G T C C G A C G C C A G G G A C A G A - - - - -
PhyseterCatodon - G T C C G A C G C C G G G A C A G A - - - - -
TursiopsTruncatus - G T C C G A C G C C G G G A C A G A - - - - -
BubalusBubalis - G T C C G A C G C C A G G G A C A G A - - - - -
OvisAries - G T C C G A C A C C A G G G A C A G A - - - - -
OtolemurGarnettii - - - - -
CallithrixJacchus - G T C C G A C A C C T G G G A C A G A - - - - -
SaimiriBoliviensis - G T C C G A C A C C T G G G A C A G A - - - - -
ChlorocebusSabaeus - G T C C G A C A C C T G G G A C A G A - - - - -
MacacaFascicularis - G T C C G A C A C C T G G G A C A G A - - - - -
HomoSapiens - G T C C G A C A C C T G G G A C A G A - - - - -
NomascusLeucogenys - G T C C G A C A C C T G G G A C A G A - - - - -
PanPaniscus - G T C C G A C A C C T G G G A C A G A - - - - -
PanTroglodytes - G T C C G A C A C C T G G G A C A G A - - - - -
PongoAbelii - G T C C G A C A C C C G G G A C A G A - - - - -
ChrysochlorisAsiatica - G T C C A A C G C C T G G G A C A G A - - - - -
EchinopsTelfairi - - - - -
DasypusNovemcinctus - G T C C A A C G C C T G G G A C G G A - - - - -
TrichechusManatus - G T C C A A C G C C C G G G A C A G A - - - - -
SarcophilusHarrisii C G T C C T C C A C C C T G G C C C C A C A C A C C C C A T T T A C C C C A C C C C A C C C A A
MonodelphisDomestica - - - - -
```

AiluropodaMelanoleuca	- - - - -	CTGC
UrsusMaritimus	- - - - -	CTGC
FelisCatus	- - - - -	CTGC
LeptonychotesWeddellii	- - - - -	CTGC
PantheraTigris	- - - - -	TTGC
EptesicusFuscus	- - - - -	CTGC
MyotisLucifugus	- - - - -	CTGC
MyotisBrandtii	- - - - -	CTGC
CeratheriumSimum	- - - - -	CTGC
EquusCaballus	- - - - -	CTGC
OrcinusOrca	- - - - -	CTGT
PhyseterCatodon	- - - - -	CTGT
TursiopsTruncatus	- - - - -	CTGT
BubalusBubalis	- - - - -	CTGC
OvisAries	- - - - -	CTGC
OtolemurGarnettii	- - - - -	- - GG
CallithrixJacchus	- - - - -	CTGC
SaimiriBoliviensis	- - - - -	CTGC
ChlorocebusSabaeus	- - - - -	CTGC
MacacaFascicularis	- - - - -	CTGC
HomoSapiens	- - - - -	CTGC
NomascusLeucogenys	- - - - -	CTGC
PanPaniscus	- - - - -	CTGC
PanTrogodytes	- - - - -	CTGC
PongoAbelii	- - - - -	CTGC
ChrysochlorisAsiatica	- - - - -	CTGT
EchinopsTelfairi	- - - - -	- - GG
DasybusNovemcinctus	- - - - -	CTGT
TrichechusManatus	- - - - -	CTGT
SarcophilusHarrisii	G T C A C C C T C T T T G G C C T C C G C A G T G C T C A G C A A T T T C T A T G A C T C T G C	
MonodelphisDomestica	- - - - -	- - GG

AiluropodaMelanoleuca	T - - - -	G - - - -	A
UrsusMaritimus	T - - - -	G - - - -	A
FelisCatus	T - - - -	G - - - -	A
LeptonychotesWeddellii	T - - - -	G - - - -	A
PantheraTigris	T - - - -	G T A G A A C C A G T T G G A G T T T T T A A	
EptesicusFuscus	T - - - -	G - - - -	A
MyotisLucifugus	T - - - -	G - - - -	A
MyotisBrandtii	T - - - -	G - - - -	A
CeratheriumSimum	T - - - -	G - - - -	A
EquusCaballus	T - - - -	G - - - -	A
OrcinusOrca	T - - - -	G - - - -	A
PhyseterCatodon	T - - - -	G - - - -	A
TursiopsTruncatus	T - - - -	G - - - -	A
BubalusBubalis	T - - - -	G - - - -	A
OvisAries	T - - - -	G - - - -	A
OtolemurGarnettii	T - - - -	A - - - -	A
CallithrixJacchus	T - - - -	G - - - -	A
SaimiriBoliviensis	T - - - -	G - - - -	A
ChlorocebusSabaeus	T - - - -	G - - - -	A
MacacaFascicularis	T - - - -	G - - - -	A
HomoSapiens	T - - - -	G - - - -	A
NomascusLeucogenys	T - - - -	G - - - -	A
PanPaniscus	T - - - -	G - - - -	A
PanTrogodytes	T - - - -	G - - - -	A
PongoAbelii	T - - - -	G - - - -	A
ChrysochlorisAsiatica	T - - - -	G - - - -	A
EchinopsTelfairi	T - - - -	A - - - -	A
DasybusNovemcinctus	T - - - -	G - - - -	A
TrichechusManatus	T - - - -	G - - - -	A
SarcophilusHarrisii	T T T A C T C A T A G A G C G A G G T G A T C G C A G C G T T T T G G T A A C A C A A T A A		
MonodelphisDomestica	T - - - -	A - - - -	A

Appendix 3 : Nucleotide alignment for mammalian CD93 sequences.

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus M P S A S A N P L H H L E G A A P A G F I L Q S V K K L P A C K Q T L R N A V S P R Q R T R P T L V
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta - - - - - M K L D D E M Q P L
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus K P K L M A S Y I G W E P G M P A F P G P L T L S S S G T L S I L R R Q V T R T G G L G G S D P Q E
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta D A S S R V T D W H K D A W P I D H M V L K P S G N T S I P G S H G R E P A S S Q A Q G H P N I S M
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus A V F H V L R T R Q L Q W T Q S S R T S A P G S T N R S H A V L L H V Q C L P P T P V A F H L P S A
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta E A T V V ? - - - - -
Papio anubis - - - - -

Otolemur garnettii - - - - -
Tarsius syrichta - - - - -
Homo sapiens - - - - -
Nomascus leucogenys - - - - -
Pan paniscus - - - - -
Pan troglodytes - - - - -
Pongo abelii - - - - -
Callithrix jacchus L P P T L V P C H L P S A L P P T L V S F H L P S A L P P T L V S F H L S
Saimiri boliviensis - - - - -
Chlorocebus sabaues - - - - -
Macaca fascicularis - - - - -
Macaca mulatta - - - - - ? A V A R F T G V P C V L
Papio anubis - - - - -

Otolemur garnettii - - - - - M A T S T H - - L L L L L L L G Q P W A T
Tarsius syrichta - - - - - M A T S T G - L L L L L L L L G Q P W V G
Homo sapiens - - - - - M A T S M G L L L L L L L L L T Q P G A G
Nomascus leucogenys - - - - - M A T P M G - L L L L L L L L S Q P G A G
Pan paniscus - - - - - M A T S M G - L L L L L L L L T Q P G A G
Pan troglodytes - - - - - M A T S M G - L L L L L L L L T Q P G A G
Pongo abelii - - - - - M A T F M G - L L L L L L L L S Q P G A G
Callithrix jacchus S A L P H T P K L L S P S S L L G F S P P A E G H M E T G M A T F T T - L L L L L L L L V Q P G A G
Saimiri boliviensis - - - - - - - M E T G M A T F T G - L L L L L L L G Q P G A G
Chlorocebus sabaues - - - - - - - M A T S M G L L L L L L L L L R Q L G A G
Macaca fascicularis - - - - - - - M A T S V G L L L L L L L L L R Q L G A G
Macaca mulatta H R G A S P G A F T K L L S L L G F S P P A E G H T E T G M A T S V G L L L L L L L L L R Q L G A G
Papio anubis - - - - - - - M A T S V G L L L L L L L L L R Q L G A G

Otolemur garnettii A G A A M E A V V C A D T A C Y T A H W G K L S A A E A Q Q H C S K N G G K L T T V K S E E E A G H
Tarsius syrichta T S V D T E A V V C G G T A C Y T A H W G K L S A A E A Q D H C Q S N G G N L A T V K S E E E A Q H
Homo sapiens T G A D T E A V V C V G T A C Y T A H S G K L S A A E A Q N H C N Q N G G N L A T V K S K E E A Q H
Nomascus leucogenys T G A N T E A V V C A G T A C Y T A H S G K L S A A E A Q N H C S Q N G G N L A T V K S E E E A Q H
Pan paniscus T G A D T E A V V C V G T A C Y T A H S G K L S A A E A Q N H C N Q N G G N L A T V K S E E E A Q H
Pan troglodytes T G A D T E A V V C V G T A C Y T A H S G K L S A A E A Q N H C N Q N G G N L A T V K S E E E A Q H
Pongo abelii T G A D T E A V V C V G T A C Y T A H S G K L S A A E A Q N H C S Q N G G N L A T V K S E E E A Q D
Callithrix jacchus T G G D T E A V V C A G M A C Y T A H W G K L S A A D A Q N H C S Q N G G N L A T V K S K E E A Q H
Saimiri boliviensis M G G D T E A V V C A E M A C Y T A H W G K L S A A E A Q S H C S Q N G G N L A T V K S R E E A Q H
Chlorocebus sabaues T G A D T E A V V C A G T A C Y T A H S G K L S A A E A Q N L C L Q N G G N L A T V K S E E E A Q H
Macaca fascicularis T G A D T E A V V C A G T A C Y T A H W G K L S A A E A Q N L C L Q N G G N L A T V K S E E E A Q H
Macaca mulatta T G A D T E A V V C A G T A C Y T A H W G K L S A A E A Q N L C L Q N G G N L A T V K S E E E A Q H
Papio anubis T G A D T E A V V C A G T A C Y T A H W G K L S A A E A Q N L C L Q N G G N L A T V K S E E E A Q H

Otolemur garnettii V Q R T L A Q L L S L Q A S L A A R M G K F W I G L Q R E K G K C Q D P R L P L K G F S W V G G G E
Tarsius syrichta V Q Q A L A Q L L T P E K A L A A R F G K F W I G L Q R E K G K C L D P S L P L K G F A W V G G G E
Homo sapiens V Q R V L A Q L L R R E A A L T A R M S K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Nomascus leucogenys V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Pan paniscus V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Pan troglodytes V Q R V L A Q L L R R E A A L T A R I G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Pongo abelii V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Callithrix jacchus I Q R A L A Q L L R L E A N L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Saimiri boliviensis I Q R A L A Q L L R L E A N L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Chlorocebus sabaues V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Macaca fascicularis V Q Q V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Macaca mulatta V Q Q V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E
Papio anubis V Q Q V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L P L K G F S W V G G G E

Otolemur garnettii D T L Y T N W H K E A R N S C I S K R C V S L L L D L S L T P T T S R L P K W S E G P C G N P V S P
Tarsius syrichta D T A Y T N W H K E V R S S C I S R R C V A L L L D L S Q P P L P G R F P K W S E G P C G N P S T P
Homo sapiens D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P S R L P K W S E G P C G S P G S P
Nomascus leucogenys D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P S R L P K W S E G P C G S P G S P
Pan paniscus D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P S R L P K W S E G P C G S P G S P
Pan troglodytes D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P S R L P K W S E G P C G S P G S P
Pongo abelii D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P S R L P K W S E G P C G S P S S P
Callithrix jacchus D T P Y T N W Y K E L R N S C I S K R C V S L L L D L S Q P L L S S Y L P R W S E G P C G S S D S P
Saimiri boliviensis D T P Y A N W Y K E L R S C V S K R C V S L L L D L S Q P L L S S H L P R W S E G P C G S S D S P
Chlorocebus sabaues D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P R R L P K W S E G P C G S P G S P
Macaca fascicularis D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P G R L P K W S E G P C G S P G S P
Macaca mulatta D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P G R L P K W S E G P C G S P G S P
Papio anubis D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P L L P R R L P K W S E G P C G S P G S P

Otolemur garnettii G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q A T S S S L D A V P F A S M A
Tarsius syrichta G S S I E G F V C K F S F K G M C R P L A L G G P G Q V T Y N T P F K A I S S S L E A V P F A S M A
Homo sapiens G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Nomascus leucogenys G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Pan paniscus G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Pan troglodytes G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Pongo abelii G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Callithrix jacchus G N N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Saimiri boliviensis G N N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Chlorocebus sabaues G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Macaca fascicularis G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Macaca mulatta G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A
Papio anubis G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F Q T T S S S L E A V P F A S A A

Otolemur garnettii S V A C G D ? - ? N E S T S H Y F L C K E K E P N V F E W N S S G P L C V S P D Y G C N F N N G G C
Tarsius syrichta Y V S C G D R A T D K S H ? - ? I L C R E K G P G V F E W G T P G P F C V N P E L G C S F N N G G C
Homo sapiens N V A C G E G D K D E T Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Nomascus leucogenys D V A C G E G D K D K S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Pan paniscus N V A C G E G D K D E S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C S F N N G G C
Pan troglodytes N V G C G E G D K D E S Q S H Y F L C K E K A P D V F D W G S S G P L C V I P K Y G C S F N N G G C
Pongo abelii T V A C G E G D K D E S Q S H Y F L C K E K A P G V F D W G S S G P L C V S P K Y G C N F N N G G C
Callithrix jacchus N V A C G D R D Q D K S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C S F N N G G C
Saimiri boliviensis N V I C G D G D Q D K S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Chlorocebus sabaues N V A C G E G D K D D S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Macaca fascicularis N V A C G E G D K D D S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Macaca mulatta N V A C G E G D K D D S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C
Papio anubis N V A C G E G D K D D S Q S H Y F L C K E K A P D V F D W G S S G P L C V S P K Y G C N F N N G G C

Otolemur garnettii Q Q A C F E G G D G S F R C G C L P G F R L L D D L V T C A S R N P C S S S P C I G E A T C V S A P
Tarsius syrichta E Q D C F E G G D G S F R C G C R P G F R L L D D L V S C A S R N P C S S S P C S G E A T C V P G P
Homo sapiens H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C V L G P
Nomascus leucogenys H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G E A T C I L G P
Pan paniscus H Q D C F E G E D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I L G P
Pan troglodytes H Q D C F E G E D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I L G P
Pongo abelii H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I L G P
Callithrix jacchus H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I Q G S
Saimiri boliviensis H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I Q G S
Chlorocebus sabaues H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I P G P
Macaca fascicularis H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I P G P
Macaca mulatta H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I P G P
Papio anubis H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P C S S S P C R G G A T C I P G P

Otolemur garnettii H G T N Y T C H C P Q G F Q V D E S Q L G C V D V D E C Q D S P C V Q A C V N T H G S F R C E C W V
Tarsius syrichta H R E D F M C R C P S G Y Q L D A S Q L S C E D V D E C Q A S P C A Q Q C V N T P G G F R C E C W V
Homo sapiens H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Nomascus leucogenys H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Pan paniscus H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Pan troglodytes H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Pongo abelii H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Callithrix jacchus Q G K N Y T C H C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Saimiri boliviensis H G K N Y T C H C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G G F R C E C W V
Chlorocebus sabaues H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G S F R C E C W V
Macaca fascicularis H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G S F R C E C W V
Macaca mulatta H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G S F R C E C W V
Papio anubis H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A Q E C V N T P G S F R C E C W V

Otolemur garnettii G Y E P S S P G E G A C Q D V D E C A L G R S P C T Q R C T N T D G S F H C S C E E G Y V L A G E D
Tarsius syrichta G Y E P G G P G E A A C R D V D E C A P S R T P C A Q N C T N T D G S F H C S C R E G Y V L A G E D
Homo sapiens G Y E P G G P G E G A C Q D V D E C A L G R S P C A Q G C T N T D G S F H C S C E E G Y V L A G E D
Nomascus leucogenys G Y E P G G P G E R T C R D V D E C A L D R S P C A Q G C T N T E G S F H C S C E E G Y V L A G E D
Pan paniscus G Y E P G S P G E G A C Q D V D E C A L G R S P C A Q G C T N T D G S F H C S C K E G Y V L A G E D
Pan troglodytes G Y E P G G P G E G A C Q D V D E C A L G R S P C A Q G C T N T D G S F H C S C K E G Y V L A G E D
Pongo abelii G Y E P G G P G E G A C R D V D E C A L G R S P C A Q G C T N T D G S F H C S C E E G Y V L A G E D
Callithrix jacchus G Y Q P D G P G E G A C R D V D E C A L D P S P C A Q G C T N T D G S F Y C S C Q E G Y V L A E E D
Saimiri boliviensis G Y E P G G P G E G V C Q D V D E C A L D P S P C A Q G C T N T D G S F Y C S C Q E G Y V L A E E D
Chlorocebus sabaues G Y E P G G P G E G V C Q D V D E C A P G R S P C A Q G C T N T E G S F H C S C E E G Y V L A G E D
Macaca fascicularis G Y E P G G P G E G A C Q D V D E C A L G R S P C A Q G C T N T E G S F H C S C E E G Y V L A G E D
Macaca mulatta G Y E P G G P G E G A C Q D V D E C A L G R S P C A Q G C T N T E G S F H C S C E E G Y V L A G E D
Papio anubis G Y E P G G P G E E A C Q D V D E C A L G R S P C A Q G C T N T E G S F H C S C E E G Y V L A G E D

Otolemur garnettii G T Q C Q D V D E C A G P G D S L C D N L C F N T Q G S F S C G C L P G M E L A P D G V S C I I A P
Tarsius syrichta G T Q C Q D V N E C E G L G S S R C D S L C L N T Q G S F L C G C L P G W E L A A D G V S C T M G P
Homo sapiens G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C L P G W V L A P N G V S C T M G P
Nomascus leucogenys G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C L P G W V L A P N G V S C T M G P
Pan paniscus G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C L P G W V L A P N G V S C T M G P
Pan troglodytes G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C L P G W V L A P N G V S C T M G P
Pongo abelii G T Q C Q D V D E C L G L G G P F C D S L C F N T Q G S F H C G C L P G W V L A P N G V S C T M G P
Callithrix jacchus G T Q C Q D V D E C A G P G V S P C D S L C F N T Q G S F R C G C L T G W E L A P N G V S C T M G L
Saimiri boliviensis G T Q C Q D V D E C A G P G V S P C D S L C F N T Q G S F L C G C L T G W E L A P N G V S C T M G L
Chlorocebus sabaues G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F R C G C L P G W V L A S N G V S C A M G P
Macaca fascicularis G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F R C G C L P G W V L A P N G V S C A M G P
Macaca mulatta G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F R C G C L P G W V L A P N G V S C A M G P
Papio anubis G T Q C H D V D E C V G P E G P L C D S L C F N T Q G S F R C G C L P G W V L A P N G V S C A M G P

Otolemur garnettii V S L V P L A G A P Q E E D N G K R E R R P M P S A T T L S P T R G P E T S F E A V P A S R ? - ? P
Tarsius syrichta V P P R S P T G L P Q E E D Q E E R E G S T I P P A A A S S P T G G S E G T S Q V A P T S G R P S L
Homo sapiens V S L G P P S G P P D E E D K G E K E G S T V P R A A T A S P T R G P E G T P K A T P T T S R P S L
Nomascus leucogenys V S L G P P S G P P D E E Y K G E K E G N T I L P A A T A S P T R G S E G T P K A T P T A R R P S L
Pan paniscus V S L G P P S G P P D E E D K G E K E G S T V P P A A T A S P T R G P E G T P K A T P T T S R P S L
Pan troglodytes V S L G P P S G P P D E E D K G E K E G S T V P P A A T A S P T R G P E G T P K A T P T T S R P S L
Pongo abelii V S L G P P S G P P D E E Y K G E K E G S T V P P A A T A S P T R G P E G T P K A T S T A R R P S L
Callithrix jacchus V S L G R P S G S P - E E Y K G K K E G S T V A P T A T A S P T R G P K G T P R A T P T T R R L S L
Saimiri boliviensis V S V G P P S G P P E E E Y K G K K E G S T V A P A A A S P T R G P E G T P R A T P T T R R L S L
Chlorocebus sabaues V S L G P P S G P P D E E Y K G E R E G S T V P P A A T A S P T R G P E G T A K S T P T T R S P S L
Macaca fascicularis V S L G P P S G P P D E E Y K G E R E G S T V P P A A T A S P T R G P E G T P K S T P T T R R P L L
Macaca mulatta V S L G P P S G P P D E E Y K G E R E G S T V P P A A T A S P T R G P E G T P K S T P T T R R P L L
Papio anubis V S L G P P S G P P D E E Y K G E R E G S T V P P A A T A S P T R G P E G T P K S T P T T R R P L L

Otolemur garnettii P S S T P I T S A L P E T L A P S G A P E V R V N P G T H Q P T A A T G H R E S A G R ? ? S V A T Q
Tarsius syrichta L F R V P I T S A P P E M L T H S G P P G I R T E S R T H H P M A A T G H W D S A A G ? ? S V D T K
Homo sapiens S S D A P I T S A P L K M L A P S G S P G V W R E P S I H H A T A A S G P Q E P A G G D S S V A T Q
Nomascus leucogenys S S D T P I T S A P L E M L A P S W S P G V W R E P S I H H A T A A S G P Q E P A G G D S S V A T Q
Pan paniscus S S D A P I T S A P L K M L A P S G S P G V W R E P S I H H A T A A S G P Q E P A G G D S S V A A Q
Pan troglodytes S S D A P I T S A P L K M L A P S G S P G V W R E P S I H H T T A A S G P Q E P A G G D S S V A A Q
Pongo abelii S S D A P I T S D P L K M L A P S G S P G V W R E P S I H H A T A A S G P Q E P A G G D S S V A A Q
Callithrix jacchus S P D A P V T S D P F E M L A P S G S P S V W K E P S I H H N T A A S G P Q E P A G G ? ? S V A K Q
Saimiri boliviensis S P D A P V T S D P L E M L A P S G S P R I W K E P S I H H V T A I S G P Q E P E G G D S S V D K Q
Chlorocebus sabaues S S D A P I T S V P L E V L A P S G S P G L W R E P S I H H T T A A S G A Q E P A G G D S S V A T Q
Macaca fascicularis S S D A P I T S V P L E V L A P S G S P G L W R E P S I H H T T A A S G A Q E P A G G D S S V A T Q
Macaca mulatta S S D A P I T S V P L E V L A P S G S P G L W R E P S I H H T T A A S G A Q E P A G G D S S V A T Q
Papio anubis S S D A P I T S V P L E V L A P S G S P G L W R E P S I H H T T A A S G A Q E P A G G D S S V A T Q

Otolemur garnettii S D D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K Q A E K K E K M P
Tarsius syrichta R D D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K Q E G K K E R P P
Homo sapiens N N D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K K E K K P
Nomascus leucogenys N D D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R Q E K K E K K P
Pan paniscus N N D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K K E K Q P
Pan troglodytes N N D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K K E K Q P
Pongo abelii N N D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K K Q K K P
Callithrix jacchus N D N G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K E D ? ? P
Saimiri boliviensis N N D G T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K E E ? ? P
Chlorocebus sabaues N D D S T D G Q K L L L F Y I L G T V V A I L L L L A L A L G L L V Y R K R R A K R E E K K E ? ? P
Macaca fascicularis N D D G T D G Q K L L L F Y I L G T V V G I L L L L A L A L G L L V Y R K R R A K R E E K K E ? ? P
Macaca mulatta N D D G T D G Q K L L L F Y I L G T V V G I L L L L A L A L G L L V Y R K R R A K R E E K K E ? ? P
Papio anubis N D D G T D G Q K L L L F Y I L G T V V G I L L L L A L A L G L L V Y R K R R A K R E E K K E ? ? P

Otolemur garnettii S N A A D S Y S W A S E R A E S R A T E N Q Y R * ? - - - - -
Tarsius syrichta Q S A A D T Y S W V P E R A E S R A S E N P Y S P T P G T D C *
Homo sapiens Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Nomascus leucogenys Q N A A D S Y S W V P E R V E S R A M E N Q Y S P T P G T D C *
Pan paniscus Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Pan troglodytes Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Pongo abelii Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Callithrix jacchus Q N A A D R Y S W V P E R A E G R A M E N E Y S P T P G T D C *
Saimiri boliviensis Q N A A D R Y S W V P E R A E G R A M E N A Y S P T P G T D C *
Chlorocebus sabaues Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Macaca fascicularis Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Macaca mulatta Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G T D C *
Papio anubis Q N A A D S Y S W V P E R A E S R A M E N Q Y S P T P G A D C *

Appendix 4 : Amino acid alignment for primate CD93 sequences

Ailuropoda melanoleuc L A T V R S E E E A W H I Q Q A L T Q L L E S E V T M A G W V G K F W I G L Q R E K G K C L D P S L
Ursus maritimus L A T V R S E E E A W H I Q R A L T Q L L E S E V T L A T W V G K F W I G L Q R E K G K C L D P S L
Felis catus L A T V K S E E E A W H I Q R A L A Q L L E L E E A L E A R M G K F W I G L Q R E K G K C L D S S L
Leptonychotes weddelli L A T V R S E E E A R H T Q R A L T Q L L E S E A P L A A R M G K F W I G L Q R E K A K C L D P S L
Panthera tigris L A T V K S E E E A W N I Q R A L A Q L L E L E E A L E A R M G K F W I G L Q R E K A K C L D S S L
Eptesicus fuscus L A T V R T E E E A Q H I Q R A L A Q L L Q P G A P - - - W T G K F W I G L Q R E R S K C L D P S L
Myotis lucifugus L A T V R T E E E A R H I H R A L A Q L L Q P G A P - - - W T G K F W I G L Q R E R G K C L D P R L
Myotis brandtii L A T V R T E E E A R H I Q R A L A Q L L Q P G A P - - - W T G K F W I G L Q R E R G K C L D P R L
Ceratotherium simum L A T V K S E E E A R H V Q R A L A Q L L Q L E A P P A A R T G K F W I G L Q R E K G K C L D P S L
Equus caballus L A T V K T E E E A R L I Q R A L A Q L L Q L E A P L V T R M G K F W M G L Q R E K G K C L D S T L
Orcinus orca L A T V K S E E E A L H V Q G A L A Q L L P P G A P L T E R M G R F W I G L Q R D K G K C L D S N L
Physeter catodon L A T M K S E E E A L Y V Q R A L A Q L L P P G A P L A E R M G R F W I G L Q R D K G K C L D S N L
Tursiops truncatus L A T V K S E E E A L H V Q G A L A Q L L P P G A P L T E R M G R F W I G L Q R D K G K C L D S S L
Bubalus bubalis L A T V K S E E E A R H I Q G A L S Q L L L L G A P L Q E R P - K F W I G L Q R E K G T C S D S S L
Ovis aries L A T V K S E E E A R H I Q G A L T Q L L L L G A S L P E R Q N K F W I G L Q R E K G N C S D S S L
Otolemur garnettii L T T V K S E E E A Q H V Q R T L A Q L L S L G A S L A A R M G K F W I G L Q R E K G K C Q D P R L
Callithrix jacchus L A T V K S K E E A Q H I Q R A L A Q L L R L E A N L T A R M G K F W I G L Q R E K G K C L D P S L
Saimiri boliviensis L A T V K S R E E A Q H I Q R A L A Q L L R L E A N L T A R M G K F W I G L Q R E K G K C L D P S L
Chlorocebus sabaeus L A T V K S E E E A Q H V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L
Macaca fascicularis L A T V K S E E E A Q H V Q Q V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L
Homo sapiens L A T V K S K E E A Q H V Q R V L A Q L L R R E A A L T A R M S K F W I G L Q R E K G K C L D P S L
Nomascus leucogenys L A T V K S E E E A Q H V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L
Pan paniscus L A T V K S E E E A Q H V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L
Pan troglodytes L A T V K S E E E A Q H V Q R V L A Q L L R R E A A L T A R I G K F W I G L Q R E K G K C L D P S L
Pongo abelii L A T V K S E E E A Q D V Q R V L A Q L L R R E A A L T A R M G K F W I G L Q R E K G K C L D P S L
Chrysochloris asiatica L A T V R N A E E A R Y I Q E V L V Q L L Q P E A L T A R M G K F W I G L Q R E K S K C L D P S L
Echinops telfairi L A T V R S A E E A R Y I Q E A L A Q L L L P E A P L T A R M A K F W I G L Q R E K G K C L D A N L
Dasylops novemcinctus L A T V K S E E E A R H I Q E A L A Q L L R P Q D P T A A R M G K F W I G L Q R E K G K C L D P N L
Trichechus manatus L A T V R S A E E A Q R V Q G A L A Q L L R P E A P L T T R T G K F W I G L Q R D K G K C L D S N L
Sarcophilus harrisii L A T V K S E E E A Q H I Q E V L T Q L P E K G A ? - ? A R T V K F W I G L Q R E K S K C M D R D D
Monodelphis domestica L A T V K N E E E A Q H I Q E A L A Q L P D R E A ? - ? G R T V K F W I G L Q R E K G K C M N P D E

*Ailuropoda melanoleuc*P L K G F S W ? ? G G G E D T L Y T N W N K E V R S S C I S R R C V S L L L Y L S Q P ? ? Q A - S H
Ursus maritimus P L K G F S W ? ? G G G E D T L Y T N W N K E V R S S C I S R R C V S L L L Y L S Q P ? ? H A - S H
Felis catus P L K G F S W ? ? G G G E D T L Y T N W N R E V R S S C I S R R C V S L L L Y L S L P ? ? H A - S H
*Leptonychotes weddelli*P L K G F S W ? ? G G G E D T L Y T N W N K E V R S S C I S R R C V S L L L Y L S Q P ? ? H A - S H
Panthera tigris P L K G F S W ? ? G G G E D T L Y T N W N R E V R S S C V S R R C V S L L L Y L S L P ? ? H A - S H
Eptesicus fuscus P L R G F S W ? ? G G G E D T L Y S N W Y K E P R N T C I S K R C A S L M L D P S L S ? ? L S - S H
Myotis lucifugus P L K G F S W ? ? G G G E D T L Y S N W Y K E A R H T C I S K R C V S L M L D P S V S ? ? L S - S H
Myotis brandtii P L K G F S W ? ? G G G E D T L Y S N W Y K E A R H T C I S K R C V S L M L D P S V S ? ? L S - S H
Ceratotherium simum P L K G F S W ? ? G G G E N T S Y A N W Y K E L K H S C I S K R C V S L V L D L S L T ? ? L T - G H
Equus caballus P L R G F S W ? ? G G G E N T S Y A N W Y K E P K N S C T F R R C V S L V L D L S L P ? ? L A - S H
Orcinus orca P L K G F S W ? ? G G G E D T S Y T N W H K E A K N S C T S K R C V S L M L D L S A P ? ? L A - S R
Physeter catodon P L K G F S W ? ? G G G E D T S Y T N W H K E A K N S C T S K R C V S L M L D L S V P ? ? L A - N R
Tursiops truncatus P L K G F S W ? ? G G G E D T S Y T N W H K E A K N S C T S K R C V S L M L D L S A P ? ? L A - S R
Bubalus bubalis P L K G F S W ? ? G D G E D S Q Y N N W Y K E V R N T C T H R R C V S L I L D L S V P ? ? L A - S S
Ovis aries P L K G F S W ? ? G D G E A S Q Y N N W Y K E V K N T C I Q R R C V S L I L D L S V P ? ? L A - S S
Otolemur garnettii P L K G F S W ? ? G G G E D T L Y T N W H K E A R N S C I S K R C V S L L L D L S L T ? ? T T - S R
Callithrix jacchus P L K G F S W ? ? G G G E D T P Y T N W Y K E L R N S C I S K R C V S L L L D L S Q P ? ? L S - S Y
Saimiri boliviensis P L K G F S W ? ? G G G E D T P Y A N W Y K E L R S S C V S K R C V S L L L D L S Q P ? ? L S - S H
Chlorocebus sabaeus P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - R R
Macaca fascicularis P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - G R
Homo sapiens P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - S R
Nomascus leucogenys P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - S R
Pan paniscus P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - S R
Pan troglodytes P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - S R
Pongo abelii P L K G F S W ? ? G G G E D T P Y S N W H K E L R N S C I S K R C V S L L L D L S Q P ? ? L P - S R
Chrysochloris asiatica P L K G F S W I G G G G N T H Y S N W H K E L K N T C V S K R C V S L M L D L S L P ? ? L T - N Q
Echinops telfairi P L K G F S W ? ? G G G E N T S Y T N W Y K E L K N T C I S K R C V S L A L D L S L L P S R T - S H
Dasylops novemcinctus P L K G F S W ? ? G G G E D T L Y S N W Y K E G K G T C I S K R C V A L L L D L S L Q ? ? L P - S H
Trichechus manatus P L K G F S W ? ? G G G D T P Y T N W Q K E P K N T C I S K R C V S L L L D L S L S ? ? P T - G R
Sarcophilus harrisii P L K G F S W ? ? G G G E N T S Y S N W H K E P M S T C L F K R C A S L L L D L S S P ? ? S A - H
Monodelphis domestica L A L K G F S W ? ? G G A E N T S Y S N W Q K E P M S T C I S K R C A S L S V D L S A S ? ? L A A A H

<i>Ailuropoda melanoleuc</i>	? ? P K W S E S P C G S P T S P G S K I E G F V C K F S F K G M C Q P L A L G G P G W V N Y T T P F
<i>Ursus maritimus</i>	? ? P K W S E S P C G S P T S P G S K I E G F V C K F S F K G M C Q P L A L G G P G W V N Y T T P F
<i>Felis catus</i>	? ? ? - ? M C Q P L A L G G P R P V E Y R T P F
<i>Leptonychotes weddelli</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C Q P L A L G G P G R V N Y T T P F
<i>Panthera tigris</i>	? ? S K W S E G P C G T P N S P G S N I E G F V C K F S F K G M C Q P L A L G G P G R V E Y R T P F
<i>Eptesicus fuscus</i>	? ? P K W S E G P C G N P G S P V S N I E G F V C K F S F K G M C R P L A L G G P G Q V N Y S T P F
<i>Myotis lucifugus</i>	? ? P K W S E G P C G S P G A P V N N I E G F V C K F S F K G M C R P L A L G G P G Q V N Y T T P F
<i>Myotis brandtii</i>	? ? P K W S E G P C G S L G A P V N N I E G F V C K F S F K G M C R P L A L G G P G Q V N Y T T P F
<i>Ceratotherium simum</i>	? ? P K W A E G P C G S P S P G S N I E G F V C K F S F K G M C R P L A L G G P G H V N Y T T P F
<i>Equus caballus</i>	? ? P K W A E G P C G N P G F S V N N I E G F V C K F S F K G M C R P L A L G G P G Q V N Y T T P F
<i>Orcinus orca</i>	? ? S K W T E G P C G S S K F S G S N I E G F V C K F S F K G M C W P L T L G G P G Q V N Y T T P F
<i>Physeter catodon</i>	? ? S K W T E G P C G S S R F S G S N I E G F V C K F S F K G M C R P L T L G G P G Q V N Y T T P F
<i>Tursiops truncatus</i>	? ? S K W T E G P C G S S K F S G S N I E G F V C K F S F K G M C W P L T L G G P G Q V N Y T T P F
<i>Bubalus bubalis</i>	? ? S K W V D G P C G H S G F P G M N I E G F V C K F S F K G M C R P L T L G G P G Q V N Y T T P F
<i>Ovis aries</i>	? ? S K W V D G P C G Q S G F P E S N I E G F V C K F S F K G M C R P L T L R G P G Q V N Y T T P F
<i>Otlemur garnettii</i>	? ? P K W S E G P C G N P V S P G S N I E G F V C K F S F K G M C R P L A L G G P G K V T Y S T P F
<i>Callithrix jacchus</i>	? ? P R W S E G P C G S S D S P G N N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Saimiri boliviensis</i>	? ? P R W S E G P C G S S D S P G N N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Chlorocebus sabaeus</i>	? ? P K W S E G P C G S P S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Macaca fascicularis</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Homo sapiens</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Nomascus leucogenys</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Pan paniscus</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Pan troglodytes</i>	? ? P K W S E G P C G S P G S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Pongo abelii</i>	? ? P K W S E G P C G S P S P G S N I E G F V C K F S F K G M C R P L A L G G P G Q V T Y T T P F
<i>Chrysochloris asiatica</i>	? ? P K W S E G P C G S H G S P G S N I E G F V C K F S F K G M C Q P L A L G G P G Q V T Y T T P F
<i>Echinops telfairi</i>	? ? P T W S E G P C G S H S G S P G S N I E G F V C K F S F R G M C R P L A L G G P G Q I S Y T T P F
<i>Dasyops novemcinctus</i>	? ? P K W S E G P C G S P N S P G S N V E G F V C K F S F K G M C R P L V L G G P G Q V T Y T T P F
<i>Trichechus manatus</i>	? ? S K W A E G P C G S P N S P G S N I E G F V C K F S F E G M C R P L A L G G P G Q V T Y T T P F
<i>Sarcophilus harrisi</i>	S V P K W S E S P C G T P G S P V R N I E G Y V C K F S F K G M C H P V A L G G P G E V T Y T T P F
<i>Monodelphis domestica</i>	S V P K W T E S P C G T T D S P G R N I E G Y V C K F S F K G M C H P V A L G G P G E V T Y T T P F
<i>Ailuropoda melanoleuc</i>	N A T S S S L E A V P F A S A A T V A C G A ? - ? E D G Q E H Y L M C R E K A P D V F D W G N L G P
<i>Ursus maritimus</i>	N A T S S S L E A V P F A S A A T V S C G D ? - ? E D G Q E H Y F M C R E K A P D V F D W G N S G P
<i>Felis catus</i>	Q A T S S S L D T V P F A S V A N V A C G D ? - ? D E G R E H Y F L C K E K A S D V F D W G S S G P
<i>Leptonychotes weddelli</i>	N A T S S S L E A V P F G S A A T V V C G A ? - ? E A G Q E D Y F M C R E K A P D V F D W G S S G P
<i>Panthera tigris</i>	Q A T S S S L D T V P F A S V A N V A C G D ? - ? D E G R E H Y F L C K E K A S D V F D W G S S G P
<i>Eptesicus fuscus</i>	Q A T S S S L E A V P F A S V A N V A C G V ? - ? G E S G Q H F F L C K E K A T D V F D W G I S G P
<i>Myotis lucifugus</i>	Q A T S S S L E A V P F A S V A N V A C R N ? - ? D K S K Q H F F L C K E K A T D V F D W G I S G P
<i>Myotis brandtii</i>	Q A T S S S L E A V P F A S V A N V A C ? - - - ? D E I R Q H F F L C K E K A T D V F D W G I S G P
<i>Ceratotherium simum</i>	Q A T S S S L D A V P F A S V A N V A C G D ? - ? R E S G H H Y F L C K E K A P D V F D W G S S G P
<i>Equus caballus</i>	Q A T S S S L E A V P F A S M A N V A C G D ? - ? N E S E W H Y F L C K E K A P D V F D W D S S G P
<i>Orcinus orca</i>	Q A T S S S L Q A V P F A S M A N V A C G D ? - ? D E S W Q H Y F L C K E K T P G V F D W D S S G P
<i>Physeter catodon</i>	Q A T S S S L Q A V P F A S M A N V A C G D ? - ? D E S W Q H Y F L C K E K A P D V F D W D S S G P
<i>Tursiops truncatus</i>	Q A T S S S L Q A V P F A S M A N V A C G D ? - ? D E S W Q H Y F L C K E K A P G V F D W D S S G P
<i>Bubalus bubalis</i>	Q A T S S S L Q A V P F A S M A T V A C E D ? - ? D E G R Q H Y F L C K E K A P S E F D W D S S G P
<i>Ovis aries</i>	Q A T S S S L Q A V P F A S M A S V C E D ? - ? D E G T P H Y F L C L E K A P S V F D W D C S R P
<i>Otlemur garnettii</i>	Q A T S S S L D A V P F A S M A S V A C G D ? - ? N E S T S H Y F L C K E K E P N V F E W N S S G P
<i>Callithrix jacchus</i>	Q T T S S S L E A V P F A S A A N V A C G D R D Q D K S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Saimiri boliviensis</i>	Q T T S S S L E A V P F A S A A N V I C G D G D Q D K S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Chlorocebus sabaeus</i>	Q T T S S S L E A V P F A S A A N V A C G E G D K D S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Macaca fascicularis</i>	Q T T S S S L E A V P F A S A A N V A C G E G D K D S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Homo sapiens</i>	Q T T S S S L E A V P F A S A A N V A C G E G D K D E T Q S H Y F L C K E K A P D V F D W G S S G P
<i>Nomascus leucogenys</i>	Q T T S S S L E A V P F A S A A D V A C G E G D K D K S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Pan paniscus</i>	Q T T S S S L E A V P F A S A A N V A C G E G D K D E S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Pan troglodytes</i>	Q T T S S S L E A V P F A S A A N V G C G E G D K D E S Q S H Y F L C K E K A P D V F D W G S S G P
<i>Pongo abelii</i>	Q T T S S S L E A V P F A S A A T V A C G E G D K D E S Q S H Y F L C K E K A P G V F D W G S S G P
<i>Chrysochloris asiatica</i>	R A T S S S L E A V P F A S V A S V C D D ? - ? D T Q K S H Y F L C K E K G A D V F N W G T S G P
<i>Echinops telfairi</i>	G A S S S L D A V P F A S I A T V A C G E ? - ? G K N G S N Y F Q C R E K G S K L F D W D T S G P
<i>Dasyops novemcinctus</i>	L A T S S S L G T V P F A S S A D V T C G E ? - ? E M E E T H Y F L C K E K D P G V F D W D S S G P
<i>Trichechus manatus</i>	Q A T S S S L E A V P F A S M A N V A C G D ? - ? G K E G S H Y F L C K K K G A D V F D W G T S G P
<i>Sarcophilus harrisi</i>	G A T S T S L A A V P F A S V A N V A C R D ? - ? G E K K N H Y L L C K E R S S N L F D W G T P G P
<i>Monodelphis domestica</i>	G A T S T S L A A V P F A S A A S V N C G Y ? - ? D E R K S H Y L V C K E R N P N Q F D W G T S G P

Ailuropoda melanoleuc L C V S A Q Y G C S F N N G G C Q Q D C F E G G N G S F R C G C R P G F R L L D D L V T C A S R N P
Ursus maritimus L C I S A Q Y G C S F N N G G C Q Q D C F E G G D G S ? - ? C R P G F R L L D D L V T C A S R N P
Felis catus L C V S P K Y G C S F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Leptonychotes weddelli L C V S P Q Y G C S F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R D P
Panthera tigris L C V S P K Y G C S F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Eptesicus fuscus L C A S A E Y K C S F N N G G C Q Q E C L E G E D G S F R C G C R P G F R L L D D L V T C I S R D P
Myotis lucifugus L C A S A E Y G C S F N N G G C Q Q E C L E G E G G S F R C G C R P G F R L L D D L V T C I S R D P
Myotis brandtii L C A S A E Y G C S F N N G G C Q Q E C L E G E G G S F R C G C R P G F R L L D D L V T C I S R D P
Ceratotherium simum L C V S P K Y G C D F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Equus caballus L C V N P K Y G C D F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Orcinus orca L C V S P K F S C D F N N G G C Q Q D C F E G G E G S F R C G C R P G F R L L D D L V T C A S R N P
Physeter catodon L C V S P K F S C D F N N G G C Q Q D C F E G G E G S F R C G C R P G F R L L D D L V T C A P R N P
Tursiops truncatus L C V S P K F S C D F N N G G C Q Q D C F E G G E G S F R C G C R P G F R L L D D L V T C A S R N P
Bubalus bubalis L C V S P K Y G C D F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Ovis aries L C V S S P K F S C D F N N G R C Q Q D C F E G K N V S F R C C R P G F R L L D D L V T C A S R N P
Otlemur garnettii L C V S P D Y G C N F N N G G C Q Q A C F E G G D G S F R C G C L P G F R L L D D L V T C A S R N P
Callithrix jacchus L C V S P K Y G C S F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Saimiri boliviensis L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Chlorocebus sabaeus L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Macaca fascicularis L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Homo sapiens L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Nomascus leucogenys L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Pan paniscus L C V S P K Y G C S F N N G G C H Q D C F E G E D G S F L C G C R P G F R L L D D L V T C A S R N P
Pan troglodytes L C V I P K Y G C S F N N G G C H Q D C F E G E D G S F L C G C R P G F R L L D D L V T C A S R N P
Pongo abelii L C V S P K Y G C N F N N G G C H Q D C F E G G D G S F L C G C R P G F R L L D D L V T C A S R N P
Chrysochloris asiatica L C V S S K L G C S F N N G G C Q Q D C F E G G D G S F R C G C R P G F R L L D D L V T C T S R N P
Echinops telfairi L C V N S K L G C S F N N G G C Q Q E C F E G L D G S F N C G C L P G Y Q L L E D M V T C A S R N P
Dasyops novemcinctus L C A S P K Y S C S F N N G G C Q Q E C F E G G D G S F R C G C R P G F R L L D D L V T C A S R N P
Trichechus manatus L C V S S K L S C S F N N G G C Q Q Y C F E G G D G S F R C G C Q P G F R L L D D L V T C T S R N P
Sarcophilus harrisii F C A S P N H G C A F N N G G C Q Q E C L E G G D G S F L C G C R P G Y R L L D D L V T C I P R D P
Monodelphis domestica L C A S P N H G C A F N N G G C Q Q E C L E G G D G S F L C G C R P G Y R L L D D L V S C V P R D P

Ailuropoda melanoleuc C S S N P C G G P A T C E Q G P H G K S Y T C H C P Q G Y Q L D S S Q R D C L D V D E C Q E S P C P
Ursus maritimus C S S N P C R G A A T C E Q G P H G K S Y T C H C P R G Y Q L D S S Q R D C L D V D E C Q D S P C P
Felis catus C S S S P C K G A A T C V L G P H R K N Y T C L C P Q G Y Q L D S S Q Q D C V D V D E C Q D S P C P
Leptonychotes weddelli C S S S P C R G A A T C V P A P H G K N Y T C R C P Q G Y Q L D S S Q R D C V D M D E C Q D S P C R
Panthera tigris C S S S P C K G A A T C V L G P H R K N Y T C L C P Q G Y Q L D S S Q Q D C V D V D E C Q D S P C P
Eptesicus fuscus C S S S P C R G V A T C V P D S L W R K Y T C Q C P E G Y Q L N A T Q G D C V D V D E C Q A S P C E
Myotis lucifugus C S S S P C R G V A T C V P E S L W K N Y T C Q C P E G Y Q L N T T Q Q D C V D V D E C Q A S P C E
Myotis brandtii C S S S P C R G V A T C V P E S L W K N Y T C Q C P E G Y Q L N A T Q Q D C V D V D E C Q A S P C E
Ceratotherium simum C S S S P C G G A A T C V P G P L G K N Y M C R C P P G Y Q L D S T Q Q D C V D V D E C Q D S P C A
Equus caballus C S S S P C R G V A T C V P E T L G K S Y L C R C P Q G Y Q L D S T Q R D C V D V D E C Q G S P C A
Orcinus orca C S S S P C G G G S T C V P G P L G K D F T C H C P P G Y R L D S T Q Q D C V D M D E C Q D A P C A
Physeter catodon C S S S P C G G G S T C V P G P L G K D F T C S C P P G Y R L D S T Q Q D C V D T D E C Q D T P C A
Tursiops truncatus C S S S P C G G G S T C V P G P L G K D F T C H C P P G Y R L D S T Q Q D C V D M D E C Q D A P C A
Bubalus bubalis C S S S P C R G E A T C F P G S L G T D F T C H C P P G Y Q L D S T Q R D C V D V D E C R D N P C A
Ovis aries C S S S P C G G E A T C F P G S L G T D F T C H C P P G Y Q L D S T Q R D C V D V D E C Q D N P C A
Otlemur garnettii C S S S P C I G E A T C V S A P H G T N Y T C H C P Q G F Q V D E S Q L G C V D V D E C Q D S P C V
Callithrix jacchus C S S S P C R G G A T C I Q G S G H K N Y T C H C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Saimiri boliviensis C S S S P C R G G A T C I Q G S H G K N Y T C H C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Chlorocebus sabaeus C S S S P C R G G A T C I P G P H G K N Y T C G C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Macaca fascicularis C S S S P C R G G A T C I P G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Homo sapiens C S S S P C R G G A T C V L G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Nomascus leucogenys C S S S P C R G E A T C I L G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Pan paniscus C S S S P C R G G A T C I L G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Pan troglodytes C S S S P C R G G A T C I L G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Pongo abelii C S S S P C R G G A T C I L G P H G K N Y T C R C P Q G Y Q L D S S Q L D C V D V D E C Q D S P C A
Chrysochloris asiatica C S S N P C K G V A T C E P G S L G E S Y K C R C P L G Y Q L D L S E L D C S D V D E C Q A S P C A
Echinops telfairi C S S N P C R G I A T C E P K P T W E S Y G C S C P L G Y Q L D P S K L G C S D I D E C Q A S P C P
Dasyops novemcinctus C S S S P C R G M A T C V P G T H G K S Y T C R C P P G Y Q L D P S Q M D C E D V D E C L A S P C P
Trichechus manatus C S S N P C R G V A T C K P D S L G K S Y R C H C P P G Y Q L D P S E L D C R D V D E C Q A S P C A
Sarcophilus harrisii C H P N P C R G K A K C S P G T H G Q H Y E C Q C P A G F K S T P N R L D C E D V D E C S R F P C T
Monodelphis domestica C H P N P C R G K A K C S P G G H G K H Y E C L C P A G F K P T P N R L D C D D V D E C D R I P C A

Ailuropoda melanoleuc Q E C V N T P G S F R C E C W V G Y E P ? ? G P G E G V C Q D V D E C A P G R S P C S Q E C T N T D
Ursus maritimus Q E C V N T P G S F R C E C W V G Y E P ? ? G P G E G A C Q D V D E C A P G R S P C A Q E C T N T D
Felis catus Q E C V N T P G G F H C E C W V G Y E L ? ? G P G E E A C Q D V D E C A P G H S P C A Q G C T N T D
Leptonychotes weddelli Q A C V N V P G G F R C E C W V G Y E P ? ? G P G E G P C R D V D E C V P G R S P C A Q E C T N T D
Panthera tigris Q E C V N T P G G F H C E C W V G Y E P ? ? G P G E E A C Q D V D E C A S G H S P C S Q D C T N T D
Eptesicus fuscus Q E C V N T P G S F H C Q C W V G Y E P ? ? G P R G E A C R D V D E C ? - - - - - - - - - - - - -
Myotis lucifugus Q E C V N T P G S F H C Q C W V G Y E P ? ? S P G G Q A C Q D V D E C ? - - - - - - - - - - - - -
Myotis brandtii Q E C V N T P G S F H C Q C W V G Y E P ? ? S P G G Q A C Q D V D E C ? - - - - - - - - - - - - -
Ceratotherium simum Q E C V N T P G G F H C Q C W V G Y E P ? ? G A G E G A C R D M D E C A P G R S P C A Q G C T N T D
Equus caballus Q E C V N T P G G F H C Q C W V G Y E P ? ? G P G E E T C R D V D E C A P G R S P C A Q D C T N T D
Orcinus orca Q E C V N T L G G F R C E C W V G Y E P ? ? G P G E G A C V D V D E C A P S H S P C A Q G C T N T D
Physeter catodon Q E C V N T L G G F R C E C W V G Y E P ? ? G P G E G A C V D V D E C A P S H S P C A Q G C T N T D
Tursiops truncatus Q E C V N T L G G F R C E C W V G Y E P ? ? G P G E G A C V D V D E C A P S H S P C A Q G C T N T D
Bubalus bubalis Q D C V N T P G S F R C E C W V G F E P ? ? G P E E G A C V D V D E C A P G R S P C A Q S C T N T E
Ovis aries Q D C V N T P G S F R C E C W V G F E P ? ? G P E E G A C V D V D E C A P G H S P C A Q S C T N T E
Otolemur garnettii Q A C V N T H G S F R C E C W V G Y E P ? ? S P G E G A C Q D V D E C A L G R S P C T Q R C T N T D
Callithrix jacchus Q E C V N T P G G F R C E C W V G Y E P ? ? G P G E G A C R D V D E C A L D P S P C A Q G C T N T D
Saimiri boliviensis Q E C V N T P G G F R C E C W V G Y E P ? ? G P G E G V C R D V D E C A L D P S P C A Q G C T N T D
Chlorocebus sabaeus Q E C V N T P G S F R C E C W V G Y E P ? ? G P G E G A C Q D V D E C A P G R S P C A Q G C T N T D
Macaca fascicularis Q E C V N T P G S F R C E C W V G Y E P ? ? G P G E G A C Q D V D E C A L G R S P C A Q G C T N T E
Homo sapiens Q E C V N T P G G F R C E C W V G Y E P ? ? G P G E G A C Q D V D E C A L G R S P C A Q G C T N T D
Nomascus leucogenys Q E C V N T P G G F R C E C W V G Y E P ? ? G P G E R T C R D V D E C A L D R S P C A Q G C T N T E
Pan paniscus Q E C V N T P G G F R C E C W V G Y E P ? ? S P G E G A C Q D V D E C A L G R S P C A Q G C T N T D
Pan troglodytes Q E C V N T P G G F R C E C W V G Y E P ? ? S P G E G A C Q D V D E C A L G R S P C A Q G C T N T D
Pongo abelii Q E C V N T P G G F R C E C W V G Y E P ? ? G P G E G A C R D V D E C A L G R S P C A Q G C T N T D
Chrysochloris asiatica Q E C I N T L G S F H C V C W V G Y E P ? - - - ? E G T C R D L D E C A P D R N P C A Q A C T N T D
Echinops telfairi Q V C I N T P G S F H C A C W V G Y E P ? - - - ? E G T C Q D I D E C V P G Q N P C D Q N C T N T Y
Dasybus novemcinctus Q E C I N T P G G F L C E C W V G Y Q L G P G E G E G A C L D V D E C A Q G L A P C A Q A C S N T L
Trichechus manatus Q E C I N T P G S F R C T C W V G Y E P ? - - - ? E G T C R D L D E C A P G R S P C A Q A C T N T D
Sarcophilus harrisii H K C V N T P G S F H C T C H L G Y E T ? ? G H N G M E C W D V D E C A G D H S P C A Q L C I N T V
Monodelphis domestica Q D C V N T P G S F H C T C R P G Y E P ? ? G H N G M E C W D V D E C A E G R S P C A Q L C N N T E

Ailuropoda melanoleuc G S F Y C S C E K G Y V L A G E D S T Q C Q D V D E C A D M E N G L C D S L C L N T Q G S F R C G C
Ursus maritimus G S F Y C S C E K G Y V L A G E D S T Q C Q D V D E C A D M E N G L C D S L C L N T Q G S F R C G C
Felis catus G S F Y C S C K K G Y V L A K E D G T Q C L D V D E C E G P E H G L C E G L C L N T Q G S F R C G C
Leptonychotes weddelli G S F Y C S C E K G Y V L A G A E G T E C Q D V D E C A D T E N S L C D S L C L N T Q G S F R C G C
Panthera tigris G S F H C F C K E G Y V L A G E D G T Q C L D V D E C E G P E H G L C E G L C L N T Q G S F R C G C
Eptesicus fuscus - ? S P E G G L C E G Y C L N T Q G S F R C T C
Myotis lucifugus - ? S P E G S L C E G Y C L N T Q G S F R C T C
Myotis brandtii - ? S P E G G L C E G Y C L N T Q G S F R C T C
Ceratotherium simum G S F F C S C E E G Y V L A G D D G T Q C K D V D E C E G ? - - ? V C D S L C F N V Q G S F R C G C
Equus caballus G S F Y C S C K E G F V L A G E D D T Q C Q D V D E C E D S E G H L C D S L C F N M Q G S F R C G C
Orcinus orca G S F Y C S C E E G Y V L A G E D G T R C V D V D E C A G P Q G G L C D S L C F N T E G S F R C G C
Physeter catodon G S F Y C P C E E G Y V L A G E D G T Q C V D V D E C A G P Q G G L C G S L C F N T E G S F R C G C
Tursiops truncatus G S F Y C S C E E G Y V L A G E D G T R C V D V D E C A G P Q G G L C D S L C F N T E G S F R C G C
Bubalus bubalis G S F Y C S C E E G Y E L A E E D G T Q C L D V D E C E V Q Q G G L C D S L C F N T E G S F R C G C
Ovis aries G S F Y C S C E E G Y E L A G E D G T Q C L D V D E C E V Q Q G G L C D S L C F N T E G S F R C G C
Otolemur garnettii G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C A G P G D S L C D N L C F N T Q G S F S C G C
Callithrix jacchus G S F Y C S C Q E G Y V L A E E D G T Q C Q D V D E C A G P G V S P C D S L C F N T Q G S F R C G C
Saimiri boliviensis G S F Y C S C Q E G Y V L A E E D G T Q C Q D V D E C A G P G V S P C D S L C F N T Q G S F L C G C
Chlorocebus sabaeus G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F R C G C
Macaca fascicularis G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F R C G C
Homo sapiens G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C
Nomascus leucogenys G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C
Pan paniscus G S F H C S C K E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C
Pan troglodytes G S F H C S C K E G Y V L A G E D G T Q C Q D V D E C V G P G G P L C D S L C F N T Q G S F H C G C
Pongo abelii G S F H C S C E E G Y V L A G E D G T Q C Q D V D E C L G L G G P F C D S L C F N T Q G S F H C G C
Chrysochloris asiatica G S F H C S C E K G Y V L A G E D G T Q C Q D V D E C T G P E A S P C E G L C F N I P G S F H C G C
Echinops telfairi G S F H C S C E E G Y V L A G E D G T Q C Q D I D E C T S P G A E H C G E Q C F N V P G S F H C G C
Dasybus novemcinctus G S F Y C S C D T G Y E V A R E D N T Q C Q D V D E C T R L E S S P C D S L C F N T P G S F Y C D C
Trichechus manatus G S F H C S C E E G Y K V A G E D G T Q C Q D V D E C T G Q G A G P C R D L C F N V P G S F R C G C
Sarcophilus harrisii G S F Q C A C Q K G Y Q T T G E D G T Q C Q D V N E C E ? ? E R N P C E G F C Y N I P G S F Q C G C
Monodelphis domestica G S F Q C T C H K G Y V A T G E D G T Q C Q D V N E C D D - E G N P C E S L C F N I Q G S F R C G C

Ailuropoda melanoleuc L P G W E L G L D G V S C T P G P T S L A P P ? ? ? - ? L P R G R - ? C G ? - - - - -
Ursus maritimus L P G W E L G P D G V S C T P G P M S L A P R ? ? ? - ? L P R G R - ? C G ? - - - - -
Felis catus L P G W E L G P D G V S C T T G S T S L A P Q ? ? ? - ? L P R E R - ? Y G ? - - - - -
Leptonychotes weddelli L P G W E L G L D G V S C T P G P T S L T L L ? ? ? - ? L P R G R - ? C R ? - - - - -
Panthera tigris L P G W E L G P D G V S C T A G S T S L A P Q ? ? ? - ? L P R E R - ? Y G ? - - - - -
Eptesicus fuscus L P G R E L A P D G V S C I T G P T S L G P S ? ? ? - ? P P R G R - ? H R ? - - - - -
Myotis lucifugus L P G M E L A P D G V S C I T G T T S L G P S ? ? ? - ? P P R S R - ? H R ? - - - - -
Myotis brandtii L P G M E L A P D G V S C I T G P T F L G P S ? ? ? - ? P P R S R - ? H R ? - - - - -
Ceratotherium simum L P G W E L A P D G V S C T M G A T T L G P P ? ? ? - ? L L R A M - ? H G ? - - - - -
Equus caballus L P G W E L A P N G V S C I M G T T L G P P ? ? ? - ? L T R G M - ? H G ? - - - - -
Orcinus orca L P G W E L S P D G V S C T G G L T S L G P T ? ? ? - ? L P K G R - ? H R ? - - - - -
Physeter catodon L P G W E L S P D G V S C T G G L T S L G P P ? ? ? - ? L P K G R - ? H R ? - - - - -
Tursiops truncatus L P G W E L S P D G V S C T G G L T S L G P T ? ? ? - ? L P K G R - ? H R ? - - - - -
Bubalus bubalis L P G W E L D P N G V S C T G P T S L G P L ? ? ? - ? L P L G K - ? H G ? - - - - -
Ovis aries L P G W E L D T N G V S C T G G P T S L G P P ? ? ? - ? L P L G K - ? H G ? - - - - -
Otlemur garnettii L P G M E L A P D G V S C I I A P V S L V P L ? ? ? - ? L P K R R - ? Q W ? - - - - -
Callithrix jacchus L T G W E L A P N G V S C T M G L V S L G R P ? ? ? - ? P ? ? R S - ? Q R ? - - - - -
Saimiri boliviensis L T G W E L A P N G V S C T M G L V S V G P P ? ? ? - ? P P R R S - ? Q R ? - - - - -
Chlorocebus sabaeus L P G W E L A S N G V S C A M G P V S L G P P ? ? ? - ? P P M R S - ? Q G ? - - - - -
Macaca fascicularis L P G W V L A P N G V S C A M G P V S L G P P ? ? ? - ? P P M R S - ? Q G ? - - - - -
Homo sapiens L P G W V L A P N G V S C T M G P V S L G P P ? ? ? - ? P P M R R - ? Q R ? - - - - -
Nomascus leucogenys L P G W V L A P N G V S C T M G P V S L G P P ? ? ? - ? P P M R S - ? Q R ? - - - - -
Pan paniscus L P G W V L A P N G V S C T M G P V S L G P P ? ? ? - ? P P M R R - ? Q R ? - - - - -
Pan troglodytes L P G W V L A P N G V S C T M G P V S L G P P ? ? ? - ? P P M R R - ? Q R ? - - - - -
Pongo abelii L P G W V L A P N G V S C T M G P V S L G P P ? ? ? - ? P P M R S - ? Q R ? - - - - -
Chrysochloris asiatica L P G W E L S P D G V S C T L N H T S S G P R ? ? ? G L H C R K K - ? ? - - - - -
Echinops telfairi L P G W E R S P D G V S C T L S H G S P E P P ? ? ? E D L H P R E K - ? ? - - - - -
Dasylops novemcinctus L P G W E L A P N G V S C T F R N V S P G T P ? ? ? - ? L A R G K - ? R G ? - - - - -
Trichechus manatus L P G W E L A P N G V S C I L G H T S P G P T E G P A P P T D R P A P Q - ? - - - - -
Sarcophilus harrisi L P G W N L A P N G V S C I A N ? - - - ? Q Q ? ? ? - ? L P E D K - ? K R ? - - - - -
Monodelphis domestica L P G W N L A P N G V S C I A N H T M S V L P ? ? ? - ? I K R R M - ? E G K K D N Q * R R E K E R G

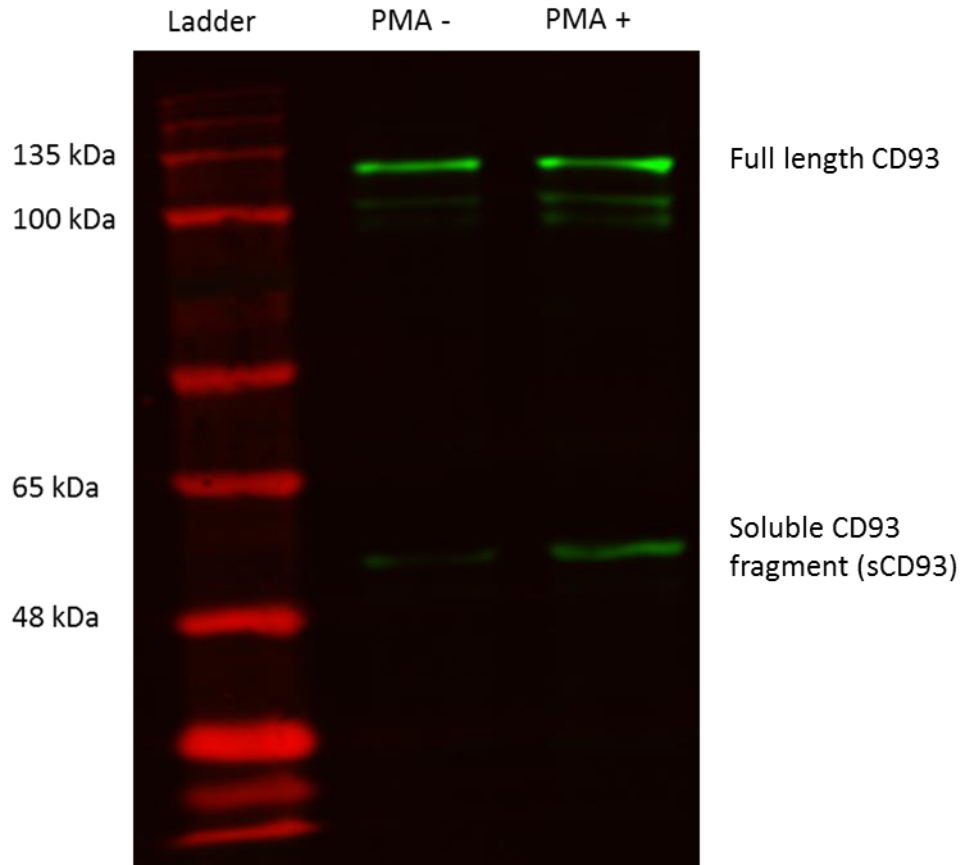
Ailuropoda melanoleuc - ? * ? ? G E A C V F C H S V Q A H Q ? ? P * G H L - - - - - Q G G T H H K G T L L P T Q C P H H
Ursus maritimus - ? * ? ? G E A C V F C H S V Q A H Q ? ? P * G H L - - - - - Q G G A H H K G T L P P T Q C P H H
Felis catus - ? W ? ? G E S C V F F H N I Q A H Q ? ? L R G H L - - - - - Q G G I Y H E D S L P P I * G P H H
Leptonychotes weddelli - ? * ? ? G E T R A F C H N V Q A H Q ? ? P * G H L - - - - - Q G G T H R K G T L P P T Q R P R H
Panthera tigris - ? * ? ? G E S C V F F H N I Q A H R ? ? L R G H L - - - - - Q G A T H H E E T L P P I * G S H H
Eptesicus fuscus - ? * ? ? G E P H A F H H N L K S N E ? ? P * G H F - - - - - Q G G T H Q M E T L P * I Q C L Y H
Myotis lucifugus - ? * ? ? K E P Q A F Y H N L K S N W ? ? P * G H F - - - - - Q G G I H Q V E T L P * I Q C L Y H
Myotis brandtii - ? * ? ? K E P Q A F Y H N L K S N W ? ? P * G H F - - - - - Q G G I H R V E T L P * I Q C L Y H
Ceratotherium simum - ? * ? ? G E P C A F C H N V Q S N Q ? ? P * G H L - - - - - Q G G S H C E Q T L P P T R C P H Y
Equus caballus - ? E ? ? G E P C A F C L N V Q S H Q ? ? P Q G H L - - - - - Q G G S H C E G P L P P T Q C S H H
Orcinus orca - ? W ? ? G E A R V F C C N V Q S H Q G Q P R G R L - - - - - H G G A H R Q E T L P P R Q R P H L
Physeter catodon - ? W ? ? G E A C V F C R N V Q S H Q G Q P R G R L - - - - - H G G S R R Q E T L P P R Q R P H L
Tursiops truncatus - ? W ? ? G E A S V F C C N V Q S H Q G Q S R G R L - - - - - H G G A H R Q E T L P P R Q R P H L
Bubalus bubalis - ? W ? ? R G A P V S C H C V Q S Q R G Q P * G Y L - - - - - H S G A L Q Q E T L P P S * S P H L
Ovis aries - ? W ? ? R G A P V F C H R A Q S Q R G Q P * G Y L - - - - - H G G T L Q Q E T L P P S * G P H L
Otlemur garnettii - ? E ? ? A E T H A L C Y Y T Q S H Q ? ? P * D K L - - - - - * S S A C L Q E A ? - ? I Q H A H H
Callithrix jacchus - ? E ? ? G E H C G P H C N S Q S H E ? ? P Q G H S - - - - - Q G H T H H K E T F T L T * R P S H
Saimiri boliviensis - ? E ? ? G E H R G P R C S S Q S H E ? ? P * G H P - - - - - Q G H T H H K K T F T L T * R P S H
Chlorocebus sabaeus - ? E ? ? G E H C A S R C N S Q S H E ? ? P R G H R - - - - - Q V Y T H H K E P F A L I * C P H H
Macaca fascicularis - ? E ? ? G E H C A S R C N S Q S H E ? ? P R G H P - - - - - Q V Y T H H K E T F A L I * C P H H
Homo sapiens - ? E ? ? R E H R A P C C N S Q S H K ? ? P R G H P - - - - - Q G Y T H H K * T F A V I * R P H H
Nomascus leucogenys - ? E ? ? G E H H T P R C N S Q S H E ? ? L R G H P - - - - - Q G Y T H R K E T F A V I * H P H H
Pan paniscus - ? E ? ? R E H R A P G C N S Q S H E ? ? P R G H P - - - - - Q G Y T H H K * T F A V I * R P H H
Pan troglodytes - ? E ? ? R E H R A P R C N S Q S H E ? ? P R G H P - - - - - Q G Y T H H K * T F A V I * R P H H
Pongo abelii - ? E ? ? G E H R A P R C N S Q S H E ? ? P R G H P - - - - - Q G Y I H R K E T F A V I * C P H H
Chrysochloris asiatica - - - ? W D H C P I Y N N I Q S P Q ? ? P * G H L - - - - - * R G S H H R E T L S T F Q H P Y H
Echinops telfairi - - - ? A E H H T F C * N I Q Y P Q ? ? L R G C L - - - - - * G G T H H R E T L L A I Q H L H H
Dasylops novemcinctus - ? W ? ? G E H S S F C N N T Q S Y P ? ? S * A H L - - - - - R R V T H H R E S L P P I * H L H H
Trichechus manatus - ? E G ? R E H R P F C H N I Q S P Q ? ? P * G H F - - - - - * G G T H H G E T L P A L Q H P L H
Sarcophilus harrisi - ? K K ? R E Q W F F S L S F G H N Q ? ? I * I H L R S * Y S L Q H S T S N G E I F P T D * Y S S H
Monodelphis domestica K G E R K R E Q * L F F P S F G H N Q ? ? T * G H P R S * H S L Q * S I Y S G E T F P T E * S S Y H

*Ailuropoda melanoleuc*P G R T * R A G S Q W A P W C L D G A Q H P S R ? ? G H H W Q S G E Y * R ? - - - - - ? - F R
Ursus maritimus P G R T * H A G S Q W A P W C L D G A Q H P S S ? ? G H H W Q S G E Y * R ? - - - - - ? - F R
Felis catus P D C A * H A G S Q W A P W R M D G A Q H P S P ? ? G Y H R W W G E Y G * ? - - - - - ? - F H
*Leptonychotes weddelli*P G R T P H A G S Q W A P * C L D G A Q H P S P ? ? G H P W P W G E Y R G ? - - - - - ? - F H
Panthera tigris P D C A * H A G S Q W A P W * M D G A H H P S P ? ? G Y H R S W G E Y G * ? - - - - - ? - F H
Eptesicus fuscus P Y V T P V S G H Q W V P R N L D G A Q Q P S P ? ? G H H W S R G V Y G W ? - - - - - ? - S H
Myotis lucifugus P Y V T P V S G H H W V P W N L D G V Q Q P S P ? ? S H H * S R G V Y G W ? - - - - - ? - S H
Myotis brandtii P Y V T P V S G H H W V P W N L D G V Q Q P S P ? ? S H H W S R G V Y G * ? - - - - - ? - S H
Ceratotherium simum S C S T Q D A G P Q W A P W R L D G A Q H P S P ? ? S H H W P * G V H G W ? - - - - - ? - F H
Equus caballus P H P T Q D D G P Q W A P W R L D G A Q H P S P ? ? G Q H W P * G V H G W ? - - - - - ? - L R
Orcinus orca P C P T * H A G P Q W V P W C L D G G Q H P S P ? ? G H H W P * G F R R * ? - - - - - ? - F H
Physeter catodon P C P T R H A G P Q W V P W C L D G G Q H P S A ? ? G H H R P * G F R R G * ? - - - - - ? - F H
Tursiops truncatus P C P T * H A G P Q W V P W C L D G G Q H P S P ? ? G H H W P * G F R R * ? - - - - - ? - F H
Bubalus bubalis P A P I G D A G P Q C D A W G L D G A Q H P L P ? ? S H H R P Q G D C R R ? - - - - - ? - F H
Ovis aries P A S T G D A G P Q * D A G G L D G A Q H P S P ? ? S H H G P Q G V C R R ? - - - - - ? - F H
Otolemur garnettii L C P A * D A G P Q W G P * G P S E S W H P P A ? ? S C H W S P * V C R * ? - - - - - ? - F G
Callithrix jacchus L * P I * N A G P * W V P K R L E G A Q H P S Q ? ? G C L W P P G A C R W ? - - - - - ? - L R
Saimiri boliviensis L * P T G N A G P * W V P T H L E G A Q H P S C ? ? G H L W P P G A * R W ? - - - - - ? L L R
Chlorocebus sabaeus L C P T * G A G P Q W V P R P L E G A Q H P S P ? ? S C L W R P G A C R W ? - - - - - ? L L R
Macaca fascicularis L C P T * G A G P Q W V P R P L E G A Q H P S H ? ? S C L W C P G A C R W ? - - - - - ? L L R
Homo sapiens I C P T Q D A G P Q W V P R R L E G A Q H P S R ? ? S C L W P P G A C R W ? - - - - - ? L L R
Nomascus leucogenys V C P T G D A G P Q L V P R R L E G A Q H P S R ? ? S C L W P P G A C R W ? - - - - - ? L L R
Pan paniscus I C P T Q D A G P Q W V P R R L E G A Q H P S R ? ? S C L W P P G A C R W ? - - - - - ? L L R
Pan troglodytes I C P T Q D A G P Q W V P R R L E G A Q H P S H ? ? S C L W P P G A C R W ? - - - - - ? L L R
Pongo abelii V * P T Q D A G P Q W V P R R L E G A Q H P S R ? ? S C L W P P G A C R W ? - - - - - ? L L R
Chrysochloris asiatica P C S N Q G P D L Q W A P * H Q G G V Q H Q P P ? ? - ? R H W P C R ? - - - - - ? - F C
Echinops telfairi S C P T Q D H G L Q W V P H H Q G R A * H E L P ? ? Y R C W P C * A C R * ? - - - - - ? - F D
Dasyops novemcinctus P H P A P D P G A * W D P Q H Q D G A K H * L P ? ? G H S R L G W V C R W G L C R W G L C R * G C R
Trichechus manatus P C P T Q A P G L Q W A P Q Q G G A Q H Q P P ? ? G C C W P C * V C R R ? - - - - - ? - F H
Sarcophilus harrisii S R S F * A S Y I Q Y A T K N S D G I Q H H P P H I N D H P * W R I S E R ? - - - - - ? - I L
*Monodelphis domestica*S K P S Q A S Y I Q * E T K T S A D L Q H C L P H R D H H * W R I A Q R Q ? - - - - - ? - L

*Ailuropoda melanoleuc*G Q A K R * G H R W A K A A V V L Y P G H R G G H L T L T G S G S G A A G L S Q A E S K E G R G E G
Ursus maritimus G Q T K R * G H R W A K A A V V L Y P G H S G G H L T L T G S G S G A A G L S E A E S K E G R G E G
Felis catus V Q T K * Q W H R W A K T A F V L Y P G H S G G H L T L T G S G S W T S G L S Q A E S K E G G G E G
*Leptonychotes weddelli*H Q T K R * G H R R T K A A V V L H P G H R G G H L T L T G S G S R A T G L P Q A E S K E R E G E G
Panthera tigris ? Q T K * Q R H R W A K A A F V L Y P G H S G G H L T L T S G S W T S G L S Q A E S K E G G G E G
Eptesicus fuscus C P K K E * R P R L A K A A F V L H P R H G G G H L I P A G S G P G A A G L P Q A E S Q E G G ? ? G
Myotis lucifugus C P T K E * Q P * L A K A A F V L Y P R H C G G H L T P A G S G P G A A G L P Q A E S Q E G G ? ? G
Myotis brandtii C P T K E * Q P R L A K A A F V L Y P R H C G G H L T P A G S G P G A A G L P Q A E S Q E G G ? ? G
Ceratotherium simum G Q T K R * W H R R A K A A L V L H P G H C G G H P T L A G S G S R A P G L S Q T E S K E G G D K G
Equus caballus G Q T E R R W H R R T K T A L I L H P G H R G G H P A L A G S G S R A P G L S Q A E S K A G G E E G
Orcinus orca R Q A K R R W H G R A E A P V L H P G H C G G H P I P A G S G S G A P G L S Q A Q S Q E G G ? ? G
Physeter catodon R Q A K R R W H G R A E A P V L H P G H S G G H P A P A G S G S G A P G L S Q A Q S Q E G G ? ? G
Tursiops truncatus R Q A K R R W H G R A E A P V L H P G H C G G H P V P A G S G S G A P G L S Q A Q S Q E G G ? ? G
Bubalus bubalis S Q A E R P G H G R T A A A L I L H S W H R G G H P A P A S S G L R A A G L S Q A Q G Q E G G ? ? E
Ovis aries S Q A E R P G H G W T A A A L I L H S W H R R G H P A P A S S G P R A A G L S Q A Q G Q E G G ? ? E
Otolemur garnettii G H T K * * W H * R T E A A F V L H P G H C G G H P A P A G S G A R A S G L S Q A E S * A G G E E G
Callithrix jacchus R Q T K Q R W H * W A K V A F V L H P G H R G G H P P P A G P G S G A A G L S Q A E S E E G G ? ? G
Saimiri boliviensis R Q T K Q R W H * R A K V A F V L H P G H R G G H P P P A G P G S G A P G L S Q A E S E E G G ? ? G
Chlorocebus sabaeus G H T E R R Q H * R A K A A F I L H P R H R G R H P T S A G P G S G A T G L S Q A E S E E G G ? ? E
Macaca fascicularis G H T K R R H * R A K A A F I L H P R H R G G H P T S A G P G S G A T G L S Q A E S E E G G ? ? E
Homo sapiens G H T K Q R W H * R A K A A F I L H P R H R G G H P T P A G P G S G A T G L S Q A E S E E G G E E G
Nomascus leucogenys G H T K * R W H * R A K A A F I L H P R H R G G H L T P A G P G S G A T G L S Q A E S E E A G E E G
Pan paniscus G R T K Q R W H * R A K A A F I L H P R H R G G Y P T P A G P G S G A T G L S Q A E S E E G G E E G
Pan troglodytes G R T K Q R W H * R A K A A F I L H P R H R G G H P T P A G P G S G A T G L S Q A E S E E G G E E G
Pongo abelii G R T K Q R W H * R A K A A F I L H P R H C G G H P T P A G P G S G A T G L S Q A E S E E G G E E A
Chrysochloris asiatica G Q A N G R H Q R W T E A A S I L H S G H C G G H L T P S G F S P S A T S L S Q A E S K K G S E K G
Echinops telfairi - - - K G R Q P Q W A E T A S V L H S G H C G G H L T T A G S S S R A T D L S Q A E S K S G R E E G
Dasyops novemcinctus G P T E R Q Q Y * W A K T A F V L Y P G H G G G I P T H A G P C S W A A G L P Q A E S Q E G G E E G
Trichechus manatus G Q T K * R Q H Q W A E T A S I L H P G H C G G H L T T A G S R P G A T G L P Q A E S K E G R E E G
Sarcophilus harrisii G K * E * - H * W S E I T P V L Y F G D S S S Y L A A F G Y D P G V S V L S Q E K S K K G R ? - ?
*Monodelphis domestica*G K W E R W * H * W T E I P P I L Y L G S S S S C L A S S G Y G P G V S V L S Q E E N K K G N ? ? E

<i>Ailuropoda melanoleuc</i>	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-			
<i>Ursus maritimus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-			
<i>Felis catus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-			
<i>Leptonychotes weddelli</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-			
<i>Panthera tigris</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	?	*	N	Q	L	E	F	L	
<i>Eptesicus fuscus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Myotis lucifugus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Myotis brandtii</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Ceratotherium simum</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Equus caballus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Orcinus orca</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Physeter catodon</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Tursiops truncatus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Bubalus bubalis</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Ovis aries</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Otolemur garnettii</i>	-	-	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Callithrix jacchus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Saimiri boliviensis</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Chlorocebus sabaeus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Macaca fascicularis</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Homo sapiens</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Nomascus leucogenys</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Pan paniscus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Pan troglodytes</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Pongo abelii</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Chrysochloris asiatica</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Echinops telfairi</i>	-	-	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Dasypus novemcinctus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Trichechus manatus</i>	-	-	-	-	-	?	C	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
<i>Sarcophilus harrisi</i>	A	Q	Q	F	L	*	L	C	F	T	H	R	A	R	*	S	Q	R	F	G	N	T	I
<i>Monodelphis domestica</i>	-	-	-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Appendix 5 : Amino acid alignment of mammalian CD93 sequences



Appendix 6: CD93 is shed from the surface of human monocytes upon stimulation with PMA. Supernatants were collected from human monocytes were incubated with (PMA +) or without (PMA -) PMA for 10 minutes and analysed by Western Blot.

Curriculum Vitae

Name: Jack W. D. Blackburn

Post-secondary Education: University of Western Ontario, London, ON, Canada
2010-2014 BSc (Hons: Genetics)

Honours and Awards: BioLegend Poster Award, CSI, 2016.
Microbiology and Immunology Travel Award, 2015, 2016.
Deans Honours List, 2011-2013.

Related Work Experience: Teaching Assistant, Univ. of Western Ontario, 2015.

Publications:

[1] Evans, A.L., Blackburn, J.W.D., Yin, C., and Heit, B. Quantitative efferocytosis assays. *Methods Mol. Biol.* In press (2016).

Poster Presentations:

Jack Blackburn and Bryan Heit (April 2016). Elucidating the role of CD93 as an opsonin of apoptotic targets in efferocytosis.
Canadian Society for Immunology, Ottawa, Ontario

Jack Blackburn and Bryan Heit (March 2016). Elucidating the role of CD93 as an opsonin of apoptotic targets in efferocytosis.
London Health Research Day, London, Ontario

Jack Blackburn, Amanda Evans, Ronald Flannagan and Bryan Heit (November 2015). Elucidating the role and function of CD93 in efferocytosis.
Infection and Immunity Research Forum, the University of Western Ontario, London, Ontario

Jack Blackburn, Amanda Evans, Ronald Flannagan and Bryan Heit (April 2015). Elucidating the role and function of CD93 in efferocytosis. London Health Research Day, London, Ontario

Jack Blackburn, Amanda Evans, Ronald Flannagan and Bryan Heit (March 2015). Elucidating the role and function of CD93 in efferocytosis.
Annual McGill Biomedical Graduate Conference, McGill University, Montréal, Québec

Jack Blackburn, Amanda Evans, Ronald Flannagan and Bryan Heit (November 2014). Elucidating the role and function of CD93 in efferocytosis.
Infection and Immunity Research Forum, the University of Western Ontario, London, Ontario.