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Provisional chapter

Plasmids as Genetic Tools and Their Applications in Ecology and Evolution

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Additional information is available at the end of the chapter

Abstract

Plasmids are genetic elements of DNA molecules in the form of small circles present within the bacterial cell cytoplasm outside the bacterial chromosome. Because they are separate from the chromosome, they reproduce independently. However, plasmids are bound to multiply in the cell by multiplying the chromosome. Plasmids differ in size and number of copies in the cell. Plasmids carry genes that add to the cell additional properties, but they are not necessary for cell life and do not affect cell vitality. Some chemicals can remove plasmids from the cell by stopping their proliferation. By bacterial cell multiplication, the number of plasmids decreases until bacterial cells free from the plasmids are obtained. Plasmids are used in the techniques and research of genetic engineering and gene therapy by gene transfer to bacterial cells or to cells of superior organisms, whether other plants, animals, or other living organisms, to improve their resistance to diseases or to improve their growth rates or to improve any other required traits.

Keywords: Plasmids, evolutionary biology, plasmid ecology, plasmid classification

1. Plasmids

A plasmid, usually circular but sometimes linear, is a small double-stranded DNA unit, which is chromosome independent and is capable of self-replication. Each plasmid carries only a few genes. Carrying only a few genes, the plasmid's size ranges from 1 to more than 1000 kbp. Genes required for organism survival and those that are generally beneficial to the host organism, such as antibiotic resistance, are often found in plasmids [1].

Mostly plasmids can be found in bacteria, but they are also present in multicellular organisms and archaea. Plasmids usually contain at least one gene and are not considered independent life forms even though they possess separate genes from their hosts [2].

2. Functions of plasmids

Plasmids perform numerous functions. For instance, the enhancement of organism survival may be found in genes containing genes responsible for killing other organisms or having defense mechanisms for the host through the production of toxins. In addition, some plasmids may also enable the bacterial replication process. The small size of plasmids limits the genes that can be found, which tend to have a certain function (in contrast to an abundant amount of noncoding DNA). A single cell may have multiple coexisting plasmids, each with various functions.

3. Specific types of plasmids

Plasmids can be divided into five main types: fertility F-plasmids, resistance plasmids, virulence plasmids, degradative plasmids, and finally Col plasmids [3].

3.1. Fertility F-plasmids

Fertility plasmids, or F-plasmids, are part of a comprehensive category of conjugative plasmids found in F+ or male bacterial cells that lead with frequent transfer and rarely to transfer of the bacterial chromosome (**Figure 1**). F-plasmids can be inserted into chromosomal DNA

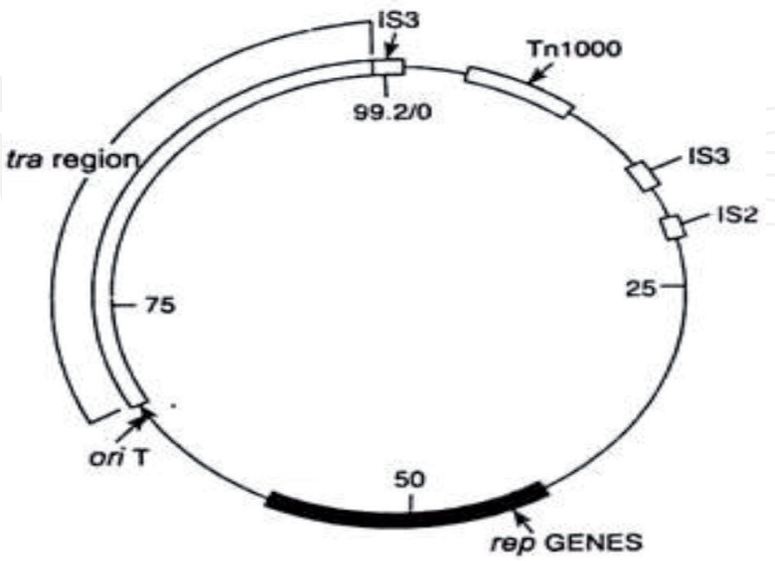

Figure 1. Genetic map of the F-plasmids of *E. coli* [3].

and are termed episomes. Bacteria containing plasmid are termed F positive (F+), and those without plasmids are F negative (F–). Two F+ bacteria result upon conjugation of an F+ bacterium with an F– bacterium. Each bacterium is only able to contain one F-plasmid [3].

3.2. Resistance plasmids

These plasmids contain antibiotics or poison resistance genes and help bacterial production of pili (historically known as R-factors before the nature of plasmid was understood). Resistance plasmids have the ability to use conjugation to transfer themselves, thus providing that bacterial strain resistance to antibiotics. The resistance to the antibiotics in bacteria may even show within 5 years. That being said, NPR stated that antibiotic overuse for treatment of infections, such as UTIs, may result in the appearance of drug-resistant strains.

3.3. Virulence plasmids

A virulence plasmid containing bacterium will render that bacterium a pathogen, or a disease agent. Disease causing bacteria easily spreads among individuals and causes infection by replication in the new host. For example, there are several virulence plasmids for the *Escherichia coli* bacterium. Although *E. coli* is found naturally in human and animal intestine, some *E. coli* strains can result in severe vomiting and diarrhea. *Salmonella enterica* is additional example of a virulence plasmid containing bacterium.

3.4. Degradative plasmids

The main function of degradative plasmids is to aid the host bacterium in the digestion of compounds, which are not commonly found in nature, such as camphor, salicylic acid, toluene, and xylene. Thus, these plasmids encompass genes for enzymes, which have a main function to break down specific compounds (**Figure 2**). Degradative plasmids can be described as conjugative.

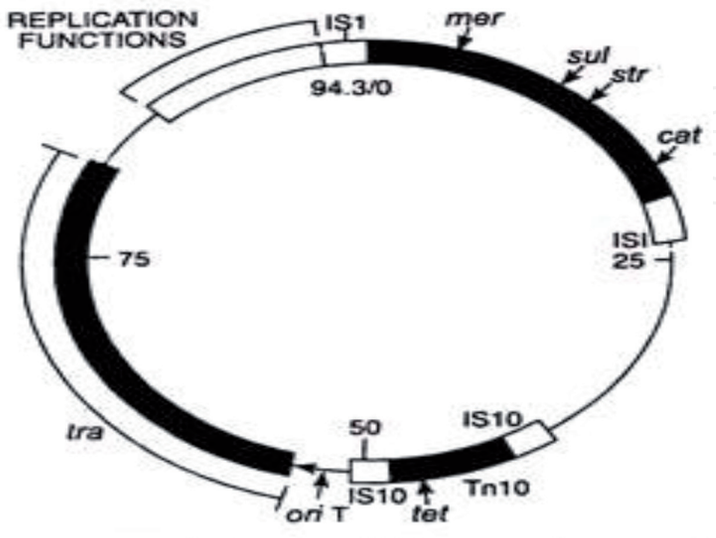

Figure 2. Genetic map of the resistance plasmids R100 [3].

3.5. Col plasmids

Col plasmids contain genes responsible for production of bacteriocins also termed colicins. These proteins can defend the host bacterium through killing other bacteria. Numerous bacteria types produce bacteriocins such as *E. coli* owing to the presence of the ColE1 plasmid [3].

4. Application of plasmids

Plasmids are used in genetic engineering to amplify, or produce many copies of certain genes. They are used in different techniques and are involved in research of genetic engineering and gene therapy by gene transfer to bacterial cells or to cells of superior organisms, whether other plants, animals or other living organisms, to improve their resistance to diseases, growth rates, or any other required traits. In molecular cloning, plasmids are types of vectors that are useful in cloning short segments of DNA. Scientists have developed many uses for plasmids and have created software to record the DNA sequences of plasmids for the use in many different techniques. For example, the artificial and cost-effective bulk production of antibiotics can be achieved by incorporating an expression vector for that antibiotic in microbial cells. Similarly, other biomolecules can also be produced. In addition, plasmids are used to administer gene therapy, which is a technique used to correct defective genes responsible for disease development. They can also be used to replicate proteins, such as the protein that codes for insulin, in large amounts [4].

5. Plasmids as genetic tools

Studies have shown that one of the essentials of gene expression regulation in bacterial genomics is the identification of promoters and transcriptional terminators. Many of the genes are organized by bacteria and then copied from the promoter itself to a single polycistronic molecule of mRNA. Many genes are also replicated in the operas that lie within adjacent genes [5, 6].

Studies also have indicated that there are many experimental methods that require the final identification of promoters either by the body of the organism or by the laboratory. The site includes the initiation of transcription with the use of purified RNA as well as the exposure of promoter activity with the use of promoter-reporter fusion and description of RNA polymerase-promoter complexes [7–9].

A study showed that bacterial genome works to encode various forms of the agent to preserve the specificity of the RNAP promoter, most copies of the bacterial cells showing growth gradually start by RNAP with a measure factor comparable to *Escherichia coli* σ70 [7–10]. The promoters for the holocaust enzyme are characterized by a major sequential element −35 and −10 hexamers, whose sequential sequence is 5′-TTGACA-3′ and 5′-TATAAT-3′, the length of which is 17 nucleotides, which is located in one place of the nucleotide upstream of hexamer-10 [10–13]. This element is mainly retained in Gram-positive bacteria (5′-TRTG-3 ‘motif) than *E. coli* (5′-TG-3′ motif) [11–13]. Plasmid promoter-probe carriers are beneficial in demonstrating the in vivo activity of a promoter that is provided by DNA fragments and contains a transgenic fusion, and it is a necessity in dealing with bacterial genome [14, 15].

One study noted that pathogenic bacteria adapt efficiently in different environments during its infectious cycle, which need a new place to examine or coordinate the change in gene expression. Catalysts and plasmid probes are useful systems for screening in a diverse selection of groups with genetic backgrounds and environmental stimuli of *S. pneumoniae* and *E. faecalis* [16].

The results of a study were found in both plasmid transcripts through the HindIII site, use of PAS plasmid as a vector-separator in *S. pneumoniae* and *E. faecalis*, the application of plasmid (PAST) as a *S. pneumoniae* and *E. faecalis* marker, and Fucose regulation of promoter PfcsK pneumococcus in the PAST vector showing that the stimulus vectors, probes, and decomposition probes are suitable for evaluating promoter activity and signals in *S. pneumoniae* and *E. faecalis*. The most important replicas are based on pMV158; these tools are likely to be of use in numbers of Gram-positive bacteria and to construct strains that express genetically desirable traits [17].

Studies have shown that expression vectors are one of the most widely used genetic manipulation tools for biocatalysis [18]. More efficient and less time-consuming genetic systems have been developed to take advantage of sequencing data to generate targeted alternative gene vectors (TGRVs) and the ability to express fusion proteins [18, 19].

If the trypanosome lacked RNA pathways, TGRVs could generate fresh, single, and double strains of *T. cruzi*, although it is now the only alternative to the elimination of the product of gene expression [18–20].

A study on the development of the pTcR vector series and the pDIY vector pathogens shows that plasmids contribute to the genetic manipulation of Crohn's tumor, which contributes to the extension of a number of breeds through the means of setting a transfection strategy and selectivity. Simple molecular building blocks have been developed to complement the work in harmony with genetic manipulation tools [21].

6. Applications of plasmid in ecology

6.1. Plasmid host range determination and plasmid cost and benefits

The host scope of a plasmid is believed to be a key parameter that decides the plasmid environment. While generally plasmids have run thinks about were finished by mating with a couple of chosen beneficiary strains under ideal conditions, a relative plasmid has run assurance in the rhizosphere of grass was attempted. In this examination, *E. coli* benefactor strains conveying IncP-1 (pTH10, pTH16, RP4), IncQ (pIE639), IncN (pIE1037), IncW (pIE1056), IncI1 (pIE1040), or IncFII (pIE1055) plasmids, all conveying the Tn7-like transposon Tn1826 were connected together with an *E. coli* beneficiary strain into soil. The most noteworthy exchange frequencies were watched for IncP-1, trailed by IncN and IncW, though under similar conditions, no exchange was identified for IncI1 and IncFII. Fifty days in the wake of presenting the *E. coli* contributor pTH16 and beneficiaries into nonsterile soil, rhizosphere microbes that caught the nourseothricin obstruction plasmid were disconnected and distinguished by BIOLOG as *Agrobacterium*, *Pseudomonas*, and *Flavobacterium*. A comparative methodology was additionally taken to distinguish the host scope of IncP-1ε pHH3414 in soil microcosms planted with *Acacia caven*. In this investigation, soil microbes that got pHH3414 were recognized by 16S rRNA quality sequencing as Gammaproteobacteria (*Enterobacter amnigenus*,

Xanthomonas codiaei) and Betaproteobacteria (*Cupriavidus campinensis*, *Alcaligenes* sp.). Soil microcosm tests were likewise used to decide the host scope of the catabolic plasmids pJP4 and pEMT1, giving the capacity to corrupt the herbicide 2,4-dichlorophenoxyacetic corrosive. Beneficiaries were for the most part distinguished as *Burkholderia* species when no extra supplements were included, while the revision of the dirts with supplements brought about extra transconjugants recognized as *Stenotrophomonas* species. Along these lines, again the plasmid hosts of the two plasmids included Beta- and Gammaproteobacteria [22].

At the rate at which new plasmid grouping data are being discharged, it is not any more conceivable to experimentally test the host scope of all recently depicted plasmids. Along these lines, genomics-based strategies might be utilized to anticipate the feasible host and host scope of a particular plasmid dependent on its DNA grouping. Microscopic organisms unmistakably contrast in the general bounty of di-, tri-, or tetra-nucleotides (additionally alluded to as their genomic succession mark), and it gives the idea that plasmids that have a long-haul relationship with hosts of a comparative mark will in general procure that signature. Interestingly, expansive host-extend plasmids rather thought to move between remotely related microscopic organisms, indicating particular genomic marks. Along these lines, we can now effortlessly look at the genomic mark of uncharacterized plasmids and construe their imaginable host or host extend. While the strategy regularly precisely predicts a plasmid's presumable has on account of very much portrayed plasmids, more exploratory approval is required for some novel key plasmids that are being sequenced as a component of genome and metagenome ventures [22].

6.2. Environment of plasmids

The ability of microbes to survive, be established, and grow as well as their genetic recombination in natural habitats is all influenced by various ecological factors. Survival ability, being established and grown, is largely reliant on the genetic constitution specific to the microbes as well as on the physical (temperature, pressure, spatial relations, surfaces, and electromagnetic radiation), chemical (growth factors, carbonaceous substrates, inorganic nutrients, toxicants, available water, ionic composition, PH, gaseous composition, and oxidation-reduction potential), and biological (features of positive and negative microbial interactions) factors associated with the different habitats. All these factors impact the ecology of microorganisms [23].

Each of these individual ecological factors exerts an influence relative to the recipient natural environment. Frequently, such an impact is more significant on introduced microbes compared with indigenous ones. In addition, not all these factors function individually but rather collectively with various additional factors. Even though some factors may be more dominant in a certain habitat, they may exert indirect and cascading effects on other traits. Subsequently, changing one environmental factor may lead to simultaneous changes to other factors, and eventually, the habitat. This alters the survival ability of both introduced microbes and of portions of the indigenous microbiota. Most of the likely permutations of interactions between these environmental factors are basically unlimited, and it is challenging to predict the survival success levels of microbes containing new genetic information as well as their ability to establish and grow in these natural habitats [23].

The intensified interest in recombinant DNA technology increases the likelihood of accidental or deliberate introduction of those genetically engineered microbes into natural habitats. Examples of such habitats are soils, waters, and sediments, being the main sources for all microbes. Such microbes will contain new sequences of DNA some unintentionally inserted also including desired and seemingly harmless sequences. This may pose a potential threat to the health of plants and animals, including humans, and to other features in the biosphere, especially if they show better growth in the recipient environment when compared to the indigenous microbiota or the experimental parental strains. Given that, even minor alterations in a single biosynthetic capability can significantly augment growth rates and hence, result in greater survival and colonization by introduced microbes. For instance, can bacteria possessing an acquired N2 fixing ability combined with existing rapid growth, efficient metabolism, and high survival value in natural habitats be able to decrease the atmospheric N2 content, ground-waters polluted with NO3, and deplete the ozone layer due to production of NO_x, from NO_3? Can organisms designed to remove oil-spills remain confined to such spills or will they extend to other areas and cause degradation of petroleum products in the gas station and refinery, especially if genes, which greatly augment their survival ability in these habitats were also acquired?

Manipulated microbes' ability to survive in natural habitats is apparently low, which minimizes the danger they pose after being established and begin proliferating in natural habitats. Furthermore, some "constructed" host organisms can be auxotrophic and debilitated to the extent that they undergo self-destruction outside the enriched laboratory conditions. However, there have been few studies investigating the survival of these microbes in natural environments. Their survival may be vastly improved by an ability of weakened recipients to obtain the genes present in the natural habitat into which they are placed which reduces their intensity of auxotrophy. To date, there are no studies investigating influence of the physicochemical features of the recipient environment on the microbial ability to survive and acquire genes. These characteristics play a major role in concluding the survival, establishment, and growth of the indigenous as well as the introduced microorganisms in natural habitats [23].

Genetic recombination studies in bacteria are mostly performed in vitro, and there is limited data proving an in-situ form of gene transfer. A few studies have been conducted in vivo using axenic animals or animals with the normal biota, usually of the intestinal tract, being significantly decreased or completely eliminated by pretreatment with antibiotic. These studies focused on conjugation, mainly R-factor transfer, as the gene transfer mechanism [23].

A demonstration of R-factor genes transfer by transduction is seen in *Staphylococcus aureus* and in *Pseudomonas aeruginosa*. Some soil-borne bacteria (e.g., species of *Arthrobacter*, *Pseudomonas*, and *Acinetobacter*) and certain nonsoil bacteria (e.g., species of *Klebsiella* and *Serratia*) seem to be evolving in terms of genetic proficiency, through plasmid transfer, for the utilization of a range of aromatic possibly recalcitrant hydrocarbons toxic to these organisms. Moreover, a demonstration of the conjugation in soil-borne bacteria in vitro such as pseudomonads is seen [23].

Increase in nosocomial infections by drug-resistant bacteria counts as empirical evidence, which implies that the gene transfer responsible for antibiotics and heavy metals resistance occurs in natural habitats. However there is few experimental support to make a solid conclusion, as most of these studies have been restricted to either using resistant bacteria isolated from natural

habitats or performing the transfer and expression of these genetic materials under carefully measured laboratory conditions. Essentially no studies have endeavored to connect these experimental extremes, probably due to lack of techniques specific to studying genetic recombination occurring in natural habitats and lack of scientists trained in microbial genetics [23].

The ability for survival, multiplication, and conjugation in sterile soils is demonstrated in both the strains of *E. coli* K12, being the auxotrophic and prototrophic strains. Clay minerals present, especially montmorillonite, increased the frequency of recombination, most probably due to the enhancement in bacterial growth ability which clay possesses. Such enhancement is partly a result of clay's ability to act as a buffer to the pH of soils, which is a function of the clay's cation exchange capacity. Numerous mechanisms, which clarify the way in which clay minerals influence the survival, growth, establishment, and metabolic activities of microbes in natural habitats, have been outlined. Initial studies on conjugation occurring in nonsterile soils have suggested that the recombination frequency is significantly lower than in sterile soils [23].

The decreased occurrence of recombination occurring in nonsterile soils confirms the obtained results with the drug-resistance plasmids transfer to an animal system. The transfer frequency of a multiple drug resistant plasmid from *Salmonella typhosa* to *E. coli* in healthy rabbits' bladder was as elevated as in in vitro systems with either sterilized urine or synthetic mating media. However, a significantly lower frequency of transfer was seen in the presence of other bacteria namely exogens such as *Proteus mirabilis* and nonconjugative *E. coli*. This observed reduction was not a consequence of the exogens interfering physically (i.e., steric) in the process of conjugation. This is demonstrated by polystyrene latex particles with the same size and concentration as that of the exogens not affecting the frequency of plasmid transfer, suggesting a chemical interference on conjugation caused by the exogens. It is unknown whether the lower frequencies of conjugation in nonsterile compared to sterile soils are attributed to such interference, but that interference could be possible since various species may be in adjacent vicinity in different natural microbial habitats [23].

Studies involving the conjugation in sterile soil also signified that rather than undergoing genetic recombination, cross-feeding (syntrophism) allows bacteria that are auxotrophic for various nutrients to co-exist, in both soil and replica-plated agar media. This observation accentuates the need to prudently investigate suggestions for seeming genetic recombination occurring in natural habitats and the ability of auxotrophs to survive in natural habitats as a viable possibility, in spite of their apparent fragility and debilitation, in the chance that other microbes present in the same habitat act as commensals providing nutrients which cannot be synthesized by auxotrophs. Sagik and Sorber showed that these auxotrophs (e.g., the EK2 host and DP50supF) are able to survive in a nutrient-rich environment such as, for example, a model sewage treatment plant. The solid fraction of the waste stream appears to be associated with this survival, once again demonstrating that particulates and the resultant increases in surface area improve the survival and growth of bacteria. Moreover, cometabolism or "shared" detoxification of inhibitors can participate to the survival of microbes sensitive to toxins without any genetic recombination [23].

There is insufficient documentation shedding light on transformation, which occurs in natural microbial habitats. The scarcity of studies on transformation in situ can be attributed to

this lack of information, but in addition, it may also reflect an unconfirmed notion which is that "naked" DNA is exceedingly susceptible to enzymatic degradation in natural habitats. Greaves and Wilson have, however, demonstrated that nucleic acids become adsorbed to soil clay minerals, particularly to montmorillonite, and that the adsorption protects the nucleic acids from degradation by enzymes. Similarly clay adsorbed viruses, proteins, peptides, and amino acids are protected to different degrees against microbial degradation. Accordingly, both naked DNA (taking part in transduction) may endure in natural habitats despite the absence of an appropriate host [23].

This adsorption to clay minerals protecting soluble organics and viruses from degradation is vital to consider in any possible exchange of genes occurring in clay containing habitats and other surface-active particulates. An inability of transforming DNA and transducing viruses to survive can be expected for long in natural habitats lacking hosts. In addition, being best, the substrate for nonhost microbes (that is they contain C, N, and P as well as S in case of viruses) means they would be swiftly degraded by the indigenous microbiota. However, there is growing evidence that DNA and viruses persevere in natural habitats due to the clay minerals adsorption process, which protects against both biological inactivation and physico-chemical. Additionally, this adsorption does not lessen the enzymes' activity regarding its catalysis capabilities but may in fact increase it; or the virus's ability to infect the hosts. Thus, if transforming DNA and viruses (no studies have investigated the ability of adsorbed DNA to transform) are able to persist in natural habitats, it is possible that it is through transmission of their genetic information to any suitable host introduced into these habitats inadvertently or deliberately. There are sporadic studies involving the survival and consequent microbial establishment of microbes, which do not inhabit a particular habitat. This is illustrated by the survival ability of enteric bacteria (including *E. coli*, *Salmonella* sp., and *Shigella* sp.) introduced into soils and waters by means of wastewater or sludge applications and of *Listeria monocytogenes* and *Clostridium botulinum* [23].

7. Evolution of plasmids

It cannot be said that plasmids are mere materials and a suitable environment for genetic exchange given that they themselves are subjects to evolutionary forces [24].

The connections of plasmid access in new bacteria result in a cost of fitness. Therefore, if the plasmid is unable to spread horizontally with the required speed ensuring its survival as a pure gene parasite, the theory predicts that it will be removed from the bacterial group. Thus, unless the plasmid-encoded traits are not selected, the plasmid of the population will be removed by purifying the selection. Furthermore, positive selections can ultimately result in any beneficial plasma genes to move to the bacterial chromosome; hence, the beneficial value of the plasmid is elminiated. However, the costs inflicted by plasmids are not irreversible. In fact, the latest reports indicate that compensatory development can often improve these costs. Extensive studies conducted by clinical microbiologists have shed light on the molecular basis and epidemiology of AR, giving a clear perception of which genes and AR plasmids proliferate in clinical conditions. In this process, the plasmid bacteria acquire genetic charge

that can provide feature. Plasmids typically impose the cost of fitness in the absence encoded properties, and compensatory mutations can constrain the spread of cloning of bacterial plasmids. This cost can be moderated over time. It is suggested that the significant relation detected between AR plasmids and clinically significant bacteria should be determined with the use of plasmid compensatory development and fitness costs. Associated plasmids are playing a mean part in the diffusion of resistance genes in the patients' intestines and are ever so relevant to diseases of intestinal pathogens. Therefore, hospital patients are provided, through dark microbes, with an exclusive opportunity to study a bacterial community described as clinically relevant [25].

Plasmids are known to be extra chromosomal genetic elements where their ecology and evolution are dependent on their host interaction as well as their genetic repertoire. Mobility and stability are qualities, which influence the plasmid lifestyle and each differs in magnitude. The relationship between plasmid traits and host biology are caused for transitions between the lifestyles, host range, invasion, persistence, and adaptation of the plasmids. In terms of plasmid ecology, kinetics is an important factor, and as for long-term plasmid evolution, plasmid stability is more relevant. Upon the transition into additional chromosomes, plasmids become no longer independent entering the host lineage. Plasmid evolution of prokaryotic chromosomes may be independent even though they are confined to their hosts. Evolution of plasmid genome within the host cell occurs after plasmids have successfully entered a host. The plasmid lifestyle is eventually affected by these molecular changes, with outcomes being seen in the development of host range, plasmid adaptation and persistence, and the transition into additional chromosomes [26–28].

Mobile elements of DNA like bacteriophages and plasmids have different genetic organization from the host's chromosomal organization. Confluence and clustering of various survival and propagation functions, arranged in functional modules, affect plasmid organization. Many traits are found in the molecular archeology of the IncW backbone and that provides an example of the way evolution, and genetic organization occurs in the conjugative plasmids' life [24].

7.1. Wellness of plasmids

The initial step to better understand the developmental elements of clinically significant plasmid bacterium affiliations is to acquire an exact gauge of the appropriation of wellness impacts of AR plasmids in their regular bacterial hosts. There are different possible ways to deal with this dissemination in accumulations of intestinal microbiota segregates. A highly evident methodology is to contemplate the wellness impacts of the plasmids officially found in the clones. This methodology needs the capacity to evacuate (fix) the plasmid followed by contrasting the overall wellness of clones and without it. Relieving plasmids from wild-type clinical strains is testing, yet there are new innovations accessible. The issue presenting itself in expelling the plasmid is given that it is difficult to determine to what extent a plasmid has been available in a bacterial clone, and it is additionally difficult to know whether any expense initially forced by the plasmid has just been reduced by compensatory development. An option is to build a new relationship by joining predominant bacterial clones with AR plasmids from the intestinal microbiome, empowering investigation of the wellness impacts

of plasmids upon entry in their hosts. This strategy may generate a more reasonable gauge of the circulation of plasmids' wellness impacts in occupant gut microscopic organisms instantly after plasmid securing.

7.2. Compensatory evolution in vivo

The enhancement of plasmid costs after some time by means of compensatory changes in the plasmid or bacterial chromosome is inevitable in test show frameworks. It is hence sensible to expect that if plasmids create an expense for their new has in the intestinal microbiome, this expense will be managed by compensatory advancement. It ought to be conceivable to affirm this speculation by concentrate fleeting arrangement of intestinal microbiota segregates from hospitalized patients. A lessening after some time in the expense at first forced by a plasmid found in a clone could show an occasion of interpatient compensatory development. Critically, testing various provinces of the plasmid-conveying clone per time point should build the odds of recuperating remunerated clones. Uncovering potential compensatory transformations aggregated after some time can come from sequencing the bacterial genomes from this worldly arrangement of separates. At long last, remaking of these changes in the genealogical plasmid-conveying clone will affirm their job [27].

8. Conclusions

In nature, gene dissemination by the means of horizontal gene transfer encompasses several different factors (plasmids, transposons, integrons, and phages) and mechanisms (homologous and site-specific recombination, conjugation, transposition, transduction, and transformation) [26–28]. In terms of their genetic organization, plasmids seem to equally possess characteristics of both phages and chromosomes. More studies should concentrate on the regulation networks of conjugative plasmids with the purpose of confirming the existence of a global organization present in their genomes, as an alternative to a meager combination of independent modules [29].

The ability of a plasmid to facilitate retrotransfer (acquire potentially beneficial genes to its host) is to a greater extent common in numerous conjugative plasmids. IncP plasmids are mainly used to study retrotransfer, but it is more noticeable for some newly defined BHR plasmids. Retrotransfer can hold vast evolutionary significance a horizontal gene transfer promoting force. After unraveling the mechanism, the subsequent move should be to comprehensively investigate the retrotransfer keeping in mind an ecological perspective, especially for plasmids showing a conjugation range larger than their replication range. These plasmids could acquire genes (either from a plasmid or a plasmid free bacterial chromosome) from a taxonomic domain much bigger than the domain within which they replicate.

This will significantly affect horizontal gene fluxes, either between natural species of bacteria or genetically modified organisms. It must be said that we have inadequate understanding of BHR plasmids, even considering IncP plasmids, which are known to self-transfer among cyanobacteria, Gram-positive bacteria, and other key bacterial branches.

Data concerning their capture range and the gene types which can be captured are scarce. Retrotransfer, biparental, and triparental mattings have resulted in the isolation of new BHR plasmids, but only a limited number of recipient hosts, mostly β- and γ-proteobacteria [30–32], and lately one species from the α-proteobacteria [33] have been put to use to capture these plasmids [25].

The progress achieved in comparative genomics and experimental evolution has been fundamental in shedding light on the involved mechanisms of plasmid trait evolution. Strong pressures for selection such as the addition of antibiotics, are often applied to study experimental evolution, thus the evolutionary dynamics of the plasmid perceived in such studies might be more imperceptible in nature. Additional studies of biology of plasmids will help expose how different plasmid traits contribute to the transitioning between the various modes of lifestyle. To further illuminate their role in evolution of prokaryotes, the interplay between plasmid stability and indispensability should be investigated. Investigating the plasmid lifestyle transitions from the plasmid standpoint provides new opportunities for the research involving the ecology and evolution of plasmids [25]. Studies concerning environmental spatial variation have mainly concentrated on maintaining genetic variation. Numerous one locus genetic models have attended to this subject, but these models, for various reasons, cannot be directly applied to quantitative (polygenic) traits. One explanation being that concerning characters which vary continuously, there is also interest in evolution of the mean phenotype expressed in different environments [34].

Investigational methods that combine clinical microbiology and evolutionary biology can help illuminate and clarify the evolutionary, ecological, and molecular mechanisms, which influence both the increase and spread of interactions deemed successful between bacterial pathogens and AR plasmids. Eventually, this information will aid in designing exclusive strategies of intervention to thwart these interactions before they are established irreversibly in the clinical setting.

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