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Mechanisms of Gene Transfer in Bacteria: A Review

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Abstract
Gene transfer in bacteria is unidirectional from a donor cell to a recipient cell and the donor usually gives only a small part of its DNA to the recipient. Therefore, complete zygotes are not formed; rather, partial zygotes (merozygotes) are formed. the objective of this review was to critically describe the various mechanism involved in the horizontal transfer of genetic information in bacteria. These mechanisms include transformation, conjugation and transduction these natural processes have been modified in the field of molecular biology so that DNA can be deliberately incorporated into host microbes. Method: The method adopted in this review is broad search of both electronic data bases, hard copies by studying and comparing the information obtained from available current published scientific researchers in peer reviewed journals, books, and conferences etc. Results: it was found that Bacterial genes are usually transferred to members of the same species but occasional transfer to other species can also occur example in members of the genus S almonellae and Escherichia. Understanding the mechanism of transfer of genetic elements in bacteria is important in order to appreciate R. plasmid mediated antibiotic resistance in bacteria. Conclusion; Bacteria can transfer genes from one strain to another by different mechanisms: these natural processes have been modified in the field of molecular biology so that DNA can be deliberately incorporated into host microbes including genes that would normally never be transferred this way

Keywords
Mechanism, Gene, Transfer, Bacteria

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INTRODUCTION
Gene transfer pertains to the transfer of genes between organisms. It may be a horizontal gene transfer or a vertical gene transfer. The transfer of genes is horizontally when a segment of DNA is copied and inserted from one site to another of the same or of a different chromosome which could be transferred from the donor organism to the recipient organism (i.e. not the donor organism's offspring) through gene copying and insertion. This kind of gene transfer is associated with the occurrence of antibiotic resistance and transmission of virulence among different bacterial species (Gyles and Boerlin, 2014). In contrast, the vertical gene transfer pertains to the transfer of genes from parents to offspring. This kind of gene transfer entails reproductive mechanisms such as by sexual reproduction or by asexual reproduction. Vertical gene transfer is applied in plant breeding (Keen, 2012).

The first evidence that horizontal gene transfer (HGT) could occur was the recognition that virulence determinants could be transferred between pneumococci in infected mice, a phenomenon that was later shown to be mediated by the uptake of the genetic material DNA in a process called transformation (Griffith, 1928). The subsequent identification of gene transfer mediated by both plasmids and viruses and the recognition of transposable elements provided the steppingstones to our current picture of gene flux and the

importance of mobile genetic elements (Thomas, 2000). Many horizontally acquired genes are likely to cause deleterious effects in the chromosome of the bacterial recipient. Therefore, these bacteria will be lost from the population over time in the same way that deleterious mutations are lost.

However, horizontally acquired chromosomal DNA that confers a selective advantage to the host, or mobile genetic elements that encode their own transfer and maintenance functions, have the potential to spread rapidly within a bacterial population. Where HGTs succeed between distantly related organisms, the genes most likely to be involved tend to belong to the simplest sets of functional networks (Jain, 1999). Therefore, informational genes of the central cellular machinery such as DNA replication, transcription or translation tend not to spread rapidly, even if they confer antibiotic resistance, compared for example to single-function resistance determinants such as β-lactamases or aminoglycoside-modifying enzymes (Christopher and Kaare, 2005).

In contrast to the evolution of new traits through the modification of existing sequences, the origin of new abilities through HGT has three requirements. First, there needs to be a means for the donor DNA to be delivered into the recipient cell. Second, the acquired sequences must be incorporated into the recipient's genome (or become associated with an autonomous replicating element). And third, the incorporated genes must be expressed in a manner that befits the recipient microorganism. The first two steps are largely indiscriminate with respect to the specific genes or functional properties encoded by the transferred regions, and can occur through three mechanisms:

A. Transformation,
B. Transduction,
C. And Conjugation (Sridhar, 2006).

TRANSFORMATION

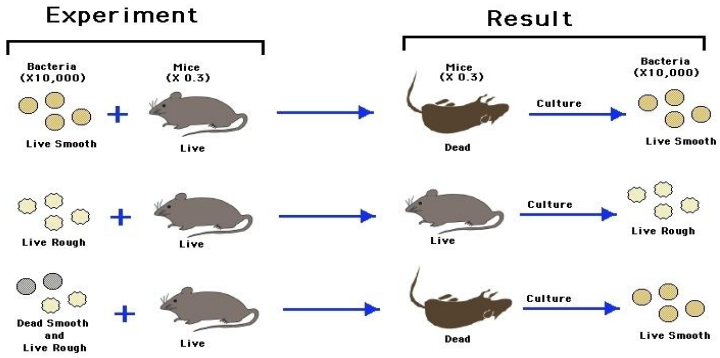
Natural transformation-the stable uptake, integration and functional expression of extracellular DNA that can occur under natural bacterial growth conditions — is the only mechanism that can potentially explain how bacteria acquire DNA from foreign species beyond the host range of mobile genetic elements or bacteriophages. For transformation to occur, bacterial cells must first develop a regulated physiological state of competence, which has been found to involve approximately 20 to 50 proteins. With the exception of *Neisseria gonorrhoeae*, most naturally transformable bacteria develop time-limited competence in response to specific environmental conditions such as altered growth conditions, nutrient access, cell density (by quorum sensing) or starvation (Christopher and Kaare, 2005). As the growth environments and factors that regulate competence development vary between bacterial species and strains, there is no universal approach to determine if a given bacterial isolate can develop competence as a part of its life cycle (Cohan, 1991).

The ability to take up naked DNA by natural transformation has been detected in archaea and divergent subdivisions (phyla) of bacteria, including representatives of the Gram-positive bacteria, cyanobacteria, *Thermus* spp., *Deinococcus* spp., green sulphur bacteria and many other Gram-negative bacteria (Paget, 1994; Lorenz, 1994). Many human pathogenic bacteria, including representatives of the genera Campylobacter, Haemophilus, Helicobacter, Neisseria, Pseudomonas, Staphylococcus and Streptococcus, are naturally transformable (Lorenz, 1994).

The conserved ability to acquire DNA molecules by natural transformation among a broad range of bacteria indicates that the genetic trait is functionally important in the environment, enabling access to DNA as a source of nutrients or genetic information. Prerequisites for natural transformation include the release and persistence of extracellular DNA, the presence of competent bacterial cells and the ability of trans located chromosomal DNA to be stabilized by integration into the bacterial genome or the ability of trans located plasmid DNA to integrate or re-circularize into self-replicating plasmids (Christopher and Kaare, 2005).

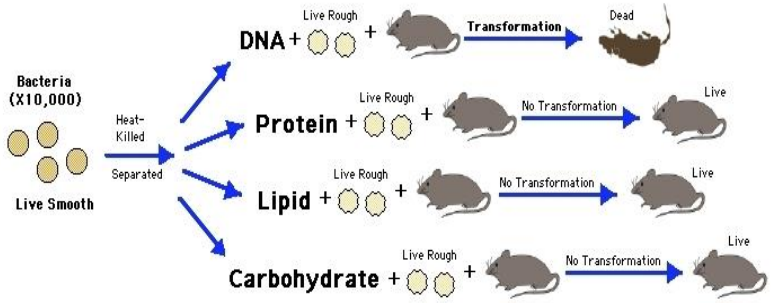
Fred Griffith Experiment.

In 1928, Fred Griffith, while working in vaccine research with *Streptococcus pneumoniae*, discovered the common phenomenon of bacterial transformation. Griffith was culturing different strains of *S. pneumoniae* and injecting them into mice to check mortality. He had a virulent (smooth) strain, one that killed mice, and another nonvirulent (rough) strain, that did not kill mice. In one particular experiment, Griffith had injected the remains of dead virulent (smooth) *S. pneumoniae* along with living nonvirulent (rough) *S. pneumoniae* into living mice. The mice died, and when he cultured the bacteria in the dead mice, he was surprised to find living *S. pneumoniae*. The dead virulent bacteria had contributed something to the living nonvirulent bacteria and transformed them. Griffith named the substance the "transforming principle" but died before he could actually identify it.



(Kuensting, 2004).

Oswald Avery, Colid MaCleod, and Maclyn McCarty continued with Griffith's experiment. They systematically purified extracts from virulent *S. pneumoniae* consisting of either carbohydrate, lipid, protein and nucleic acid. The only extract that was capable of transforming nonvirulent (rough) bacteria into virulent (smooth) bacteria was the DNA extract. In 1944, their conclusion was that DNA was the hereditary substance that caused bacterial transformation.



(Kuensting, 2004)

Release of extracellular DNA in the environment.

Natural transformation relies on bacterial exposure to extracellular DNA molecules in the environment. DNA continually enters the environment upon release from decomposing cells, disrupted cells or viral particles, or through excretion from living cells. The release of intact DNA from decomposing cells depends on the activity and location of nucleases and reactive chemicals. (Moscoso, 2004; Lorenz, 1994). Passive release of DNA from dead bacteria occurs after self-induced lysis, a process that results in broken cell walls and membranes and the subsequent exposure to, and release of cytoplasmic contents, including DNA, in the environment (Palmen, 1995). Pathogenic microorganisms can also undergo lysis caused either by the host immune system or the antibiotic treatment of infections (Christopher and Kaare, 2005).

Stability of extracellular DNA in the environment.

The persistence of extracellular DNA will determine the bacterial exposure time, and therefore the natural transformation frequency. The degradation kinetics of extracellular DNA vary considerably depending on environmental conditions (Worthey, 1999; Widmer, 1996).

Uptake of DNA into the bacterial cytoplasm.

Upon exposure to competent bacteria, the extracellular DNA binds non-covalently to sites present on the cell surface (30 to 80 binding surfaces in *Streptococcus pneumoniae*) (Palmen and Hellingwerf, 1997; Dubnau, 1999). The subsequent DNA translocation process varies among bacteria and remains to be fully characterized (Dreiseikelmann, 1994; Puyet, 1990). Double stranded DNA is converted to single-stranded DNA during translocation across the inner membrane (Chen, 2004). Although some competent bacterial species, for example, *N. gonorrhoeae* and *H. influenzae*, are selective in the DNA they translocate across the membrane, whereas most other species take up DNA independently of its sequence (Lorenz, 1994).

Recombination with the host genome.

With the exception of plasmids that succeed in reconstituting a replication-proficient form, the horizontally transferred DNA transiently present in the bacterial cytoplasm must integrate into the bacterial genome to persist for many generations. For homologous recombination, depending on the system, the incoming DNA must contain regions between 25 to 200 bp in length of high similarity to the recipient genome. These regions will initiate DNA pairing and strand exchange (Christopher and Kaare, 2005).

CONJUGATION.

In 1946 Joshua Lederberg and Tatum discovered that some bacteria can transfer genetic information to

other bacteria through a process known as conjugation. Bacterial conjugation is the transfer of DNA from a living donor bacterium to a recipient bacterium. Plasmids are small autonomously replicating circular pieces of double-stranded circular DNA. Conjugation involves the transfer of plasmids from donor bacterium to recipient bacterium. Some plasmids are designated as F factor (F plasmid, fertility factor or sex factor) because they carry genes that mediate their own transfer. The F factor can replicate autonomously in the cell. These genes code for the production of the sex pilus and enzymes necessary for conjugation. Cells possessing F plasmids are F+ (male) and act as donors. Those cells lacking this plasmid are F-(female) and act as recipient (Sridhar 2006).

Plasmid transfer in Gram-negative bacteria occurs only between strains of the same species or closely related species and each Gram-negative F+ bacterium has 1 to 3 sex pili that bind to a specific outer membrane protein on recipient bacteria to initiate mating. The sex pilus then retracts, bringing the two bacteria in contact and the two cells become bound together at a point of direct envelope-to-envelope contact. In Gram-positive bacteria sticky surface molecules are produced which bring the two bacteria into contact. Gram-positive donor bacteria produce adhesins that cause them to aggregate with recipient cells, but sex pili are not involved. DNA is then transferred from the donor to the recipient. Plasmid-mediated conjugation occurs in *Bacillus subtilis*, *Streptococcus lactis*, and *Enterococcus faecalis* but is not found as commonly in the Gram-positive bacteria as compared to the Gram-negative bacteria.

Despite the diversity of mechanisms mediating genetic exchange among prokaryotes, the introduction of DNA into a recipient cell's cytoplasm does not ensure successful gene transfer unless the transferred sequences are stably maintained in the recipient microorganism. DNA assimilation into the bacterial genome can exploit one of a number of processes including:

(1) Persistence as an episome, which requires selection to avoid stochastic loss.

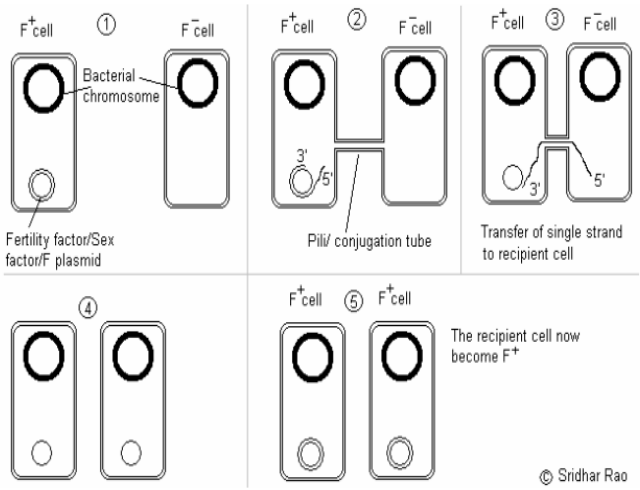
(2) Homologous recombination, which will serve primarily to reassert variation among closely related taxa and is unlikely to allow introduction of novel traits.

(3) Integration mediated by bacteriophage integrases or mobile element transposases; and

(4) Illegitimate incorporation through chance double-strand break repair, as postulated for the integration of mitochondrial sequences into the yeast genome (Ricchetti *et al.,* 1999).

F+ conjugation:

This results in the transfer of an F+ plasmid (coding only for a sex pilus) but not chromosomal DNA from a male donor bacterium to a female recipient bacterium. The two strands of the plasmid separate. One strand enters the recipient bacterium progressing in the 5' to 3' direction while one strand remains in the donor. The complementary strands are synthesized in both donor and recipient cells. The recipient then becomes an F+ male and can make a sex pilus. During conjugation, no cytoplasm or cell material except DNA passes from donor to recipient (Sridhar, 2006).



(Sridhar, 2006)

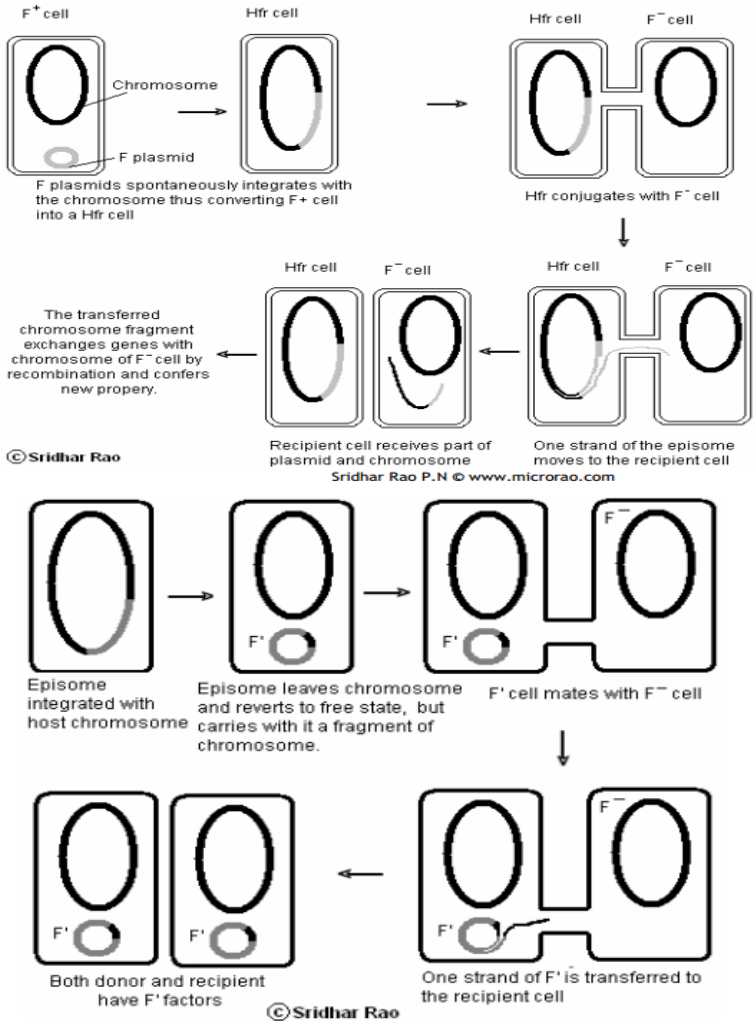
Resistance plasmid conjugation:

Some Gram-negative bacteria harbor plasmids that contain antibiotic resistance genes, such plasmids are called R factors. The R factor has two components, one that codes for self-transfer (like F factor) called RTF (resistance transfer factor) and the other R determinant that contains genes coding for antibiotic resistance. R plasmids may confer

resistance to as many as five different antibiotics at once upon the cell and by conjugation; they can be rapidly disseminated through the bacterial population (Sridhar, 2006).

Hfr (high frequency recombinant) conjugation:

Plasmids may integrate into the bacterial chromosome by a recombination event depending upon the extent of DNA homology between the two. After integration, both plasmid and chromosome will replicate as a single unit. A plasmid that is capable of integrating into the chromosome is called an episome. If the F plasmid is integrated into the chromosome it is called an Hfr cell. After integration, both chromosome and plasmid can be conjugally transferred to a recipient cell. Hfr cells are called so because they are able to transfer chromosomal genes to recipient cells with high frequency. The DNA is nicked at the origin of transfer and is replicated. One DNA strand begins to pass through a cytoplasmic bridge to the F- cell, where its complementary strand is synthesized. Along with the portion of integrated plasmid, the chromosome is also transmitted to the F cell. The bacterial connection usually breaks before the transfer of the entire chromosome is completed so the remainder of the F+ plasmid rarely enters the recipient. Usually only a part of the Hfr chromosome as well as the plasmid is transferred during conjugation and the recipient cell does not receive complete F factor. After conjugation the Hfr cell remains Hfr but the F cell does not become F+ and continues to remain F. However, the transferred chromosome fragment recombines with the chromosome of F cell thereby transferring some new property to the recipient cell (Sridhar, 2006).



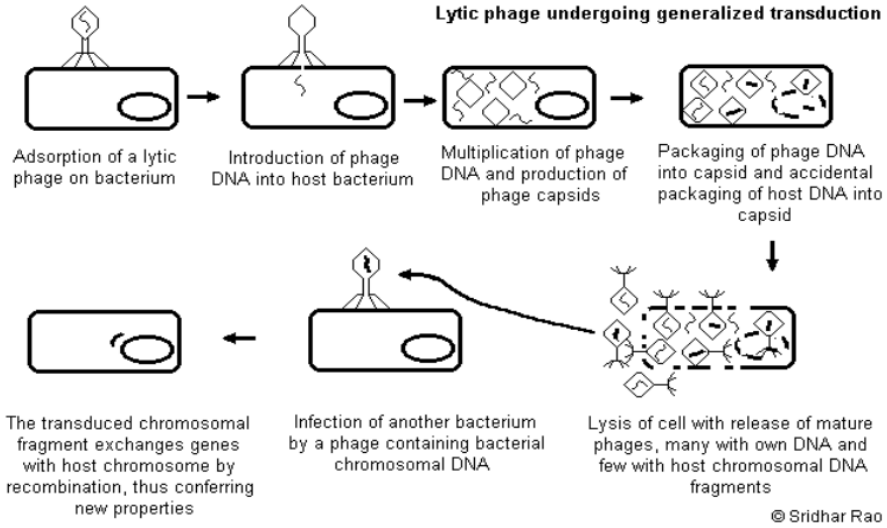
(Sridhar, 2006)

The integration of episome into the chromosome is not stable and the episomes are known to revert back to Free State. While doing so, the episomes sometimes carry fragments of chromosomal genes along with it. Such an F factor that incorporates some chromosomal genes is called F prime (F') factor. When such an F' cell mates with F- recipient cell, it not only transfers the F factor but also the host genes that it carried with it. This process of transfer of

chromosomal genes along with F factor is known is sexduction.

TRANSDUCTION

Transduction is the process by which DNA is transferred from one bacterium to another by a virus. It also refers to the process whereby foreign DNA is introduced into another cell via a viral vector. This is a common tool used by molecular biologists to stably introduce a foreign gene into a host cell's genome. When bacteriophages (viruses that infect bacteria) infect a bacterial cell; their normal mode of reproduction is to harness the replicational, transcriptional, and translation machinery of the host bacterial cell to make numerous virions, or complete viral particles, including the viral DNA or RNA and the protein coat (Carpa, 2010).



Sridhar, 2006)

Transduction happens through either the lytic cycle or the lysogenic cycle. If the lysogenic cycle is adopted; the phage chromosome is integrated into the bacterial chromosome, where it can remain dormant for thousands of generations. If the lysogen is induced (by UV light for example), the phage genome is excised from the bacterial chromosome and initiates the lytic cycle, which culminates in lysis of the cell and the release of phage particles. The lytic cycle leads to the production of new phage particles which are released by lysis of the host (Carpa, 2010).

The packaging of bacteriophage DNA has low fidelity and small pieces of bacterial DNA, together with the bacteriophage genome, may become packaged into the bacteriophage genome. At the same time, some phage genes are left behind in the bacterial chromosome. There are generally three types of recombination events that can lead to this incorporation of bacterial DNA into the viral DNA, leading to two modes of recombination (Perales-Graván et al 2009).

Generalized transduction may occur in two main ways, recombination and headful packaging. If bacteriophages undertake the lytic cycle of infection upon entering a bacterium, the virus will take control of the cell's machinery for use in replicating its own viral DNA. If by chance bacterial chromosomal DNA is inserted into the viral capsid used to encapsulate the viral DNA, the mistake will lead to generalized transduction. If the virus replicates using "headful packaging", it attempts to fill the nucleocapsid with genetic material. If the viral genome results in spare capacity, viral packaging mechanisms may incorporate bacterial genetic material into the new virion. The new virus capsule now loaded with part bacterial DNA continues to infect another bacterial cell. This bacterial material may become recombined into another bacterium upon infection (Clarck 2005).

CONCLUSION

Bacteria can transfer genes from one strain to another by three different mechanisms: transformation, conjugation and transduction, these natural processes have been modified in the field of molecular biology so that DNA can be deliberately incorporated into host microbes inclusive of genes/ antibiotic resistance markers that normally would never be transferred among bacteia this way.

RECOMMENDATION

For better understanding of antibiotic resistance in bacteria, a significant level of knowledge on mechanisms of horizontal gene transfer is essential.

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