Bacterial Genetic Exchange

Secondary article

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Exchange of genetic material between bacterial species is mediated by the basic processes of conjugation, transduction and transformation. This exchange is fundamental for bacterial evolution and adaptation in a dynamic environment.

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Introduction

The primary goals of a bacterium are to survive and replicate in its environment. To reach these goals, bacteria must rely on their complement of genes. As many bacterial species exist in multiple and potentially hostile environments, an organism's genes may be insufficient to survive in all of the environments it encounters. An organism that rigidly maintains the same genetic material from one generation to the next may have little chance for survival. Thus, bacteria have evolved mechanisms of genetic exchange as a survival tool. Indeed, nearly all known bacteria have at least one of the three basic mechanisms of genetic exchange: conjugation, transduction and transformation. Several notable exceptions are *Treponema* spp., *Rickettsia* spp. and *Mycoplasma* spp., in which genetic exchange has not been observed. That bacterial genetic exchange is widespread across most genera, in both Gram-positive and Gram-negative organisms, suggests that exchange of genetic material is a very important trait for survival. Conjugation, transduction and transformation are responsible for horizontal or lateral gene transfer, the transfer of genes from a donor bacterium to a recipient bacterium.

DNA elements, such as plasmids, transposons, insertion sequences, integrons, transducing phages or naked DNA, are required as the substrate for bacterial genetic exchange. Plasmids are small, circular pieces of DNA that replicate autonomously from the bacterial chromosome; these elements are probably the most common type of DNA element transferred during genetic exchange. Insertion sequences are small mobile DNA elements that contain direct or inverted repeats at their ends and genes for transposition (transposase and resolvase). Transposons are mobile DNA elements that contain insertion sequences, transposition genes and genes conferring antimicrobial resistance or metal ion resistance, or other genes. There are also conjugative plasmids and conjugative transposons, which contain genes required for conjugation. Integrons will be discussed below in the antimicrobial resistance section.

We will summarize conjugation, transduction and transformation and review the role of genetic exchange in nature with specific reference to antimicrobial resistance and acquisition of virulence traits.

Conjugation

Conjugation (**Figure 1**) is the transfer of a plasmid or other self-transmissible DNA element and sometimes chromosomal DNA from a donor cell to a recipient cell via direct contact usually mediated by a conjugation or sex pilus. Recipients of the DNA transferred by conjugation are called transconjugants. Conjugation was discovered to occur in *Escherichia coli* by Lederberg and Tatum in 1946. The process of conjugation can transfer DNA regions of hundreds to thousands of kilobases and has the broadest host range for DNA transfer among the methods for bacterial exchange. Conjugation occurs in and between many species of bacteria, including Gram-negative as well as Gram-positive bacteria, and even occurs between bacteria and plants. Although numerous examples of conjugative plasmids exist, we will focus on the F plasmid and briefly describe several other conjugation systems.

The F plasmid

Of all the conjugative plasmids, the F (fertility) plasmid of *E. coli* was the first discovered and is one of the best studied. The F plasmid is present in one or two copies per cell and is very large (about 100 kilobases). *E. coli* harbouring the F plasmid are referred to as donor (F^+; male) cells and *E. coli* lacking the F plasmid are referred to as recipient (F^-; female) cells. Only donor cells are capable of transferring the F plasmid to recipient cells.

For transfer of the F plasmid from donor to recipient, a series of events must occur. Intimate contact between cells, resulting in mating-pair formation, is required for efficient DNA transfer. In *E. coli* this is apparently mediated by a sex pilus produced by the donor cell. Once intimate contact

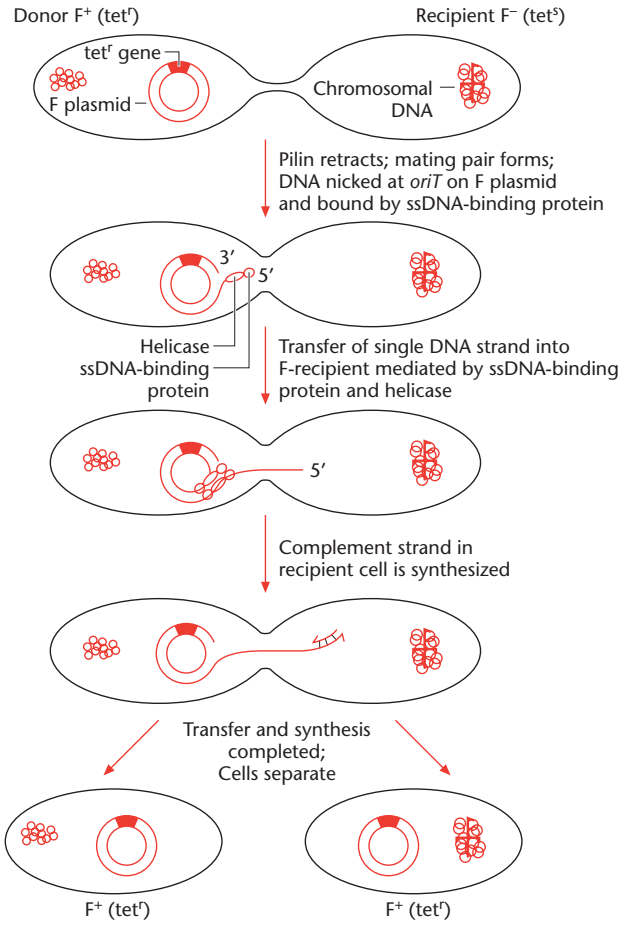

Figure 1 Conjugation. Conjugation is the transfer of a plasmid or other self-transmissible DNA element and sometimes chromosomal DNA from a donor cell to a recipient cell via direct contact, usually mediated by a conjugation or sex pilus. Cell-to-cell contact is required and the process is resistant to DNAase. In this example the F plasmid (F^+) is being transferred from a donor cell to a recipient cell. The donor is resistant to the antibiotic tetracycline (tet^r) which is encoded by the F plasmid. The F plasmid DNA is transferred to the recipient cell as a single-stranded (ssDNA) bound by ssDNA-binding protein. The complement DNA strand is synthesized in the recipient cell and the resulting transconjugant is tet^r and can act as a donor cell.

is established, the F plasmid is transferred to the recipient cell as a single-stranded DNA molecule. The complementary strand is synthesized in both cells; thus, both the donor and recipient are F^+. A number of proteins play a role in the process of conjugation and these are all encoded by the *tra* (transfer) genes found on the F plasmid. The *tra* genes encode proteins that are responsible for production and assembly of the sex pilus, stable mating-pair formation, nicking of the plasmid DNA at *oriT* (origin of transfer site) required for single strand transfer, and the unwinding and priming of DNA required for replication that follows DNA transfer. In addition to the mechanical process of DNA transfer, some *tra* genes encode proteins that are required for regulation of transfer and prevention of the introduction of DNA of the same type as the F plasmid resident in the host bacterium (exclusion). The *tra* region of the F plasmid consists of 35 open reading frames, indicating the complexity of conjugative DNA transfer.

Other conjugative DNA elements

The F plasmid is an example of a conjugative DNA element with a narrow host range (i.e. conjugation occurs within the same or a small number of closely related species). Broad-host-range conjugative plasmids, such as RK2, can be transferred among many bacterial genera and even from bacteria to yeast. In addition, there exist plasmids that harbour *oriT*, but that are not self-transmissible because they lack some or all of the necessary *tra* genes. If the *tra* genes are provided on a separate replicon (*in-trans* complementation) these plasmids can be mobilized for transfer. Such plasmids are called mobilizable plasmids. Broad-host-range conjugative plasmids have been used in molecular biology to introduce recombinant genes into bacterial species that are refractory to routine transformation or transduction methods.

Conjugative transposons have features that are similar to transposons in that they encode antimicrobial resistance markers and may integrate into and excise from the host cell genome as a single element. They have features similar to conjugative plasmids in that they are self-transmissible to recipient cells where they integrate into the recipient cell's genome. The exact mechanism of transfer has yet to be elucidated; however, it is known that mating-pair formation is required. Conjugative transposons are found in Gram-negative and Gram-positive bacteria.

Agrobacterium tumefaciens causes crown gall tumour in plants by transferring the T DNA element, a part of the T*i* (tumor inducing) plasmid present in this bacterium, into a plant cell where the T element becomes incorporated into the plant cell's genome. The T*i* plasmid itself acts as a conjugative factor by expressing proteins responsible for the excision and transfer of the T DNA. The T*i* plasmid is not transferred to the plant cell. Once the T DNA is integrated into the plant cell genome, the plant cells proliferate (tumour formation) and synthesize opine compounds that *Agrobacterium* can utilize for growth and replication. This DNA transfer mechanism has been used to introduce recombinant genes into plant cells (genetic engineering).

Role of conjugation in bacterial evolution

Transconjugants are cells that have acquired additional genetic information. Enhanced survival may occur if the new genetic information encodes resistance to antibiotics or heavy metal compounds. Antimicrobial resistance is associated with many naturally occurring conjugative

plasmids and conjugative transposons. Conjugative plasmids encoding antimicrobial resistance genes are called R plasmids or factors. Bacteria harbouring R plasmids survive in the presence of the appropriate antibiotic. However, the transfer of R plasmids to susceptible recipient bacteria can occur in the absence or presence of the antibiotic. Therefore, R factors play a large role in the dissemination of antimicrobial resistance genes. Indeed, R factors were discovered because of a widespread outbreak of antibiotic-resistant *Shigella*-mediated dysentery. In addition to antimicrobial resistance, conjugative plasmids can transfer metabolic genes to a recipient cell. If the environment contains a compound that can be metabolized by enzymes encoded by these genes, the transconjugant will have a selective growth advantage over cells that do not harbour the metabolic genes and may replace these cells in the environment (an example of 'selection').

Transduction

Transduction (**Figure 2**) is the transfer of bacterial DNA from a donor to a recipient bacterium via a virus particle. A

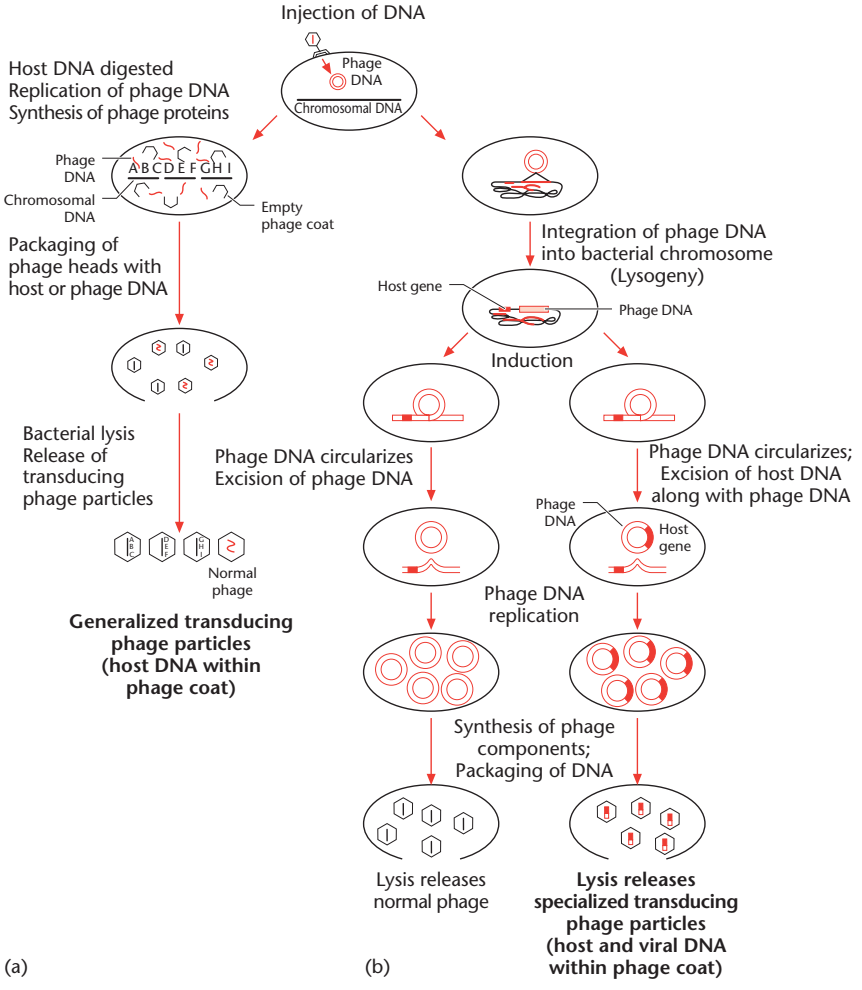

Figure 2 Transduction. Transduction is the transfer of bacterial DNA from a donor cell into a recipient bacterium via a virus particle. Transduction requires phages and is resistant to DNAase. (a) Generalized transduction. The bacterial chromosome is degraded as a result of an initial round of phage infection. Portions of the degraded chromosome encoding genes (A, B, C, etc.) are mistakenly packaged into phage particles during phage assembly. These particles can now act as generalized transducing phages which are able to deliver their portion of the bacterial chromosome to another bacterium during a second round of phage infection. (b) Specialized transduction. After initial infection, phage DNA is integrated into the host cell genome at a specific site (lysogeny). During induction (the replicative stage of phage development) the phage genome can be excised intact or aberrantly. Intact phage genomes are packaged into phage particles resulting in mature normal phage. Aberrantly excised phage genomes contain host cell genes and are packaged into phage particles producing specialized transducing phage. The specialized transducing phage are now able to introduce the host cell DNA into another bacterium during a second round of infection.

virus particle that infects bacteria is called a bacteriophage or phage. Phages attach to a specific bacterial cell surface receptor and inject their DNA into the bacterial cytoplasm. Depending on the phage, the DNA integrates into the bacterial genome (lysogeny), replicates in the cytoplasm as a plasmid (phagemid; also lysogeny), or replicates immediately (lytic cycle) producing phage progeny. There are two types of transduction: (1) specialized, in which only specific bacterial genes near the attachment site of a lysogenic phage are transferred from one bacterium to another, and (2) general, in which virtually any bacterial gene is transferred. Cells that have received DNA from another bacterium by transduction are called transductants. Transduction was discovered by Zinder and Lederberg in 1952 when genetic transfer of nutritional markers occurred despite the presence of a membranous filter that would inhibit conjugation and in the presence of DNAase, which would inhibit transformation (Zinder and Lederberg, 1952). Since DNA of the phage is protected by a protein coat, transduction is DNAase-resistant. Not all phages are transducing phages. The process of transduction can transfer DNA regions of tens to hundreds of kilobases. Due to the high specificity of phages for cell surface receptors, transduction has the narrowest host range of DNA transfer among the methods of bacterial genetic exchange.

Generalized transduction

In generalized transduction, phage mistakenly package bacterial DNA instead of their own phage DNA during phage assembly. This results in an infectious virus particle containing bacterial DNA, but one that can no longer replicate in the bacterium due to loss of all of the phage DNA. The phage particle can, however, attach to a bacterial cell surface receptor and inject the packaged DNA into the cytoplasm of the bacterium. If the bacterial DNA in the phage is from the bacterial chromosome, the DNA can recombine with homologous DNA of the bacterial recipient to generate stable transductants. This process requires a host recombinase (e.g. RecA). However, studies have indicated that the majority of transductants are abortive, meaning the transduced DNA is not stably integrated into the bacterial genome but rather remains extrachromosomal and is transferred to only one daughter cell at cell division. If the transduced DNA is a plasmid, the plasmid may replicate and be maintained in the recipient. If the DNA contains a transposon or insertion sequence, the element may insert itself onto a resident plasmid or the bacterial genome. Generalized transduction is a rare event, but if a powerful selection method is available, such as amino acid utilization or antimicrobial resistance, transduction can be a very efficient method to transfer genetic markers to different strains. A good example of a generalized transducing phage is P1, which can transduce *E. coli* DNA to numerous Gram-negative bacteria. Indeed P1 transduction is a tool used for construction of strains differing in only one genetic trait. Generalized transducing phages, such as P1 and P22, are also used for mapping genes, mutagenesis, transferring plasmids and transposons, and determining whether different genera of bacteria have homologous genes.

Specialized transduction

Specialized transduction requires that the phage undergo lysogeny usually at specific locations in the bacterial genome called attachment sites. Lysogeny is a process in which the phage genome usually integrates into the bacterial chromosome; virus replication is repressed during lysogeny. Unlike a generalized transducing phage, a specialized transducing phage contains both phage and bacterial genes. Usually under stress conditions, the phage genome excises from the bacterial genome and, due to imprecise excision and recombination, adjacent bacterial genes are also excised. If such bacterial genes are introduced via the specialized transducing phage into a recipient that lacks the bacterial gene, the recipient can express the newly acquired genetic trait. The newly acquired gene is inserted into the bacterial genome along with phage DNA to form a new round of lysogeny. Specialized transduction is independent of host homologous recombination and *recA* but requires phage integrase. Specialized transduction, like generalized transduction, is a rare event, and its detection requires powerful selection tools. Specialized transducing phages were instrumental in the isolation of the first genes in molecular biology, and in the discovery of insertion elements, which often serve as attachment sites for phage DNA integration. *E. coli* phage lambda is a classic example of a specialized transducing phage: it integrates its DNA precisely between operons encoding enzymes responsible for galactose (*gal*) and biotin (*bio*) utilization in the *E. coli* chromosome and, during excision, occasionally incorporates the *gal* or *bio* region along with the phage DNA into mature phage particles.

Role of transduction in bacterial evolution

Transducing phages play a crucial role in bacterial evolution by promoting horizontal gene transfer among populations of a bacterial species and through the interactions among transduction, transformation and conjugation. The transduced DNA can be in the form of chromosome, broad-host-range plasmids, conjugative plasmids, transposons or insertion sequences. Phages and these DNA elements form a symbiosis with bacteria, with the primary selfish goal of replicating the DNA. Bacteria continue to shuffle around these DNA elements via phage transduction in a trial-and-error fashion. Those elements

that enhance the survivability of the bacterium are maintained. For their part, phage can evolve with altered host range, altered regulation of genes involved in lysogeny and altered replication capacity.

In addition to the role of phages in bacterial evolution, it is possible for phages to obtain eukaryotic genes if the bacterial host for the phage interacts with eukaryotic cells. Analysis of multiple bacterial genome sequences suggests the presence of some genes in bacteria that are most closely related to eukaryotic genes. These genes may have arrived in bacteria by horizontal gene transfer through transducing phage.

Transformation

Transformation (**Figure 3**) is the transfer of free DNA released from a donor bacterium into the extracellular environment that results in assimilation and usually expression of the newly acquired trait in a recipient bacterium. The term transfection is used to describe transfer of free DNA into a eukaryotic cell. The recipient that successfully propagates the new DNA is called the transformant. Transformation can be inhibited by incubation of the free DNA with DNAase. The free DNA can be circular or linear and can be plasmids, transposons, integrons or chromosomal DNA fragments. The process of transformation can transfer DNA regions of one to tens of kilobases.

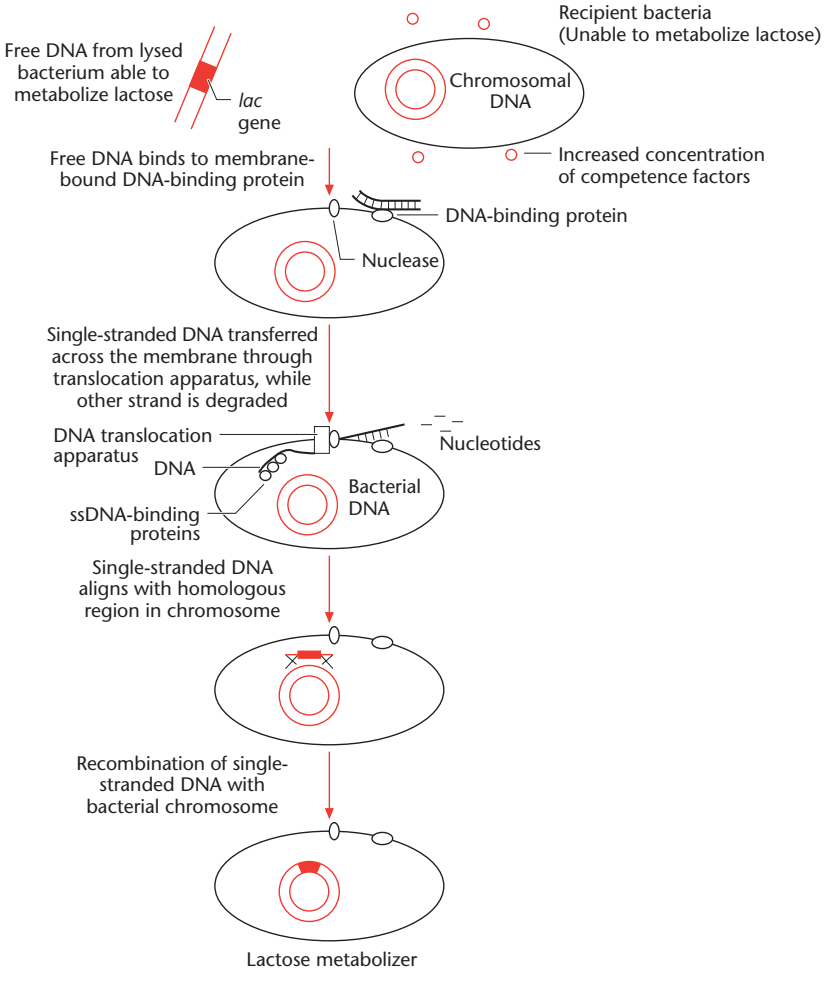

Figure 3 Transformation. Transformation is the transfer of free DNA, present in the extracellular environment, to a recipient bacterium. In the example free DNA binds to the recipient cell membrane in a protein-dependent manner. The DNA is transferred across the membrane as a single strand via a DNA translocation apparatus, bound by single-stranded DNA-binding protein, and subsequently pairs with homologous DNA sequences on the recipient's chromosome. Homologous recombination occurs and the new DNA is assimilated into the chromosome. Newly acquired traits (genes responsible for lactose utilization in the example) encoded by the assimilated DNA are expressed. The process of transformation is sensitive to DNAase.

In 1928 transformation became the first mechanism of bacterial genetic exchange to be recognized, when Fred Griffith discovered that smooth capsule-positive colonies of *Streptococcus pneumoniae* were pathogenic and rough capsule-negative colonies were nonpathogenic for mice. When rough colonies were mixed with dead smooth bacteria (containing DNA) and injected into mice, the mice died and smooth colonies were isolated. That DNA was the transforming principle became evident when in 1944 Avery, Macleod and McCarty showed that the transformation of rough colonies to smooth colonies was due to DNA. Thus, DNA was established as the hereditary material (Avery *et al*., 1944).

Natural competence

A number of Gram-positive (*Bacillus subtilis*, *Streptococcus pneumoniae*, *Enterococcus faecalis*) and Gram-negative (*Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Acinetobacter*, *Pseudomonas*, *Moraxella*, *Haemophilus influenzae*, *Campylobacter jejuni* and *Helicobacter pylori*) organisms are naturally competent or naturally transformable, meaning they readily take up extracellular DNA. Organisms that are naturally transformable spontaneously release their DNA in late stationary phase via autolysis. A number of bacteria, including *Escherichia coli*, can be artificially treated in the laboratory to increase their transformability by chemicals, such as calcium, or by applying a strong electric field (electroporation); these organisms are not considered to be naturally transformable. Transformants can be selected if the transformed DNA contains a selectable marker, such as antimicrobial resistance, or if the DNA encodes for utilization of a growth factor, such as an amino acid.

Mechanism of transformation

There are four steps in transformation: development of competence, binding of DNA to the cell surface, processing and uptake of free DNA (usually in a 3′ to 5′ direction), and integration of the DNA into the chromosome by recombination. In *S. pneumoniae* and *B. subtilis*, double-stranded DNA released from lysed cells binds noncovalently to cell surface receptors. There is no DNA sequence-specific recognition; thus, these organisms can potentially incorporate DNA from outside their species. The bound double-stranded DNA is nicked and cleaved into smaller fragments by membrane-bound endonucleases, and one of the two DNA strands is exonucleolytically cleaved by a membrane-bound DNAase, allowing the remaining single strand to enter the cell through a membrane-spanning DNA translocation channel. An alternative model for DNA translocation describes the formation of a polyhydroxybutyrate–calcium polyphosphate helical complex that forms a central pore in the bacterial membrane through which single-stranded DNA (the polyphosphate component) enters. For either model, the single-stranded DNA is coated by single-stranded DNA-binding proteins to protect the DNA from further nuclease digestion. The transformed DNA integrates into the chromosome and replaces the chromosomal DNA fragment by homologous recombination; this is called allelic exchange and the process requires *recA*. Allelic exchange requires significant nucleotide sequence homology between the donating DNA fragment and the resident fragment in the chromosome. Sometimes, the transformed DNA is a plasmid capable of replicating autonomously from the chromosome. If the transferred trait is present both in the chromosome and on a plasmid, the bacterium is merodiploid for that trait.

Transformation in *B. subtilis* is regulated by a two-component regulatory system: ComP/ComA. ComP is a membrane sensor protein kinase that becomes autophosphorylated during high culture density. The phosphorylation of ComP is triggered through small competence pheromone peptides (competence factors), which are secreted into the extracellular environment and participate in sensing cell density. The phosphoryl group from ComP is transferred to the DNA-binding response protein, ComA, which then transcriptionally activates early and late competence genes, including the genes for additional transcription factors, *comC*, and the *comE*, *comF* and *comG* operons. ComE and G are believed to form the DNA translocation channel. ComC is a leader peptidase that processes some of the other competence proteins necessary for the DNA translocation apparatus.

Neisseria spp. and *H. influenzae* can only take up DNA from their own species; this occurs by species-specific recognition by cell surface machinery of a 10–12 bp DNA uptake sequence on the linearized DNA molecule. Pili, surface appendages used for attachment to host cell surfaces, are required for efficient transformation of *Neisseria*.

For *Haemophilus*, linear double-stranded DNA binds to receptor proteins at the surface of membrane compartments called transformasomes via a specific 11-bp DNA sequence and is then translocated into the transformasome in a DNAase-protected manner. The DNA is converted to a single-stranded molecule as it rapidly passes into the cell followed by recombination into the bacterial chromosome.

Role of transformation in bacterial evolution

Many of the genes required for competence are homologous among naturally competent organisms. Additionally, some of the transporter proteins share amino acid homology with conjugation secretion apparatuses from a wide range of organisms. Since these genes are conserved at the DNA and protein levels in such a diverse group of organisms it is likely that DNA transformation mechanisms arose in the early stages of bacterial evolution.

There are three possible benefits of transformation in nature: nutrition, repair and recombinational diversity. All three have survival of the bacterium as an underlying theme. The nutrition aspect suggests that naturally transformable organisms use DNA they take up as a source of nucleotides, carbon and nitrogen. The repair aspect suggests that when DNA of the bacterium is damaged, some of the lysed bacteria of the population release nonmutated DNA that can replace damaged DNA of live cells. Indeed, some repair genes in some organisms are induced during competence development. The recombinational diversity aspect suggests that naturally transformable organisms allow new combinations of genes, thereby increasing diversity and fitness. For example, the pilus proteins of *Neisseria* spp. undergo antigenic variation due to the allelic replacement of expressed native pilus genes in a bacterium (at the *pilE* locus) by pilus gene cassettes (*pilS* – silent gene pilin), contributed by the surrounding population, as a result of natural transformation. The newly transformed bacterium is able to express a new set of antigenically distinct pili, which results in avoidance of the human host immune response (Seifert *et al*., 1988).

Genetic Exchange and Antimicrobial Drug Resistance

Many antimicrobial resistance genes found in pathogenic bacteria (especially Gram-negatives) are situated on resistance (R) plasmids, transposons or integrons.

R plasmids

As discussed earlier, R plasmids are conjugative plasmids that encode antimicrobial resistance genes.

Transposons

Transposons are mobile genetic elements that often carry an antimicrobial resistance gene. These elements can insert randomly, move from plasmids to the chromosome, and vice versa and can be moved from one bacterium to another by conjugation, transformation or transduction.

Integrons

Integrons (**Figure 4**) are site-specific recombination elements often found within transposons or defective transposons that capture and mobilize bacterial-derived genes, especially multiple antimicrobial resistance gene cassettes. Unlike other transposons, integrons do not randomly insert into the bacterial genome but rather are highly selective in their insertion site, with an especially high predilection for conjugative plasmids. Because of their presence in conjugative plasmids, integrons can be transferred readily from one bacterium to another, with concomitant transfer of antimicrobial resistance genes. Integrons usually have less than eight genes, but recently, 'super-integrons' containing 100 or more genes have been discovered from *Vibrio cholerae*; most of these genes do not encode antibiotic resistance. The site-specific recombinase/integrase of integrons, IntI, is a member of the phage integrase family of proteins; the *intI* gene is found in the 5′ conserved segment of the integron. Integrons contain a very strong promoter, P_{ant}, found in the *intI* gene, for coordinated expression of antimicrobial resistance genes and other captured genes. Integrons also have a specific attachment site (*attI*) recognized by the recombinase that serves as the site for capture of genes. Promoterless gene cassettes containing a 59-bp element, speculated to have arisen by reverse transcription from mRNA and present as nonreplicating circular forms, are able to insert into integrons immediately downstream of P_{ant}. Most integrons identified in nature have a gene conferring sulfonamide resistance, which is found in the 3′ conserved segment of the integron. Integrons play a role in horizontal gene transfer between bacteria and eukaryotic cells (e.g. yeast), as well as transfer between bacterial species and contribute immensely to widespread antimicrobial resistance of bacteria.

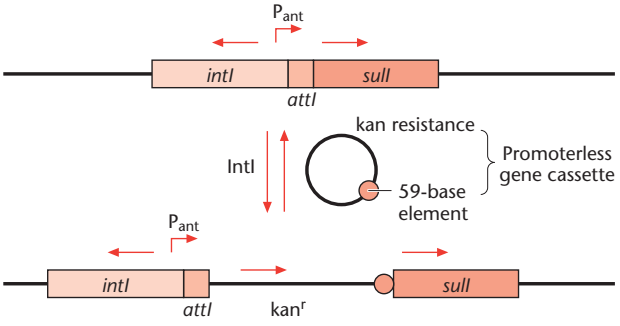

Figure 4 Integrons. Integrons are site-specific recombination elements often found within transposons or defective transposons that capture and mobilize bacterial-derived genes, especially multiple antimicrobial resistance gene cassettes. In the example, the integrase IntI integrates a circular piece of DNA encoding kanamycin resistance (kan^r). The integration occurs at a specific attachment site (*attI*), immediately downstream of a strong promoter (P_{ant}). This results in two adjacent antimicrobial resistance genes encoded by the integron: kan^r and sulfonamide resistance encoded by *sulI*.

Genetic Exchange and Acquisition of Virulence Traits

There are numerous examples of phages that integrate into the transfer RNA (tRNA) genes of bacteria. The reason for integration into tRNA genes could be that tRNA genes are highly conserved and are essential for bacterial protein

synthesis. There is selective pressure to maintain precisely these genes and, thus, this integration site. Alternatively, this could allow the phage to expand its tropism to other bacterial species. Another possibility is that phage prefer to integrate into sequences containing 2-fold rotational symmetry at attachment sites; tRNA genes have such symmetry. Interestingly, there are large blocks of virulence genes called pathogenicity islands that are found inserted within or near tRNA genes. Pathogenicity islands are large DNA fragments (> 10 kb) containing virulence genes, such as genes that encode secreted proteins. Pathogenicity islands have a G + C% DNA content different from that of the rest of the bacterial genome and often contain a phage integrase gene and insertion sequences. These findings suggest that pathogenicity islands of virulent pathogens, such as uropathogenic, enteropathogenic and enterohaemorrhagic *E. coli*, *Salmonella* spp., *Yersinia* spp., and *Helicobacter pylori*, may have been acquired by horizontal gene transfer, perhaps through the help of transducing phages. Indeed, the VPI (*Vibrio cholerae* pathogenicity island) of *V. cholerae* is encoded by the intact pathophage VPIϕ (Karaolis *et al*., 1999). VPIϕ encodes the TCP (toxin-coregulated pilus), which has a dual function as a colonization factor for *V. cholerae* and serves as the receptor for another virulence gene-encoding phage of *V. cholerae*, CTXϕ, which encodes cholera toxin (see Waldor, 1998).

Another example of horizontal gene transfer mediated by bacterial genetic exchange is the presence of bacterial toxins within prophages lysogenized in the bacterial chromosome: examples include diphtheria toxin, Shiga toxins 1 and 2, botulinum toxin types C_1 and D, erythrogenic toxin (scarlet fever), staphylococcal enterotoxin A, *Pseudomonas aeruginosa* cytotoxin, tetanus toxin and cholera toxin. These toxins are all crucial for the pathogenesis of each of the respective bacteria, as bacteria lacking the toxins are nonpathogenic (i.e. not able to cause disease). Such lysogenic conversion of nonpathogenic strains to pathogenic strains occurs in both Gram-positive and Gram-negative bacteria. In addition to toxins, there are examples of other virulence traits being encoded by phages, including extracellular enzymes, lipopolysaccharide-modifying enzymes and outer membrane proteins.

The presence of toxins and pathogenicity islands in bacteria that exhibit phage-like elements and insertion sequences suggests that transduction is a common method of transferring virulence traits to other bacterial species in nature. Presence of toxins and other virulence genes on a moveable piece of DNA may allow faster adaptation of bacteria to their host, without having to carry the virulence trait in environments where the trait is unnecessary and potentially energetically wasteful.

Summary

Conjugation, transduction and transformation, and the DNA elements for bacterial genetic exchange (plasmids, transposons, insertion sequences, integrons, and naked DNA) offer bacteria access to the genomes of other bacterial strains, species and genera, and even eukaryotes. This creates a large library of genetic information from which bacteria may obtain genes, enhancing their survivability. This is the fundamental evolutionary result of bacterial genetic exchange. The ubiquity of bacterial genetic exchange suggests that it has been selected for in nature over millions of years of evolution as the most efficient means to enhance genetic diversity and survival, while maintaining the integrity of the bacterial genome. Bacterial genetic exchange plays a major role in the development of bacterial pathogens virulent for humans, as well as promotes the widespread transfer of antimicrobial resistance genes.

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