Functions of plasmids

Many plasmids control medically important properties of pathogenic bacteria. These include (*a*) resistance to one or several antibiotics, (*b*) production of toxins, and (*c*) synthesis of cell surface structures required for adherence or colonization. Plasmid determined properties are summarized in Box 7-1. Some plasmids are cryptic and have no recognizable effects on the bacterial cells that harbor them. Comparing plasmid profiles is a useful method for assessing possible relatedness of individual clinical isolates of a particular bacterial species for epidemiological studies.

Transfer of DNA within the bacterial cells can occur by (*a*) transposons (*b*) integrative conjugating elements, and (*c*) programed rearrangement.

Transposons

Transposons are a type of mobile DNA of 2000–20,000 bp. They can transfer DNA from one site of the bacterial chromosome to another site or to a plasmid. The idea of transposons or jumping genes was first given by Barbara McClintock, a geneticist working in the field of maize genetics.

The mode of genetic transfer by transposon is called ***transposition***. The transposition differs from recombination in that a segment of DNA can be transferred from one to another molecule that has no genetic homology with either the transposable element or the donor DNA.

Transposons do not occur independently but have the characteristic of jumping from one part of a chromosome to another or to a plasmid. They can also jump from one plasmid to another

or back to the chromosome, hence, are called as ***jumping genes***. Transposition in prokaryotes usually involves two steps— selfreplication
and recombination. They jump from one part to another by synthesizing a copy of their DNA and inserting the
copy at another site in the bacterial chromosome or the plasmid. Transposons, unlike plasmids, are not self-replicating
and depend on chromosomal or plasmid DNA for replication. Transposons do not require homology with the recipient site for its transfer.

Integrative Conjugative Elements

Integrative conjugative elements (ICEs) are ways of horizontal gene transfer and self-transmissible mobile genetic elements. The elements exchange by conjugation, but need to integrate into chromosome to propagate. They cannot replicate autonomously.
ICEs integrate into and replicate along with the host
cell chromosome, whereas plasmids exist as extra-chromosomal (usually circular) autonomously replicating DNA molecules.

Programed Rearrangements

The transfer of DNA within bacteria can also occur by programed
rearrangement. In this programed rearrangement, there is a movement
of a gene from a silent site where the gene is not expressed to an active site where transcription and translation occur. Many silent genes are present in the DNA that encode variants of the antigens. Presentation of the new gene into the active site occurs in a sequential and repeated manner, which then manifests in antigenic variations in the bacteria and parasites. This mechanism is responsible for antigenic variations seen in *Neisseria gonorrhoeae*, *Borrelia recurrentis*, and *Trypanosoma brucei*.

Transfer of DNA between Bacterial cell

The genetic information can be transferred from one bacterium to another. There are three general methods for genetic exchange in bacteria: (*a*) transformation, (*b*) transduction, and (*c*) conjugation.

Transformation

Transformation is a process of the transfer of DNA itself from one bacterium to another. This may occur either in nature or in a laboratory. In nature, DNA is released from a bacterium by lysis, which may be taken up by recipient bacterium that must be competent. This natural process of transfer of genetic material appears to play no role in disease. In laboratory conditions, DNA may be extracted from one type of bacterium and introduced into genetically different bacteria. The cell walls of bacteria *in vitro* are made more permeable for DNA uptake by using substances, such as calcium chloride.

Griffith (1922) in his classical experiment on mice demonstrated that neither of the mice died when injected separately with a live, noncapsulated Pneumococcus (nonvirulent) and heat-killed, capsulated Pneumococcus (nonvirulent), but the mice died when they were injected with a mixture of both these strains. From the dead mice, he could isolate live, capsulated pneumococci, which were virulent. He demonstrated that some factor in heat-killed, capsulated pneumococci had transferred the material for capsule synthesis in the noncapsulated strains of the bacteria, making them virulent (Fig. 7-1).

McLeod and McCarthy in 1944 demonstrated that DNA extracted from encapsulated, smooth pneumococci could transform nonencapsulated, rough pneumococci into capsulated, smooth organisms. They demonstrated the transforming principle of DNA. The experimental use of transformation was the first experiment to reveal important information about DNA and was the first example of genetic exchange in bacteria.

Another bacterium where transformation is observed is *Haemophilus influenzae*.

Transduction

The transfer of a portion of DNA from one bacterium to another mediated by a bacteriophage is known as ***transduction***. During replication of virus within the cell, a piece of bacterial DNA is incorporated into the bacteriophage and is carried into the recipient bacterium at the time of infection. The phage DNA within the recipient bacterial cell integrates into the cell DNA during a process called ***lysogenic conversion***. The process of lysogenic conversion confers a new property to the bacterial cell; for example, by lysogenic conversion nonpathogenic bacteria can become pathogenic. Bacteriophages encode diphtheria toxin, botulinum toxin, cholera toxin, and erythrogenic toxin and can be transferred from one bacterium to another by transduction (Fig. 7-2). Transduction is of two types: (*a*) generalized transduction and (*b*) specialized transduction.

Conjugation

Conjugation is a process of transfer of DNA from the donor bacterium to the recipient bacterium during the mating of two bacterial cells. In conjugation, direct contact between the donor and recipient bacteria leads to formation of a cytoplasmic bridge between them and transfer of part or all of the donor genome to the recipient (Fig. 7-3). Conjugation takes place between two closely related species and occurs mostly in Gramnegative bacteria. Conjugation also occurs in Gram-positive bacteria.

Donor ability of bacteria is determined by specific conjugative plasmids called fertility (F_) plasmids or sex plasmids. The F plasmid controls the mating process of bacteria. Pilus is the most important protein that forms the sex pilus or conjugation tube. The sex pilus produces a bridge between

conjugating cells in Gram-negative bacteria. Mating occurs between the donor male bacterium carrying the F factor (F_) and the recipient female bacterium that does not contain F factor (F_). It begins when the pilus of F_ bacterium attaches to a receptor on the surface of a female (F_) bacterium. The cells are then brought into direct contact by the link in the pilus. This is followed by an enzymatic cleavage of the F factor DNA in which one strand of bacterial DNA is transferred into the recipient cell through the conjugation bridge. The synthesis of the complementary strand to form a double-stranded F-factor plasmid in both the donor and recipient cells completes the process of conjugation. The recipient cell becomes F_ male that is capable of transmitting the plasmid to other F_ cells.

High-frequency recombination (Hfr): Long length of DNA can be transferred by process of conjugation. Hfr strain is a type of F+ cells that have an F plasmid integrated into the bacterial DNA. Hence they acquire the capability of transferring the chromosome to another cell. A whole chromosome can be transferred if it is integrated with F plasmid. In this process, the single strand of DNA that enters the recipient F_ cell contains a part of the F factor at one end, followed by the bacterial chromosome, and then by the remainder of the F factor. The bacterial genes adjacent to the leading piece of F factor are the most frequently transferred. The newly acquired DNA recombines with the recipient DNA and becomes an integral component of genetic material. The complete transfer of the bacterial DNA is usually completed in approximately 100 minutes.

In matings between F+ and F□ bacteria, only the F plasmid is transferred with high efficiency to recipients. Chromosomal genes are transferred with very low efficiency, which is mediated

by the spontaneous Hfr mutants in F_ populations. In matings between Hfr and F_ strains, the segment of the F plasmid

containing the tra region is transferred last, after the entire bacterial chromosome has been transferred. Most recombinants

produced after matings between Hfr and F_ cells fail to inherit the entire set of F-plasmid genes and are phenotypically F_. In matings between F_ and F_ strains, the F plasmid spreads rapidly throughout the bacterial population and most recombinants are F_.

Conjugation also occurs in Gram-positive bacteria. Grampositive donor bacteria produce adhesions that cause them to aggregate with recipient cells, but sex pili are not involved. In some *Streptococcus* spp., recipient bacteria produce extracellular sex pheromones that facilitate conjugation. Table 7-1 shows a comparison of transformation, transduction, and conjugation

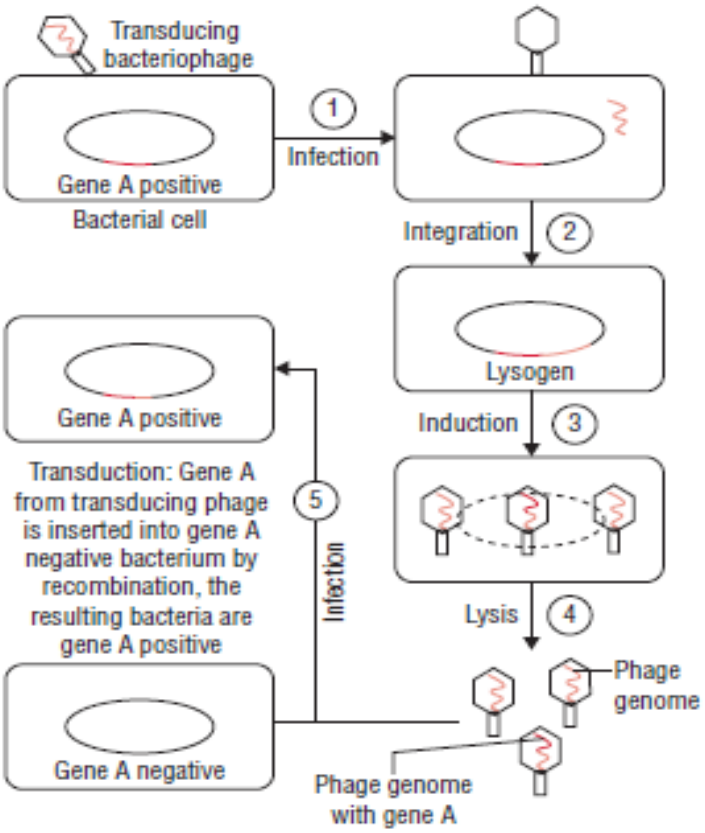

FIG. 7-2. A schematic diagram showing transmission of genetic material by bacteriophage-mediated transduction.

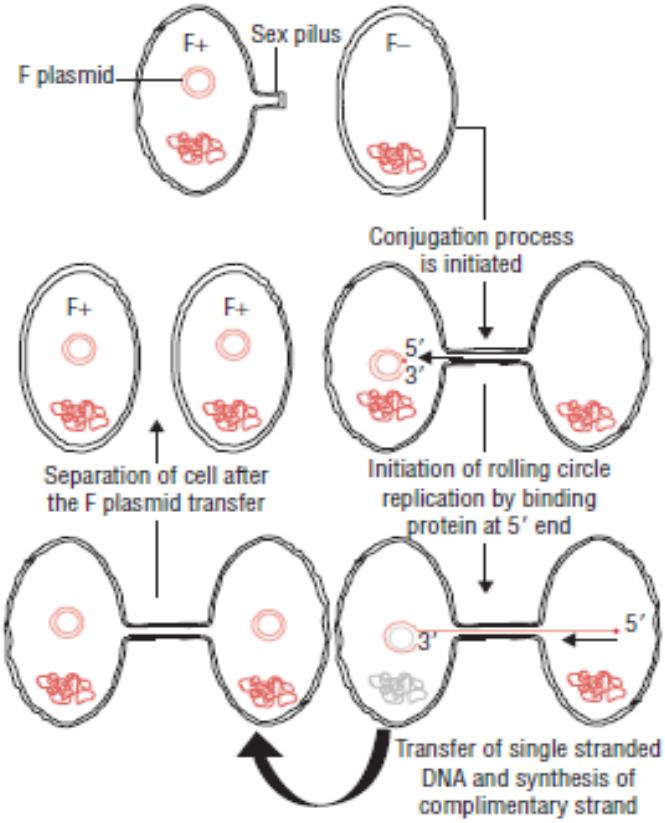

FIG. 7-3. A schematic diagram showing transmission of genetic material by conjugation.