

SELF MOBILIZATION AND SELF TRANSMISSIBLE PLASMIDS

A plasmid that codes for its own set of MPF(mating pair formation) genes is called self - transmissible or conjugative. If it uses an MPF of another genetic element present in the cell, it is called mobilizable . Some plasmids are called nonmobilizable because they are neither conjugative nor mobilizable

Plasmids are key vectors of horizontal gene transfer and essential genetic engineering tools. They code for genes involved in many aspects of microbial biology, including detoxication, virulence, ecological interactions, and antibiotic resistance.

GENERAL PROPERTIES OF PLASMID MOBILITY

Biological function and agents of plasmid mobility.

Genetic information flows at high rates among prokaryotes, leading bacteria and archaea to have a small core genome that is conserved within a species and a large genome that is highly variable .

Widespread horizontal gene transfer has profound evolutionary implications. First, it allows homologous recombination between closely related strains or species in a process resembling eukaryotic sex.

Second, it leads to the integration of new genetic information, creating large functional leaps that allow fast adaptation to new environments or to stressful conditions .

Third, gene mobility has been proposed to drive microbial cooperative processes.

From the three classical mechanisms of horizontal transfer, transformation, transduction, and conjugation, the latter is thought to be quantitatively more important. This is because phages have restricted host ranges and small cargo regions, whereas some plasmids can conjugate between remotely related organisms, including conjugation from bacteria to eukaryotes.

Plasmids, along with integrative conjugative elements (ICEs), are the major players in conjugation processes. Many of the genes allowing bacteria to metabolize toxic organic compounds such as antibiotics are carried by plasmids.

Plasmids also often code for information essential for the interaction of bacteria with multicellular eukaryotes, including nitrogen fixation by rhizobia, plant cell manipulation by *Agrobacterium* species, and virulence by *Shigella* species, among many other human pathogens. Plasmids are also molecular biology workhorses whose mobility opened up the possibility of genetic manipulation.

Essential lexicon of plasmid conjugation.

Mobility is an essential part of plasmid fitness. It is also a key element to an understanding of the epidemiology of plasmid-carried traits such as virulence and antibiotic resistance. As such, two functions are deemed essential for plasmid survival: DNA replication and horizontal spread. The latter may occur by conjugation if a plasmid carries two sets of genes. The set of mobility (MOB) genes is essential and allows conjugative DNA processing (the MOB genes were also called Dtr genes, for DNA-transfer replication). Besides, a membrane-associated mating pair formation (MPF) complex, which is a form of a type 4 secretion system (T4SS), provides the mating channel. A plasmid that codes for its own set of MPF genes is

called self-transmissible or conjugative. If it uses an MPF of another genetic element present in the cell, it is called mobilizable. Some plasmids are called nonmobilizable because they are neither conjugative nor mobilizable. They spread by natural transformation or by transduction. Hence, plasmids can be classified into three categories according to mobility: conjugative, mobilizable, and nonmobilizable.

Mechanism of conjugation.

The only protein component of the conjugative machinery that is common to all transmissible, i.e., conjugative or mobilizable, plasmids is the relaxase .

The relaxase is a key protein in conjugation, since it recognizes the origin of transfer (*oriT*), a short DNA sequence which is the only sequence required in *cis* for a plasmid to be conjugally transmissible. The relaxase catalyzes the initial and final stages in conjugation, that is, the initial cleavage of *oriT* in the donor, to ultimately produce the DNA strand that will be transferred, and the final ligation of the transported DNA in the recipient cell that reconstitutes the conjugated plasmid.

Conjugative relaxases are structurally related to rolling-circle replication initiator proteins, and they catalyze similar biochemical reactions. However, they are easily distinguished because relaxase amino acid sequences are linear permutations of the replication initiator sequences, as discussed previously .

Mobilizable plasmids carry only the relaxosomal components *oriT*, a relaxase gene, and one or more nicking auxiliary proteins. On the other hand, conjugative plasmids carry all the machinery needed for self-transfer. This includes, besides the above-mentioned relaxosome components, the type IV coupling protein (T4CP) and the components of the mating channel that assemble a T4SS. The T4CP is involved in the

connection between the relaxosome and the transport channel

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It is also thought to energize the process of DNA transport .

The conjugative mating channel is basically a protein secretion channel, which transports the relaxase protein bound to the DNA to be transferred .

According to the nomenclature of protein secretion mechanisms, it is a T4SS .

The phylogenetic relationship among relaxases has been traced, leading to a classification of conjugative systems into six MOB families: MOB_F, MOB_H, MOB_Q, MOB_C, MOB_P, and MOB_V .

This classification extends to the entire mobility region, which includes the nicking auxiliary proteins and the T4CPs \

There have been reports on the classification and phylogenetic relationships among NTPases

yet little is known about the classification of conjugative T4SSs in prokaryotes, except for some specific clades such as *Rickettsia* .or for VirB4 of T4SSs involved in pathogenicity.

While the manuscript was being finished, a review giving an extensive description of known T4SSs in prokaryotes, including many conjugative systems, was published That analysis showed some common themes among T4SSs as well as an important diversity, and here we aim to quantify them.