Available online at www.sciencedirect.com
SCIENCE DIRECT®
PLASMID
Plasmid 54 (2005) 1–25
www.elsevier.com/locate/yplas

Review

# The mating pair formation system of conjugative plasmids—A versatile secretion machinery for transfer of proteins and DNA

Gunnar Schröder [a,*], Erich Lanka [b]

[a] *Division of Molecular Microbiology, Biozentrum, University of Basel, Klingelbergstrasse 50/70, CH-4056 Basel, Switzerland*
[b] *Max-Planck-Institut für Molekulare Genetik, Ihnestrasse 73, Dahlem, D-14195 Berlin, Germany*

Received 17 January 2005, revised 21 February 2005
Available online 27 April 2005

Communicated by D.K. Chattoraj

**Abstract**

The mating pair formation (Mpf) system functions as a secretion machinery for intercellular DNA transfer during bacterial conjugation. The components of the Mpf system, comprising a minimal set of 10 conserved proteins, form a membrane-spanning protein complex and a surface-exposed sex pilus, which both serve to establish intimate physical contacts with a recipient bacterium. To function as a DNA secretion apparatus the Mpf complex additionally requires the coupling protein (CP). The CP interacts with the DNA substrate and couples it to the secretion pore formed by the Mpf system. Mpf/CP conjugation systems belong to the family of type IV secretion systems (T4SS), which also includes DNA-uptake and -release systems, as well as effector protein translocation systems of bacterial pathogens such as *Agrobacterium tumefaciens* (VirB/VirD4) and *Helicobacter pylori* (Cag). The increased efforts to unravel the molecular mechanisms of type IV secretion have largely advanced our current understanding of the Mpf/CP system of bacterial conjugation systems. It has become apparent that proteins coupled to DNA rather than DNA itself are the actively transported substrates during bacterial conjugation. We here present a unified and updated view of the functioning and the molecular architecture of the Mpf/CP machinery.


*Keywords:* Mating pair formation; Mpf system; Bacterial conjugation; Type IV secretion; DNA transfer; Protein secretion

## 1. Introduction

Bacterial conjugation, often referred to as 'bacterial sex' is one of the major routes of horizontal gene transfer and accounts for the rapid spread of antibiotic resistance genes among pathogenic

* Corresponding author. Fax: +41 0 61 267 2118.
*E-mail addresses:* gunnar.schroeder@unibas.ch (G. Schröder), lanka@molgen.mpg.de (E. Lanka).

0147-619X/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.plasmid.2005.02.001

bacteria (Waters, 1999). Mechanistically, conjugative plasmids first undergo processing into a transfer-competent form, and are then transferred into a recipient bacterium where they subsequently replicate. Conjugative plasmids can spread autonomously since they are equipped with the entire set of genes that are required for plasmid transfer. Many of the conjugative plasmids are supplied with broad host range properties among Gram-negative species and a small number of these plasmids can also transfer between and replicate in both Gram-negative and Gram-positive bacteria (Charpentier et al., 1999; Gormley and Davis, 1991; Kurenbach et al., 2003; Trieu-Cuot et al., 1987). Intriguingly, conjugative DNA transfer between bacteria and eukaryotic cells has also been reported (Heinemann and Sprague, 1989; Waters, 2001), demonstrating that bacterial conjugation contributes to genetic exchange going even beyond the bacterial kingdom.

The genetic framework of conjugation systems has been grouped into two functional subsets belonging to the DNA transfer and replication (Dtr) and the mating pair formation (Mpf) systems (Willetts, 1981). The Dtr system is responsible for plasmid replication and processing of the conjugative plasmid into a transfer-competent intermediate (a protein–DNA conjugate). The Mpf system is essential for production of exocellular pili and formation of a trans-envelope channel structure presumably serving as a conduit for protein and DNA substrates. A third function, mediating between Dtr and Mpf, is carried out by the coupling protein (CP, VirD4). The CP first delivers the protein–DNA substrate generated by the Dtr to the entry of the Mpf channel and then probably participates in the active secretion of the substrate. Plasmids that lack a Mpf system but encode their own Dtr and, optionally, their own CP, are frequently found. Such plasmids, called mobilizable (Mob) plasmids, can be transferred from one bacterium to another in case a Mpf system able to interact with the Dtr system of the Mob plasmid is present in the same donor bacterium (encoded either on a second plasmid or on the chromosome). Studies carried out with Mob plasmids have therefore largely contributed in identifying the genetic determinants of the Mpf and Dtr systems and, specifically, the role of the CP.

Long after the first discovery of bacterial conjugation, which dates back to 1946 (Lederberg and Tatum, 1946), a series of pathogenicity-associated secretion systems delivering toxic protein or DNA substrates into eukaryotic host cells were discovered to be sequence-related to bacterial conjugation systems (Lessl and Lanka, 1994; Lessl et al., 1992). These secretion systems are grouped into the family of type IV secretion systems (T4SS), as originally proposed by Salmond (1994) (Table 1). The family of T4SS includes the VirB/VirD4 system encoded by the *Agrobacterium tumefaciens* Ti plasmid, which is responsible for the formation of tumors in infected plant tissues. The VirB/VirD4 system secretes an oncogenic DNA fragment (T-DNA), which, similar to conjugation systems, is processed into a transfer-competent protein–DNA conjugate before transfer. Proteins that are secreted along with the T-DNA enable import of the T-DNA into the nucleus and integration of the T-DNA into the plant chromosome. Other T4SS target effector proteins or toxins into infected host cells. These include the T4SS of *Bordetella pertussis* (Ptl), *Helicobacter pylori* (Cag), and *Bartonella henselae* (VirB/VirD4), responsible for whooping cough, gastric diseases, and cat scratch disease, respectively (Cascales and Christie, 2003; Schröder et al., 2005).

Numerous studies on Mpf/CP systems of bacterial conjugation systems and of other T4SS have aimed to assign specific functions to individual Mpf components and their contribution to the secretion process. Since these components are networked within a tight complex that is integrated into the bacterial membranes, this has often been a difficult objective. However, based on a conserved set of proteins that are found in most T4SS (Fig. 1), we are now able to present a unified view of a 'model' Mpf system, assigning functions to the 'key players' VirB1–VirB11 and the CP (VirD4).

## 2. The foreplay of bacterial sex: mating pair formation

How do bacteria have sex? The first requirements are: find a partner cell, get close to it, and