

Structural Biology of Type IV Secretion System

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Type IV secretion systems (T4SSs) are machineries used for the transport of macromolecules across the bacterial cell envelopes of Gram-negative bacteria. The archetypal T4SS, the VirB/D system was first defined in *Agrobacterium tumefaciens* where it is naturally responsible for the delivery of the T-DNA to the plant host-cell. The *A. tumefaciens* VirB/D system comprises 12 proteins (VirB1 to 11 and VirD4) whereas T4SS in other bacteria can display homologues for only a subset of those proteins. T4SSs are highly versatile and have been found in many bacterial pathogens such as *Helicobacter pylori* (Cag PAI), *Brucella suis* (VirB/D), and *Legionella pneumophila* (Dot, Icm). The secretion machinery spans both bacterial membranes and translocates substrates from the cytoplasm to the external milieu (secretion) or vice-versa (uptake).

In the past few years, crystal structures of the components VirD4, VirB11 and VirB5 have become available and have provided seminal insights into the mechanism of T4SS assembly and substrate secretion. We here describe and analyse the structures of the periplasmic domains of VirB8 from *B. suis* and Comb10 from *H. pylori* (homologues of VirB8 and VirB10 from *A. tumefaciens*, respectively) which were solved by X-ray crystallography. These structures defines prototypes for their respective families of proteins and, together with other studies, will help define the secretion mechanism and/or machinery assembly of T4SSs.

Keywords: DNA/protein transport, molecular machinery, bacterial pathogenesis