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Crystal Structure of Filamentous Hemagglutinin Secretion Domain. V. Villeret¹, B. Clantin¹, H. Hodak², E. Willery², C. Locht², F. Jacob-Dubuisson², ¹UMR8525 CNRS and ²U447 INSERM, Institut de Biologie de Lille, Institut Pasteur de Lille, 59021 Lille Cedex, FRANCE.

Filamentous hemagglutinin (FHA), the major 230-kDa adhesin of the whooping cough agent *Bordetella pertussis*, is one of the most efficiently secreted proteins in Gram-negative bacteria. FHA is secreted via the Two-Partner Secretion (TPS) pathway. Several important human, animal and plant pathogens also secrete adhesins and other virulence factors using this mode of secretion. All TPS secreted proteins contain a distinctive N-proximal module essential for secretion, the TPS domain. We have determined the 1.7Å structure of a functionally secreted 30-kDa N-terminal fragment of FHA. This structure is representative of the TPS domains found so far in over one hundred secreted proteins from pathogenic bacteria. It reveals that the TPS domain folds into a β-helix, with three extra-helical motifs, a β-hairpin, a four-stranded β-sheet and an N-terminal capping, mostly formed by the non-conserved regions of the TPS domain. It also provides a first mechanistic insight into how protein folding may be linked to secretion in the TPS pathway. The structure and its biological implications for TPS secretion will be presented.