

forms a polyproline-II-like helix that seems to be a common feature of many Gram-positive cell-wall anchored virulence factors, and particularly of basal pilins. Together, we identified structural characteristics of pilins that direct their incorporation into the pilus polymer.

Keywords: bacterial adhesion, pilus assembly, *Streptococcus pyogenes*

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Identification, characterisation and exploitation of novel Gram-negative drug targets. Gunter Schneider, Tatyana Sandalova, Jolanta Kopec, Jason Schmidberger, Robert Schnell. *Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden.*

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Increases in the rates of bacterial infection and resistance to available antibiotics present an alarming health-problem worldwide. The situation is particularly serious with respect to Gram-negative bacteria and the identification and structural characterisation of novel, genetically validated drug targets for these bacteria would represent a major advance in biomedical science. The EC-funded AEROPATH project aims to contribute to early stage drug discovery by advancing, at the molecular level, fundamental and important aspects of Gram-negative bacteria using the important pathogen model *Pseudomonas aeruginosa*. Secondly the consortium wishes to exploit these discoveries and develop inhibitors as hit and lead compounds for further antibiotic development. The consortium consists of the University of Dundee, University of St. Andrews, Lionex GmbH, MFD Diagnostics GmbH, and Karolinska Institutet. Target validation is based on gene knock-out studies focusing on individual genes flagged as essential and an infection model in the mouse. Hits will be identified by virtual screening based on three-dimensional structures, HTS screens at the Scottish Hit Discovery Facility, and fragment-based screening using a combination of thermofluor/Stargazer technologies, NMR and X-ray methods. Enzyme inhibition assays, x-ray crystallography and Isothermal Calorimetry are used to characterize the binding mode and the kinetic parameters of the identified ligands. The progress on the 43 targets assigned to the consortium partner KI will be presented.

Keywords: infectious diseases, macromolecular crystallography, lead compounds