Characterisation of the interactions of the *Streptococcus pneumoniae* toxin, pneumolysin, with soluble molecules of the immune system.

**Application deadline:** Applications accepted all year round

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**Summary**

The human pathogen *Streptococcus pneumoniae* is a major cause of disease worldwide. It is a principal agent for bacterial pneumonia, septicaemia, and meningitis. A major cause of its virulence is the pneumolysin toxin. The toxin has two distinct activities (modulation of host cell activities and binding to antibodies and activation of the complement system of immunity) and both are required for the full impact of the toxin *in vivo*. Complement is a key part of the host’s immune system, which normally activates only on the surface of pathogens to stimulate protective responses including phagocytosis, inflammation and adaptive immunity. By triggering activation in serum, pneumolysin diverts complement attack away from invading bacteria and simultaneously depletes complement in the serum. Despite its importance to virulence the underlying mechanism of complement activation by pneumolysin is poorly understood. The aim of the project is to understand the molecular basis of complement activation by pneumolysin by identifying the targets to which the toxin binds and by characterisation of the affinities, kinetics and stoichiometries of pneumolysin-complement interactions. Binding domains and key binding residues will be identified using mutagenesis approaches and candidate complexes will be selected for further structural and functional analysis. The project will use molecular biological techniques, protein expression using bacterial and eukaryotic expression systems, protein purification and biophysical techniques for the analysis of protein-protein interactions.