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Project title: Characterisation and vaccine potential of novel pneumococcal virulence factors expressed during invasive disease

The factors and/or events that trigger the progression of *Streptococcus pneumoniae* (the pneumococcus) from asymptomatic nasopharyngeal colonisation to invasive disease in certain individuals are not fully understood, but presumably require expression of a distinct array of bacterial genes. To date, we have conducted comprehensive microarray comparisons of gene expression profiles between pneumococci in various *in vivo* niches of mice, and identified candidate genes that may be required for progression from colonisation to invasive disease.

Accordingly, the **specific aims** of this project are:

1. To confirm the role in pathogenesis of candidate genes by targeted mutagenesis.
2. To assess the efficacy of promising vaccine antigens for prevention of pneumococcal pneumonia and sepsis.

Study design:

Both Aims will be carried out *in vitro* (using state-of-the-art molecular biology techniques) and *in vivo*, including mouse immunisation (to generate antisera) and challenge studies, as well as mouse models of pneumonia and sepsis.

Techniques to be employed/learned include:

RNA purification
Microarray analysis
real-time quantitative reverse transcription (RT)-PCR
molecular cloning
gene sequencing
targeted mutagenesis
protein expression and purification
mouse immunisation and challenge