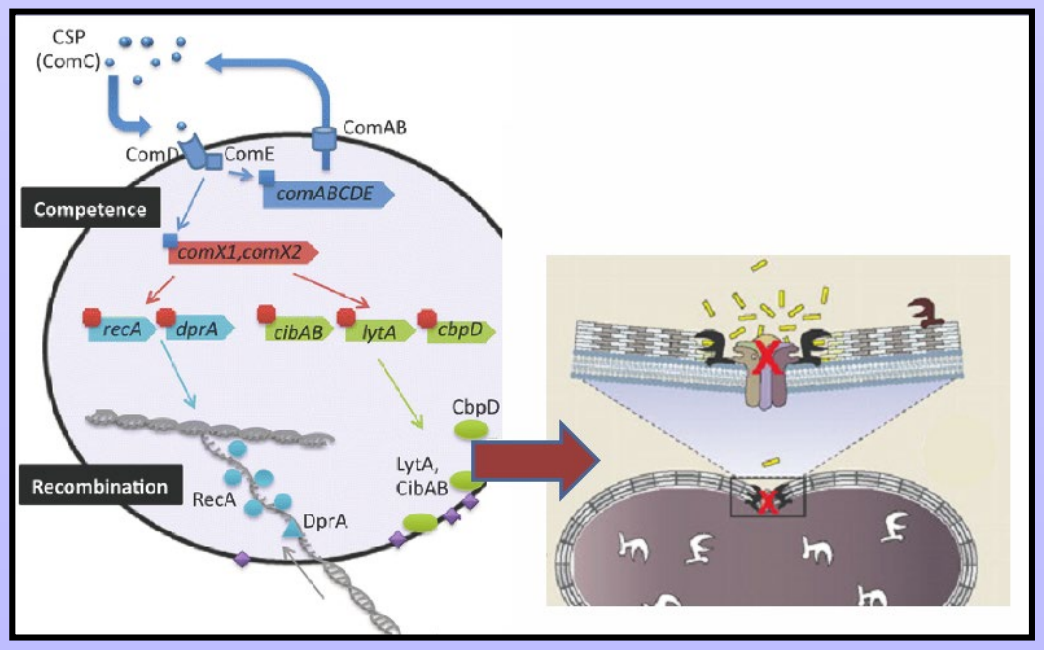
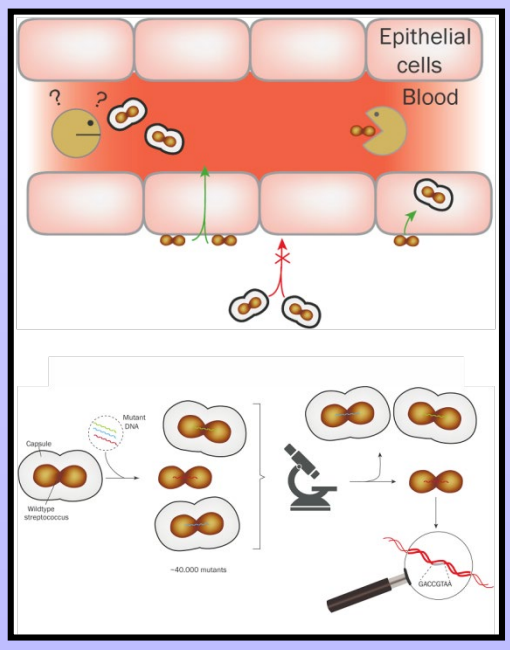
Virulence Streptococcus pneumoniae

Forskningsleder Mikkel Girke Jørgensen

Gruppens kerneforskningsområder

Over a century ago Sir William Osler proclaimed, that in the mortality bills *S. pneumoniae* has become 'the captain of the men of death'. This statement is as true today as it was then, despite the development of vaccines and antibiotics. It is a leading cause of bacterial pneumonia, meningitis, and sepsis worldwide, and causes an annual ~ 1 million deaths in children younger than 5 years. *S. pneumoniae* frequently resides in the upper respiratory tract of healthy individuals, and from there, it can transverse the human epithelial cells and cause severe invasive infections by migrating to other parts of the body (i.e. crossing the blood-brain barrier and cause meningitis). It is still poorly understood how and why *S. pneumoniae* switches from its commensal mode to its pathogenic life style, and it is the aim of this project to better understand this process.
Treatment of pneumococcal diseases are today primarily focused on prevention by vaccination using pneumococcal vaccines that target the most virulent capsular serotypes of *S. pneumoniae*. Sadly, there are increasing incidences of pneumococcal diseases caused by serotypes not covered by current vaccines. In addition, antimicrobial resistant pneumococci have a worldwide distribution and is posing a threat to effective treatment. This is particular worrisome for the case of meningitis because most antibiotics do not penetrate effectively into the cerebrospinal fluid. This is already causing treatment failures as penicillin-resistant pneumococcal meningitis has become common.





Er du interesseret i at skrive projekt i gruppen, så kontakt : mikkelj@bmb.sdu.dk

Projekter	Beskrivelse
The streptococcal cloak of invisibility	One of the critical virulence factors of *S. pneumoniae* is its capsule. The capsule consists of polysaccharides excreted outside the cell wall. The capsule enables the pneumococci to avoid detection by the host immune system as it prevents phagocytosis of the bacteria by macrophages and recognition from the complement system. Very interestingly, colonization of the nasopharynx requires less or no expression of capsule in order to expose the bacterial cell surface adhesions to promote binding to the epithelial cells. In this project, we investigate how the capsule expression is regulated at the genetic level by making random transposons mutagenesis.
Small non-coding RNA-mediated control of virulence gene expression	Recent findings have evidenced small non-coding RNAs as critical elements of bacterial pathogenesis. These sRNAs act at the post-transcriptional level to regulate gene expression through direct base-pairing with the mRNA of their target gene. sRNAs accomplish a large variety of regulatory functions in response to environmental changes and stress conditions. Certainly, human disease progression exposes *S. pneumoniae* to many different environmental niches where rapid adaptation is a key factor for pneumococcal growth and survival. Here we use advanced next generation sequencing techniques (GRIL-seq) to uncover the genetic virulence traits associated with pneumococcal bacteremia.
Competence induced autolysis	Streptococcal cells can evolve rapidly. In fact, one strain of *S. pneumoniae* replaced 7.8% of its genome during a human infection. One way for genetic changes to occur in pneumococcus is through activation of the competence system, resulting in uptake of genetic material from the surroundings. During this process, some of the bacterial cells are marked for death and others remain unharmed through mechanisms regulated by the proteins, LytA and CbpD. In this project, we use a combination of single cell fluorescence microscopy and genetic manipulation to elucidate these mechanisms.