Host-Pathogen Interactions in Bacterial Infections

Forskningsleder Jakob Møller-Jensen

Gruppens kerneforskningsområder

We work in the field of molecular microbiology with focus on extraintestinal pathogenic strains of Escherichia coli and their interactions with host cells. We seek to understand what distinguishes pathogenic bacteria from harmless ones, and how pathogenic bacteria control the expression of virulence factors in response to a particular host environment.

We employ infection models of varying complexity, ranging form simple in vitro systems to live-animal models. Current research activities include the identification of bacterial virulence genes using transposon mutagenesis and high-thoughput sequencing (Tn-seq), investigation of bacterial gene expression inside human cells using RNA sequencing and proteome analysis.

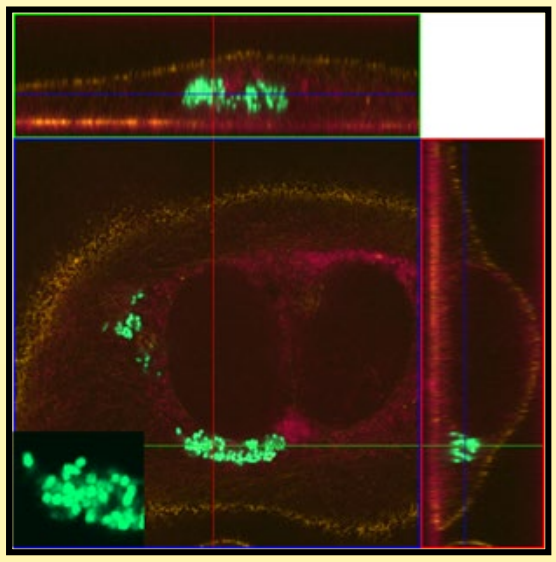
Er du interesseret i at skrive projekt i gruppen, så kontakt: jakobm@bmb.sdu.dk

Beskæftigelse af tidligere studerende

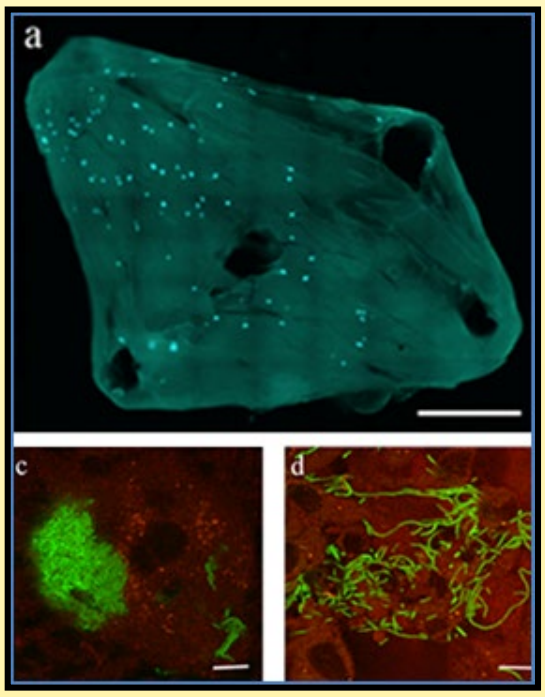
Thøger Jensen Krogh, PhD student in the JMJ group
Andreas Kjær, PhD student at Oxford University;
Grith Hermansen, PhD student at DTU

Carsten Mamsen Jessen, Molecular Biologist at Ampliqon
Nadia Davidsen, Research Chemist at Novo Nordisk
Louisa Fredberg, Biologist at Eurofins Steins Laboratory

Nadia Rahbæk Dyrberg Kristensen, Academic Administrative Officer, SDU Faculty of Science.



Mouse bladder infected by GFP-labelled UPEC (green). The bacteria are located as intracellular colonies and as filaments on the bladder cell surface.



Human bladder cell infected by GFP-labelled UPEC. The bacteria form intracellular colonies.

Projekter	Beskrivelse
Identification of biofilm-associated genes in *Escherichia coli* through high-throughput transposon screening (ongoing)	The majority of complicated urinary tract infections are associated with use of indwelling catheters. These abiotic devises are often colonized by uropathogenic *Escherichia coli* (UPEC), which express adhesive surface fimbriae that bind to the catheter material. In this project we screen a library of 120.000 different UPEC transposon mutants for the inability to colonize silicone catheter material. Selection of non-adherent bacterial mutants will be performed by iterative passaging of the library through a silicone tube catheter model in artificial urine. Transposon insertion sites in enriched mutants will be identified by high-throughput sequencing.
Investigation of the molecular mechanism underlying DamX-mediated cell division inhibition in uropathogenic *Escherichia coli* (ongoing).	Uropathogenic *Escherichia coli* (UPEC) invade bladder cells and multiply to form intracellular bacterial communities. Subsequently, the infecting bacteria exit the host cell, and during this process change their morphology into filaments of more than 100 times normal cell length. This morphological switch is reversible and important for long-lasting bacterial infection of the urinary tract. Morphology-switching is controlled by DamX, a bacterial cell division inhibitor that is produced when UPEC is intracellular. The purpose of this project is to determine the molecular mechanism behind DamX-mediated UPEC morphology switching. We use fluorescence microscopy to monitor the intracelluar localization of DamX and other components of the cell division machinery during UPEC filament formation and reversal.
Adapting to foreign territory: cyclic-di-GMP signaling in *E. coli* during urinary tract infection	The intracellular signaling molecule c-di-GMP plays a primary role in regulation of motility, surface adhesion and biofilm formation in many bacteria including E. coli. The genes encoding enzymes for production and degradation of c-di-GMP are highly conserved among commensal and uropathogenic E. coli (UPEC) strains. In this project the role of c-di-GMP signaling during UPEC infection will be investigated. The intracellular levels of c-di-GMP will be manipulated by gene deletion or overexpression, followed by investigation of phenotypic consequences by e.g. tissue culture infection assays, biofilm- and motility assays, immunofluorescence microscopy and flow cytometry.