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Medizinische Fakultät Mannheim
der Universität Heidelberg

Universitätsklinikum Mannheim

mi3 MANNHEIM INSTITUTE for INNATE IMMUNOSCIENCE

UMM Universitätsmedizin Mannheim, 68135 Mannheim

The Institute for Medical Microbiology and Hygiene, Medical Faculty Mannheim, Heidelberg University, is seeking a

doctoral candidate (m/f/d)

The completely sequenced uropathogenic *Escherichia coli* strain CFT073 harbors the Toll/Interleukin 1 receptor (TIR) containing protein C gene (*tcpC*) in its genome. TcpC modulates innate immunity by binding to Toll-like receptor 4 and MyD88 as well as NLRP3 and caspase 1, key components of two important pathogen recognition receptors and their signaling cascade. CFT073 causes kidney abscesses TcpC-dependently, which consist of bacteria and polymorphonuclear neutrophils. The composition of the invading cells is characterized only superficially and the influence of TcpC on the different cellular subsets in terms of recruitment and function is not explored. Therefore, this project intends to analyze the interaction of TcpC with epithelial and invading innate immune cells in the infected kidney in detail. We will use multicolor flow cytometry to differentiate and quantify infiltrating cells and explore how TcpC changes the cellular infiltrate and its function. We will apply multi-photon microscopy and light sheet microscopy to locate the promoter activity of the *tcpC* gene within the kidney. Further, we will explore the functional relevance of those pattern-recognition receptors, which are functionally modulated by TcpC, on the composition of the cellular infiltrate, replication of CFT073 and the promotor activity of the *tcpC* gene. Finally, we will use dual RNA sequencing to study the influence of TcpC on the transcriptome of the host and the pathogen. The overall aim is to uncover the spatial relationship of CFT073 and the activity of its *tcpC* promoter with invading innate immune cells and kidney epithelial cells, to explore the distribution of pattern recognition receptors or alternatively their signaling cascade and the innate immune response and to analyze the influence of TcpC on these parameters. This knowledge will provide mechanisms in vivo how an important virulence factor of uropathogenic *E. coli* strains interacts with the innate immune system to cause pyelonephritis. Interference with these mechanisms may lead to new treatment options for pyelonephritis aside from classical antibiotics. We complement the work in mice with the analysis of the TcpC-dependent response of a human kidney epithelial cell line upon infection with CFT073 and the exploration of the inflammatory response in human kidney tissue samples from pyelonephritis patients.

The DFG-funded (MI 471/14-1) project “Influence of the TIR domain-containing protein C on the cellular infiltrate and kidney epithelium during pyelonephritis caused by the UPEC strain CFT073” is embedded at the Heidelberg Biosciences International Graduate School (HBIGS) to provide profound supervision and additional training.

Your profile:

- Completed M.Sc. in life sciences (biology, molecular medicine, immunology, etc.)
- Proficiency in English language
- High level of interest in the areas of infection immunity
- Motivated and independent working style and team spirit
- Knowledge in innate immunity, microbiology
- Practical experience in cell culture, PCR, microscopy, flow cytometry, ELISA, ideally handling of mice

The position is a fixed-term position (65% TVL-E13) to be filled by 01.09.2024

Please submit your application (including a 1-page letter of motivation, CV, academic transcripts and a summary of your master thesis as one single PDF file to Thomas.Miethke@medma.uni-heidelberg.de.

For further information please contact:

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