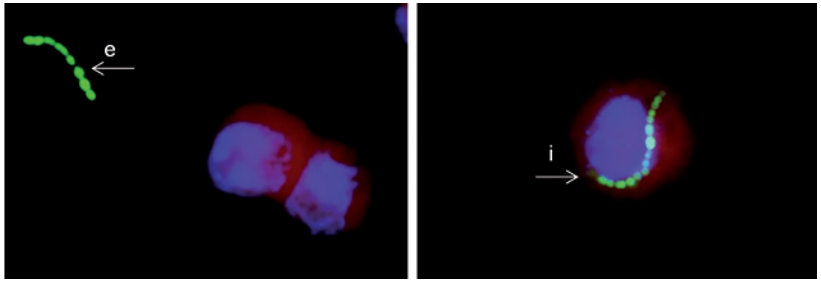
Institute of Medical Microbiology and Hygiene

Work Group: MyTB-Lab

Head: Steffen Stenger

The successful defense against an infection with *Mycobacterium tuberculosis* requires the innate as well as the adaptive immune system. In this context, our group focuses on infection immunology aspects important in mycobacterial host interactions. The goal is to elucidate the details of known immunity mechanisms and to identify novel mycobacterial clearance mechanisms. The overall goal lies in improving prevention strategies against tuberculosis and to contribute to novel therapeutic approaches. For this purpose, we use clinically relevant specimens in our experimental approaches, such as human blood, pulmonary cells and tissue samples from tuberculosis patients. Stephanie Kallert is enrolled as a graduate student in IGradU and pursues the design and evaluation of strategies to optimize Lipid-specific T cell responses against *Mycobacterium tuberculosis*. Hydrophobic molecules, such as lipids and lipoproteins, are a new class of antigens which can activate cytotoxic T cells and therefore play an important part in protection from infectious disease. For optimal use of this characteristic, it is important to bring the hydrophobic antigens efficiently into antigen-presenting cells, e.g. macrophages. The goal of this project is to develop methods for the introduction of hydrophobic molecules through the eukaryotic cell wall into macrophages in order to reach an optimal activation of the immune system resulting in the elimination of pathogenic microorganisms.

The Team:
Head of Institute: S. Stenger
Professor: B. Spellerberg
PhD Students: D. Asam, M. Busch, C. Florindo, S. Kallert, A. Sagar, S. Shabayek
Study Programme Experimental Medicine Students: J. Dick, H. Unger



Depicted are streptococci *(S. agalactiae)* following the incubation with human monocyte-derived cells. Bacteria are fluorescently labeled with EGFP. On the left, bacteria are located extracellularly (e), while on the right, bacteria are found intracellulary (i) in the cytoplasm of the eukaryotic cell.

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Work Group: Molecular Mechanisms of Streptococcal Pathogenicity

Head: Barbara Spellerberg

The work of our group focuses on molecular mechanisms of streptococci that are important for human infections. Bacterial pathogenicity represents a complex multifactorial interaction between microbial pathogens and their hosts. Innate immunity mechanisms play an important role in the defense against invasive bacterial infections. To survive in human blood, invasive microbial pathogens interfere with the humoral and cellular innate immunity of the host. Many bacterial virulence factors play an important and specific role in this interaction. One of the main goals of our group is to elucidate the molecular details of these encounters. Within this context, we were able to elucidate different streptococcal virulence factors that are crucial for human infections. These include the pyruvate oxidase of *Streptococcus pneumoniae*, the genetic background of *Streptococcus agalactiae* hemolysin production and a composite transposon of *S. agalactiae* harboring genes that are involved in adhesion to host extracellular matrix structures and interference with the human complement system.

At the Graduate School, we pursue two projects. One investigates the role of bacterial cell wall structures for human streptococcal infections. While CRP has been detected and named for its ability to bind to the cell wall of *S. pneumoniae*, the molecular details of this interaction are not completely understood. Especially puzzling is the fact that, while CRP has been shown to interact with the phosphorylcholine in the pneumococcal cell wall, streptococci and other bacteria lacking this molecule in their cell walls still cause massive CRP rises. Within the second project, we were able to elucidate the genetic background of *Streptococcus anginosus* ß-hemolysin production. While *S. anginosus* strains are often isolated from various abscesses and are regarded as an emerging pathogen in cystic fibrosis patients, very little is known about the molecular mechanisms of pathogenicity in *S. anginosus*. The identification of the ß-hemolysin genes by our group will allow us to investigate their specific role in *S. anginosus* infections.

Selected Publications:

- *Aymanns S, Mauerer S, van Zandbergen G, Wolz C, Spellerberg B (2011): High level fluorescence labeling of gram-positive pathogens. PLoS ONE 6, e19822.*
- *Brandt CM, Spellerberg B (2009): Human infections due to Streptococcus dysgalactiae subspecies equisimilis. Clin Infect Dis. 49, 766-72.*
- *Bruns H, Meinken C, Schauenberg P, Härter G, Kern P, Modlin RL, Antoni C, Stenger S. (2009): Anti-TNF immunotherapy reduces CD8+ T cell-mediated antimicrobial activity against Mycobacterium tuberculosis in humans. J Clin Invest. 119, 1167-77.*
- *Bruns H, Stegelmann F, Fabri M, Döhner K, van Zandbergen G, Wagner M, Skinner M, Modlin RL, Stenger S (2012): Abelson tyrosine kinase controls phagosomalacidification required for killing of Mycobacterium tuberculosis in human macrophages. J Immunol. 189, 4069-78.*
- *Gleich-Theurer U, Aymanns S, Haas G, Mauerer S, Vogt J, Spellerberg B (2009): Human serum induces streptococcal C5a peptidase expression. Infect Immun. 77, 3817-25.*
- *Nickel D, Busch M, Mayer D, Hagemann B, Knoll V, Stenger S (2012): Hypoxia triggers the expression of human β defensin 2 and antimicrobial activity against Mycobacterium tuberculosis in human macrophages. J Immunol. 188, 4001-7.*