Vandana Arakandy

Metabolic cross talk between host and *S. aureus* during chronic osteomyelitis

Staphylococcus aureus is a frequent cause of invasive tissue infections. In particular bone infections can develop from an acute inflammatory to a chronic stage that is extremely difficult to treat and often requires surgery, e.g. amputation. *S. aureus* persistence strategies are associated with the bacterial ability to invade host cells and dynamically change phenotypes from the aggressive wild-type to small colony variants (SCVs) which are adapted for long-term persistence. In our previous work we found that SCVs down-regulate their metabolism via dynamic global regulators. Thus, they can rapidly adjust to the altered environmental conditions and escape from the host defense system. Only recently, we could demonstrate that sigma factor B (*sigB*), a global bacterial stress regulator, is essential for SCV-formation and long-term persistence. Furthermore, we observed that during intracellular persistence the bacteria developed a thickened cell membrane/wall. Membranes consist of fatty acids (FAs) and in *S. aureus* their synthesis is mainly regulated by the type II fatty acid pathway (FASII) that is highly energy consumptive. An alternative way is to gain FA from external sources, such as host cells. *S. aureus* is able to incorporate extracellular FAs into their phospholipids that might be a crucial bacterial step for persistence. In this project we plan to investigate the function of SigB for the generation or uptake of FA and their impact on chronic infection development. We will characterize the cell envelope changes of *S. aureus* in our long-term infection models by electron microscopy and biochemical approaches. The impact of virulence factors, global regulators and proteins involved in FA synthesis will be analyzed by molecular methods

(e.g. mutants, RNA seq, real-time PCR). By this means we aim to better explore the cross talk between *S. aureus* and their host cells, which is the prerequisite to develop novel therapeutic strategies against persisting infections.

Publications

Jordan PM, Gerstmeier J, Pace S, Bilancia R, Rao Z, Börner F, Miek L, Gutiérrez-Gutiérrez O, Arakandy V, Rossi A, Ialenti A, González-Estévez C, Löffler B, Tuchscherr L, Serhan CN, Werz O (2020) *Staphylococcus aureus*-Derived α-Hemolysin Evokes Generation of Specialized Pro-resolving Mediators Promoting Inflammation Resolution *Cell Reports* 33(2), 108247. Details Open Access

Romp E, Arakandy V, Fischer J, Wolz C, Siegmund A, Löffler B, Tuchscherr L, Werz O, Garscha U (2019) Exotoxins from Staphylococcus aureus activate 5-lipoxygenase and induce leukotriene biosynthesis *Cell Mol Life Sci* [Epub ahead of print] Details PubMed

Supervisor

Bettina Löffler

Co-Supervisors

Lorena Tuchscherr de Hauschopp

Start of PhD

April 4, 2016