Prof. Dr. Ulrich E. Schaible
Research Center Borstel, Leibniz Center for Medicine & Biosciences

will give a presentation entitled

“Host-pathogen interaction studies in tuberculosis identify targets for host-directed therapies“

Monday, July 31, 2017, at 17:00 s.t.
in Blg E8.1, Seminar Room (Ground Floor)

Host: Prof. Dr. Claus-Michael Lehr

There is opportunity to talk with the speaker before the talk.

For details and for making appointments please contact: Karin Groß, 0681-98806-1010 or per email: Karin.gross@helmholtz-hzi.de

Guests are welcome!
Abstract

In less than 10% of infected persons, Mycobacterium tuberculosis (Mtb) infection causes active Tuberculosis (TB) whereas 90% remain in a latent state. In latent TB, granuloma formation and protective immunity sequesters Mtb and controls growth. In contrast, active TB is characterized by uncontrolled mycobacterial growth, exacerbated immunopathology and necrotizing granulomas, which eventually break open into the airways to allow transmission of Mtb. Emerging drug resistant Mtb isolates calls for alternative therapies by modulating immunity and metabolism to support antibiotic treatment.

Active TB is characterized by polymorphonuclear neutrophils (PMN) within lesions and PMN associated peripheral blood transcriptome signatures. We observed that PMN failed to kill virulent Mtb but succumbed to necrotic cell death via their own reactive oxygen intermediates (ROI). When macrophages (MO) take up necrotic infected PMN, only virulent Mtb but not those lacking the ESX1 secretion system were able to grow in the new host cells. Subsequent necrosis of these MO starts a vicious cycle of cell death and Mtb growth, a scenario likely to happen in exacerbating active TB granulomas. However, specific inhibition of ROI rescued PMN from necrosis and, following uptake by MO, facilitated killing of Mtb thereby defining PMN as targets for host-directed therapy (HDT). PMN are also prominent in granulomas of Mtb susceptible mouse models. Small lipid mediator (SLM) lipidomics revealed differential SLM production in these mice upon Mtb infection including enhanced production of leukotriene B4, which attracts PMN. Treatment with Zileuton, an inhibitor aloo5-mediated LTB4 synthesis, was able to reduce Mtb loads at those time points when aloo5 expression and LTB4 production was enhanced. Taken together, PMN associated pathways are intriguing targets for HDT to support anti-Mtb treatment in a personalized medicine approach.

CV

Education and Training
2002 Specialty degree, Immunology (German Society of Immunology)
2002 Habilitation, Microbiology-Immunology, Free University of Berlin
1991 Dissertation, Max-Planck-Institute of Immunobiology, Freiburg
1986 Diploma Biology - Zoology, Geobotany, Microbiology, Ethnology, Freiburg
1978-86 Studies in Biology, Philosophy and Ethnology, University of Freiburg

Academic Appointments
1998-06 Research Group Leader, Max-Planck-Institute for Infection Biology, Berlin
2006-08 Prof./Chair in Immunology, London School of Hygiene & Tropical Medicine, UK
2008-12 Director, Molecular Infectiology, Forschungszentrum Borstel, Germany
2008-15 Honorary Professor, London School of Hygiene & Tropical Medicine, UK
2008-now Professor Immunochemistry and Biochemical Microbiology, University of Lübeck
2012-now Program Director, Priority Area Infections, and Deputy Director, Forschungszentrum Borstel, Germany

Mission
The RG Cellular Microbiology studies host-pathogen interactions in tuberculosis on the molecular, cellular and animal model level. We focus on the question how the intracellular niche of Mycobacterium tuberculosis in phagocytes such as macrophages and neutrophils determines the pathogens fate and transmission as well as innate and acquired immune responses and pathogenesis in tuberculosis and, ultimately, antimycobacterial drug efficacy.