K264
Keynote Lecture
Mycobacterium tuberculosis: success through dormancy

Tuberculosis belongs to the deadliest health threats globally. Every year ca. 9 million new cases develop, a fifth of them with fatal outcome. An estimated 2 billion individuals are infected with the etiologic agent, Mycobacterium tuberculosis (Mtb). In the vast majority of these individuals, the pathogen persists in a dormant stage. Control of Mtb is the result of a complex crosstalk between different cells and molecules of the immune system which is focused on the granuloma. The pathogen resides in mononuclear phagocytes which serve both as habitat and effectors of protective immunity. The innate immune response is not only responsible for early containment of Mtb but also initiates long-term protection mediated by T lymphocytes. Critical to protection are CD4 T lymphocytes; CD8 T lymphocytes contribute to protection in addition. The cytokines Inteferon-gamma (IFN-gamma as well Tumor Necrosis Factor-alpha (TNF-alpha both produced by Th1 CD4 T cells, are crucial activators of antibacterial macrophage capacities. Probably IL-17 produced by Th17 CD4 T cells contributes to early protective immunity by directing blood cells to the site of Mtb growth. CD8 T cell contribution to protection involves cytolytic activities and secretion of IFN-gamma and TNF-alpha. The current TB vaccine Bacille Calmette-Guérin (BCG) provides insufficient protection. Hence, novel vaccination strategies are needed and several vaccine candidates have entered clinical trials. These are subunit vaccines which booster BCG or viable attenuated vaccines which replace BCG. All current vaccine candidates aim at preventing active TB disease without eradicating the pathogen Mtb. Future vaccination strategies should attempt to prevent or eradicate Mtb infection. Critical to rational vaccine design are biomarkers which define latent TB infection, vaccine induced host responses and active TB disease and can predict risk of developing active TB. Moreover, biomarkers can facilitate participant stratification and monitoring of clinical trials and provide deeper insights into mechanisms underlying protection against TB to the future custom-made biosignatures will significantly contribute to rational design of novel intervention measures for TB control.