

Research Areas

Diagnosics of mycobacterial diseases

Mycobacterial disease, e.g. tuberculosis as well as non-tuberculous mycobacterial diseases are of growing importance worldwide. Diagnostic blood tests for latent tuberculosis have recently developed and approved by FDA using specific mycobacterial antigens to stimulate T-cells for Interferon-g-secretion. The evaluability of these test in immunocompromised patients is unclear and is evaluated by our group in two studies, one in cooperation with the

TB-NET

. Interferon-g is one of several cytokines secreted upon T-cell stimulation, another project is the evaluation of other cytokines for the diagnosis of latent tuberculosis in supernatants of full blood stimulated by specific TB-antigen.

Diagnosis of non-tuberculous pulmonary disease in adults is hampered by the difficulties to distinguish colonization and infection and requires the isolation of the same mycobacterium from respiratory secretions at two separate occasions. The need for a diagnostic method for measurements of specific T-cell immunity is evident. We therefore pursue a diagnostic trial for the detection of specific antibodies and T-cell immunity to specific *M. avium* proteins.

Epidemiology of NTM-infections

Severe infections with nontuberculous mycobacteria (NTM) are marker diseases for several defined immunodeficiency disorders. However, host and environmental factors that predispose humans without overt immunodeficiency to NTM infections have not been sufficiently elucidated. In cooperation with Alexandra Nieters (Tandem project 12) we are in the progress of starting a multinational patient cohort of children and adults with NTM infections and matched controls. In a pilot study, we will explore the relevance of DNA methylation patterns of candidate genes with putative roles in anti-mycobacterial immunity.

Pathogenicity of mycobacterial diseases

Virulent mycobacteria as *M. tuberculosis* (MTB) persist and grow in macrophages whereas *M. bovis*-Bacillus Calmette-Guérin (BCG) are avirulent and attenuated in macrophages. Inhibition of apoptosis is one method that may be important for intracellular survival, since less virulent mycobacteria are capable of inducing significant higher levels of apoptosis, we focus on type VII-secretion systems as putative anti-apoptotic factors. For this purpose we use MTB-knock out strains with deletion mutants within these secretion systems.