Interaction between mycobacterial ManLAM and the host immune response

*Mycobacterium tuberculosis* is a 'successful' pathogen as it is estimated that around one-third of the world population is infected. Only 5 to 10% of the infected population develops active tuberculosis (TB), but the bacteria remain present in the body of infected persons in the other cases. *M. tuberculosis* is able to survive inside human cells leading to a latent, asymptomatic form of TB-infection, that can still become 'reactivated' TB at a later stage in life. Hence, the *Mycobacterium*-host interactions are both interesting, and, considering the need for new drugs and more effective vaccines against TB, important to study. The complex and thick mycobacterial cell wall contains large amounts of glycans, proteins, and lipids with known or hypothesized roles in the targeting or modulating of the host immune response, of which mannose-capped lipoarabinomannan (mannose-capped LAM; ManLAM) is one example.

Simultaneously with the discovery of C-type lectin Dendritic Cell-Specific ICAM3-Grabbing Non-Integrin (DC-SIGN) as the major receptor on dendritic cells (DCs) for *M. tuberculosis*, the mannose cap of ManLAM appeared essential for the recognition of LAM by DC-SIGN. Other studies also showed that DCs can form a reservoir for mycobacteria and as antigen-presenting cells, DCs are important in the regulation of the immune response. Hence, the characteristics of the interaction between on the one hand Mycobacterium and ManLAM, and on the other hand DCs and DC-SIGN are of interest in the understanding of the immune response against *M. tuberculosis*: is ManLAM the key ligand in the interaction between mycobacteria and DC-SIGN? Does inhibition of this interaction prevent or reduce TB-infection? And is the mannose cap on LAM a virulence factor restricted to the slow-growing pathogenic *Mycobacterium* species? This thesis attempts to answer these questions.