

Interaction of dormant M.tb with the immune system

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1/3 of the world's population is suffering from Latent tuberculosis (TB) and no vaccine exists against this disease. Furthermore, only little is known about the immune response required to combat latent TB, and how MTB can avoid being eradicated by the immune system. Latent TB describes a condition where *Mycobacterium Tuberculosis* (MTB) is thought to exist in a non-replicating dormant condition, here termed "DorMTB". In contrast to this is the exponentially growing MTB which is responsible for transmission of the disease and represents another state of the bacterium, termed "LogMTB".

To study the mechanisms that dormant intracellular bacterium *Mycobacterium tuberculosis* (DorMTB) use to survive in the host during latency we have compared how it interacts with the immune system with that of the active growing bacteria (LogMTB). In addition, we have compared the protein expression profile of DorMTB and LogMTB.

To generate a state of dormancy, M.tb was grown in PBS for up to 8 months. Thereafter these bacteria were used to infect mice. Our results involving infection of mice with dormant MTB (as opposed to LogMTB) showed that the transition from active (LogMTB) to dormant MTB is accompanied by a surprising ability of the bacteria to counteract the immune system. Thus, in the initial phase of the infection, DorMTB induced a strong CD4 and CD8 T cell response compared to LogMTB. However, after 6 weeks the response had waned and most of the T cells were at a terminally differentiated state. As a consequence the bacterial numbers in DorMTB infected mice significantly exceeded that observed in LogMTB infected mice.

On a protein expression level, we found that DorMTB showed a specific expression profile compared to LogMTB, and we are currently determining the identity of these proteins.