New mechanisms of *Mycobacterium tuberculosis* immune evasion: impact on disease outcome and strategies of immune intervention

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**Introduction**: *Mycobacterium tuberculosis* (Mtb) is the etiological agent of tuberculosis (TB), a disease that affects nearly one-third of the world’s population, causing the death of almost 3 million people per year. One of the possible causes for the chronicity of TB is the peculiar capacity of Mtb to induce evasion of host immune-surveillance.

**Background**: We have recently suggested that a possible mechanism for Mtb immuno evasion may rely on its ability to hijack monocyte differentiation into dendritic cells (DCs). DCs are cells with a crucial role in the induction of a microorganism-specific cellular immune response. Thus, affecting the generation of functionally active DCs, Mtb could block the afferent limb of the specific immune response, preventing a functional T cell response development. Recently, type I IFN has been found to regulate the immune system through the control of proliferation, differentiation, and maturation of different leukocytic populations, including DCs. Interestingly, we have shown that whilst Mtb induces a high expression of type I IFN, it inhibits the IFN -induced monocyte differentiation into DCs. We have also recently demonstrated that Mtb stimulates type-I IFN gene transcription, but also affects the type-I IFN signal transduction in monocyte, macrophages and DCs.

**Specific aims**: i) characterization of the molecular basis of the Mtb-caused blockade of type I IFN induced monocyte differentiation in DC, ii) analysis of the transcriptome induced by type I IFN in Mtb-infected monocytes versus uninfected cells, iii) evaluation of the functional role of T lymphocytes primed by cells derived from Mtb-infected monocytes in the disease control iv) identification of possible targets for innovative therapeutic strategies to counteract Mtb persistence in infected host.

This joint project complies with the development and pursuance of common research interests of the two partners, that so far it has allowed the progress of complementary studies on TB immunopathogenesis and the achievement of interesting results.

**Pubblicazioni rilevanti relative al progetto**:


