PREFACE: Manipulation of Macrophage Functions by *Mycobacterium Tuberculosis*

Tuberculosis remains one of the infection diseases with high mortality in humans, leading to 3 million deaths annually worldwide. It is also estimated that one-third of the world's population is asymptotically infected by *Mycobacterium tuberculosis* (Mtb). Development of Mtb resistance to various anti-mycobacterial drugs contributes to a dramatic increase in an active tuberculosis. The low effectiveness of existing vaccines is also an essential problem. In addition, despite extensive research, our understanding of the virulence factors of Mtb is still incomplete. Therefore, many research groups are seeking to identify new factors that are important for the progression of tuberculosis. Better understanding of the mechanisms of Mtb virulence and pathogenicity will lead to new strategies for the battle with tuberculosis.

This special section is focused on some of the recently discussed and tested strategies that Mtb uses during the infection process. To survive inside host cells, bacteria secrete several effector proteins like kinases and phosphatases (PknA, PknB, PtpA, and PtpB) that affect the signaling system of macrophages. Consequently, to ensure Mtb survival, phagosome maturation is arrested, apoptosis of infected macrophages is inhibited, and pro-inflammatory cytokine production is modulated. Another key proteins, PE/PPE, belonging to the ESAT-6 (ESX) secretion system, have a great potential to act as virulent factors during mycobacterial pathogenesis. It is assumed that they inhibit free-radical production, influence macrophage phagosome acidification and phagosome-lysosome fusion, and modulate the cytokine response of macrophages, allowing intracellular replication of Mtb. Numerous *in vitro* studies have demonstrated that Mtb induces the autophagy process in infected macrophages. However, its level is relatively low, suggesting that inhibitory mechanisms of Mtb play an important role during infection. Mtb may repress autophagy via upregulation of inhibitory genes as well as secretion of factors that act on the posttranslation level, e.g. by blocking fusion of lysosomes with autophagosomes. Recognition

and phagocytosis of Mtb engages innate immune receptor TLR2, which also plays an essential role in macrophage response to infection by tubercle bacilli. TLR2 signaling cascades could be either pro- or anti-inflammatory, depending on the activation by the distinct Mtb agonists (glykolipids, PE/PPE proteins, lipoproteins) with receptors. Understanding the interaction between Mtb and TLR2 seems to be a key finding of new ways to eliminate Mtb infection. Strategies used by tubercle bacilli to avoid killing by macrophages are based not only on the secretion of various factors but also on the protection of the integrity of its genome. Mtb proteins involved in DNA repair pathways participate in the survival of Mtb inside macrophages and have a potential role in the modulation of macrophages functional activity. Discussed in this special section mechanisms used by Mtb to survive inside macrophages can be potentially rich source of diagnostic and vaccine candidates. Finally, this special section is focused on BCG interactions with human dendritic cells involving the role of dendritic cell receptors in BCG recognition as well as the significance of the pro-inflammatory cytokines produced by BCG-infected DCs.

This collective work summarizes the mechanisms used by *Mycobacterium tuberculosis* to avoid killing by host cells. Identification of new mechanisms of protective immunity could be helpful in designing new safer and more efficacious vaccines.

Finally, I would like to express my gratitude to all the authors who have contributed to this special section. Their vast knowledge and experience in the field of *Mycobacterium tuberculosis* have made this special section possible.

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