[PS2.9]

Role of Mycobacterial Lipids for Survival of Bacteria inside the Macrophage

E Patin*[1], S Willcocks[1], U E Schaible[2]

[1]London School of Hygiene and Tropical Medicine, United Kingdom, [2]Research Centre Borstel, Germany

Mycobacterium tuberculosis and its relatives are important pathogens in humans and animals. Tuberculosis is a major health problem worldwide, with approximately one-third of the population infected and 1.6 million deaths estimated in 2005 by the World Health Organization. *M. tuberculosis* mainly causes chronic pulmonary diseases with the remarkable capacity to persist as a long-term asymptomatic infection. Inadequate treatment and immunodeficiency have contributed to the emergence of strains with multiple resistances to common anti-tuberculosis drugs.

M. tuberculosis has the ability to survive inside macrophages by modulating the host cell defence through blocking of phagosome maturation. Mycobacterial phagosomes retain many of the early endosomal characteristics that are normally removed from the maturating phagosomes.

Mycobacterial lipids have been highlighted during recent years as key virulence factors of *M. tuberculosis*. The failure of mycobacterial phagosomes to fuse with lysosomes was suggested to be due to the mycobacterial cell wall lipids such as lipoarabinomannan (LAM), phosphatidyl inositol mannosides (PIMs) and trehalose dimycolate (TDM). Further studies are required to fully understand how these lipids execute inhibition of phagosome maturation and how the host response interferes with this virulence function. More importantly, we hypothesise that TDM synergises with other mycobacterial lipids to maintain the intracellular niche.

In my PhD, mycobacterial lipids coated onto beads were analysed for their intracellular fate in murine macrophages using an array of cell biological methods. Our preliminary results suggest a synergistic effect of TDM and mannosylated LAM on phagosome maturation. Future studies will establish the intracellular lipidome of *M. tuberculosis* to purify and identify lipids upregulated within the host cell environment. These lipids will be further investigated for their effect on phagosome maturation. It is our goal to identify the mycobacterial virulence factors promoting survival of bacteria inside macrophages by inhibiting phagosome maturation in order to target respective synthesis pathways.

Keywords: Mycobacteria, Lipids, Macrophages, Innate Immunity