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The Interaction of Anti-Microbial Peptides with *Mycobacterium spp.*

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Anti-Microbial Peptides (AMP) are a highly conserved group of proteins, produced by various cell types, including alveolar macrophages (Mφ) and epithelial cells (EC), thus making them of interest in pulmonary mycobacteria infection. Their cationic properties along with hydrophobic regions assist their integration into membranes to weaken cell integrity and contribute to killing of the pathogen. Various AMP have been shown to act either intra- or extra-cellularly, and against Gram-positive and Gram-negative bacteria. Certain AMP have been shown to be expressed during latent *Mycobacterium tuberculosis* (M.TB) infection, but are downregulated upon re-activation, suggesting a delicate relationship between the two. It has been described that mycobacterial membrane lipids, such as trehalose dimycolate (TDM) have a key role in preventing phago-lysosome fusion and therefore in facilitating intracellular survival. In the present work, we describe a potential additional role for TDM in resisting membrane attack by AMP. We use thin layer chromatography to demonstrate a shift in the mycobacterial lipidome toward more hydrophobic components inside the host macrophage and electron microscopy and model liposomes to demonstrate the potential resistance of TDM to AMP. Viability and metabolic assays were employed to measure the effect of AMP on mycobacteria at a population, rather than individual level. Our data support the hypothesis that AMP can permeabilise and kill mycobacteria but TDM can protect mycobacterial cell walls from destruction. TDM can be considered a virulence factor due to its counter activity to innate AMP function.

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