

**P010** The role of Nuclear Factor kappa B (NF $\kappa$ B) in the pathophysiology of Buruli ulcer (BU) disease

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BU, is characterised by an extracellular and poorly inflammatory infection caused by *M. ulcerans*. Immune response to the disease is poorly understood. The virulence factor has been identified as a macrolide, mycolactone. Mycolactone suppresses NF $\kappa$ B activity, attenuating the expression of pro-inflammatory cytokines in primary human monocytes, consistent with the poorly inflammatory response to this pathogen since NF $\kappa$ B plays a critical role both upstream and downstream of many inflammatory genes. Recent studies suggest that inflammation plays an important role in the progression and metastases of tumors. This has focused interest on NF $\kappa$ B, as an anti-tumor target and trials are underway. However, it has also been reported that in the epithelial cells of the skin, the classical NF $\kappa$ B pathway unusually plays a tumor suppressor role. Consistent with these observations, animals studies in which NF $\kappa$ B activity has been inhibited have developed epithelial cell carcinoma. These cancers may be related to the scar site squamous cell carcinoma reported in some cases of healed BU. The mechanism by which mycolactone suppresses NF $\kappa$ B regulated gene expression remains unclear. The identification of it's molecular target will greatly improve our understanding NF $\kappa$ B regulation as well as the peculiarities of cell cycle induction in different tissues.