

P007 LL-37 enhances host immunity by modulating apoptosis and differentiation of leukocytes and epithelial cells.

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Cationic host defence peptides are microbicidal agents with immunomodulatory properties. The human cathelicidin LL-37 is expressed by neutrophils and epithelial cells and upregulated by infection and inflammation. This peptide is anti-endotoxic, chemotactic, angiogenic, and modifies cytokine and chemokine expression by mammalian cells. We demonstrate that LL-37 inhibited spontaneous apoptosis of human neutrophils, acting as a potent survival factor, but in striking contrast LL-37 induced apoptosis in airway epithelial cells *in vitro* and *in vivo*. We propose that both mechanisms enhance host bacterial clearance. Furthermore, we demonstrate that LL-37 modulates the differentiation of human monocyte-derived macrophages and dendritic cells, generating functionally enhanced LL-37-primed antigen-presenting cells. We propose that LL-37 is a multi-potent, tissue microenvironmental modifier, modulating apoptosis and differentiation and/or function of leukocytes and epithelial cells to enhance immune responses to acute infectious diseases. Synthetic analogues with microbicidal and targeted immunomodulatory activities represent attractive potential therapeutics for antibiotic resistant infectious diseases. Funding: Salvesen Trust, Wellcome Trust, Canadian CF Foundation, CIHR