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Bioactivity of the recombinant human antimicrobial peptide LL37: a key role in wound healing through vascularization

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Antimicrobial peptides (AMPs) are usually defined as small, cationic, amphipathic peptides making part of the innate immune system. Human cathelicidin AMP LL37 is overexpressed in different cells, tissues and body fluids and, in addition to its antimicrobial activity, induces chemotaxis of immune system's cells, arteriogenesis, angiogenesis and promotes wound healing. Our group developed a new, low-cost method for the expression and purification of LL37, by fusing it with the Carbohydrate Binding Module from family 3 (CBM3) from CipA from *Clostridium thermocellum*. The CBM3-LL37 protein is overexpressed in *E. coli* and retained both the antibacterial and immunophysiological properties. Additionally, it induced proliferation, migration and formation of tubule-like structures by endothelial cells. Topical application of rLL37 also increased vascularization and re-epithelialization, thus accelerating the wound healing process, in wounds of dexamethasone-treated mice. This indicates a key role for LL37 in wound regeneration, mainly mediated by its proangiogenic activity, which is currently being studied with further detail in diabetic mice, a chronic wound model. Moreover, we are working on the development of natural polymer-based delivery systems for the topical sustained release of LL37 that can be applied to wound sites, thus promoting faster and more efficient wound regeneration. Acknowledgements: JPS and RR are supported by FCT grants SFRH/BPD/64958/2009 and SFRH/BD/27404/2006.