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Therapeutic Potentials of Antimicrobial Peptides

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Antimicrobial peptides (AMPs) are small proteins (<100 amino acids) which include alpha-defensins, beta-defensins and the cathelicidin LL-37 in humans [1]. Alpha-defensins are expressed in neutrophils as part of their non-oxidative antimicrobial mechanisms and are also found in Paneth cells in the intestine [2,3]. They are synthesized as precursors that are proteolytically activated and released during inflammation [4]. The human beta-defensins (hBDs) are cationic antimicrobial peptides made primarily by epithelial cells and expressed in all human epithelia tested to date [5]. The defensins are secreted in biological fluids, including urine, bronchial fluids, nasal secretions, saliva and gingival crevicular fluid [5-7]. hBD-1 is expressed constitutively in epithelial tissues, whereas hBD-2 and hBD-3 are expressed when epithelia are stimulated with bacteria, *Candida albicans*, IL-1, or TNF-α [8,9]. LL-37 is an amphipathic cationic peptide expressed in various epithelial cell types, including inflam206-543-4339 ed epidermal keratinocytes and in human tongue, buccal mucosa and saliva following inflammatory stimulation [10,11].

These AMPs are synthesized in various locations of the human body and provide a broad spectrum of antimicrobial activity against Gram-negative and Gram-positive bacteria, as well as against yeast and some viruses [12,13], thus may have future therapeutic potential [14]. The effectiveness of human AMPs has been tested in a few animal studies, such as investigating how a subcutaneous administration of HNP-1 significantly reduces *Mycobacterium tuberculosis* infection in lung and spleen of the infected mice [15,16]. Furthermore, hBD-2 has been shown to be protective against pneumonia and sepsis, as rats receiving a recombinant adenovirus carrying rat beta-defensin-2 (BD-2), which is very similar to hBD-2, showed significantly lower amounts of *P. aeruginosa* colony-forming units in the infected compared to the control rats [17]. Although these animal studies suggest administration of AMPs as a valuable candidate for a new therapeutic approach, their effectiveness in human clinical studies is yet to be determined.

As the level and the frequency of bacterial resistance to systemic antibiotics increase, the need to develop suitable alternatives to the current antibiotic therapy becomes more urgent. Fortunately, AMPs have shown a broad spectrum of antimicrobial activities with little bacterial resistance to this date, making them promising alternatives to the current therapy [18,19]. In addition, another desirable characteristic of AMPs is the fact that they are synthesized in various body sites and may act synergistically to fight infections caused by different microorganisms. Other potential applications of AMPs include utilization as adjuvants to enhance antibody production, as AMPs show chemotactic abilities and can stimulate the acquired immune system [20,21]. AMPs also promise to be a viable candidate to be used in cancer therapies. For instance, hBD-1 shows potential as an agent to suppress the growth of OSCC cells, as its recombinant protein can be developed to support tumor therapy and prevent tumor recurrence [22]. Feedback regulation of hBD-1 expression in OSCC cells may also be useful in developing new ways to control tumor cell proliferation [22]. The strong evidence presented in this commentary will help us leap forward to new and innovative ways to develop antimicrobial compounds against many infectious diseases.

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