

Integration of Defensins: A Promising Clinical Tool

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DEAR EDITOR,

Defensins are cationic peptides, 20-40 amino acids in length, containing six cysteines, which form three intramolecular disulfide bonds. They are classified as α -, β -, or θ -defensins, based on the relative positions of these disulfide bonds. α -Defensins were first isolated from the rabbit alveolar macrophages.^[1] Subsequently, homologous peptides were discovered in the neutrophils of most species examined. These peptides are characterized by the maintenance of a six-cysteine consensus sequence as well as several other highly conserved amino acids.^[2-5] They exhibit antimicrobial activity *in vitro* against bacteria,^[6,7] fungi and enveloped viruses.^[7,8] They are expressed in host defense settings (in phagocytes and epithelia) and display a broad spectrum of antimicrobial activity. The production of many defensins is constitutive, but others are induced by infectious or inflammatory stimuli. Some defensins are chemoattractant for monocytes, lymphocytes, and dendritic cells.

Initial naming of several defensins put emphasis on their tissue of origin, e.g. human neutrophil peptides 1-3 (HNP-1 to HNP-3) also known as human defensins 1-3, macrophage cationic peptides 1 and 2 also known as rabbit defensins 1 and 2, or skin antimicrobial peptide, now known as human β -defensin 2 (HBD-2). Other designations emphasized alternative activity, e.g., corticostatins, so named because of the inhibitory effect of

some defensins on the production of cortisol by adrenal cells.^[7-9] Defensins have a broad-spectrum antimicrobial activity *in vitro* against gram-positive and gram-negative bacteria, yeasts, and fungi and enveloped viruses. Their common mechanism of action is membrane permeabilization followed by interactions with additional as yet undefined intracellular targets. The human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) epidemic is in its third decade and has reached to alarming proportions world-wide. Diagnosis of HIV/AIDS via early testing along with pretest and post-test counseling is important for psychosocial stabilization and destigmatization.^[10]

Between 2011 and 2015, World AIDS Days are held under the theme of "Getting to Zero: Zero New HIV Infections, Zero Discrimination, and Zero AIDS-Related Deaths." In this context, a global vision was developed for all countries; working together toward zeros, but a big question is how we can approach these ambitious targets?^[11] When attacked by HIV, the immune system counteracts infection with elicitation of HIV-specific antibodies and cytotoxic T lymphocytes. In most cases however, these defenses are unable to resolve HIV infection, which progresses if left untreated, ravaging the immune system and leading to AIDS and eventually, to death. β -Defensins are associated with improved clinical status and in some cases, even with protection from infection due to HIV.

β -Defensins are produced by epithelial cells, and thus are important in controlling infection at mucosal sites thereby playing a major role in preventive and therapeutic approaches to combat HIV infection. During past decades, hepatitis C virus (HCV) infection has become the cause of the second major epidemic of viral infection after HIV. So, it is considered as a critical public health problem world-wide. HCV infection can progress to chronic hepatitis, cirrhosis, and hepatocellular carcinoma.^[12] α -Defensin, also known as HNP1, has been shown to have activity against RNA viruses, including HIV and HCV.

Due to their wide variety of functions, human defensins are a promising tool for clinical application. For instance, these molecules could be directly applied on a lesion, in order to work as local antibiotics. Furthermore, their ability to influence and direct the adaptive immune system makes defensins promising immune modulators in systemic anti-inflammatory or anti-cancer treatment. In the treatment of guided tissue repair, defensins might be useful when applied locally after infection is under control, thus helping to overcome the problems of failed wound healing. Finally, their role in carcinogenesis makes them a tremendous target in the diagnosis and therapy of a growing number of cancers involving head and neck, bone, as well as the gastrointestinal and urogenital tracts. Hence, many efforts and researches have recently been made to focus on the pharmaceutical administration and modification of defensins as new leads for clinical therapeutic applications.^[13-16] These remarkable peptides may be a boon for the future treatment modalities.

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