**INTRODUCTION**

Defensins are small cationic antimicrobial peptides involved in innate immunity and highly conserved in vertebrates. In humans, defensins are classified into two subgroups (α and β) based on both unique amino acid sequences and disulfide bonds. α-defensins are mostly expressed by neutrophils and β-defensins are secreted by epithelial cells of the skin and mucosae. Despite their antimicrobial activity against bacteria, viruses, fungi and protozoa, they are modulators of the adaptive immunity. The most studied human β-defensins are HBD1, HBD2 and HBD3 but the predicted peptide sequence is available for all human β-defensins known.

**STRUCTURE**

The different subfamilies of defensins are thought to share a common ancestry. Human α- and β-defensins gene family is in the main locus on chromosome 8p22-23. The tertiary structures of human β-defensins are similar despite low sequence conservation in their amino acids. Their cationic structure is composed of 3 β-strands arranged in an antiparallel sheet stabilized by 3 intramolecular disulfide bonds between 6 cysteine and flanked by an α-helix.

**ANTIMICROBIAL ACTIVITY**

Despite HBD4 has not been isolated in vivo, this peptide exhibits the strongest antimicrobial activity but only at low ionic strength. Moreover, HBD3 has a broad spectrum activity but weaker than HBD4 and it is not inhibit at high salt concentrations. My aim is to modify the HBD4 amino acid sequence mimicking the HBD3 sequence to introduce its features in a synthetic HBD4.

**AIMS**

β-defensins are a rapidly evolving peptide family with low sequence similarity between paralogs. However, some gene regions evolve under positive selection and are directly involved in mature peptide function. According to my aim, I have changed some HBD4 residues subject to positive selection mimicking the HBD3 homologues sites and increasing the net charge of own peptide.

**DESIGN OF PEPTIDES**

![Image](image1.png)

**Figure 1.** β-defensins sequences and properties. Cysteine residues highlighted in red, basic residues in blue and conserved glycine in green.

**Figure 2.** The attachment of peptides is initiated by electrostatic interactions with the negatively charged membranes of pathogens. The hydrophobic residues enable their internalization and pore formation until pathogen is killed by osmotic shock. High salt concentrations inhibit the attachment of β-defensins except HBD3.

**EXPECTED RESULTS**

If the results of antimicrobial assay are good, we can expect an improvement of own peptides functions. The first four peptides possess a α-helix like HBD3 which is responsible of the attachment to pathogens membrane, therefore we could expect a wider spectrum activity. The second group of peptides have a higher number of basic residues which increase the net charge and allegedly their antimicrobial activity and salt concentrations resistance. This assumption is supported by the fact that HBD3 possess the highest net charge value and it is not inhibit at high salt concentrations. Finally, the last group of peptides have been designed to incorporate the previous features into one peptide.

The analysis of the structural and functional characteristics of β-defensins opens the way to the engineering of these peptides with therapeutic applications. This study could show that the rational design of these hybrid peptides is possible.

**REFERENCES**


Figure 2. Rivas-Santiago B, Sada E, Hernández-Pando R, Tsutsumi V. Peptidos antimicrobianos en la inmunidad innata de enfermedades infecciosas. Salut Pública Mèx, 2006.