X-ray Structures of Mixed-chirality α-Helical Antimicrobial Peptides

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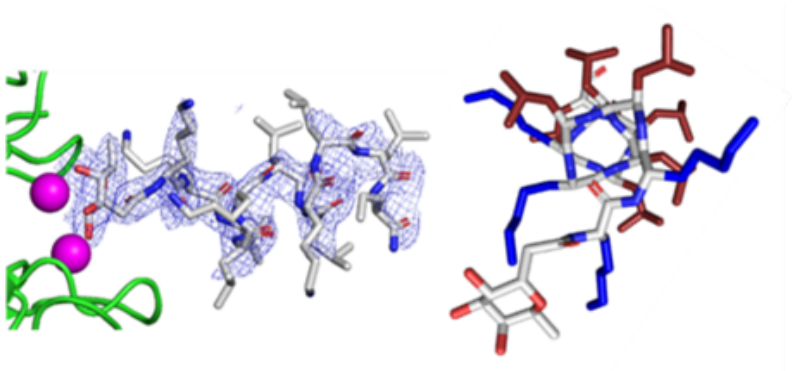
Peptide α-helicity mostly depends on its amino acid sequence and is right or left-handed depending on amino acids chirality (respectively L- or D-). However, mixed-chirality sequences are usually unfolded. In case of antimicrobial peptides (AMPs), an amphiphilic α-helix is generally required to be active and research on mixed chirality AMPs is poorly documented. We recently reported the first X-ray crystal structures of mixed chirality short bicyclic and linear AMPs forming α-helices as complexes of fucosylated analogs with the bacterial lectin LecB (see figure: X-ray structure of lectin-bound fucosylated AMP dln69, KKllKllKlll).[1] Following up the study on our mixed-chirality peptide ln69, we discovered new chirality patterns also presenting α-helical conformation both in membrane-like environment and in aqueous condition determined by X-ray crystallography. Compared to their homochiral parent, these mixed chirality peptides display better stability in human serum, as well as, in selected cases, improved antimicrobial activity.



[1] Stéphane Baeriswyl, Hippolyte Personne, Ivan Di Bonaventura, Thilo Köhler, Christian van Delden, Achim Stocker, Sacha Javor and Jean-Louis Reymond, *RSC Chem. Biol.*, **2021**, 2, 1608-1617