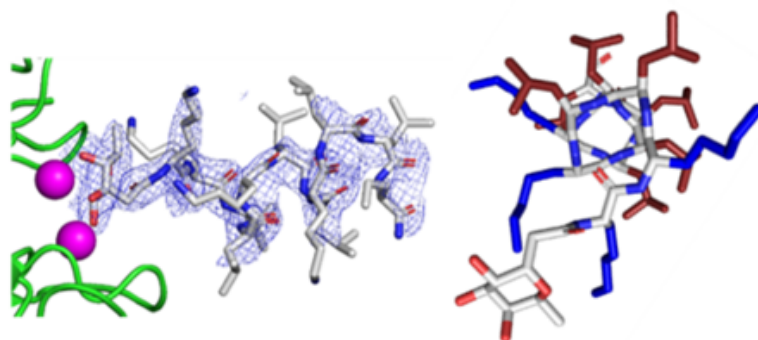


X-ray Structures of Mixed-chirality α -Helical Antimicrobial Peptides

Hippolyte Personne, Achim Stocker, Sacha Javor and Jean-Louis Reymond

Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern, Freiestrasse 3,
3012 Bern, Switzerland
hippolyte.personne@unibe.ch

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 dIn69, KKIIKKIIKKIII).¹ Following up the study on our mixed-chirality peptide In69, 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