Characterization of Alpha-Helix Distortion in an Arginine Containing Peptide Bound at the Membrane Surface

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Introduction

Understanding the principles responsible for the structure, dynamics and function of integral membrane proteins is essential for the enhancement of computer modeling of these properties of protein-lipid systems. Experiments that determine the dynamics, orientation and structural integrity of simple transmembrane peptides within lipid bilayers can be used as benchmarks for validating such computational methods. Here we report recent progress in characterizing the backbone structure of a membrane surface-bound peptide variant based on the GW^{4,20}ALP23 sequence [1] containing a central Arg residue and two opposing terminal Trp residues. Solid-state NMR experiments with mechanically oriented samples containing peptide in biologically relevant lipid bilayers are utilized to determine the location and integrity of the peptide helix.

Experimental

Oriented sample (OS) ^{15}N solid-state NMR experiments were performed at the NHMFL NMR-MRI/S Facility using a 600 MHz 89 mm bore magnet and NHMFL Low-E static probe. Mechanically aligned samples containing residue specific ^{15}N-labeled peptide in lipid bilayers were analyzed using the SAMPI4 pulse sequence.

Results and Discussion

OS solid-state NMR has previously been used with model transmembrane peptides to analyze helix kinking when a central proline is present [2], confirmed by two distinct PISA wheels for the sequences on either side of the proline. Here, a central Arg residue within the GW^{4,20}ALP23 sequence not only brings the peptide to the bilayer surface but also likely induces helical distortion. As shown in **Fig.1**, the N-terminal residues do not fall on the same PISA wheel as the C-terminal residues. Whether or not the N-terminal residues retain a helical conformation or instead unwind remains to be further investigated.

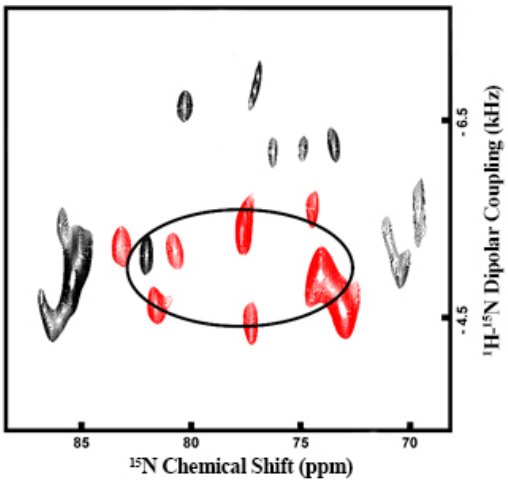

Fig.1 SAMPI4 spectra were obtained with NHMFL WB600 Spectrometer and a NHMFL Low-E Probe. (Red) C-terminal labeled residues. (Black) N-terminal labeled residues. The ellipse shown corresponds to the predicted helical wheel of the C-terminal helix.

Conclusions

Arginine is an important and conserved residue in many transmembrane proteins which carry out essential biological functions. Further experiments are planned to characterize the N-terminal conformation. Understanding the dominance this residue exerts on the structure of a simple transmembrane peptide sequence with NMR experiments such as these will influence computational models of more complex systems.

Acknowledgements

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References

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