Structural Analysis of the C-Terminus of Lung Surfactant Protein B (SP-B)

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Introduction

Pulmonary surfactant (PS) is a surface-active lipid–protein complex that is found in the alveoli of the lungs, and is mainly composed of phospholipids, with the rest being neutral lipids and proteins [1]. Surfactant proteins B and C (SP-B and SP-C) are required as mediators at relatively low concentration to make the transfer of phospholipids through the aqueous hypophase rapid and efficient. In contrast with SP-C, SP-B is absolutely critical for survival and normal respiration.

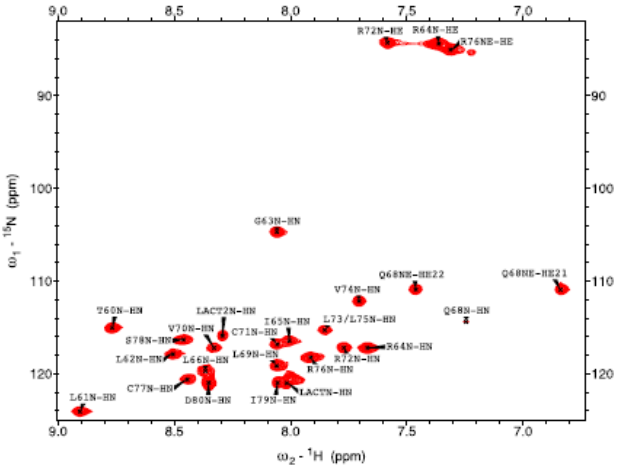
The C-terminal fragment of SP-B, specifically residues 59–80 (SP-$B_{59–80}$), can efficiently transfer phospholipids to air-water interfaces and lower surface tension; *in vivo* studies have demonstrated gain of function in surfactant-deficient fetal rabbits on application of synthetic surfactant-containing SP-B_{59-80} [2]. Despite its vital importance, little is known about the atomic-level structure and dynamics in the lipid environment present in lung surfactant. So hereby, it is our primary interest to probe the structure and dynamics of the C-terminus (SP-$B_{59–80}$) in either detergent micelles or lipid vesicles by means of high resolution as well as solid state NMR.

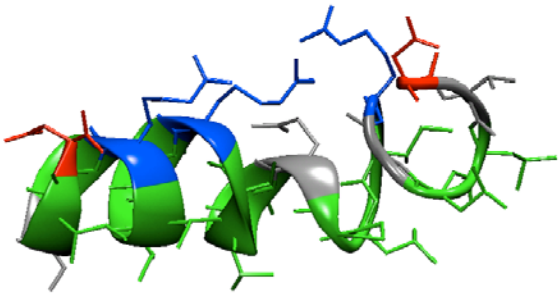
Experimental

Uniformly ^{15}N labeled SP-B_{59-80} was synthesized. Previous CD studies indicate the peptide adopts helical conformation in both methanol and lipid vesicles. In this study, we utilize high resolution NMR to characterize the structure of SP-B_{59-80} reconstituted into detergent micelles, which mimics its native lipid environment with a high curvature. All the NMR data were collected on the 600-cryo or 750 MHz magnets at the AMRIS facility.

Results and Discussion

Shown on the lower left is a ^{15}N HSQC spectrum of SP-B_{59-80}. All the resonances are well spread and isolated. With the full assignment done on various spectra, the structure of this peptide in the detergent micelles has been calculated and is shown on the lower right.





Conclusions

Based on the calculated structures of SP-B_{59-80} in lipid vesicles, and the fact that it's different from the conformation it adopts in methanol, we propose a "rolling" mechanism for how SP-B works as a lipid transporter.

Acknowledgements

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References

[1] Goerke J., Biochim Biophys Acta., **1408**, 79-89 (1998).
[2] Revak, S. D., *et al*., Pediatr Res., **29**:460-465 (1991).