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, 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, our primary interest is 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 NMR.

Experimental

Uniformly ^{15}N labeled SP-B_{59-80} was expressed and purified. 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

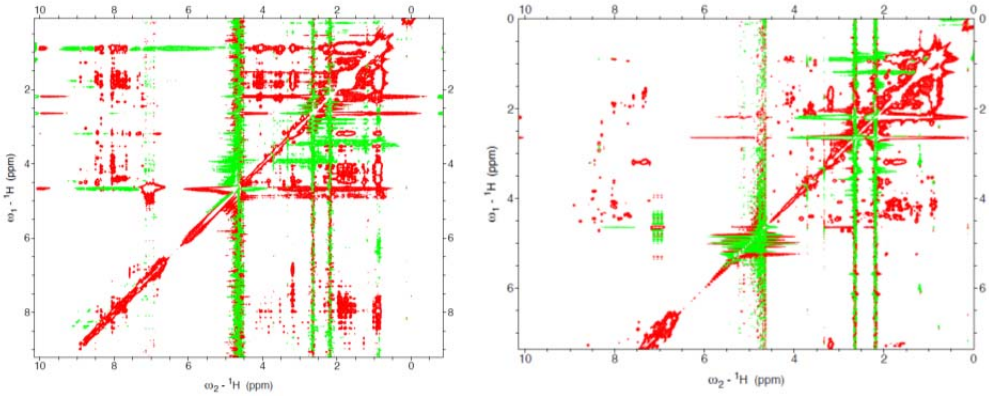

Figure 1 and 2: Shown above are the TOCSY and NOESY spectra of uniformly ^{15}N labeled SP-B_{59-80}. We're currently in the process of assigning resonances.

Conclusions

We have successfully optimized the condition for NMR experiments. By finishing the assignment, we'll gain more insights into the conformational changes of SPBC in different environments, hence, leading us to a better understanding of how SPBC traffics lipids in its native environment.

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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).