Delineation of the Dynamic Properties of Individual Lipid Species in Native and Synthetic Pulmonary Surfactants

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Introduction

Pulmonary surfactant (PS) is characterized by a highly conserved lipid composition and the formation of unique multilamellar structures within the lung. An unusually high concentration of DPPC is a hallmark of PS and is critical to the formation of a high surface area, stable air/water interface; the unusual lipid polymorphisms observed in PS are dependent on surfactant proteins, particularly lung surfactant protein B (SP-B). The molecular mechanisms of lipid trafficking and assembly in PS remain largely uncharacterized.

Experimental

Using ^{2}H and ^{31}P NMR, we characterize the dynamics and polymorphisms of the major lipid species in native PS and synthetic lipid mixtures as a function of SP-B_{1-25} addition.

Results and Discussion

Our findings point to increased dynamics and a departure from a lamellar behavior for DPPC on addition of the peptide, consistent with our observations of DPPC phase separation in native surfactant. The monounsaturated lipids POPC, POPG and POPE remain in a lamellar phase and are less affected than DPPC by surfactant peptide addition. Additionally, we demonstrate that the properties of a native PS can be successfully mimicked using a fully synthetic lipid mixture allowing the efficient evaluation of peptidomimetics under development for PS replacement therapies via NMR spectroscopy. The specificity of the dynamic changes in DPPC relative to POPC suggests the importance of tuning partitioning properties in successful peptidomimetic design.

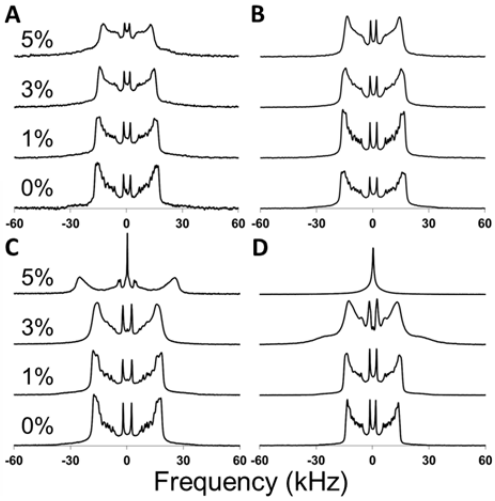

Figure 1. A comparison of the effects of SP-B_{1-25} addition on DPPC dynamics at 38 ºC in A) native CLSE lipids, B) a synthetic lipid mixture mimicking CLSE, C) 8:2:1 DPPC/POPG/Chol, and D) 4:1 DPPC/POPG. A clear change in DPPC dynamics with peptide addition is seen in all the lipid environments; it first appears as broadening in the lamellar lineshapes leading to a loss of resolution for the individual deuterated acyl chain positions and culminates in an isotropic lineshape in the simpler lipid mixtures.

Conclusions

The specificity of the dynamic changes in DPPC relative to POPC suggests the importance of tuning partitioning properties in successful peptidomimetic design.

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References

[1] Farver, S. et al., Biochimica et Biophysica Acta - Biomembranes, **1848** (1B), 203–210 (2015)