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## **(POS-43) Molecular Dynamics Simulation of Lung Surfactant Protein SP-B fragments in model bilayers**

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In lungs, a lipid-protein surfactant layer enables breathing by reducing surface tension at the air-water interface. Lung surfactant function requires cycling of material between bilayer reservoirs and an active surfactant layer, presumably involving transient formation of highly curved lipid structures. Surfactant protein SP-B, a 79-residue protein that forms homodimers, is essential for lung function. To study how lipid-SP-B interactions might contribute to implied lipid assembly reorganization, GROMACS molecular dynamics simulations were used to study conformation and orientation of SP-B fragments SP-B<sub>1-9</sub> and SP-B<sub>1-25</sub> in DPPC/POPG (7:3) model lipid bilayers. SP-B<sub>1-9</sub> includes SP-B's initial 7-residue insertion sequence. SP-B<sub>1-25</sub> also includes the first of SP-B's four amphipathic helices. To obtain averages and test for protein-induced bilayer perturbation, each simulation involved multiple copies of each fragment (18 SP-B<sub>1-9</sub> or 9 SP-B<sub>1-25</sub> copies per bilayer leaflet). Simulations were also run with no peptide and with only one copy of SP-B<sub>1-9</sub> per leaflet. The simulation with multiple copies of SP-B<sub>1-9</sub> started with randomly oriented peptides inserted in the lipid bilayer and ran for 450 ns. SP-B<sub>1-25</sub> simulations started with (i) randomly oriented peptides, (ii) peptides oriented along the bilayer surfaces, and (iii) peptides inserted across the bilayer (trans). On average, SP-B<sub>1-9</sub> was found to tilt only slightly into the bilayer with its N-terminal phenylalanine staying within about 0.75 nm of the bilayer phosphate layer. Comprising the insertion sequence plus first SP-B helix, SP-B<sub>1-25</sub> tended to remain in the trans-bilayer orientation when started in that orientation. If started roughly parallel to the bilayer surface, SP-B<sub>1-25</sub> tended to settle into non-trans orientations but with excursions toward the trans configuration. When starting from random peptide orientations, SP-B<sub>1-25</sub> largely settled into a mixture of trans and surface orientations. SP-B<sub>1-25</sub> is nearly the first third of the SP-B monomer. Its capacity to be accommodated in both trans-bilayer and single-leaflet environments may reflect SP-B's role in promoting lipid assembly reorganization implied by the cycling between bilayer reservoir and surface-active layer structures. Supported by NSERC, ACENet, and Digital Research Alliance of Canada.

### **Keyword-1**

Lipid-protein interaction

### **Keyword-2**

Lung surfactant

### **Keyword-3**

Molecular Dynamics Simulation

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