

Improving the Biophysical Activity of Dysfunctional Lung Surfactant

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INTRODUCTION

Lung surfactant enables respiration by lowering the surface tension within the lungs to near-zero levels. Dysfunctional lung surfactant results in high surface tensions which makes breathing difficult and can lead to alveolar collapse.

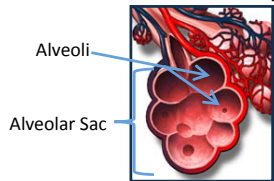
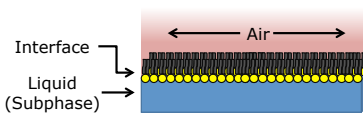


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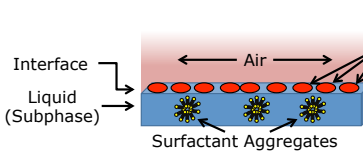
Acute Respiratory Distress Syndrome (ARDS) results from a lung injury and is characterized by a lung surfactant dysfunction. In the United States alone, 150,000 cases of ARDS are diagnosed each year; 40% of the patients do not survive¹. Our research focuses on studying the underlying mechanisms behind the surfactant dysfunction seen during ARDS.

Normal Interfacial Behavior of Lung Surfactant (Healthy Lung)



Lung surfactant occurs in the alveoli and occupies the interface between the air and the thin layer of liquid that lines the alveolar walls.

Competitive Adsorption by Albumin (Dysfunctional Lung)



Albumin is a protein found in blood serum that flows into the lungs after injury. It occupies the air-liquid interface and prevents lung surfactant from properly adsorbing.

EXPERIMENTAL TECHNIQUES

The Langmuir trough mimics the normal expansion and contraction of the alveoli through moveable metal barriers. Surface pressure and temperature are measured at the interface.

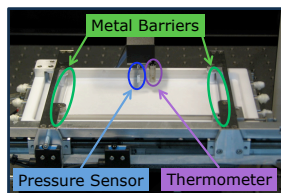


Image: http://aboutnutrition.com/images/en-115/brands/survanta/brand_survanta.jpg

Survanta, a clinical therapy for premature babies, acts as our model lung surfactant.

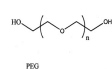
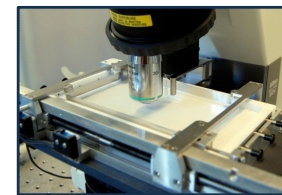


Image: http://web.mit.edu/3.082/www/team2_s02/PEG.jpg

Previous experiments in our lab have shown that polyethylene glycol (PEG) reverses albumin's inhibition of Survanta².

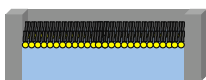
Confocal microscopy enables us to simultaneously view and track our fluorescently dyed albumin and Survanta.



It also allows us to take thin image slices so we can focus on interfacial behavior.

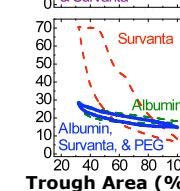
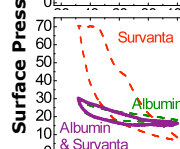
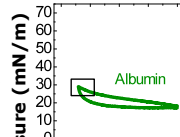
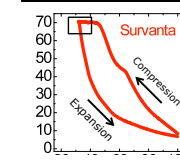
RESULTS

Healthy Lung

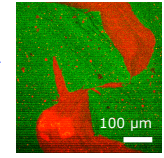
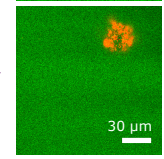
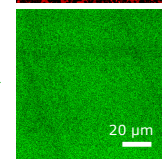
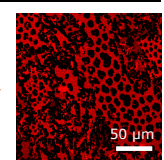


Characteristic Survanta Curve
Healthy lung surfactant (Survanta) enables us to breathe by reaching surface pressures near 70 mN/m upon compression; this corresponds to a surface tension near zero (see boxed area).

Langmuir Trough Isotherms at 25°C



Interfacial Confocal Microscope Images



Albumin Only

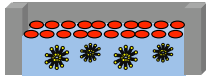


Characteristic Albumin Curve
Albumin alone would make normal respiration impossible because it does not reach sufficiently high surface pressures (boxed area).

Characteristic Survanta Structure

Characteristic Albumin Structure

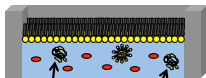
ARDS



Albumin Inhibition of Survanta
Albumin appears to dominate the interface when present with Survanta because the isotherm matches that of the characteristic albumin curve.

An albumin dominated interface with a Survanta aggregate that is blocked from adsorbing.

Inhibition Reversal



Unsuccessful Reversal by PEG
Curve was expected to match that of Survanta. In our experiment, PEG did not reverse albumin's inhibition of Survanta, as evidenced by the shape of the isotherm.

An albumin dominated interface with regions of Survanta that have adsorbed to, but not spread over, the interface.

CONCLUSIONS

1. Albumin clearly inhibits Survanta (healthy lung surfactant), and can therefore provide a model of the inhibition seen during ARDS.
2. Our inhibition reversal model, which has been successful in previous experiments, was unsuccessful here. We suspect this may be due to the batch-to-batch variability of Survanta.
4. PEG helped Survanta adsorb to an albumin-covered interface, but the Survanta failed to spread.



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References

1. R. H. Notter, Ed., *Lung Surfactants: Basic Science and Clinical Applications*, vol. 149 (Marcel Dekker, Inc., New York, N.Y., ed. 1, 2000), pp. 444.
2. P. C. Stenger, J. A. Zasadzinski, *Biophysical Journal* **92**, 3 (Jan, 2007).