

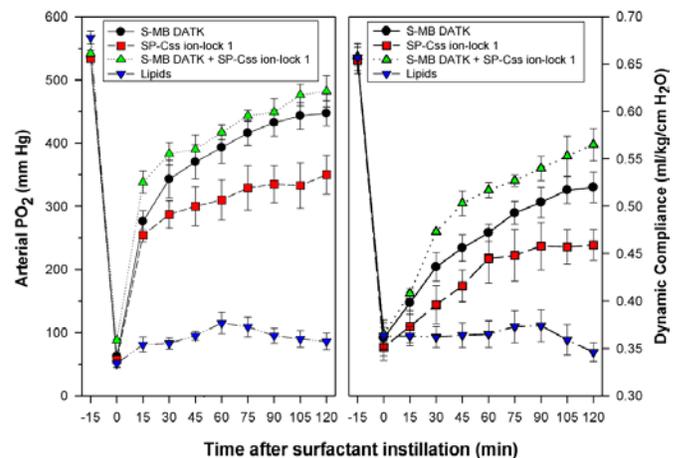
# Fully Synthetic Phospholipase-Resistant Lung Surfactant to Treat Surfactant-Deficient Lung Tissue [LAB0132]

## Background

- The airsacs in mammalian lungs are stabilized by pulmonary surfactant, a complex mixture containing glycerophospholipids and specific surfactant proteins.
- A deficiency or dysfunction of pulmonary surfactant is associated with severe respiratory conditions, such as neonatal respiratory distress syndrome (NRDS), and can lead to death.
- NRDS affects about 1% of pregnancies, or approximately 30,000 infants per year.
- The administration of animal-derived surfactants greatly reduces morbidity and mortality.
- However, compared to animal-derived surfactants, fully-synthetic surfactants have significant advantages in purity, reproducibility, consistency of activity, and manufacturing economy. In addition, synthetic surfactants can be synthesized to incorporate special molecular properties such as resistance to degradation by phospholipases.
- Synthetic, exogenous surfactants with high surface activity and resistance to degradation would greatly reduce the fatal outcomes associated with respiratory conditions involving surfactant deficiency, especially in neonates.

## Innovation

- Dr. Franz Walther and his team have developed a fully synthetic lung surfactant to treat surfactant deficiency and associated conditions, such as NRDS.
- The surfactant comprises synthetic analogs of surfactant proteins SP-B and/or SP-C and a phospholipase-resistant phospholipid.
- The two core surfactant proteins drive the reduction in alveolar surface tension at the monolayer covering the alveolar epithelium.
- The SP-B mimic Super Mini-B (SMB) shows excellent surface activity as a single peptide in various lipid mixtures.
- SP-C mimic (SP-Css\_ion-locks) stimulates the structural and functional properties of the native SP-C.
- The combination of SMB and SP-Css\_ion-locks, outperforms clinical, animal-derived lung surfactant in animals with surfactant deficiency.
- The lung surfactant is aerosolizable, simplifying delivery to collapsed lungs and lowering maintenance cost.
- *In vivo* studies have been completed in rats and rabbits.



Synthetic surfactants were administered to ventilated rats with ARDS by intratracheal instillation. Single-peptide surfactant (S-MB DATK, an analog of human SP-B) significantly improved both arterial oxygenation and dynamic lung compliance. Two-peptide surfactant (S-MB DATK + SP-Css ion-lock 1, an analog of human SP-C) showed even greater improvement in Arterial PO<sub>2</sub> and dynamic compliance than single-peptide surfactant.

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## Advantages

- Improved purity, reproducibility, consistency of activity, and manufacturing economy compared to animal-derived surfactants
- Greater stability and resistance to degradation than animal-derived surfactants
- Outperforms animal-derived surfactants
- Can be aerosolized for improved delivery

## Applications

- Synthetic lung surfactant to treat premature babies with NRDS
- Synthetic lung surfactant to treat patients with collapsed lungs from sepsis, inhalation of harmful substances, severe pneumonia, or major injuries to the chest

**Lead Inventor:** Franz Walther, MD, PhD

## IP Status

- U.S. Patent No. 7,538,090 titled “Exogenous Surfactant Protein B Mimic” issued May 26, 2009
- U.S. Patent No. 9,815,869 titled “Novel SP-B & SP-C peptides, Synthetic Lung Surfactants, and Use Thereof” issued November 14, 2017
- U.S. Patent No. 10,358,465 titled “Novel SP-B & SP-C peptides, Synthetic Lung Surfactants, and Use Thereof” issued July 23, 2019
- European Patent No. 2812018 titled “Novel SP-B & SP-C peptides, Synthetic Lung Surfactants, and Use Thereof” nationalized in Germany, France, UK and issued December 5, 2018
- European Patent Application No. 18203081.7 titled “Synthetic Analogs of Lung Surfactant Proteins SP-C and Their Use” filed Dec. 29, 2018 – pending

## Related Publications

- Notter RH, Gupta R, Schwan AL, Wang Z, Shkooor MG, Walther FJ. Synthetic lung surfactants containing SP-B and SP-C peptides plus novel phospholipase-resistant lipids or glycerophospholipids. PeerJ. 2016;4:e2635.
- Walther FJ, Hernández-juviel JM, Gordon LM, Waring AJ. Synthetic surfactant containing SP-B and SP-C mimics is superior to single-peptide formulations in rabbits with chemical acute lung injury. PeerJ. 2014;2:e393.
- Walther FJ, Waring AJ, Hernandez-juviel JM, et al. Dynamic surface activity of a fully synthetic phospholipase-resistant lipid/peptide lung surfactant. PLoS ONE. 2007;2(10):e1039.