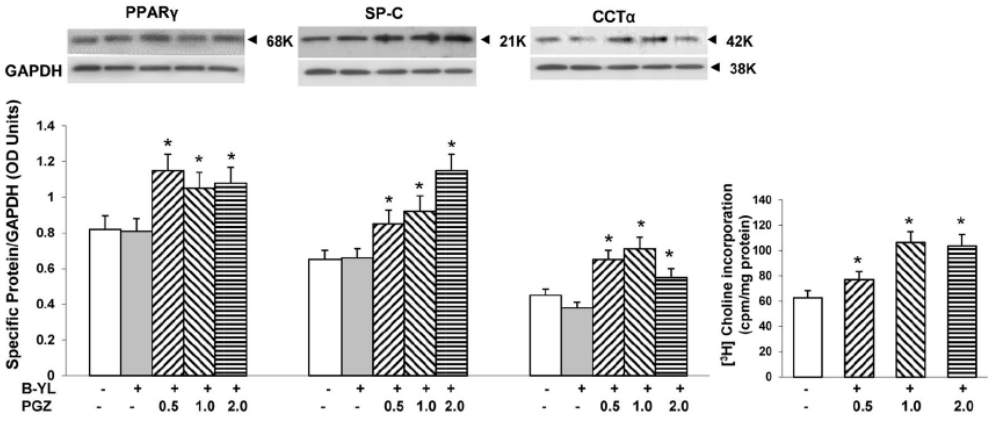
Synthetic Lung Surfactant for the Prevention of Neonatal Lung Injury
[LAB0163]

Background

- The World Health Organization estimates that 15 million babies are born preterm every year.
- Production of endogenous lung surfactant typically begins after 32 weeks of gestation. As such, premature infants born around or before 32 weeks often lack the ability to produce sufficient surfactant and may develop respiratory conditions, including respiratory distress syndrome (RDS), which results directly from the lack of surfactant.
- Infants who do not adequately recover from RDS can develop bronchopulmonary dysplasia (BPD), which results from hyperoxia.
- The current standard of care calls for the administration of exogenous animal-derived surfactant during oxygen therapy. While surfactant is effective in treating RDS, it has not been shown to be effective in reducing BPD.
- BPD can cause long-term breathing difficulties, chronic lung disease, and other related conditions as the affected infants grow older.
- A treatment that addresses both RDS and BPD would greatly benefit neonates that suffer from insufficient surfactant production and hyperoxia.

Innovation

- Drs. Frans Walther and Virender Rehan have developed a new synthetic lung surfactant to treat the symptoms and disorders associated with both insufficient surfactant production and hyperoxia in neonates.
- The composition comprises the Peroxisome Proliferator-Activated Receptor gamma (PPARγ) agonist pioglitazone (PGZ), the synthetic surfactant peptide B-YL, and one or more phospholipids. Treatment with this mixture at early stages of RDS can prevent both acute and chronic lung injury in very premature infants.
- The treatment can be formulated for aerosol delivery during ventilation therapy.
- *In vivo* experiments have been completed in rats. PGZ attenuates lung injury in neonatal rats and promotes lung maturation, while B-YL reduces RDS.



Lung explants from fetal rats subjected to hyperoxia were cultured with B-YL and PGZ. Explants cultured with both molecules had significantly increased levels of PPARγ, SP-C, CCTα, and choline incorporation, which are all markers of lung maturation and/or injury repair.

Advantage

- Multipronged treatment for premature infants who lack sufficient lung surfactant
  - Surfactant peptides and phospholipids address surfactant insufficiency and RDS
  - PPARγ agonists promote lung development, maturation, and also reduce hyperoxia-induced lung injury and BPD

For partnering opportunities and collaborations:
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Applications

- Dual approach that reduces RDS and prevents BPD in neonates with immature lungs
- Can also be developed to treat acute lung injury/acute respiratory distress syndrome (ALI/ARDS) in children and adults

Lead Inventors: Frans Walther, MD, PhD & Virender Rehan, MD

IP Status

- PCT Application No. PCT/US2017/020881 filed on March 6, 2017
    - National Stage CA 3,016,810 – pending
    - National Stage EP 177639818.6 – pending
    - National Stage HK 19129661.5 – pending
    - National Stage US 11,179,446 – issued on November 23, 2021

Related Publications

- Sakurai R, Lee C, Shen H, Waring AJ, Walther FJ, Rehan VK. A Combination of the Aerosolized PPAR-γ Agonist Pioglitazone and a Synthetic Surfactant Protein B Peptide Mimic Prevents Hyperoxia-Induced Neonatal Lung Injury in Rats. Neonatology. 2018;113(4):296-304.

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