Docket #: S21-426

Inhibition of Syt2 by PEN-SP9 to Prevent Airway Mucus Obstruction

Stanford inventors have engineered a therapy (PEN-SP9) that blocks rapid mucin secretion without impairing lung health. Common lung diseases, such as asthma, COPD, cystic fibrosis, and bronchiectasis are exacerbated by mucin hypersecretion and subsequent formation of airway mucin plaques. PEN-SP9 is a cell-penetrating peptide conjugated to a functional stapled peptide that blocks interactions between Syt2 and SNARE in airway epithelial cells to prevent rapid mucin secretion. Aerosolized delivery of PEN-SP9 enabled substantial peptide uptake in the distal airway epithelial cells and decreased airway mucus occlusion in mouse models, demonstrating that the therapeutic may be promising for treating acute and chronic mucin occlusion.

Stage of Development
The invention decreases rapid secretion of mucins without adverse side effects in mouse in vivo models.

Applications

- May prevent death caused by acute airflow obstruction
- Could prevent mucus plaque formation in patients with chronic airway obstruction

Advantages

- Currently no therapies exist to treat airway dysfunction caused by rapid mucin secretion

Publications

- Lai Y, Fois G, Flores JR, Tuvim MJ, Zhou Q, Yang K, Leitz J, Peters J, Zhang Y, Pfuetzner RA, Esquivies L, Jones P, Frick M, Dickey BF, Brunger AT. 2022. Inhibition of calcium-triggered secretion by hydrocarbon-stapled peptides. Nature 603:949–956.
- Y.Lai, M.J.Tuvim, J.Leitz, J.Peters, R.A.Pfuetzner, L.Esquivies, Q.Zhou, B.Czako, J.B.Cross, P.Jones, B.F.Dickey, A.T.Brunger. Screening of hydrocarbon-stapled peptides for inhibition of calcium-triggered exocytosis. Preprint in bioRxiv (2022).

Patents

- Published Application: WO2023159137
- Published Application: 20250163122

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