THREE LAKES
FOUNDATION

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Key Journal Publishes a Study Focused on Delivering Drugs Directly to Cells

CHICAGO, October 28, 2020 — The Science Translational Medicine has recently published a groundbreaking study which describes the potential to deliver drugs directly to cells that develop to idiopathic Pulmonary Fibrosis. The interdisciplinary journal covers basic, translational, and clinical research on human diseases.

The study was led by Philip S. Low, et al, and was funded by Three Lakes Foundation, a nonprofit dedicated to improving time to diagnosis and accelerating therapies for pulmonary fibrosis (PF).

“Targeted inhibition of PI3 kinase/mTOR specifically in fibrotic lung fibroblasts suppresses pulmonary fibrosis in experimental models” was published in the October issue of the journal. Results of this study may lead to accelerating new therapies for this devastating lung disease.

Article Abstract:

Idiopathic pulmonary fibrosis (IPF) is a lethal disease with an average life expectancy of 3 to 5 years. IPF is characterized by progressive stiffening of the lung parenchyma due to excessive deposition of collagen, leading to gradual failure of gas exchange. Although two therapeutic agents have been approved from the FDA for IPF, they only slow disease progression with little impact on outcome. To develop a more effective therapy, we have exploited the fact that collagen-producing myofibroblasts express a membrane-spanning protein, fibroblast activation protein (FAP), that exhibits limited if

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any expression on other cell types. Because collagen-producing myofibroblasts are only found in fibrotic tissues, solid tumors, and healing wounds, FAP constitutes an excellent marker for targeted delivery of drugs to tissues undergoing pathologic fibrosis. We demonstrate here that a low–molecular weight FAP ligand can be used to deliver imaging and therapeutic agents selectively to FAP-expressing cells. Because induction of collagen synthesis is associated with phosphatidylinositol 3-kinase (PI3K) activation, we designed a FAP-targeted PI3K inhibitor that selectively targets FAP-expressing human IPF lung fibroblasts and potently inhibited collagen synthesis. Moreover, we showed that administration of the inhibitor in a mouse model of IPF inhibited PI3K activation in fibrotic lungs, suppressed production of hydroxyproline (major building block of collagen), reduced collagen deposition, and increased mouse survival. Collectively, these studies suggest that a FAP-targeted PI3K inhibitor might be promising for treating IPF.

To obtain a copy of the article, visit: https://bit.ly/34Gu1xf

About Three Lakes Foundation

Three Lakes Foundation (TLF) is a nonprofit organization focused on uniting researchers, industries and philanthropy in pulmonary fibrosis. We connect entrepreneurs, advocates and institutions to an innovation ecosystem that will transform our approach to improve time to diagnosis and accelerate new therapies. To learn more, visit **threelakesfoundation.org**.

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