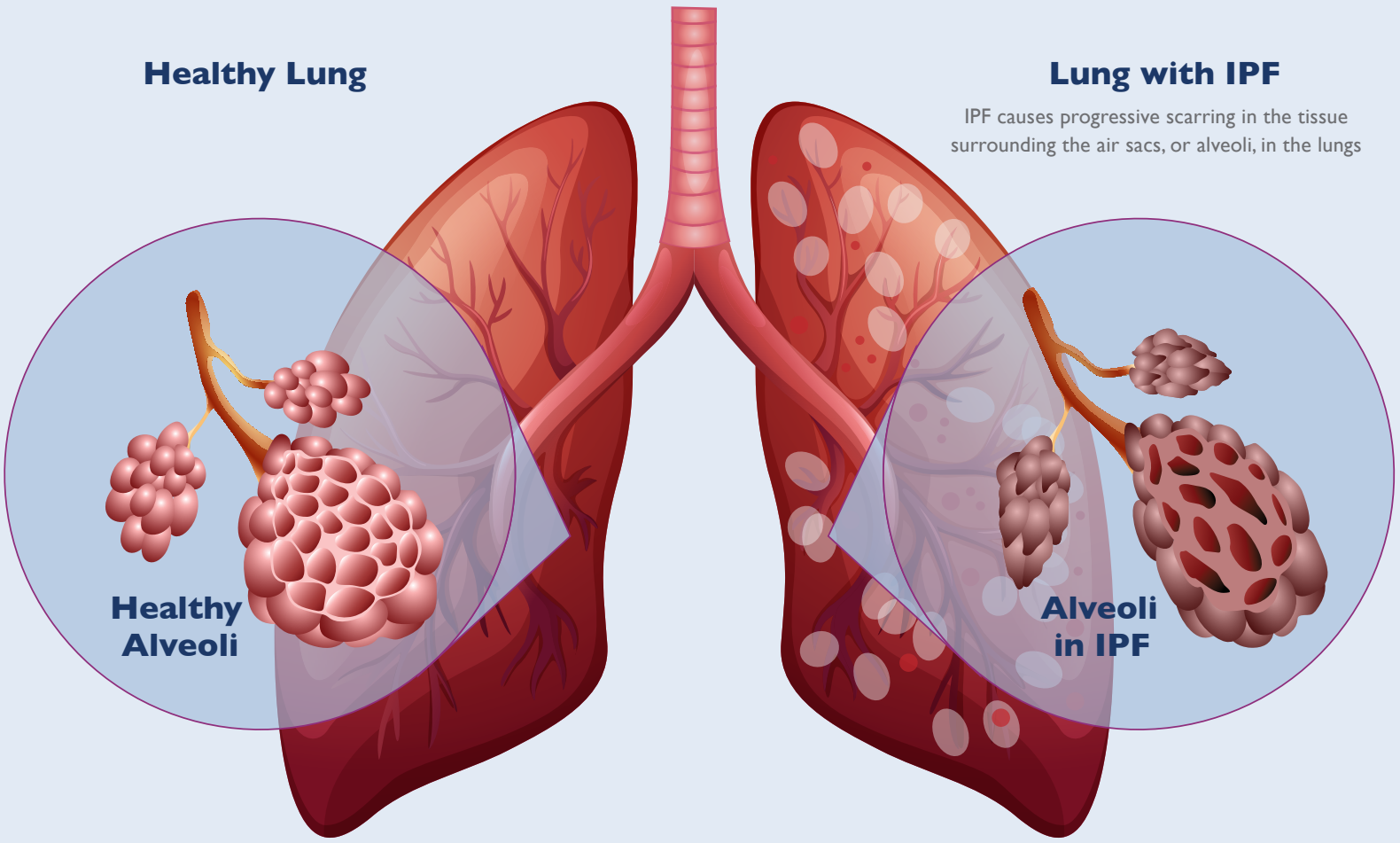
Lysophosphatidic acid (LPA) in IPF

What is IPF?

Pulmonary fibrosis (PF) is one of 200 interstitial lung diseases that cause scarring (fibrosis) in the lungs.[1] The most common type of PF is idiopathic pulmonary fibrosis (IPF). Unlike other forms of PF that can be caused by immune-mediated diseases or the use of certain medications, the cause of IPF is unknown.[1]

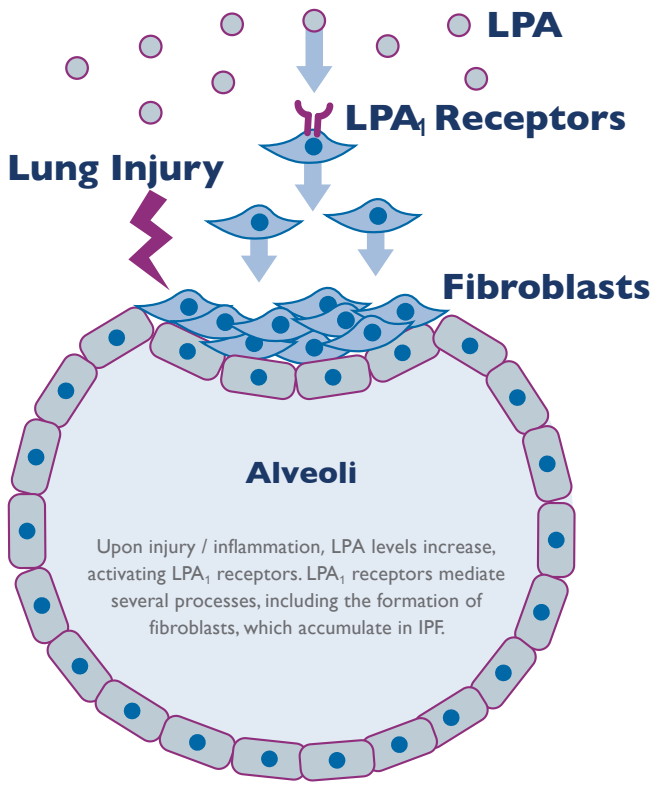
IPF causes lung tissue to become thickened, scarred and stiff, leading to lung damage and severe breathing difficulties.[2] IPF is difficult to diagnose, associated with a poor prognosis and has limited treatment options that can only slow disease progression.[3]

Researchers are working to develop a deeper understanding of IPF pathophysiology in order to develop innovative therapeutics that can halt or reverse lung fibrosis.



Identifying the Culprits of Fibrosis

- Several biological targets have been implicated in the development of fibrosis in IPF, including lysophosphatidic acid (LPA).[4]
- LPA production is stimulated in response to lung cell injury, and can activate several receptors, including LPA_1.[5]
- LPA_1 receptor activation promotes pro-fibrotic processes, including the generation and accumulation of fibroblasts.[5]
- Levels of LPA are elevated in the lungs of individuals with IPF.[6]
- Preclinical studies antagonizing – or blocking – LPA_1 receptors report reduced pulmonary fibrosis development, establishing the potential of LPA_1 receptors as a clinical target for IPF.[7]



Research Implications

- Therapeutics that block the LPA_1 receptor have the potential to address the altered fibrotic processes observed in IPF.

Bristol-Myers Squibb is currently investigating a LPA_1 receptor antagonist for the treatment of IPF. Learn more about our work in fibrosis by visiting:

www.bms.com/researchers-and-partners/areas-of-focus.html

[1]American Lung Association. "Pulmonary Fibrosis" https://www.lung.org/lung-health-and-diseases/lung-disease-lookup/pulmonary-fibrosis/introduction/types-causes-and-risk-factors.html [2]National Heart, Lung, and Blood Institute. "Idiopathic Pulmonary Fibrosis" https://www.nhlbi.nih.gov/health-topics/idiopathic-pulmonary-fibrosis [3]Fujimoto H, Kobayashi T, & Azuma A. "Idiopathic pulmonary fibrosis: treatment and prognosis." Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine. 2015; 9: CCRPM-S23321. https://journals.sagepub.com/doi/full/10.4137/CCRPM.S23321 [4]Ahluwalia N., Shea B. S., & Tager, A. M. "New therapeutic targets in idiopathic pulmonary fibrosis. Aiming to rein in runaway wound-healing responses." American journal of respiratory and critical care medicine. 2014; 190(8), 867-878. https://www.atsjournals.org/doi/full/10.1164/rccm.201403-0509PP [5]Shea B. S., & Tager A. M. (2012). "Role of the lysophospholipid mediators lysophosphatidic acid and sphingosine 1-phosphate in lung fibrosis." Proceedings of the American Thoracic Society. 2012; 9(3); 102-110. [6]Tager A.M. et. al. "The lysophosphatidic acid receptor LPA 1 links pulmonary fibrosis to lung injury by mediating fibroblast recruitment and vascular leak." Nature medicine. 2008; 14(1); 45. https://www.ncbi.nlm.nih.gov/pubmed/?term=The+lysophosphatidic+acid+receptor+LPA1+links+pulmonary+fibrosis+to+lung+injury+by+mediating+fibroblast+recruitment+and+vascular+leak [7]Swaney, J.S. et. al. "A novel, orally active LPA1 receptor antagonist inhibits lung fibrosis in the mouse bleomycin model." British journal of pharmacology. 2010; 160.7: 1699-1713.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2936842/

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