# Researchers identify protein connected to aging and idiopathic pulmonary fibrosis

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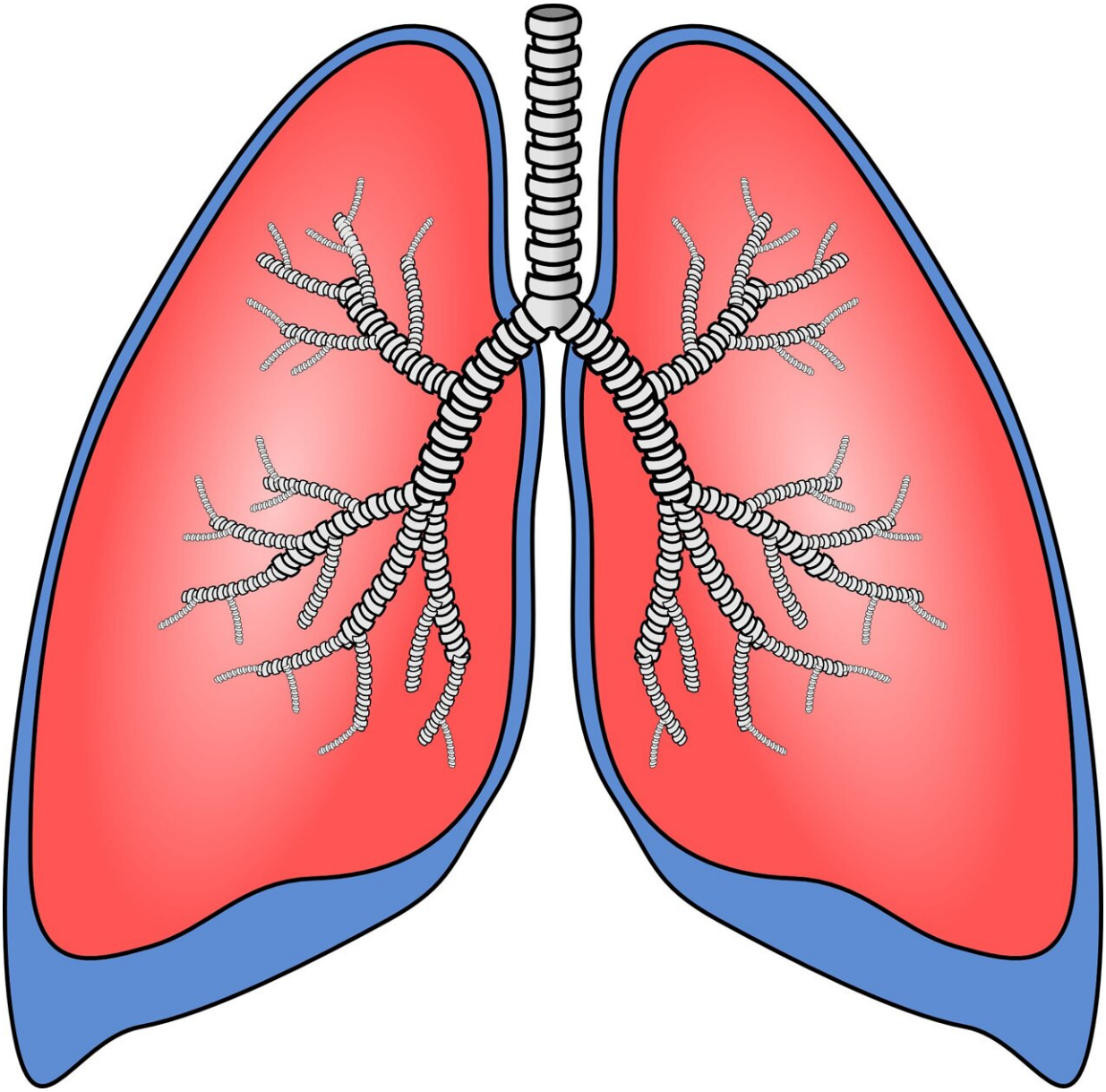

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Idiopathic pulmonary fibrosis (IPF) is an aging-associated disease caused by progressive scarring of the lungs, leading to respiratory failure and death. Therapies to treat IPF are limited, making studies on the mechanisms responsible for this crippling disease a priority. Now for the first time, researchers at the Arthritis and Autoimmune Diseases Center (AADC) at Boston University School of Medicine (BUSM) in collaboration with those at Mayo Clinic, Rochester, Minn., have discovered a new mechanism linking the aging of blood vessels to the development of pulmonary fibrosis.

More specifically, they found that ERG, a protein that normally controls the regenerative properties of endothelial cells (the inner lining of blood vessels), is implicated in the progression of IPF, an aging-associated disease that causes progressive scarring of the lungs, respiratory failure and death.

"Although the lungs of IPF patients manifest multiple vascular abnormalities, the contribution of these alterations to the progression of IPF has remained largely unexplored. "Our findings demonstrated the impact of the aged lung vasculature on the pathogenesis of IPF," said corresponding author Giovanni Ligresti, Ph.D., associate professor of medicine at BUSM. "This work is also relevant to other fibrotic disorders, including lung fibrosis associated with scleroderma," said BUSM professor of medicine Maria Trojanowska, Ph.D., director of the AADC and collaborator of this study.

The researchers used experimental models of pulmonary fibrosis, human lung cells and lung tissues from human patients with IPF to investigate how aging-associated dysfunction of the pulmonary vasculature

contributes to the progression of IPF.

In addition, they created a new experimental model in which the gene ERG was depleted from blood vessels. "Upon lung injury, models with deleted ERG were no longer able to properly repair from the injury resulting in progressive lung scarring as observed in aged mice, as well as in patients with IPF. Furthermore, even in absence of injury, models without ERG exhibited features of advanced aging, including increased inflammation and an enhanced predisposition to develop chronic conditions, which are typically observed in elderly," explained Ligresti.

According to the researchers, given that many chronic diseases in elderly are characterized by dysfunctional blood vessels, targeting molecular mechanisms that can promote blood vessel regeneration, such as ERG, will be beneficial in multiple organs besides lungs. "These findings may also have important implications in elderly patients with COVID-19, in which vascular abnormalities and elevated vascular inflammation are often responsible for disease exacerbation and death," adds Ligresti.

These findings appear online in the journal *Nature Communications*.

**More information:** Nunzia Caporarello et al, Dysfunctional ERG signaling drives pulmonary vascular aging and persistent fibrosis, *Nature Communications* (2022). DOI: 10.1038/s41467-022-31890-4

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