Potential new treatment combats COPD and other lung diseases

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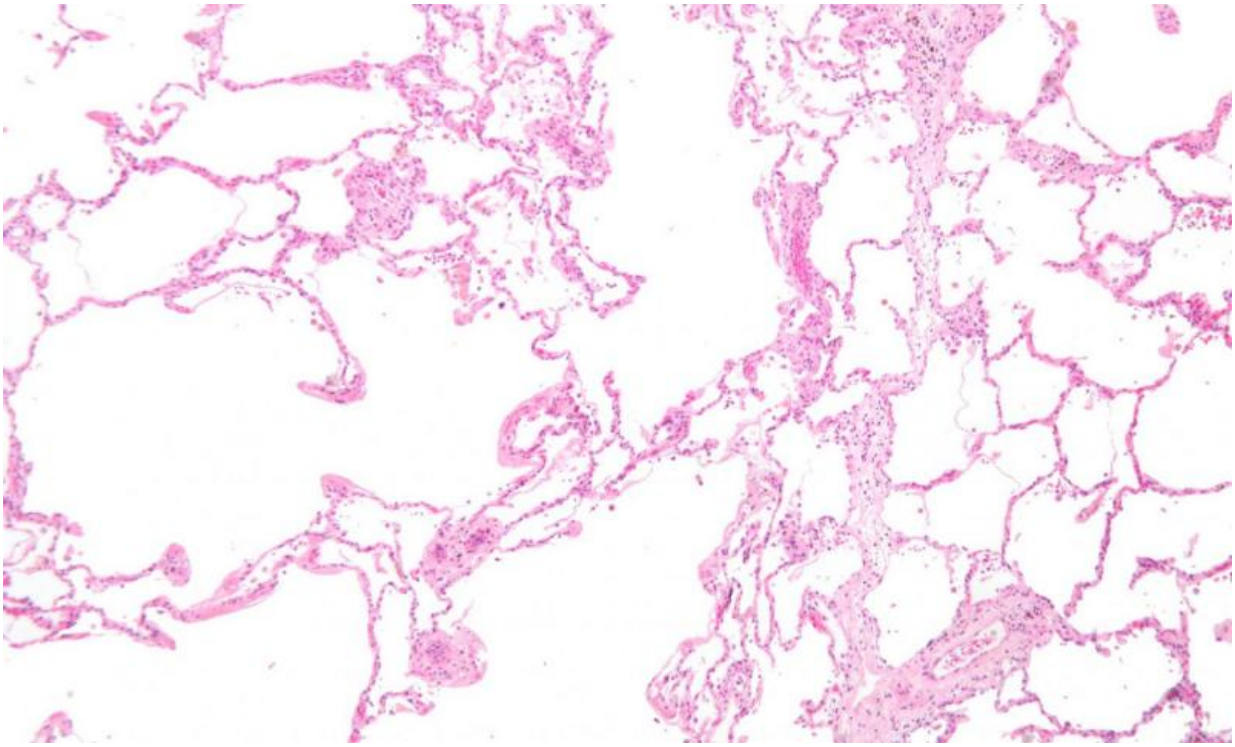

Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

New research published online in *The FASEB Journal* reveals a potential drug to combat the life-threatening effects of chronic obstructive pulmonary disease (COPD). Specifically, the study investigated the efficacy of a receptor for advanced glycan end-products

(RAGE)-specific antagonist chemical compound, FPS-ZM1, in mice, and found that this compound reverses the inflammatory response and has a protective role in COPD.

"RAGE disturbances in pulmonary disorders are precise and effective strategies with beneficial clinical effects," said Se-Ran Yang, D.V.M., Ph.D., a researcher involved in the work and an associate professor at the Department of Thoracic and Cardiovascular Surgery in the School of Medicine at Kangwon National University in Gangwon, Korea. "Blockade of RAGE as a novel clinical therapeutic for COPD ameliorates emphysema/COPD development and progression."

In their study, Yang and colleagues investigated the efficacy of RAGE-specific antagonist FPS-ZM1 administration in both in vivo and in vitro COPD models to determine the molecular mechanism by which RAGE influences COPD. The researchers injected mice with an in vivo COPD inducer and the RAGE antagonist FPS-ZM1. Then they assessed the infiltrated inflammatory cells and their production of cytokines. Cellular expression of RAGE, initiating inflammatory response, and soluble RAGE, acting as a "decoy," was determined in protein, serum, and bronchoalveolar lavage fluid in the mice, as well as in the serum of human donors and patients with COPD. They analyzed downstream damage-associated molecular patterns (DAMPs) and danger signals in vivo and in vitro and in patients with COPD, and found that RAGE was associated with the up-regulation of DAMP-related signaling pathways via Nrf2 (a master regulator of the total antioxidant system in humans). FPS-ZM1 administration also significantly reversed emphysematous lung symptoms in mice.

"No one expected the pathogenic roots of COPD to be simple, and this study gives us an indication of the complexity involved.," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*. "The current pharmacological armamentarium is limited, and studies like this are thus

extremely valuable as a foundation."

More information: Hanbyeol Lee et al, Blockade of RAGE ameliorates elastase-induced emphysema development and progressionRAGE-DAMP signaling, *The FASEB Journal* (2017). DOI: 10.1096/fj.201601155R

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