Susceptibility to pathogenic T cells in chronic lung disease may have genetic basis

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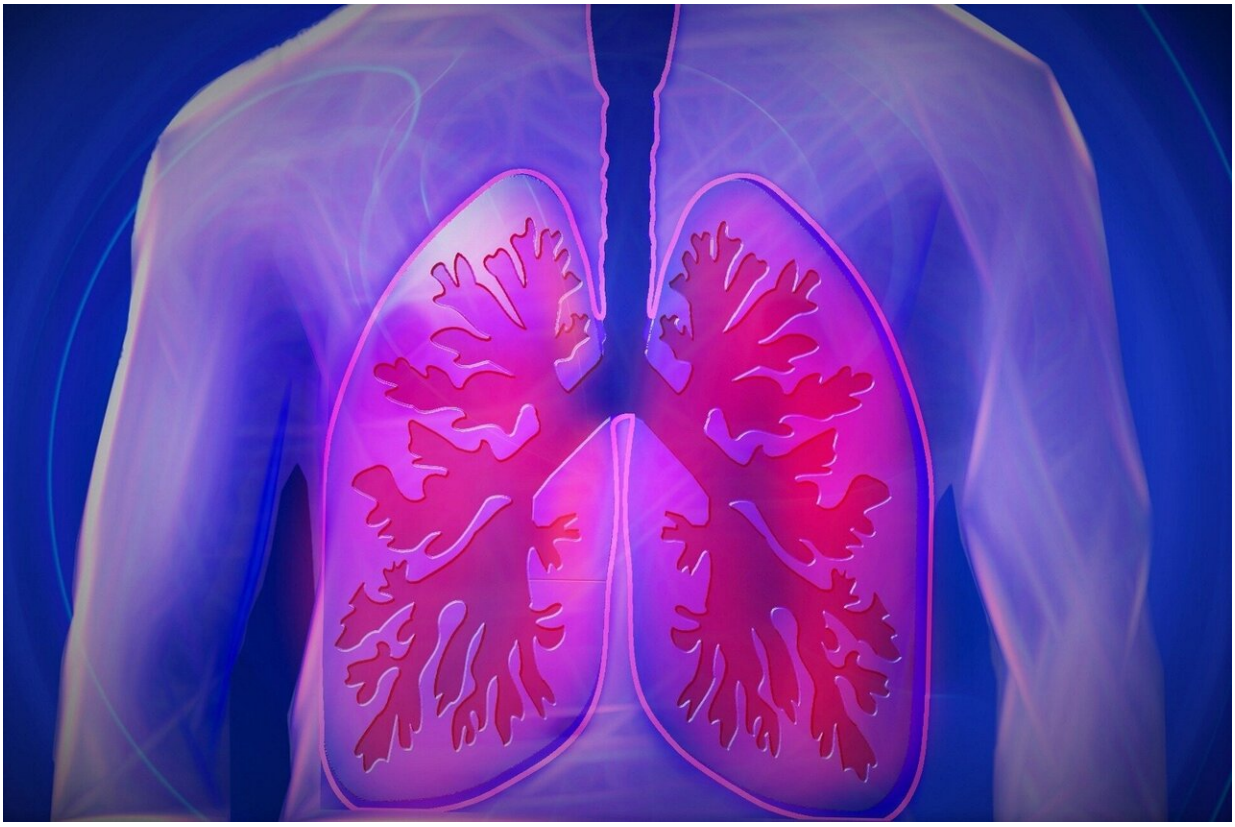

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Respiratory viral infections pose significant morbidity and mortality to patients with chronic lung diseases like emphysema and COPD, causing exacerbations that drive destruction of normal lung tissue, and leading to

one of the most common diagnoses for hospital admissions.

UC San Francisco researchers have uncovered a surprising role for fibroblasts in the lungs in activating T cell inflammation that drives lung destruction in COPD exacerbation triggered by viral infection. They have also identified a T cell subset that can be targeted to treat COPD exacerbations.

In a study publishing February 22, 2023 in *Immunity*, author Chaoqun Wang, Ph.D., a UCSF postdoctoral fellow in the laboratory of Tien Peng, MD, identified a fibroblast-secreted factor encoded by a COPD-susceptibility gene, HHIP, that suppresses viral inflammation in the lung. In collaboration with Ari Molofsky, MD, Ph.D., UCSF associate professor of Laboratory Medicine, the authors demonstrated that loss of HHIP promotes the expansion of tissue resident T cells that accumulate in the lung, leading to inflammatory destruction of resident lung stem cells.

The researchers discovered a pathogenic T cell subset (Tissue resident lymphocytes) in human emphysema using high-definition single cell sequencing of patient samples. They found that therapeutic targeting of these pathogenic T cells improves disease in pre-clinical models of emphysema.

These findings shed important insights on why certain patients with COPD-susceptibility gene variants are more likely to develop worsening COPD and present a novel therapeutic approach to treat COPD progression through the restoration of tissue factors in the lung.

"Discovery of a new lung stem cell subset in human emphysema lungs that is susceptible to these pathogenic T cells will provide more opportunity for therapeutic targeting of these pathogenic T cells to eventually improve disease treatment," said Peng, UCSF associate

professor of Medicine.

More information: Chaoqun Wang et al, Dysregulated lung stroma drives emphysema exacerbation by potentiating resident lymphocytes to suppress an epithelial stem cell reservoir, *Immunity* (2023). DOI: 10.1016/j.immuni.2023.01.032 , doi.org/10.1016/j.immuni.2023.01.032

Stanislav Dikiy et al, Principles of regulatory T cell function, *Immunity* (2023). DOI: 10.1016/j.immuni.2023.01.004

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