Antibody discovery may lead to a cure for age-related lung diseases

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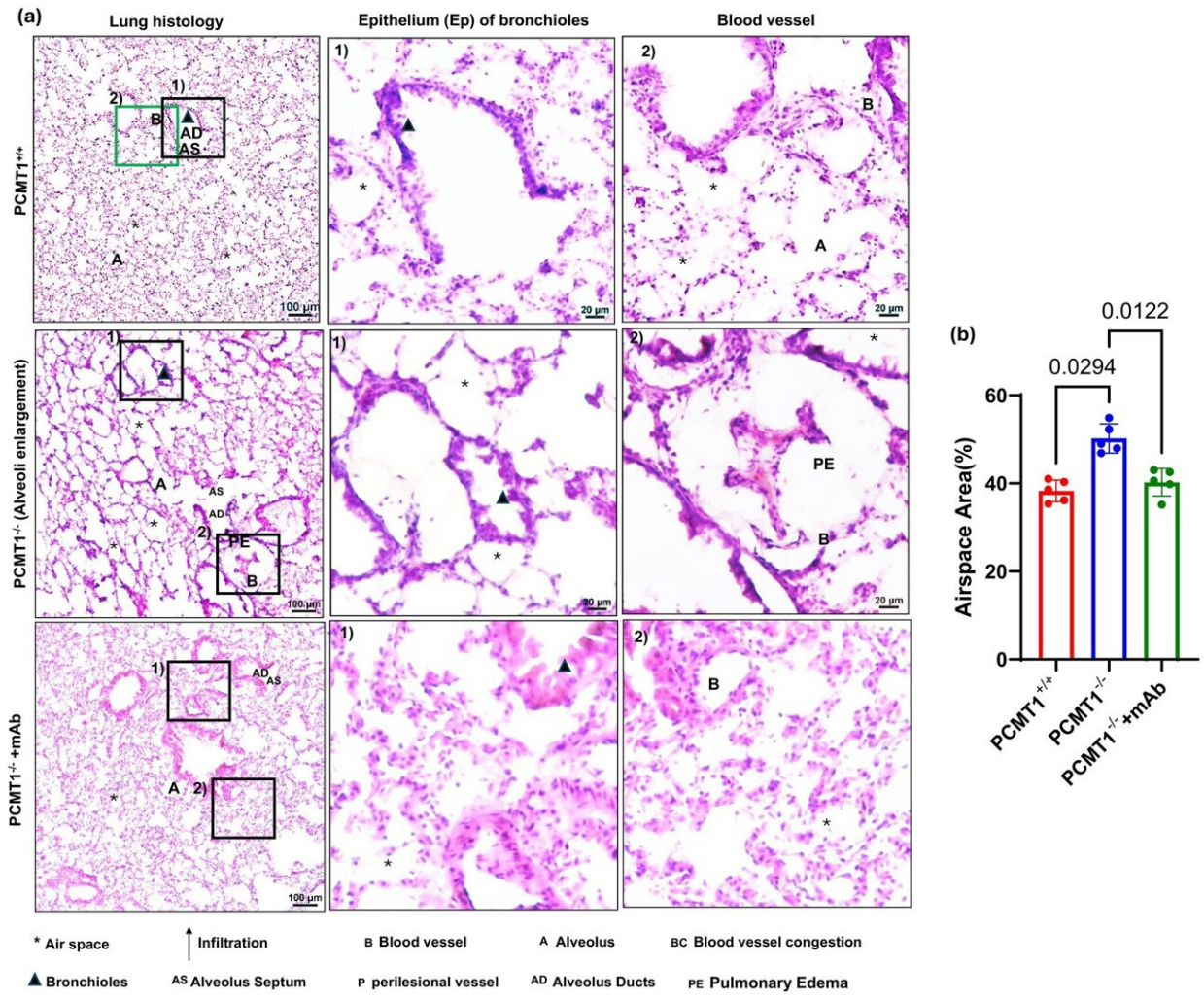

IsoDGR mAb treatment improves emphysema phenotype in lungs from Pcmt$^{-/-}$ mice Representative H&E-stained lung sections from 5 to 6 week-old Pcmt1$^{+/+}$, and Pcmt1$^{-/-}$ mice, displaying airspace enlargement, severe pulmonary oedema, and alveolar destruction, except in Pcmt1$^{-/-}$ mice treated with anti-isoDGR mAb

therapy. Credit: *Aging Cell* (2025). DOI: 10.1111/acel.14425

Research led by Brock University has found a possible cure for lung diseases typically found in older adults, such as pulmonary fibrosis. The findings are published in the journal *Aging Cell*.

Professor of Health Sciences Newman Sze and his international team have identified a specific antibody that targets age-related damage to proteins, a type of biomolecule, in lung tissue and reduces inflammation in the lungs.

"Treatments for chronic lung disease are currently focused on symptom management," says Sze, who is the Canada Research Chair in Mechanisms of Health and Disease. "The antibody we identified is treating the root cause of the disease, so this would be a cure instead of just making the patient feel better."

As time passes, biomolecules damaged by lifestyle and environmental factors accumulate in body tissues, fueling the aging process and age-related chronic diseases.

Since this damage often occurs spontaneously, both the damage itself and subsequent age-related chronic diseases were thought to be incurable, says Sze. Typical therapeutic strategies targeting genes or enzymes were also ineffective.

In their study, "Immunotherapeutic Targeting of Aging-Associated isoDGR Motif in Chronic Lung Inflammation," Sze and his team examined isoDGR, a type of biomolecule called a peptide motif that contains three amino acids—molecules that combine to form proteins. The amino acids in isoDGR are damaged.

The researchers began their study by examining the presence of isoDGR in human lung tissues obtained from people having a variety of ages and backgrounds as well as from patients diagnosed with lung fibrosis.

The team found isoDGR concentrations increased with age, with levels being eight times as high in tissues from fibrosis patients.

Using animal models to better understand how and why isoDGR gathers in the lungs, the researchers created an antibody—a protein produced by the immune system to fight off harmful substances—that binds specifically with isoDGR.

"This antibody activated the immune system to remove isoDGR from the body," says Sze. "Because this damaged protein is the root cause of pulmonary fibrosis, when it was removed, the tissue actually became healthy again."

Pulmonary fibrosis is one of many diseases triggered by isoDGR. Other conditions include chronic inflammation, cardiovascular disease, lung edema, hypoxemia and vascular congestion.

In fact, isoDGR is stored in areas throughout the body such as the blood vessels, says Sze.

"Since biomolecular damage is a main cause of many chronic age-related diseases, targeting and removing the damaged proteins with antibodies may offer therapeutic benefits beyond lung diseases," says Sze.

"This immunotherapeutic approach holds significant promise for reducing the burden of age-related diseases and supporting healthy aging in elderly populations."

Sze says the next steps in the research are working with companies to

modify the antibody for compatibility with the human immune system for clinical trials and further developing it for patient use.

More information: Pazhanichamy Kalailingam et al, Immunotherapeutic targeting of aging-associated isoDGR motif in chronic lung inflammation, *Aging Cell* (2025). DOI: 10.1111/acel.14425

Provided by Brock University