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Human Alveolar Stem Cells for Lung Regeneration and Treatment of Chronic Lung Disease

Stanford researchers have discovered and characterized a novel population of human alveolar stem cells, termed AT2-s cells, with robust self-renewal and regenerative capacity. This technology enables the purification, expansion, and transplantation of these cells to regenerate damaged lung tissue, offering a first-in-class regenerative therapy for currently incurable lung diseases.

Chronic lung diseases such as idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD), along with acute conditions like acute respiratory distress syndrome (ARDS), affect millions of patients worldwide and represent leading causes of mortality. Current therapies only slow disease progression or provide symptomatic relief, and none can restore or regenerate damaged alveolar tissue. This critical gap leaves patients with progressive lung function decline and limited treatment options beyond lung transplantation.

The inventors have identified a distinct subpopulation of alveolar type 2 (AT2) epithelial cells with unique stem cell properties: they self-renew, form three-dimensional alveolospheres in culture, and differentiate into both AT2 and AT1 cells—the two cell types essential for gas exchange in the alveoli. These AT2-s cells can be isolated from donor lung tissue, expanded in culture, and transplanted into patients to regenerate damaged alveolar tissue. Proof-of-concept engraftment has been demonstrated in ex vivo perfused human lungs, with transplanted cells successfully incorporating into alveolar structures and differentiating into functional gas-exchange epithelium. This platform enables both autologous and allogeneic cell therapy approaches for lung regeneration.

Stage of Development
Preclinical—*ex vivo* validation in human tissue; *in vivo* validation and

immunogenicity testing ongoing

Applications

- Regenerative cell therapy for IPF and other fibrotic lung diseases
- Treatment of COPD and emphysema featuring alveolar tissue loss
- Lung repair following acute lung injury (ALI) and ARDS
- *Ex vivo* lung perfusion (EVLP)-based enhancement for donor lung reconditioning prior to transplantation
- Disease modeling and drug discovery using patient-derived alveolar organoids

Advantages

- First-in-class regenerative therapy for restoring and regenerating damaged alveolar tissue
- Dual differentiation capacity of AT2-s cells leads to generation of both AT2 and AT1 cells, reconstituting complete alveolar epithelium
- Uses FDA-approved surface markers and standard cell sorting technology, facilitating clinical translation
- Self-renewing cells maintain stemness properties during expansion, enabling scalable production
- Human-derived approach avoids species translation challenges and supports both autologous and allogeneic therapeutic modalities

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