Bottling a mouse 'superpower' may heal lungs damaged by premature birth

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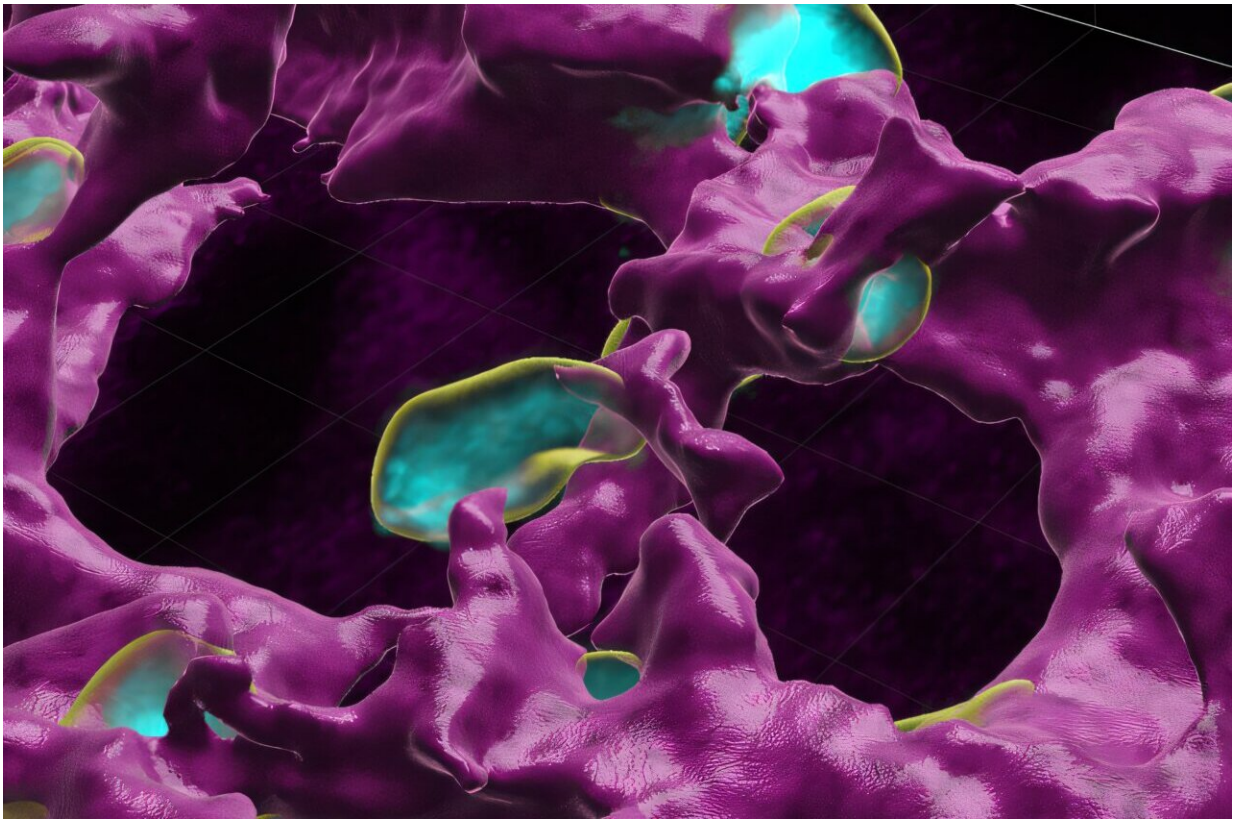


Alveolar epithelial cells (cyan) bud from mesenchymal rings of myofibroblasts and other cells (magenta). Image credit: Nick Negretti, Ph.D., and Jennifer Sucre, MD. Credit: Vanderbilt University Medical Center

Understanding resilience—the ability of injured lung tissue to heal and regenerate—may be key to advancing the treatment and prevention of

life-threatening lung disease that occurs in extremely premature babies, a new study suggests.

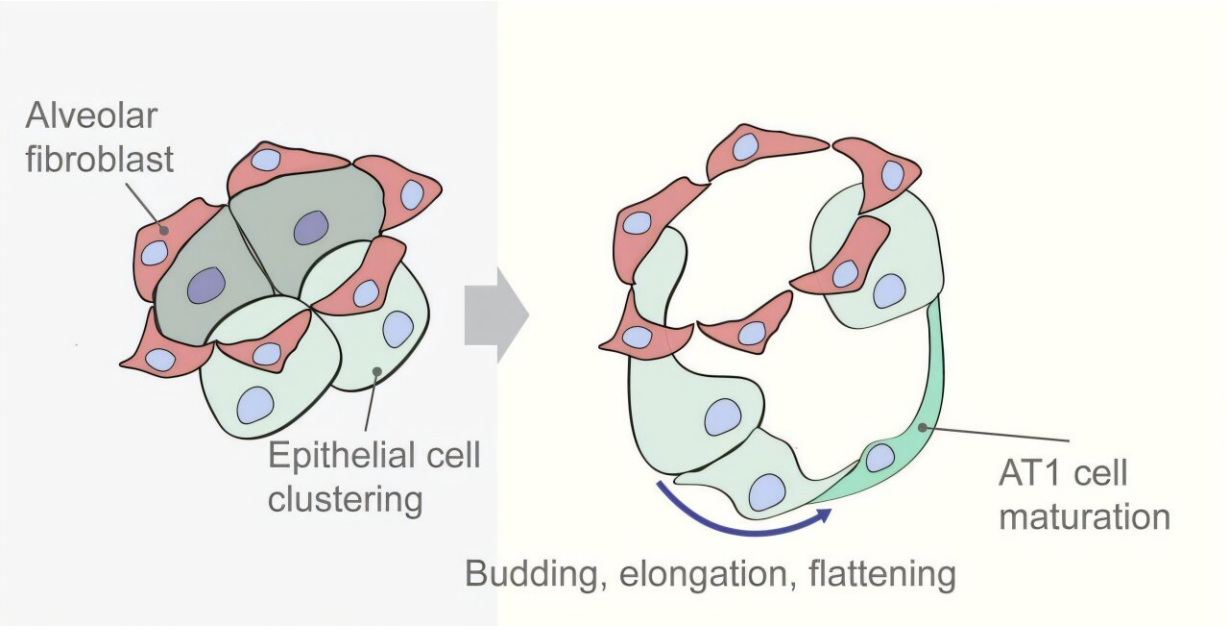
Using a four-dimensional microscopy technique, researchers at Vanderbilt University and Vanderbilt University Medical Center have created 3D video images of mouse lung tissue grown in the laboratory. What they have learned has been nothing short of groundbreaking.

"For the first time, we've been able to live-image the lung as it forms, and quantify and measure those cellular movements that come together to make an organ with a surface area large enough for gas exchange," said Jennifer Sucre, MD, associate professor of Pediatrics and Cell and Developmental Biology.

The group's findings, published Feb. 24 as the cover article in *JCI Insight*, represent a significant step toward improved treatment and prevention of bronchopulmonary dysplasia (BPD), which occurs in about 50% of infants born two to four months prematurely.

"If we can understand how the lung forms, then we have a blueprint for how to grow new lungs after injury," said the paper's first author, Nick Negretti, Ph.D., a senior post-doctoral fellow in the Sucre lab who co-led the research.

"Mice have an extraordinary ability to repair the lung," said Sucre, the paper's senior author, who directs the Biodevelopmental Origins of Lung Disease (BOLD) Center at VUMC. "I want to give babies the superpower of the mouse."



Graphical abstract. Credit: *JCI Insight* (2025). DOI: 10.1172/jci.insight.187876

Premature babies with BPD require oxygen and mechanical ventilation in the early days after birth to help them breathe. Oxygen therapy is a double-edged sword, however, because it can also damage delicate lung tissue.

Though many premature babies can be weaned off the ventilator after a few days, they are at increased risk for developing serious breathing problems later in life, including chronic obstructive pulmonary disease.

Respiration—the exchange of oxygen for carbon dioxide—occurs in the alveoli of the lungs across a fragile basement membrane between epithelial cells and blood vessels. According to the traditional view of lung development, ingrowing septa (dividers) emerge from a layer of epithelial, endothelial and mesenchymal cells to divide airspaces into the alveoli.

But when the researchers imaged slices of living neonatal mouse lung over three days, a different view emerged, one of a ballooning outgrowth of epithelial cells supported by a ring of myofibroblasts, or cells that promote tissue formation.

The innovative technology implemented by the Sucre lab allows for testing and identification of the specific molecules and pathways that guide this process. It is also a discovery tool for drugs that can promote tissue regeneration after injury.

Sucre said her lab is "keen to understand … what are the pathways in the resilient (mouse) lung that can repair it after infection and injury? How do we bottle that?"

More information: Nicholas M. Negretti et al, Epithelial outgrowth through mesenchymal rings drives lung alveologenesis, *JCI Insight* (2025). DOI: 10.1172/jci.insight.187876

Provided by Vanderbilt University Medical Center