

## Breathing New Life into Old Lungs

Nidhi Subbaraman

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For the first time, researchers have built a functioning lung by growing cells on the skeleton of a donor lung. The engineered organ was transplanted in a live rat, where it exchanged carbon dioxide with oxygen in the blood--just as a normal lung would--for two hours. The study is the first proof that old lung scaffolds can be used as a scaffold on which new lung tissue can grow.

Lung tissue does not regenerate, so the only way to replace a damaged lung, for example in those with emphysema and cystic fibrosis, is by transplant. "But it's a difficult procedure and there aren't enough lungs to go around for transplants," says Laura Niklason, professor of anesthesiology and biomedicine at Yale University and the corresponding author on the study. Only about 10 percent of patients who have undergone a transplant survive after 10 years, with infection and organ rejection being major problems. Growing lungs by combining a donor lung seeded with a patient's own lung cells could decrease the chance of rejection, and potentially improve the success of lung transplants.

"I think this is a groundbreaking work," says Peter Lelkes, Calhoun Chair professor of cellular tissue engineering at Drexel University. "No one has dared and actually succeeded in implanting such a complex tissue-engineered organ and kept an animal alive."

To achieve this, the team extracted the lungs of dead rats and flushed out the cells using a mixture of detergents. "Cells are just watery sacs," says Niklason. "When we remove them with detergents, what's left behind is the skeleton." Fetal lung cells and

blood vessel cells were injected into the scaffold and incubated in a bioreactor--a machine that mechanically ventilated the lung for a week. By the end of the week, the cells had multiplied, differentiated, and covered the scaffolding. "We provided the right mix of cells and the right conditions and the cells kind of figured it out--they went to the right places," says Thomas Petersen, a researcher at Yale and the first author on the study.

The rebuilt lung was implanted in a rat and hooked up to airways and key blood vessels. The blood leaving the implanted lung was rich in oxygen, showing that the lung could replace carbon dioxide with oxygen as blood passed through it. The implanted lung met the team's goal of exchanging gases for two hours. The work was published today in Science Express.

Recently, other groups have used similar "decellularized" scaffolds to grow animal heart and liver tissue. Lungs are more complex than either of these organs, containing several different cell types that form delicate, hairlike capillaries and a maze of branching air sacs. Previous attempts at creating lung tissue in the lab have only yielded small swatches of cells.

This method shows strong potential for organ regrowth, but the team is several steps away from making human lungs from repopulated scaffolds. For now, the team hopes to design a lung that will last longer when implanted in rats. One of the team's immediate next steps, Petersen says, is to optimize the coating of cells on the blood vessels, and ensure that blood doesn't leak out of the blood vessels into the airways.

"I hope that this will eventually find its way into clinical reality," says Lelkes. "I believe this is not on the horizon for tomorrow, but an outlook that I look forward to seeing in my lifetime."

"Realistically it'll probably be 20 years before we're there," says

Niklason. "There are some advances in stem cell biology and lung cell biology that still need to occur. We're just a piece of the puzzle."