

# Scientists coax stem cells to form 3-D mini lungs

24 March 2015



Scientists, led by the University of Michigan Medical School, coax stem cells to form mini lungs, 3-D structures that mimic human lungs and survived in the lab for 100 days. Credit: University of Michigan Health System

Scientists have coaxed stem cells to grow the first three-dimensional mini lungs.

Previous research has focused on deriving lung tissue from flat cell systems or growing cells onto scaffolds made from donated organs.

In a study published in the online journal *eLife* the multi-institution team defined the system for generating the self-organizing human lung organoids, 3D structures that mimic the structure and complexity of human lungs.

"These mini lungs can mimic the responses of real tissues and will be a good model to study how organs form, change with disease, and how they

might respond to new drugs," says senior study author Jason R. Spence, Ph.D., assistant professor of internal medicine and cell and developmental biology at the University of Michigan Medical School.

The scientists succeeded in growing structures resembling both the large airways known as bronchi and small lung sacs called alveoli.

Since the mini lung structures were developed in a dish, they lack several components of the human lung, including blood vessels, which are a critical component of gas exchange during breathing.

Still, the organoids may serve as a discovery tool for researchers as they churn basic science ideas into clinical innovations. A practical solution lies in using the 3-D structures as a next step from, or complement to, animal research.

Cell behavior has traditionally been studied in the lab in 2-D situations where cells are grown in thin layers on cell-culture dishes. But most cells in the body exist in a three-dimensional environment as part of complex tissues and organs.

Researchers have been attempting to re-create these environments in the lab, successfully generating organoids that serve as models of the stomach, brain, liver and human intestine.

The advantage of growing 3-D structures of lung tissue, Spence says, is that their organization bears greater similarity to the human lung.

## How to make a human lung in a dish

To make these lung organoids, researchers at the U-M's Spence Lab and colleagues from the University of California, San Francisco; Cincinnati

Children's Hospital Medical Center; Seattle  
Children's Hospital and University of Washington,  
Seattle manipulated several of the signaling  
pathways that control the formation of organs.

First, stem cells - the body's master cells—were  
instructed to form a type of tissue called endoderm,  
which is found in early embryos and gives rise to  
the lung, liver and several other internal organs.

Scientists activated two important development  
pathways that are known to make endoderm form  
three-dimensional tissue. By inhibiting two other  
key development pathways at the same time, the  
endoderm became tissue that resembles the early  
lung found in embryos.

In the lab, this early lung-like tissue spontaneously  
formed three-dimensional spherical structures as it  
developed. The next challenge was to make these  
structures expand and develop into lung tissue. To  
do this, the team exposed the cells to additional  
proteins that are involved in lung development.

The resulting lung organoids survived in the lab for  
over 100 days.

"We expected different cells types to form, but their  
organization into structures resembling human  
airways was a very exciting result," says lead study  
author Briana Dye, a graduate student in the U-M  
Department of Cell and Developmental Biology.

**More information:** "In vitro generation of human  
pluripotent stem cell derived lung organoids," *eLife*,  
DOI: <http://dx.doi.org/10.7554/eLife.05098.001>

Provided by University of Michigan Health System

APA citation: Scientists coax stem cells to form 3-D mini lungs (2015, March 24) retrieved 26 March 2015  
from <http://medicalxpress.com/news/2015-03-scientists-coax-stem-cells-d.html>

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