

Scientist develops protein mimic to help injured lungs breathe

April 30 2018, by Bruce Goldman



Anneliese Barron and her colleagues have synthesized a protein that's an essential part of a thin film that coats the inner surface of lungs. The synthesized protein could lead to better and less-expensive treatments for injured lungs. Credit: Joel Simon Images

The material could be used to synthesize a film that coats the inner

surface of lungs, possibly leading to better, cheaper treatments for acute lung injury in humans.

A Stanford University researcher has bioengineered an effective protein mimic that restored breathing capacity to the injured lungs of rats, according to a new study.

This synthetic product could lead to better, cheaper treatments for [acute lung injury](#) in humans. When used in the rats, it equaled or outperformed a costly natural counterpart in several physiological measures, the study said.

A paper describing the research was published online May 1 in *Scientific Reports*.

Imagine the force you'd need to blow up a balloon whose surface area nearly matched that of a tennis court. To make things challenging, imagine further that the balloon is made of exquisitely delicate material. That balloon is your lungs, and every breath you take is a miracle. What makes it possible is a thin coating of a soaplike film, or [surfactant](#), that lowers the tension of the lung's inner surface, radically reducing the amount of force required to inhale. Without this surfactant, you couldn't breathe.

"Lung surfactant is endowed with amazing biological properties," said Annelise Barron, Ph.D., associate professor of bioengineering. "The key to this is the presence, in the surfactant, of two special proteins whose structures uniquely enable them to cut surface tension." But those same amazing structural properties, she said, also make these proteins difficult to synthesize and purify, and relatively unstable in solution, limiting shelf-life and increasing price.

"One of them contains the most hydrophobic, or fat-resembling, stretch

of chemical constituents of all known human proteins," Barron said. "It's really hard to work with because that fatty stretch makes it tend to clump up, ruining its activity."

With the new study, Barron, who's been working on stable, synthetic substitutes for these special proteins for two decades, appears to be nearing success. She shares senior authorship of the study with Ruud Veldhuizen, Ph.D., associate professor of medicine and of physiology and oncology at Western University in Ontario, whose team performed the animal experiments. The study's lead author is Ann Czyzewski, Ph.D., Barron's former graduate student at Northwestern University, where Barron worked before coming to Stanford.

The first big challenge

Breathing is the first big challenge a newborn faces. Each year in the United States, some 20,000-30,000 infants born too early to produce their own natural surfactant are treated with an animal-derived variety, which is expensive. It's only in richer countries that this life-saving therapy occurs: The cost of a single vial containing enough animal-derived natural surfactant to coat the tiny lungs of a newborn infant is prohibitive in developing countries.

An adult's lungs are more than 20 times bigger than a baby's—their surface area approaches that of a tennis court, Barron said—pricing natural surfactant out of reach for many life-threatening cases of acute lung injury, which affects 200,000 adults annually in the United States. Surfactant dysfunction can result from severe lung infections, including bacterial and viral pneumonia; lung-collapsing trauma from impacts, such as those that occur in a car accident; inhalation of water in near-drownings; or aspiration of foreign materials in a drug overdose.

Ironically, attempts to keep patients breathing via mechanical ventilators

often cause a surfactant-depleting lung infection, Barron said. "People who wind up on ventilation in intensive-care units are intubated. A breathing tube is inserted into their nose and threaded down to their lungs," she said. "If that intubation lasts for more than three days, their chance of acquiring a [lung infection](#) rises to 100 percent." Even four hours spent on a ventilator spells a 1-in-6 chance of [lung](#) infection.

Until recently, the only way to obtain functional surfactant was to rinse it from the lungs of cattle, or chemically extract it from the lungs of pigs farmed for that purpose. "You get only a tiny amount per animal," Barron said. "And whatever you've collected, you have to purify very carefully, as the material is so fragile you can't treat it with high heat to kill microbial pathogens."

In recent years, a somewhat cheaper substitute has become available. It contains a water-based dispersion of fatty lipids along with short [protein](#) snippets that, to an extent, mimic the surface-tension-reducing capabilities of their natural counterparts, the surfactant proteins. While much better than nothing, this mixture is not quite as effective as animal-derived surfactant.

Synthetic mimics of two proteins

Barron's designer polymers, called peptoids, have specific sequences and helical structures that mimic key bioactive portions of the two important proteins, surfactant proteins B and C, found in the lungs. The mimics, which she calls pB and pC, resemble the proteins. But their component building blocks differ subtly from those of proteins in a way that makes them extremely resistant to breakdown by heat or naturally occurring bodily enzymes called proteases. In addition, they are much less inclined to aggregate into clumps and lose their bioactivity than their natural counterparts. They can be synthesized at one-quarter to one-third of the cost of obtaining the surfactant from animals or of the available

synthetic version.

Most important, the rodent study indicated that a surfactant containing pC was superior to the animal-derived surfactant in oxygenating blood, which is the lungs' main purpose.

The trial pitted the two designer substances against the animal extract and against a control solution. The researchers administered different surfactant candidates to anesthetized rats whose lungs had been rinsed to rid them of their own natural surfactant, and then assessed several physiological outcomes at various time points. The solution containing pC was equal to or better than the animal surfactant in every outcome—a "shocking result," according to Barron.

"This opens up new frontiers," Barron said. "Our relatively simple synthetic mimic of a very complex material will have a much longer shelf life and can be made in large amounts at reasonable prices. Reasonable enough, we hope, that it may for the first time be possible to conduct a clinical trial in adults in intensive care units who've been intubated and who might benefit substantially from surfactant replacement. And it would, finally, also be available to premature babies in developing countries like Bolivia, where my father was born."

Further preclinical and clinical trials lie ahead before that day comes, she added.

The work is an example of Stanford Medicine's focus on precision health, the goal of which is to anticipate and prevent disease in the healthy and precisely diagnose and treat disease in the ill.

Provided by Stanford University Medical Center

Citation: Scientist develops protein mimic to help injured lungs breathe (2018, April 30)
retrieved 7 May 2024 from

<https://medicalxpress.com/news/2018-04-scientist-protein-mimic-lungs.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.