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UVA researchers are developing ways to increase vastly the supply of transplant lungs

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Rescuing Unusable Lungs
A team of UVA researchers is out to change that, developing a way to restore damaged, unusable lungs that could revolutionize the field of lung transplantation and potentially end the organ shortage.

The UVA researchers, led by Irving L. Kron, MD, and Victor E. Laubach, PhD, are testing a new drug developed at UVA in combination with an existing technology called ex-vivo lung perfusion (EVLP). UVA’s drug has been shown to greatly reduce inflammation and damage to lungs in experimental transplantations, and the researchers hope that combining it with EVLP will allow them to rehabilitate and successfully use many of the lungs that now go to waste.

“One of the big problems with any transplant is a shortage of organ donors, but with lungs it is particularly bad. The reason is, if you have a brain injury, the lungs almost always get involved. If you’re in the ICU a long period of time with a brain injury, the lungs get infected. So only about 10 percent of brain-dead patients are lung donors,” Kron said.

“We believe we have a technology to take some of those lungs out, clean them up using some of the things we’ve been working on, and use them for patients.”

“The theory is that we would be able to use a whole lot more of these lungs,” he said. “People dying on the waiting list, we’d be able to treat.”

An extraordinary number of donor lungs go to waste each year, even as people in need die on the transplant waiting list. It’s estimated that only 15 percent of donor lungs end up being usable.
This new approach could allow doctors to use lungs from a vast numbers of donors whose lungs are currently deemed unusable, such as those who die outside of hospitals. In such cases, physicians are often left with little clue as to how badly damaged the lungs are. “Someone who had a fatal car accident, a young person otherwise healthy, currently we have no mechanism to use those lungs,” said Kron, chairman of UVA’s Department of Surgery and a founder of UVA’s lung transplant program.

Laubach, of the Division of Thoracic and Cardiovascular Surgery, explained the fundamental goal and its potential implication: “We want to be able to utilize a much larger pool of potential donor lungs: the non-heart-beating donors,” he said. “And if we can do that using this system, we can significantly reduce or maybe even eliminate the wait list for transplants. And that would save a lot of lives.”

The anti-inflammatory drug developed at UVA, an agonist that binds to an adenosine receptor, would be combined with EVLP, in which the lungs are perfused outside the body, to allow doctors to overcome the critical problem of reperfusion injury, when lungs are damaged by the restoration of interrupted blood flow (reperfusion).

“Ironically, the lung not only needs reperfusion to live – it will die without it – but it introduces acute injury, and that’s the inflammation we’re studying in the lab,” Laubach said. “Sadly, only about 50 percent of lung transplant recipients survive to five years because of the development of...
chronic rejection called obliterative bronchiolitis (OB). However, there is hope for these patients because the OB appears to be associated with reperfusion injury, and thus we believe that prevention of reperfusion injury via EVLP-mediated therapy will also reduce the risk for OB.

The approach would also extend the time lungs could remain outside the body, a critical concern today and a major limitation for donor lung transport. “Normally, we try to stay under six hours for preservation on ice,” Laubach said. “We’re testing how far beyond that we can go with the combination of this new drug and EVLP. Some of our preliminary data provides hope that we can go significantly beyond that.” And that extension would be significant indeed: possibly to 24 hours or longer. Just imagine: A patient in Boston could receive a well-matched lung from a deceased donor in Los Angeles with time to spare.

The UVA research is on the fast track. In addition to testing their approach in animal models, the researchers will be working with unusable human lungs thanks to a $3.3 million grant from the National Institutes of Health. Kron credited the rapid pace of the research, in part, to the collaborative environment at UVA. “A lot of places are siloed up, and people are very protective of their work. Here you can make one phone call and get anyone to collaborate with you. You don’t hesitate,” he said. “The concept of bench to bedside is real here. We have a problem with an operation we’re doing, we have the folks to solve the problem.”

The team is also spurred on, of course, by the scope of the problem and the desperate need for usable lungs. What they are developing could ultimately prove to be the answer to many prayers.

“If someone is listed for a lung transplant, they’d be able to get one within a week or two instead of six months, a year or two years. The timing wouldn’t be an issue. We wouldn’t need to do them in the middle of the night. We’d make the lung work perfectly and we’d put it in,” Kron said. “We would be able to liberalize our criteria for lung transplant. For example, we have age limits on lung transplantations. But a lot of 70-year-olds are really young. I think it would change everything.”

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– Irving L. Kron, MD
Chairman, UVA Department of Surgery

Cynthia Wagner, MD | Wagner is a key member of the research team, using ex vivo lung perfusion in combination with the new drug developed at UVA to push the boundaries of transplant lung viability.