Lab-grown kidneys transplanted into rats

Engineered organs produce urine, though not as efficiently as natural ones.

Ed Yong

14 April 2013 | Corrected: 16 April 2013

Scientists at Massachusetts General Hospital in Boston have fitted rats with kidneys that were grown in a lab from stripped-down kidney scaffolds. When transplanted, these 'bioengineered' organs starting filtering the rodents' blood and making urine.

The team, led by organ-regeneration specialist Harald Ott, started with the kidneys of recently deceased rats and used detergent to strip away the cells, leaving behind the underlying scaffold of connective tissues such as the structural components of blood vessels. They then regenerated the organ by seeding this scaffold with two cell types: human umbilical-vein cells to line the blood vessels, and kidney cells from newborn rats to produce the other tissues that make up the organ. The work is described today in *Nature Medicine*[1]. Ott and his colleagues developed this method in 2008, and he has since used it to grow hearts[2] and lungs.

"This study reports important milestones toward engineering replacement kidney grafts [and] shows the potential for this strategy," says urologist Anthony Atala, who directs the Institute for Regenerative Medicine at Wake Forest School of Medicine in Winston-Salem, North Carolina.

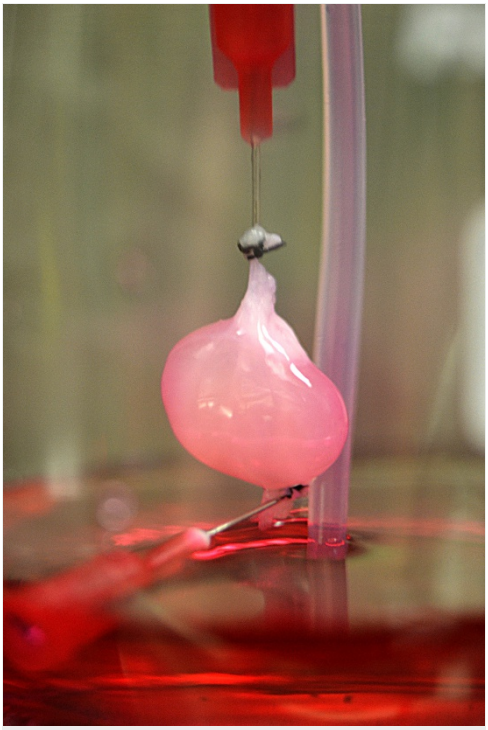
"If the work can be replicated, the scientists involved have clearly accomplished a tour de force and deserve accolades," adds William Fissell, a nephrologist at Vanderbilt University in Nashville, Tennessee.

Currently, patients who develop the most severe forms of kidney disease can be kept alive with dialysis, but only a transplant will cure them. And in the United States alone, around 100,000 people are waiting for a donor kidney.

Other research groups have used tissue-engineering techniques to develop external kidney-assisting devices using human cells, and some have already passed early clinical trials[3,4]. But Ott argues that his bioengineered kidneys, although much farther behind in development, have the benefit of being implantable just like a donor organ.

Organs on demand

If he and his team can scale up their technique to produce human kidneys, they could provide ready-made, genetically tailored organs



Ott Lab, Center for Regenerative Medicine, Massachusetts General Hospital

The connective scaffold of a rat kidney, seeded with human endothelial and rat kidney cells, growing in an organ bioreactor.

that would be much less likely to be rejected by a patient's immune system. The scaffolds could come from existing donors — with no need for a genetic match — or perhaps even from animals, such as pigs. In some cases, bioengineers might be able to strip the patient's own diseased kidney and rebuild it.

"In an ideal world, if someone walks into the hospital and has a kidney grown on demand, there's no donor organ shortage and there are no immune problems," Ott says.

Ott's method preserves the kidney's three-dimensional architecture, blood-vessel structure and molecules that help to guide and organize growing cells. For example, the team saw that cells called podocytes largely ended up in the right place in their engineered organs — around blood-filtering structures called glomeruli.

However, the resulting organs are far from ready for the clinic. When transplanted into rats, they produced only around one-third as much urine as normal kidneys, and cleared creatinine — a waste product of muscles that is used to assess kidney health — 36 times more slowly than normal.

Ott blames this poor performance on the immaturity of the engineered organs, and the fact that they probably had not created the full gamut of cell types found in adult kidneys. But he notes that many patients with kidney disease start dialysis only when their kidney function falls below 15%. "If we can make a graft that works at 20%, that would already make patients independent of haemodialysis," he says.

The team is now testing the same technique using pig and human kidneys. They are also developing more sophisticated ways of steering the development of the seeded cells, and Ott is hoping that his latest publication will attract interest from other biologists. "We'll need collaborators, and a lot more brain power chiming in," he says.

A regenerated kidney that could be implanted in humans "remains very, very far in the future", says Fissell. "In almost every area in medicine, the leap from rodent to man has been extraordinarily difficult, and that has seemed to be the case with organ scaffolds as well." However, he says that the team's work still provides a platform for understanding how kidneys develop and repair themselves. "This may end up being the area in which the paper has the most impact," Fissell says.

Nature | doi:10.1038/nature.2013.12791

Corrections

Corrected: An earlier version of this article incorrectly stated that William Fissell is at the University of California, San Francisco. He is at Vanderbilt University.

References

1. Song, J. J. *et al. Nature Med.* http://dx.doi.org/10.1038/nm.3154 (2013).
2. Ott, H. C. *et al. Nature Med.* **14**, 213–221 (2008).
3. Tasnim, F. *et al. Fibrogenesis Tissue Repair* **3**, 14 (2010).
4. Tumlin, J. *et al. J. Am. Soc. Nephrol.* **19**, 1034–1040 (2008).