K. MORIMOTO *ET AL.*/BIORXIV

The transplanted tissue grew into a kidney and the host's blood vessels began infiltrating it.

FIRST FETUS-TO-FETUS TRANSPLANT DEMONSTRATED IN RATS

The tissue developed into functioning kidneys and produced urine.

By Smriti Mallapaty

Surgeons in Japan have transplanted kidney tissue from one rat fetus to another, while the recipient was still in its mother's womb. Study lead Takashi Yokoo, a nephrologist at Jikei University School of Medicine in Tokyo, says the surgery is the first step to one day transplanting fetal pig kidneys into human fetuses that develop without functioning kidneys.

"Our project is the first of its kind," says Yokoo. Researchers have previously injected cells and amniotic fluid into fetuses (J. L. Miller *et al. JAMA* **330**, 2096–2105; 2023), including human ones, but these are the first reports of organ and tissue transplants *in utero*, he says.

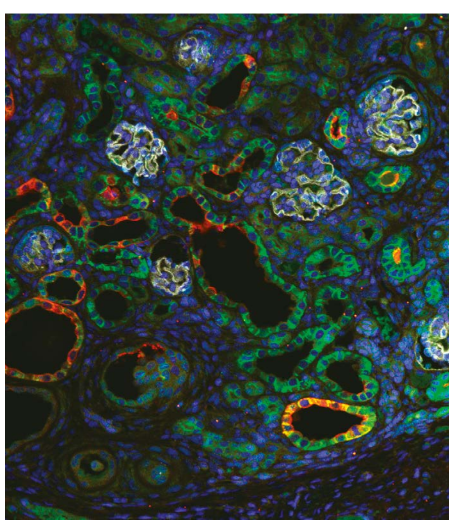
Transplanting an organ before birth could allow it to grow and develop with the fetus, so that the organ is functioning at birth, and there is less risk of rejection.

"It's lovely data," says Glenn Gardener, a fetal surgeon at Mater Mothers' Hospital in Brisbane, Australia.

Green kidneys

In their study, Yokoo and his colleagues genetically modified rats to express a green fluorescent protein in their kidneys, so that the tissue could be tracked. They then extracted the green kidney tissue from rat fetuses, and used a tiny needle to insert it under the skin of the backs of 18-day-old rat fetuses developing in their mothers' wombs. The rat pups were born after the normal gestation period of around 22 days (K. Morimoto *et al*. Preprint at bioRxiv https://doi.org/mtqr; 2024).

The tissue gradually developed, forming waste-filtering units known as glomeruli and well-divided inner and outer kidney structures. Two-and-a-half weeks later, the kidneys began to produce urine. "The timeline is considered to be almost identical to normal development," says Yokoo. But because the transplanted kidney was not connected to the ureter, the urine had nowhere to go, so the researchers drained the kidney continuously until the rats were euthanized at around five months of age.



K. MORIMOTO *ET AL.*/BIORXIV

The filtering structure of the kidney.

Of the nine fetuses that underwent surgical transplants in four pregnant rats, eight developed fluorescent-green kidneys. In the ninth fetus, the transplanted tissue probably did not embed successfully, says Yokoo.

A close look at the kidneys revealed that the fetuses' blood vessels had grown inside the donated tissue, which made them less likely to be rejected by the immune system. A major cause of organ-transplant rejection is incompatibility between donor blood vessels and the host's body, says Gardener. "In this case, the host is infiltrating the organ, and you overcome that. That was really cool."

The rat study results were posted on the bioRxiv preprint server on 20 April and have not yet been peer reviewed.

Pig, monkey, human

Yokoo's long-term goal is to transplant fetal pig kidneys into human fetuses with Potter syndrome, a condition in which the infant doesn't develop functioning kidneys during gestation, and usually dies hours after birth.

To test xenotransplantation – the use of animal organs in recipients of another species – Yokoo transplanted mouse kidney tissue into rat fetuses. The intervention was successful in four rats, and the kidneys developed for ten days without being rejected. By 18 days, the tissue showed signs of rejection, which could be quelled by immunosuppressant drugs. Yokoo says fetal tissue is less likely to induce an immune response than is adult tissue, which means that it does not need to be genetically modified before transplant to avoid rejection.

So far, researchers have attempted to genetically modify fully developed organs to bring xenotransplantation closer to the clinic. Last month, surgeons in the United States conducted the first transplant of a kidney from gene-edited pigs into a living adult. Surgeons in the United States and China have previously transplanted gene-modified pig hearts into living people, and gene-edited pig kidneys and a liver into people who lacked brain function.

Yokoo says he has also conducted pig-to-pig fetal transplants in 38 pig fetuses in 11 sows, and 18 recipient piglets were born. These results have not been published. He is also conducting pig-to-monkey fetal transplants in marmosets, and hopes to start work on cynomolgus macaques (*Macaca fascicularis*) in a few months.

Yokoo's rat experiments are a "small first step, but a very important one" on the path to xenotransplantation in people in Japan, says Maria Yasuoka, a medical anthropologist who studies organ transplantation at Otaru University of Commerce in Hokkaido, Japan.

Gardener says the results in rats are fascinating but still a long way from being applicable to humans.

Other researchers agree: "In principle, the prospect of organ transplantation *in utero* is an amazing concept," says Ahmet Baschat, a specialist in fetal interventions at Johns Hopkins University in Baltimore, Maryland. "Scientifically, it's novel. It's a beginning." But Baschat says he wouldn't get too excited yet.

Yokoo has started engaging with members of the public to inform them of the benefits of human fetal xenotransplantation and gain their trust. He will continue his research and plans to apply for approval to conduct research in people from ethics boards at his university and hospital, and Japan's regulatory agency.

SUPERCONDUCTIVITY HUNT BOOSTED BY CHINA'S PHYSICS 'PLAYGROUND'

US$220-million facility provides conditions for researching potential wonder materials.

By Gemma Conroy in Beijing

On the outskirts of Beijing sits a set of unassuming buildings marked 'X', for 'extreme'. Inside the Synergetic Extreme Condition User Facility (SECUF), researchers from all over the world are pushing matter to its limits with extreme magnetic fields, pressures and temperatures, and examining it in new ways with extremely precise resolution in time.

One particularly tantalizing goal of many researchers using this US$220-million playground for physicists is to discover new superconductors — materials that conduct electricity without resistance. "This kind of combination of extreme conditions offers a very good chance for new discoveries," says SECUF founding director Li Lu, a condensed-matter physicist at the Chinese Academy of Science's Institute of Physics (IOP) in Beijing.

Understanding the mechanisms that underlie superconductivity is an important step in the global race to finding a material that exhibits this phenomenon at room temperature, instead of under frigid conditions.

Such a discovery could open the door to faster computers and cut electricity consumption, among other benefits.

The Synergetic Extreme Condition User Facility can put samples through a battery of tests.

INSTITUTE OF PHYSICS, CHINESE ACADEMY OF SCIENCES

Under extreme conditions, matter exhibits properties that would otherwise remain hidden. For instance, when some ordinary-seeming materials are subjected to high pressures and extreme cold, they become superconductors. But measuring superconductivity can be finicky, because it can show up differently depending on the technique used, says Konstantin Kamenev, a physicist at the University of Edinburgh, UK, who specializes in extreme-conditions engineering and instrumentation. The ability to mix and match such conditions at a single facility allows researchers to characterize their samples more fully and efficiently than they could otherwise. "It's like a one-stop shop," says Jinguang Cheng, a condensed-matter physicist at the IOP.

Extreme toolbox

Since September last year, all 22 experimental stations at SECUF have moved to full operation after a one-year trial period. Tucked into a corner of one of SECUF's brightly lit rooms, Cheng oversees a station that combines a cubic anvil cell — a device that squeezes materials under enormous pressure on six sides — with two superconducting magnets and helium-based cooling systems. The sample-torturing instrument can be used to measure a range of electronic properties and characteristics. Although conventional high-pressure tools, such as diamond anvils, can accommodate samples that are only the width of a human hair, SECUF's cubic anvil cell can compress larger samples, making it easier to measure electronic properties in finer detail, says Cheng.

He says that he and his colleagues have, in this way, discovered a handful of superconductors, including a rare magnetic one[1] and another based on manganese[2].

Behind a yellow warning barrier at the other end of the room sits a powerful superconducting magnet. Rui Zhou, a condensed-matter physicist at the IOP, and his colleagues have set up a station that combines the magnet with ultra-low temperatures to perform nuclear magnetic resonance (NMR) measurements. The technique tracks the behaviour of atomic nuclei in high magnetic fields. It offers a way of peering into the mechanisms that underlie high-temperature superconductors — those that operate above −195.8 °C.

SECUF's magnet produces a weaker field — just 26 tesla — than do those at other facilities, such as the record-holding 45-T hybrid magnet, which is partially superconducting, at the US National High Magnetic Field Laboratory (NHMFL) in Tallahassee, Florida, and the 37-T resistive magnet at France's National Laboratory for Intense Magnetic Fields in Grenoble. But these require a lot of power to run. Because it guzzles much less power, the SECUF magnet can maintain a stable magnetic field for up to