

# Human kidneys partially grown in pigs offer transplant hope

Alice Klein

KIDNEYS that are more than 50 per cent human have been partly grown in pigs for the first time.

The research, conducted by Miguel Esteban at Guangzhou Institutes of Biomedicine and Health in China and his colleagues, brings us a step closer to being able to grow human kidneys in other animals to address the shortage of organ donors. Over 100,000 people in the US alone are currently waiting for a kidney transplant, with 13 dying per day.

To get around the need for donors, it may be possible to grow human kidneys in other species with similar organ sizes and physiology to us. Esteban and his colleagues explored this idea by creating pig embryos that couldn't form kidneys of their own, by disabling two key genes involved in the development of the organs.

Next, they introduced human stem cells into the pig embryos,

hoping they would transform into kidney cells in the animals and assemble into the relevant organs. The human cells were genetically engineered to help them integrate in the foreign environment by increasing the expression of two pro-survival genes.

## 1800+

Number of pig-human embryos implanted in sows

The researchers implanted more than 1800 of these hybrid embryos in the reproductive tracts of 13 sows. They only allowed the embryos to grow for 25 to 28 days before removing and analysing them because of various ethical considerations, including the possibility of producing pigs with human-like brains if the human cells spread beyond the kidneys.

Only five of the embryos

successfully implanted, but these developed early kidney structures, including miniature tubules, that were made of 50 to 65 per cent human cells and the rest pig cells.

"This is a very important study," says Jun Wu at the University of Texas Southwestern Medical Center. Wu and his team reported the creation of the first human-pig embryos in 2017, but were only able to incorporate a very small proportion of human cells, which didn't assemble into organs.

Esteban and his colleagues tracked where the human cells went in their embryos by tagging them with a red fluorescent marker. Very few became incorporated in the early central nervous system or other organs, which Wu says is reassuring (*Cell Stem Cell*, doi.org/ksjh).

The researchers in China have now received approval from their institute's ethics committee to let

such human-pig embryos develop for up to 35 days to see if the humanised kidneys continue to mature properly and to ensure minimal human cells end up in other organs. "We will move forward step by step," says Esteban. They are also looking at growing other human organs like the heart and liver in pigs, he says.

Other groups are trying pig-only organs for transplants. On 14 July, for example, surgeons at NYU Langone Health in New York transplanted a pig kidney into a brain-dead man. This came from an animal that had a gene knocked out so its organs wouldn't trigger an immune reaction in a recipient.

Wu believes that a combination of both of these approaches – growing kidneys that are mostly human in pigs and also knocking out genes that might trigger immune reactions – may end up working best. ■

## Invasive species

### Red fire ants with painful bites have taken hold in Europe

DOZENS of red imported fire ant nests have been found in Sicily, Italy – a sign that the invasive insects have become established in Europe.

The red imported fire ant (*Solenopsis invicta*) is a venomous species that originally comes from South America.

Since it was first described by science in 1916, the species has spread around the world, including to Australia, China and the US, primarily due to imports of soil and plants from its native region to other countries.

"It's considered one of the worst invasive species," says Mattia Menchetti at the Institute

of Evolutionary Biology in Barcelona, Spain. For people, red fire ant bites can be extremely painful due to their venom, which some people may even be allergic to, he says.

Red fire ants also pose a threat to nature by preying on other species, such as birds and reptiles, and displacing native ant species.

Local reports of painful ant stings from around the coastal city of Syracuse on the island of Sicily have been circulating for a few years, says Menchetti.

He and his colleagues went to collect some of the ants responsible for the bites and quickly identified them as *S. invicta*. The team found a total of 88 red imported fire ant nests spread over 4.7 hectares in the area.

DNA from these ants was found to be most similar to red imported



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fires ants in China and the US – a clue that the now-established Sicily population may have come from either of those countries.

According to the team's models, the ants could spread to 7 per cent of Europe under current

Red imported fire ants are an invasive species in many parts of the world

environmental conditions, although climate change could increase their range further. They are most likely to spread to warm, well-connected regions, such as coastal Mediterranean cities.

But urban areas across the continent, including Paris and London, may be suitable for the species to thrive because of their many heat sources, such as buildings (*Current Biology*, doi.org/kszn).

Menchetti's team is working with authorities to continue monitoring the region and to establish the extent of the population, which will help guide eradication plans. ■  
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