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# First human-pig embryos open route to growing transplant organs in chimeras

- **Marcus Strom**

Scientists have grown the first human-pig hybrid embryos and taken them a third of the way through pregnancy inside a sow.

Geneticists at the Salk Institute in California hope this research will pave the way to grow fully-functioning human transplant organs inside hybrid animals.

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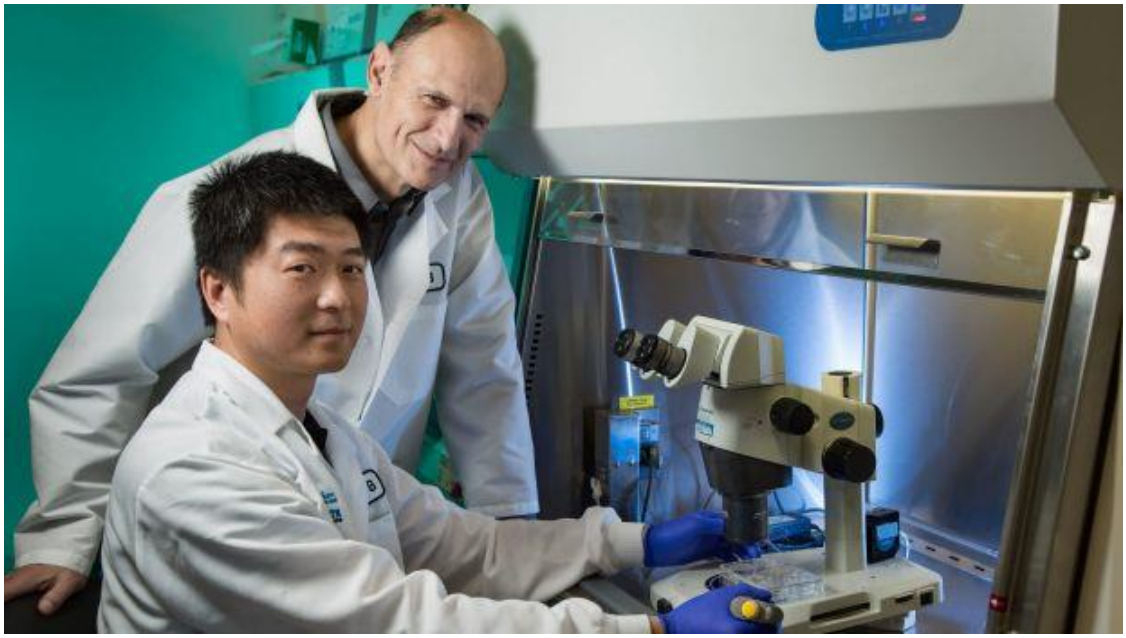
A team of scientists have grown the first human-pig hybrid embryos, opening up a route for growing transplant organs. *Vision courtesy Salk Institute.*

That, however, is a long way off. The immediate use for this research promises to revolutionise drug testing and help create personalised medicine for treatment of cancers and genetic diseases.

"The ultimate goal of this research is to generate organs that can match to your immune system," said Dr Jun Wu from the Salk Institute, lead author of the research.



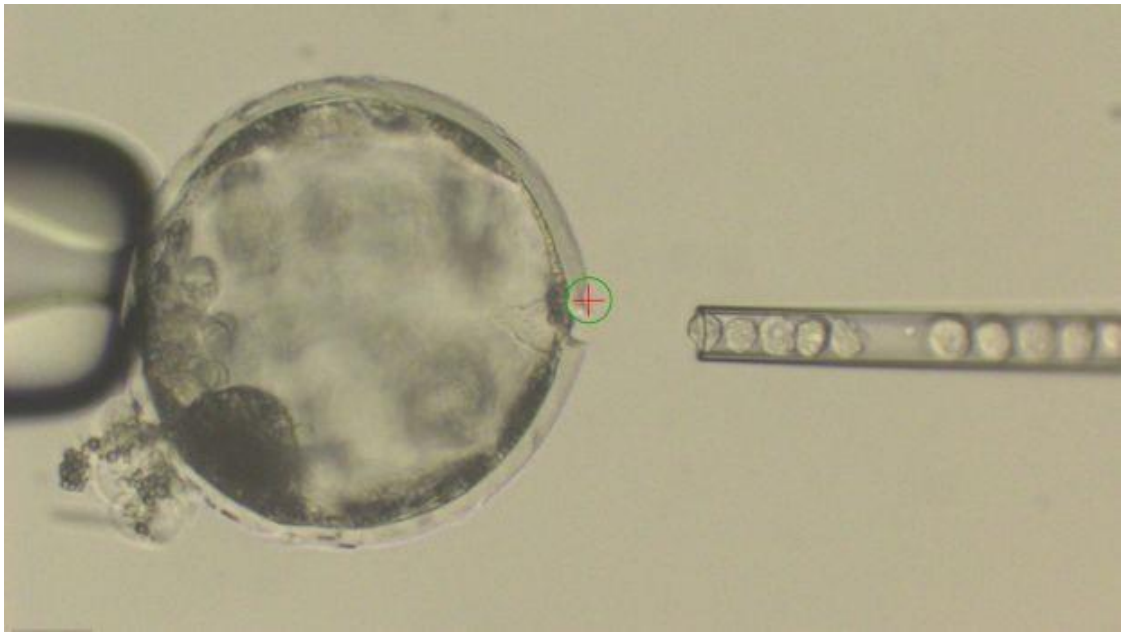
Dr Jun Wu (seated) and Professor Juan Carlos Izpisua Belmonte. *Photo: Joe Belcovson*

The hybrid embryos grown by the researchers developed the precursors to human pancreatic, liver, gut, lung, heart and muscle cells.

Dr Wu said: "Organ generation based on this technology is in the future. We need to overcome many technical, social and ethical challenges first.

"More immediate applications will be in disease modelling and drug testing."

He said you can imagine a pig born with a human liver being tested with pharmaceuticals before they are tested on humans.



Injection of human stem cells into a pig blastocyst, a precursor to the embryo. *Photo: Salk Institute/Cell*

The central ethical concern for Dr Wu was to ensure that pig-human chimeras did not develop brains or sperm/egg cells containing human cells.

"No human cells emerged in the developing brains of the 17 embryos. But we did observe neurons in the spinal cord but we don't know why yet," Dr Wu said.

A four-week-old human-pig embryo. *Photo: Salk Institute/Cell*

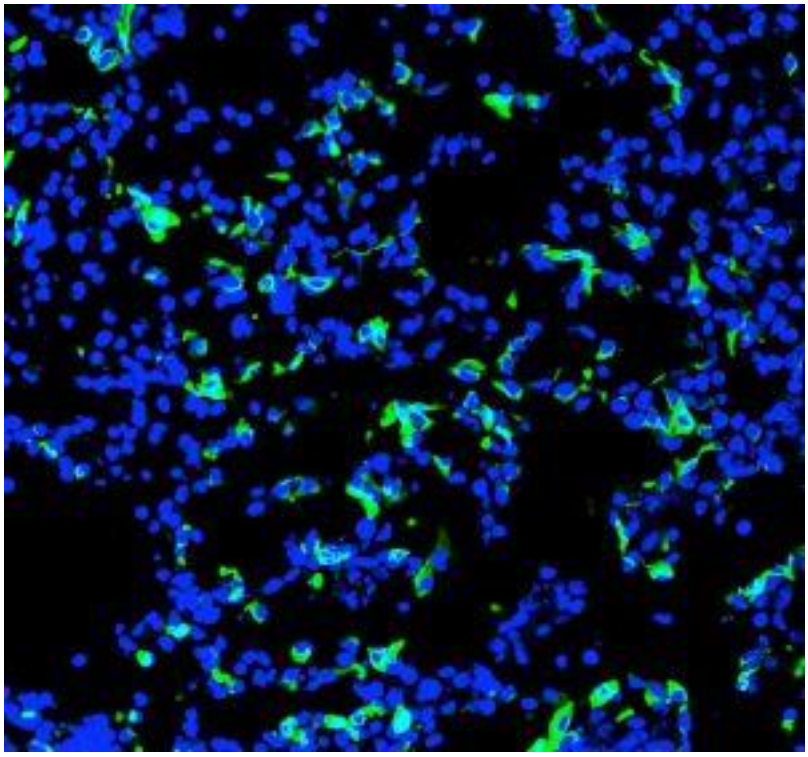
The embryos were allowed to develop to between three and four weeks. "This is long enough for us to try to understand how the human and pig cells mix without raising ethical concerns about mature chimeric animals," said co-author Professor Juan Carlos Izpisua Belmonte from Salk Institute.

Dr Wu said: "We wanted to stop the process early and analyse the results in order to understand the process better. We want to guide the human cells to be the organs we want them to be rather than going randomly everywhere."

Pigs at the Agropor facility in Spain are being used in the chimera experiments. *Photo: Salk Institute/Cell*

Professor John Rasko, head of cell and molecular therapies at Royal Prince Alfred Hospital in Sydney described the paper, published in *Cell* on Friday, as a "landmark in the field".

"We will be referencing this paper for many years to come," he said.



Human cells in pig embryos. *Photo: Salk Institute/Cell*

And while he said the research shows great potential for regenerative medicine, "I don't think this is the main importance of this study".

"What this paper shows is that if you inject early developmental cells from humans into the another species' embryo at the same developmental stage then they are better able to 'take' and contribute to the final growing embryo," he said.

Illustration: Cathy Wilcox

Professor Rasko, who is not connected to the study, described the technology used as "nothing less than enthralling".

"What they have created is the ability to place 'ticking time-bombs' inside cells that contribute to specific organs in a rat, mouse or pig body."

He said this allows the researchers to ask the question: when these cells die are there any cells nearby that can replace them?

"This allows us to develop very specific disease modelling and eventually drug-testing capabilities," he said.

"We could recreate human leukemia from an individual in a mouse and then test a whole bunch of drugs in that mouse. We could take 100 mice and test 100 drugs.

"This is a big deal. It's going to accelerate drug development and personalised medicine," he said.

Dr Wu said the human stem cells used in their study were generated using skin cells. This is done using a technique known as "cell reprogramming" pioneered by Japanese researchers in 2006. John Gurdon and Shinya Yamanaka received the Nobel Prize for medicine in 2012 for this research.

Dr Wu said: "The perfect situation is where we have human cells contributing only to the organs where we want them to go.

"The fact that these hybrids have a low contribution of their genetics from humans lowers the risk that human cells will go everywhere."

The development of human cells in the embryos was a random process. In future studies Dr Wu and his colleagues will develop techniques using the CRISPR gene-editing technology to control this process.

He said: "We were disappointed at first to see such a low-level contribution from human cells in the chimera. However, we realised this was not a bad thing. We know it is not easy to produce something that is 'unnatural'."

The next step for the research team is to enrich the human cells in specific organs and develop strategies to prevent brain development with human cells.

They will then extend the pregnancy in the pigs to the second trimester. "At that stage we will have much bigger organs to analyse," he said.

http://www.theage.com.au/technology/sci-tech/first-humanpig-embryos-open-route-to-growing-transplant-organs-in-chimeras-20170126-gtz621.html