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EXPLAINED

Relevant for: Science & Technology | Topic: Science and Technology- developments and their applications and effects in everyday life

Xenotransplantation might be the future of organ transplants. Photo: University of Maryland School of Medicine via Reuters

The story so far: On January 7, David Bennett, a 57-year-old from Baltimore, Maryland, U.S. became the first person to receive a heart transplant from a genetically-modified pig. Surgeons at the University of Maryland Medical Center transplanted the porcine heart into Mr. Bennett suffering from terminal heart failure. Since transplantation of a pig heart into a human, called xenotransplantation, is an experimental procedure, doctors had to seek an emergency authorisation from the U.S. FDA (Food and Drug Administration). Approval was granted as Mr. Bennett was facing near-certain death due to his condition and was too ill to qualify for a routine human heart transplantor, an artificial ventricular assist device.

In late September last year, surgeons at the New York University Langone Health medical centre transplanted a kidney of a genetically modified pig into a brain-dead person. The second such pig kidney experiment at the same university was carried out on November 22, 2021 on a person maintained on a ventilator. The genetic modification was to deceive the human immune system from recognising the kidney as foreign and reject it. Since the recipients were already brain-dead, the purpose of the transplantation was not to save the patient; it was purely an experiment to find out if an organ from a genetically modified pig would be compatible, function normally and not be rejected.

A pig heart transplant in Assam in 1997

Since the human immune system rejects anything that is foreign, whether from another person who is immunologically matched to the recipient or from a different species such as a pig, scientists had to tweak the pig genome to make the organ less likely to be rejected. According to the *New Scientist*, Revivicor, a U.S.-based company, is raising a small herd of genetically engineered pigs. These pigs have 10 of their genes genetically modified to reduce the possibility of rejection. Of the 10 genes, four were inactivated, including one that causes an aggressive immune response and another that causes the heart to grow after transplantation. In addition, six human genes were inserted into the pig genome to further reduce the risk of rejection. The recipient is also on an experimental drug to suppress the immune system so that the transplanted pig heart is not rejected.

In the early 1990s, it became clear that all human immune reaction were directed at one pig antigen — a sugar molecule present on cell surfaces. Knocking out the gene that produces an enzyme, which in turn, produces the sugar molecule, helps in reducing the risk of an immune reaction leading to rejection. The DNA of pigs also contains many retroviruses that can infect human cells. The presence of such a virus in the transplanted organ raises the risk of infection in human recipients. Dozens of retroviruses have been removed from the organ to make it safer when transplanted.

Unlike the traditional breeding techniques to know both copies of a gene, the advent of genome-editing tools such as CRISPR/Cas9, which allows precise removal of specific genes has made gene modification simpler, fast and accurate. A genetically modified pig cell is fused with a pig ovum that has its DNA removed. The ova that contain only the genetically engineered genome start dividing to become pig foetuses. This is the same technique that was used to clone Dolly,

the sheep. The embryos are then implanted into surrogate mothers. The gestation period is just 114 days, unlike in the case of humans. Pigs have been preferred as ideal candidates for xenotransplantation despite their immune system being different from humans for the simple reason that the porcine organs are anatomically similar to those of humans.

Last year, nearly 4,000 people in the U.S. received human donor hearts, but the need is far more. The highest demand is for kidneys. According to the health ministry, around 0.18 million people in India are estimated to suffer from renal failure every year, but only about 6,000 renal transplants are carried out in the country. About 25,000-30,000 liver transplants are needed annually in India but only about 1,500 are being performed. In the case of the heart, 50,000 people suffer from heart failure and are in need of a heart transplant. Yet, only 10-15 heart transplants are carried out in India each year. Harvesting organs from genetically engineered pigs is seen as a viable alternative to meet organs shortage. Besides scientific challenges, there are several ethical challenges to overcome before xenotransplantation of porcine organs become a reality.

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In what way does the sub-lineage, BA.2, differ from the original? Will this make it harder to track?

The extension was approved by the Central Drugs Standard Control Organisation

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