

# Pig Chimeras Offer Glimpse of Future Human Organ Development



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On January 26, 2017, a team led by Dr. Juan Carlos Izpisua Belmonte of the Salk Institute for Biological Studies successfully created pig embryos that had the potential to generate human organs. The team’s experimental results marked a key development in the artificial generation of chimeras, which are organisms that derive cells from various other embryos. Harnessing the full potential of artificial organ development would help many patients and hospitals that face organ donor shortages.

Traditionally, chimeras have been difficult to produce in a laboratory setting due to the complexity involved in assimilating two or more distinct genomes into a single organism. Scientists in the past have generally injected pluripotent stem cells, which are capable of the full extent of cell differentiation, from a donor species into a host species. Cell differentiation is the process by which immature embryo cells develop unique characteristics and form mature organs. Theoretically, the injected stem cells would differentiate as the host embryo matures and grow into full-fledged organs, generating a viable hybrid embryo. However, many such attempts have ended in failure. In fact, a seminal 2009 Nature report written by Robert Lanza of Advanced Cell Technology claimed that human-animal hybrids simply could not grow beyond 16 cells because they failed to express genes needed to keep pluripotent stem cells alive.

In an attempt to approach the chimera problem from a different angle, Belmonte’s team aimed to tackle a simpler problem by creating mouse-rat hybrids. Unlike humans, rats possess a smaller, simpler genome and exhibit more similarities with their mouse counterparts. To conduct this experiment, they relied on the popular CRISPR-Cas9 technique, which has allowed for cheaper and more efficient modifications to DNA.

Armed with this cutting-edge technology, Belmonte’s team removed the genes responsible for stem cell differentiation from mouse embryos and implanted rat stem cells that harbored rat organ development genes. The resulting chimeras mostly contained rat organs and lived for up to two years, just like their unmodified mouse counterparts.

After ensuring that their innovative experiment strategy worked, the Belmonte team turned to solve the human-animal chimera question. Because of the large litter sizes of pigs, the scientists were able to inject more than 1400 pig embryos with one of three types of human cells: Normal, fully developed human cells, pluripotent stem cells that would later develop into mature tissue, and “intermediate” cells that were neither fully normal nor immature. The third group of mice with the “intermediate” cells led to the highest number of hybrid embryos that showed signs of healthy organ development.

While the Belmonte team’s results produced great excitement

in the scientific community, several roadblocks still bar researchers from generating functional human organs through pig chimeras. To begin with, only 1 in 100,000 cells in each of the pig-human chimeras were of human origin. The scientists hypothesize that the host pigs’ immune system prevented a large number of the human stem cells from embedding within the pigs. Such a low yield of human cells raises the question of whether the resulting organs would truly be human. Dr. Hiromitsu Nakauchi of Stanford University, skeptical of the low number of human cells, stated, “It’s a good try, but the result seems like more a negative result.” Moreover, scientists and ethicists have voiced their concerns regarding the morality of generating human-pig chimeras for organ growth purposes. Indeed, ethical and scientific hurdles must be overcome before the pig-human chimera can solve the world’s organ transplant shortages.

## SOURCES

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