

Xenotransplantation: A Solution To Organ Shortage

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ABSTRACT

The problem of insufficient donor organs is still one of the most important problems that exist in the field of healthcare, as the needs of patients are rarely satisfied. The use of organs or tissues from other species, known as xenotransplantation, may become a solution to this problem. Recent advancements in genetic engineering, including the discovery of the CRISPR/Cas9 gene editing system, have allowed researchers to change multiple genes in animal organs to overcome the problem of inflammation or rejection by human bodies.

However, xenotransplantation raises complex ethical concerns. These include issues related to animal welfare, religious and cultural beliefs, and questions surrounding human identity. Additionally, there are medical and societal risks, such as the potential transmission of zoonotic diseases and the long-term effects of immunosuppressive treatments required after transplantation.

This paper reviews how xenotransplantation can address the global organ shortage while taking medical and ethical ideas into consideration, highlighting both its potential and the challenges that must be addressed before widespread implementation. Despite the great promise shown by xenotransplantation, it requires further advances in technology as well as the establishment of ethical considerations that will ensure its proper application.

INTRODUCTION

Organ shortage is a problem across the globe, where the *World Health Organization* estimates only **10% of organ transplant needs are met globally**. Organ transplantation is one of the most significant medical technologies and advancements utilised today. This shortage can lead to increased mortality and reduced quality of life for patients, including long waiting times and limited treatment options. Despite its success, there is a severe global organ transplant shortage which ranks among top causes of mortality worldwide. Scientists have been working on finding a viable solution. *CRISPR* technology has been rapidly revolutionising the medical industry, and researchers have found a way to link it to xenotransplantation, and it shows promise for revolutionizing xenotransplantation in a way that could supplement the global organ shortage. Xenotransplantation is essentially the transplantation of animal organs into humans, with the most commonly used animals being pigs and primates.

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METHOD

This literature review was conducted using Google Scholar as the main database. Articles were selected based on their relevance to xenotransplantation, genetic modification, and ethical considerations. This literature search was conducted during March-May 2026. Most of the sources used were published within the last 10–15 years in order to ensure that the information is recent and reliable. Searches were performed using keywords and phrases such as “xenotransplantation,” “ethics,” and “genetic modification.” The review primarily relied on peer-reviewed journal articles identified through Google Scholar. A limited number of reliable scientific news sources were included to provide information on real life examples. All sources were carefully chosen based on their credibility and relevance to the topic. Studies were included if they discussed xenotransplantation, genetic modification, medical challenges, or ethical considerations relevant to the review. Sources which had no contribution to the research question or lacked scientific credibility were excluded.

SCIENTIFIC EVALUATION

Xenotransplantation is a procedure that involves the transplantation, implantation or infusion of one species to another, typically from an animal to a human. This process began in 1667 in order to transfuse blood from a lamb into a human. Similarly, several studies were carried out in the 1900s regarding the kidneys, hearts, and livers of non-human primates. However, due to major ethical concerns, risk of transmitting infectious diseases and problems in reproducing the animals and vast differences in organ size, the research regarding the utilization of primates was withdrawn. (*Ryczek et al. 2021*)

THE PROCESS

Therefore, since the 1990s, researchers have attempted to implement pigs for their xenotransplantation research. The domestic pig is considered the most appropriate species because they are easy to reproduce, they have a large litter size, short maturation period and the size of the organs is similar to human ones. Even so, there are issues between pigs and humans which ultimately results in the development of an immune response which decreases the success rate of a successful xenotransplantation. (*Ryczek et al. 2021*).

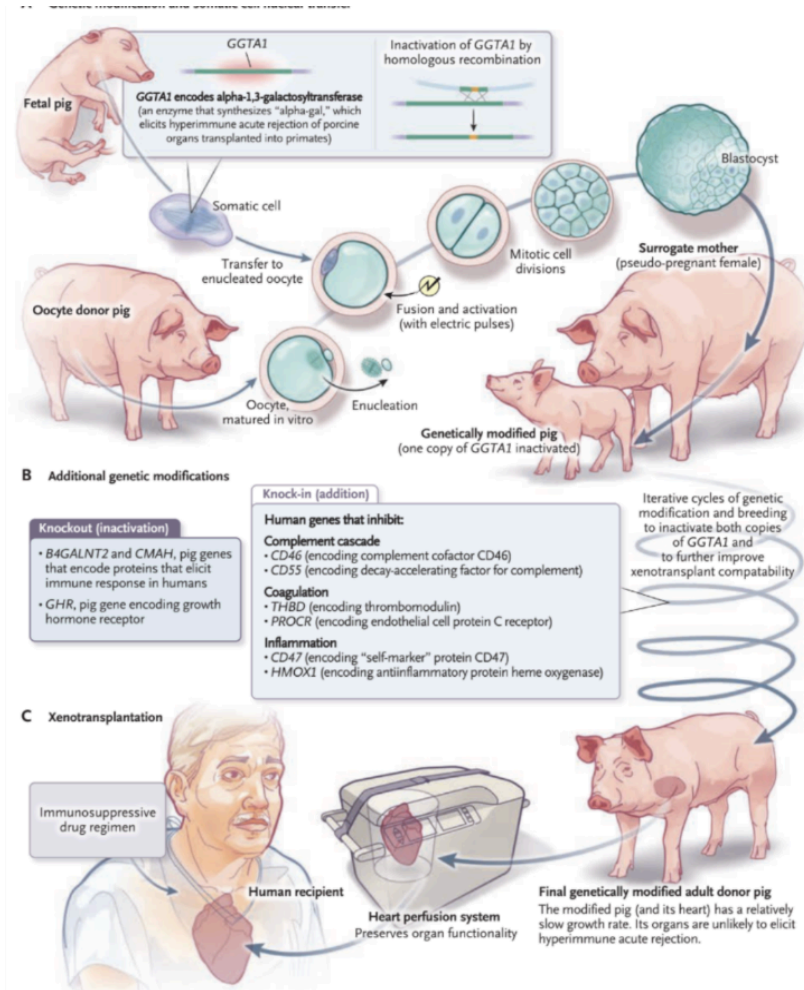


Fig. 1. Genetic modification strategies used in pig-to-human transplantation. Adapted from Phimister, Elizabeth G., "Genetic Modification in Pig-to-Human Transplantation," *New England Journal of Medicine*, vol. 387, no. 1, 2022, pp. 79–82.

The process begins with targeting the *GGTA1* gene in pig cells with *CRISPR/Cas9*, which produces the alpha gene antigen. This antigen is the reason for immediate immune rejection in humans, meaning that the transplant can fail within a few minutes to a few hours. Therefore, *GGTA1* is inactivated in somatic cells taken from a fetal pig using homologous recombination to reduce immunogenicity (Phimister 2022).

The modified somatic cells are used in a cell nuclear transfer where the nucleus moves in an enucleated oocyte from a donor pig. The fusion of this cell leads to activation via electric pulses, thus promoting cell division. Cell mitosis and development lead to the formation of a blastocyst, which is later transplanted into a female surrogate pig. In due course of time, a genetically modified pig is born. (Phimister 2022).

Further genetic modifications are made to improve compatibility. Scientists knock out pig genes like *B4GALNT2*, *CMAH*, and *GHR* to lower immune responses and manage growth. They also add human

genes to better control complement activation, coagulation, and inflammation. The inserted genes include *CD46* and *CD55* for complement control, *THBD* and *PROCR* for coagulation, and *CD47* and *HMOX1* for immune modulation. After several rounds of modifications and breeding, researchers produce a suitable donor pig. They preserve its organs in a perfusion system before transplantation. The organ is then transplanted into a human recipient, who must take immunosuppressive drugs to avoid rejection (Phimister 2022). This process shows how genetic engineering and cloning techniques can help tackle organ shortages.

While these strategies have reduced the risk of hyperacute rejection, sources suggest that a single modification is not enough by itself. Phimister mentions that combining multiple gene knockouts with some regular human genes allows for a longer lifespan and greater compatibility, thus reducing the chances of hyperacute rejection more effectively. In a similar vein, Ryczek et al. highlights that incorporating CRISPR has increased xenotransplantation by enabling several genetic modifications at once. Both of these studies demonstrate a common resolution that successful xenotransplantation requires multiple complementary genetic modifications rather than a single genetic intervention.

IMPACT OF IMMUNOSUPPRESSANTS

However, there are multiple impacts of immunosuppressive drugs which are life altering. These drugs do not simply prevent the immune system from attacking the transplanted organ—they also interfere with the body's cellular functions—inclusive of the metabolism of T cells. Immunosuppressive drugs make it harder for the body to mount effective immune responses by disrupting the metabolic processes that give T-cells energy to grow, activate, and work. As a result, while they are necessary for preventing organ rejection, they can leave individuals more vulnerable to infections and other health complications which significantly reduces the overall quality of life (Pallet et al. 2026).

THE LONGEST LASTING XENOTRANSPLANTATION CASE

The following case study reveals the role played by progress in genetic engineering in solving the problem of the lack of donor organs around the world. An American patient, Tim Andrews, aged 67, underwent a surgery where he received a kidney that had been genetically engineered from a pig. The patient lived for 271 days until his body finally rejected the transplant, but fortunately, another donor was found for him (WMUR-TV 2026). At the time of the transplantation, Tim Andrews had been suffering from the final stage of kidney disease, during which he went under dialysis treatment for more than two years. Living through six months of life is quite an accomplishment because it is at this point in time that a person is exposed to the greatest risk of developing complications like organ rejection, anemia, or infection. Comparing this achievement to the longest previous life span after a similar operation, we see that the latter took place just four months and nine days (Fieldhouse 2025). Despite the fact that this case is certainly a landmark in the development of the field of xenotransplantation, it also illustrates the constraints associated with existing transplantation methods. According to reports, the genetically

engineered kidney of the pig had to be extracted because of a slow decrease in its functioning, the reason for which remains unknown to the public. This shows that despite all the achievements in genetic engineering through CRISPR technology and immunosuppression therapy, current methods of treatment cannot provide long-term graft functionality. However, due to multi-gene editing techniques, which helped to minimize the risk of hyperacute rejection, scientists still have a number of debates concerning overcoming the other obstacles related to long-term immunity response, physiological incompatibility, and immunosuppression effects. Hence, such cases not only show the significant achievements but also the challenges that scientists face.

RECENT MILESTONES

Recently, the FDA cleared the first human clinical trial of a genetically modified pig heart. The trial, known as EXPRESS, will be evaluating UHeart, a pig heart which has undergone 10 genetic modifications. The criteria is for patients with severe heart failure left with no other options who are ≥ 50 . The trial is still experimental and there are still safety procedures to be done (*“United Therapeutics Corporation”*) (2026).

ETHICAL CONSIDERATIONS

One may consider Xenotransplantation a successful process overall, but there are multiple ethical considerations which must be taken into account while including religious beliefs, personal identity between the poles of body, soul and mind and social ethics (Rydzek *et al.* 2021).

From a religious standpoint, this advancement may be considered unethical in some contexts, as religions such as Hinduism, Judaism, and Islam place restrictions on the use and treatment of certain animals. Hinduism considers the cow to be a sacred animal, while Judaism and Islam prohibit the consumption of pigs; however, in life-threatening medical situations, these restrictions may be reconsidered or overridden.

To be specific, in Judaism, the principle of preserving human rights overrides most religious restrictions. Transplantation, including xenotransplantation, is not only permitted but may be considered a moral duty (*mitzvah*) in life-threatening situations. Similarly, in Islam, while certain animals are considered impure and dietary restrictions exist, the preservation of human life is considered more important. Islamic teachings emphasize that health is a responsibility entrusted to humans by God, and therefore, medical necessity can justify the use of otherwise prohibited materials (Sautermeister *et al.* 2015).

From a Christian perspective, this process is not strictly forbidden but not completely endorsed. Christian ethics focus on human dignity, saving lives, and responsibility toward animals. While organ transplantation is generally accepted, xenotransplantation raises concerns about animal welfare, human identity, and social acceptance. Biblical teachings do not directly address this issue but emphasize treating

animals responsibly. Therefore, xenotransplantation may be considered acceptable if it saves human lives, but it requires careful ethical consideration (*Sautermeister et al. 2015*).

However, from a Hinduism outlook, this treatment may be considered unethical, as the concept of karma extends beyond human beings to include all living creatures, since every being is believed to possess a soul. Because xenotransplantation involves harm or killing of animals, it is viewed as problematic, particularly when it involves sacred animals such as cows (*Hurst et al. 2025*).

MEDICAL CONSIDERATIONS

In terms of medical or genetic modification ethics, *Zoonosis* is another possibility, which means diseases passing from animals (like pigs) to humans through transplants. The worry is not only for the patient, but also for the chance that the infection could spread to other people in the community. This is an important ethical issue because the effects are not limited to the person who gets the transplant. Before they start working on animals, scientists need to carefully study animal viruses and figure out how likely they are to infect people and spread. There are some early warnings, but there is no way to know for sure if the risk can be completely removed because zoonotic viruses are constantly evolving (*Hurst et al. 2025*). There is a wide range of these diseases, each with different impacts. Firstly, *Porcine cytomegalovirus (PCMV/PRV)* is a virus commonly found in pigs which, rather than fully infecting the human recipient, significantly reduces the survival time of transplanted organs. This makes it one of the major barriers to successful xenotransplantation. Another virus found in pigs is *Porcine Lymphotropic Herpesvirus (PLHV-1, -2, -3)*, which can cause *post-transplant lymphoproliferative disorder (PTLD)*, a condition where immune cells grow uncontrollably after a transplant, potentially leading to serious complications (*Denner 2021*).

Building upon this, another key medical ethical issue which should be taken into account is consequentialism, where choices are made by understanding the benefits and the risks. In this case, it means considering whether giving a patient an organ will be more beneficial than harmful. Transplants can elongate a patient's life, it also carries many risks including organ rejection, side effects and at times death. Since this procedure is still being altered and experimented with, the outcomes are uncertain. Moreover, the benefits and harms may affect different people in different ways, for example, one patient may benefit, while others face risks like infections. These variables make outcomes difficult to compare. Therefore, relying only on the risks can also lead to unethical choices, so it has to be balanced with other ethical choices (*George 2022*).

DISCUSSION

The literature suggests a common consensus between researchers that advances in CRISPR/Cas9 technology have resulted in revolutionary changes in xenotransplantation. According to Ryczek et al.

(2021) and Phimister (2022), in order to ensure the success of xenotransplantation, several more genetic manipulations are needed that imply the knocking in and knocking out of different genes for different reasons. For instance, genes such as CD46, CD55, PROCR, etc. are knocked in order to control complement activation, coagulation, and inflammation.

The 271-day survival of a genetically modified pig kidney was a considerable improvement compared to all other results and showed the potential of multi-gene modification and immunosuppressive treatment. Nevertheless, the failure of kidney function and its removal reveal the fact that there are still no solutions to this problem. This corresponds to the majority of literature that regards immune response, physiological incompatibility, infection, and influence of immunosuppressive treatment as the obstacles. In spite of the evidence that the genetically modified organs can work in human patients for a long period of time, it is still required to conduct more research in order to increase graft survival both reliability and longevity.

It is still necessary to use immunosuppressive drugs so that the human immune system will not reject the organ of the pig. It shows that genetic modification alone is not sufficient to attain total immune tolerance. Currently, the use of immunosuppressants makes it possible to increase survival rate by lowering immune response. But as mentioned by Pallet et al. (2026), such medications interfere with the metabolism of T cells making the risk of infections higher.

This literature also highlights the importance of ethical and medical concerns. Various religious perspectives do and do not support the concept of xenotransplantation. For example: Some question the use of animals while others deem it acceptable when human life is at stake. Animal welfare and chances of the transmission of zoonotic diseases also raise concerns about the wider impacts of the transplants. That's why along scientific research and developments, ethical considerations must be addressed before everyone can accept it.

Overall, the literature suggests that xenotransplantation has made significant overall progress due to the advances of genetic engineering, immunosuppressants, etc. However, clinical evidence shows that long-term survival is uncertain while immunosuppression, infection, and ethical concerns continue to present challenges. Therefore, although xenotransplantation shows a lot of promise for helping reduce the global organ shortage, more research is needed before it can become a safe, reliable, and widely accepted solution.

LIMITATIONS OF THIS LITERATURE REVIEW

Since Google Scholar was the main database used, some relevant studies may have been missed, which could have limited the depth of the analysis. A limited number of scientific news sources were also included, meaning that not all sources were peer-reviewed. In addition, publication bias may have influenced the available literature, as studies which were found to be more successful were likely to have

been published. Lastly, since xenotransplantation is a relatively newer topic and constantly evolving, new findings can change the overall understanding of this paper in 5-10 years time.

CONCLUSION

Conclusively, xenotransplantation remains a controversial yet evolving solution to the global organ shortage. It involves transferring animal organs into humans, with early attempts facing ethical and disease-related challenges. Since the 1990s, pigs have been preferred due to compatible organ size and reproduction advantages. Moreover, genetic modification, such as inactivating the *GGTA1* gene, has helped reduce immune rejection. However, its effectiveness is currently restricted by medical challenges such as organ rejection, the need for lifelong immunosuppressants, and the risk of zoonotic diseases. In addition, ethical and religious concerns further complicate its widespread acceptance. Therefore, while xenotransplantation has the potential to substantially reduce the organ shortage in the future, it cannot yet serve as a complete or universally accepted solution without further scientific advancements and ethical consensus.

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