



## Editorial

### Xenotransplantation: Fact or Magic

Batool Mutar Mahdi\*

HLA Research Unit, Al-Kindy College of Medicine, University of Baghdad, Baghdad, Iraq

\* Corresponding author: batoolmutar@kmc.uobaghdad.edu.iq

#### Article history:

Received 1 July 2022

Accepted 4 August 2022

Available online 31 August 2022

<https://doi.org/10.47723/kcmj.v18i2.869>

**Keywords:** HLA, Transplantation, Genetic



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license

<http://creativecommons.org/licenses/by/4.0/>

The knowledge of transferring body organs or tissues appears in ancient mythology of Roman, Greek, Indian, Chinese, and Egyptian civilizations. The stories of organ transplants performed by GODs and health care's using organs from cadaveric and after that transplantation change from lore to medical training (1). One of the obstacles that faced this brunch of medicine is shortage of organs donation and patients still waiting on the waiting list for long time to get the organ from brain death human on car accidents or any other diseases. The best example is kidney transplantation is used for treatment chronic renal failure and there is a limited numbers of organ donations. So, the best solution is xenogenic kidney transplantation that fill the gap of shortage in the graft donation (2). Many trails were done to transplant organs from animals known as xenotransplantation (3). There is an important number of fences to xeno-transplantation in human beings for example immunologic challenges like human leukocytes antigen (HLA) incompatibility that affect the survival rates of the graft (4). HLA is a group of antigens were coded from genes located on the short arm of chromosome number six and these were divided into three Classes (Class I, II, III) and the most important one is class II that coded HLA-DR and DP which is so important in transplantation that need either a fully compatible or limited degree of HLA mismatching with acceptable results in many cases (5). A prodigious deal of development and researches are needed in immunological strategies to make xeno-transplantation a clinical reality and truth. The greatest exciting view nowadays is the use of organs from pigs that used previously with a monkeys' by genetically eliminating the epitope that responsible for hyperacute and acute xenograft rejection and tolerance induction on cellular and chronic xenograft rejection (6). Now adays the newscast of three pig to human transplantation cases has roused public and community interest and attention. Team of surgeons at Alabama Transplant Institute have successfully achieved a pig kidney transplant to human using a genetically modified pig as the donor after several approaches. Two of porcine kidneys were transplanted into a brain-dead recipient after doing gene-editing to pig kidney graft that included species-specific antigen has been removed by genetic engineering by removing the galactose-alpha-1,3-galactose (alpha-gal) epitope by means of alpha-1,3-galactosyltransferase gene knockout (GTKO) with subcapsular autologous thymic tissue (7). Then, preoperative laboratory tests like

crossmatching between donor lymphocytes and patients' serum for detection any preformed antibodies through performing panel reactive antibodies (PRA) and screening for viral infection. The xenotransplantation kidney between pig and human had also some obstacles during surgery or evidence of hyperacute rejection during operation due to antibody mediated rejection. Genetically modified pigs kidney remained viable and functioning in brain-dead human recipients for 54 hours without hyperacute immune rejection (8). Unfortunately, the grafts did not work properly and decompensation of the patient. Even though, this study shed a light on new achievement in this research part and move xenotransplantation to the clinic. So, the use of successful immunosuppressive protocols of drugs like anti-CD154 antibody will be critical to maximize the success in the first trail in human (9). Improvements in this field are needed by recent clinical experimentation, and trails then general dissemination of organ xenotransplantation has begun to appear a possible near-term ambition.

---

## References

- [1] Barker CF, Markmann JF. Historical overview of transplantation. *Cold Spring Harb Perspect Med.* 2013;3(4):a014977. Published 2013 Apr 1. doi:10.1101/cshperspect.a014977
- [2] Ramackers W, Klose J, Winkler M. Xeno-kidney transplantation: from idea to reality. *Transplant Proc.* 2012 Jul-Aug;44(6):1773-5. doi: 10.1016/j.transproceed.2012.05.041. PMID: 22841270.
- [3] Purdy L. Should we add "xeno" to "transplantation"? *Politics Life Sci.* 2000 Sep;19(2):247-59. doi: 10.1017/s0730938400014854. PMID: 15468488.
- [4] Borenstein SH, Graham J, Zhang XL, Chamberlain JW. CD8+ T cells are necessary for recognition of allelic, but not locus-mismatched or xeno-, HLA class I transplantation antigens. *J Immunol.* 2000 Sep 1;165(5):2341-53. doi: 10.4049/jimmunol.165.5.2341. PMID: 10946256.
- [5] Petersdorf EW. In celebration of Ruggero Ceppellini: HLA in transplantation. *HLA.* 2017;89(2):71-7. doi:10.1111/tan.12955
- [6] Hoerbelt R, Madsen JC. Feasibility of xeno-transplantation. *Surg Clin North Am.* 2004 Feb;84(1):289-307. doi: 10.1016/S0039-6109(03)00208-1. PMID: 15053194.
- [7] Montgomery RA, Stern JM, Lonze BE, et al. Results of Two Cases of Pig-to-Human Kidney Xenotransplantation. *N Engl J Med.* 2022;386(20):1889-1898. doi:10.1056/NEJMoa2120238
- [8] Porrett PM, Orandi BJ, Kumar V, et al. First clinical-grade porcine kidney xenotransplant using a human decedent model. *Am J Transplant.* 2022;22(4):1037-1053. doi:10.1111/ajt.16930
- [9] Ganchiku Y, Riella LV. Pig-to-human kidney transplantation using brain-dead donors as recipients: One giant leap, or only one small step for transplant kind? *Xenotransplantation.* 2022 May 26:e12748. doi: 10.1111/xen.12748. Epub ahead of print. PMID: 35616243.

**To cite this article:** Mahdi B. Xenotransplantation: Fact or Magic. *Al-Kindy College Medical Journal.* 2022;18(2):82-83.