



# XENOTRANSPLANTATION: A BRIEF OVERVIEW HOW GENETICALLY MODIFIED PIG OVERCOME XENOTRANSPLANTATION REJECTIONS:

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## INTRODUCTION:

Xenotransplantation is defined as any procedure involving transplantation, implantation, or infusion into a human recipient of live cells, tissues, or organs from a non-human animal source. It also includes any procedure in which human body fluids, cell tissues, or organs have *ex vivo* contact with live human animal cells, tissues, or organs. More generally, xenotransplantation defines any cross-species transplantation (e.g., mouse to rat, pig to primate, and sheep to human). In recent bio-medical approaches, pigs are majorly used as source animals for xenotransplantation.<sup>1</sup>

The main challenges that have come across xenotransplantation are hyperacute rejection (HAR), acute humoral xenograft rejection (AHXR), acute cellular rejection, immune cell-mediated rejection, and chronic rejection.<sup>2</sup>

## Why only pigs, not NHPs?

As NHPs are of other species, there is a probability of cross-species transmission of infection, differences in organ size, and difficulty in breeding.

## Pigs

As they have relatively large litter size, short maturation period, and low risk of xenozoonosis and their size and physiology are similar to humans, genetic engineering techniques produce porcine organ which is resistant to rejection, though immune rejection is shown.<sup>3</sup>

## BACKGROUND:

To overcome hyperacute rejection and subsequent rejection mechanisms, such as acute vascular and cellular rejection, a plethora of genetic modifications (gene knockouts and transgenes) has been introduced into the porcine genome. These modifications aim at:

Elimination of the  $\alpha$ Gal, Neu5Gc, and Sd(a) epitopes by disrupting the genes encoding  $\alpha$ -1,3-galactosyltransferase (*GGTA1*), CMP-N-acetylneuraminic acid hydroxylase (*CMAH*), and  $\beta$ -1,4-N-acetyl-galactosaminyltransferase 2 (*B4GALNT2*).

Inhibition of regulatory proteins (CD46, CD55, and CD59).

Prevention of coagulation dysfunction by transgenic regulatory proteins.

Inhibition of T-cell activation by transgenic expression of CTLA4-Ig.<sup>4</sup>

### Subjecting heart(Immune system)

Genetically modified pigs underwent 10 gene modifications.

Knocked down of 3 immune rejection-related genes.

Inserted 6 human genes and 1 growth gene for inactivation of the immune system and to control the size of heart.

Removal of Xeno antigens by gene manipulation of alpha,1-3-galactoside encoded by (GGTAI) is important cell surface Xeno antigen and N-glycolylneuraminic acid and hydroxylase (mah) is related to cross-species immunity response.

These genes are knocked out and less evoke the immune system.

In another group by deletion of SLA.

Inhibition of CD59.CD46.CD47.

It is still unknown whether immunosuppressants truly work or not.<sup>5</sup>

Conclusion:

Xenotransplantation is a life saving procedure. In detail study of anatomy, genetics is needed to go forward. Pigs played a succeeded role in organ transplantation. Using of advance biomedical research is needed for detail study.

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