**What is it?**

Xenotransplantation is any transplantation procedure in which organs, tissues, or cells are transferred from a donor whose species is different than that of the recipient.

Xenotransplantation has implications in human medicine.

Animal heart valves have been long available for transplant into human patients, and we will likely see corneal xenotransplantation, for vision impairments due to damaged cornea, and pancreatic islet cell xenotransplantation, for type I diabetes, in clinical trials soon.

Pigs have been identified as a good donor species for human patients, but current problems of antibody- and cell-mediated graft rejection, as well as cross-species viral transmission, must be resolved.

One solution has been to genetically modify donor pigs so they do not produce an enzyme called alpha-1,3-galactosyltransferase, which is antigenic in humans; as we develop an inflammatory immune response in its presence.

Another solution is to cleanse the grafts of antigenic cells and repopulate them with stem cells from the recipient. This is called semi-xenotransplantation and reduces the risk of disease transmission as well as need for immunosuppressive treatments following the transplantation procedure.

**Pros**

- Unlimited supply of organs could end human transplant wait list
- Infectious microbe transfer could be reduced by monitoring donor herd
- Creates new research opportunities
- Extend human life span

**Cons**

- High risk of rejection
- Longevity of transplant is currently questionable
- Welfare of donor animals
- Could be seen as ‘unnatural’

**How will we get xenotransplantation into clinical practice?**

Who might be involved in review of a xenograftic therapy?
- FDA or equivalent agency in another country
- Office of Cellular, Tissue, and Gene Therapies
- Center for Biologies Evaluation and Research
- Outside scientific consultants
- Patient advocates

Early Experiments & Historical Cases

Select donor species and transgenes

Preclinical Research

Establish clinical development plan

Clinical Research

Approved Xenogeneic Therapy

- What will it take to get here?
  - Reproducible preclinical & clinical data
  - Regulatory consensus
  - Infectious risk management
  - Organ farming
  - Ethical consent process
  - Public and patient education

Preclinical research will evaluate graft survival, appropriate immunosuppressive regimen, and parameters for patient monitoring.

Obtaining donor organs will require:
- Establishment of donor herd
- Animal husbandry
- Health and infectious agent testing
- Organ harvest and transport
- Use and disposal of byproducts