Online Ethics Center
FOR ENGINEERING AND SCIENCE

Unit 8 - Final Case

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Description

This is the eighth unit in an extensive Course on Genomics, Ethics and, Society. This unit (8) contains the final case study. This is the concluding piece of assessment for the course.

Body

Case Study

“Xenotransplantation” refers to the practice of transplanting organs, cells, and tissues from nonhumans into human beings. Currently, there are 122,875 people in the U.S. awaiting organ transplants (as of July 6, 2015). With the recent sequencing of the pig genome, and breakthroughs in modifying the pig genome to be more amenable to the human immune system, many researchers have begun discussing the possibility of using organs from genetically modified pigs for xenotransplantation. If successful xenotransplantation with pigs were to be achieved, the technology could then be applied to other species that, if genetically

modified, might be able to produce organs for human beings in need.

Xenotransplantation is part of a broader trend towards genetically modifying animals to provide medical products for human beings. For instance, in 2009 the FDA granted approval for milk produced by domestic goats that had been genetically engineered to produce antithrombin, a protein used in various medicines to prevent blood-clotting (Pollack, 2009). This milk was created by inserting the human gene for antithrombin into part of the goat genome that controls milk production. Typically antithrombin is collected from human plasma donations. However, this herd of goats, reportedly, can produce as much antithrombin in a year as 90,000 blood donations.

Domestic pigs (*Sus scrofa*) have been the focus of recent efforts for a number of reasons. They are much more anatomically and physiologically similar to human beings than most other animals used to develop medicines and study diseases (e.g., mice). Pigs also have a short gestation time and large litter size, enhancing their productivity and shortening the amount of time between tests. They have already proved useful in providing insights into very complicated human diseases, such as cystic fibrosis, diabetes, and Alzheimer's (Fan & Lai, 2013; Prather, 2013; Prather, Shen, & Dai, 2008; Whyte & Prather, 2011).

1,644 people in the U.S. are currently awaiting lung transplants. A longstanding challenge for conducting organ transplants even between humans is avoiding what is called *hyperacute rejection* of the transplanted organ (Cooper 2012; Groenen et al., 2012). This occurs within 24 hours of transplantation and results from the production of the antigen α-Gal, which is synthesized by the enzyme GGTA1. Xenotransplantation typically increases the risk of hyperacute rejection because differences between species are much more likely to trigger rejection than differences between individuals within a species.

Recently researchers were able to "knock out" the gene for GGTA1 in pigs and replace it with a gene that produces antigens amenable to the human immune system (Cooper 2012; Groenen et al., 2012). Further modifications have also successfully been made to other pig genes likely to produce antigens that would cause human transplants to fail. Additional research specific to lung transplants has suggested that modifications could be made to genes that manage "von Willebrand factors," which control blood clotting, and it has been suggested that these could prevent rejection of lung xenotransplants.

A population of pigs with these modifications could potentially be used as lung donors. These specific changes are unique to lung xenotransplantation, but progress on other organs would likely follow. Perhaps more importantly, the technique used to prevent hyperacute rejection could also be applied to other species (e.g., cows) whose organs might prove compatible with the human immune system, once additional research can be conducted (Garrels, Ivics, & Kues, 2012).

As with other kinds of genetic modification of animals, pigs modified for use in xenotransplantation raise a variety of concerns (Anderson, 2006; Hughes, 1998; Nuffield Council on Bioethics, 1996). For instance, diseases could unwittingly be transmitted to humans from animals in the xenotransplantation process. Before xenotransplantation can move forward, researchers might need to modify other genes that would protect against infection more generally, not just those that cause hyperacute rejection of the transplanted organ.

There are also concerns that genetically modified animals could escape and breed with non-modified populations. Containment for the antithrombin goats, mentioned above, includes two fences, 24-hour security, and video surveillance (Pollack, 2009). Every goat also receives ear tattoos, neck tags, and electronic transponders in order to facilitate identification. Similar procedures are required in the U.S. for all genetically modified animals, in accordance with the degree of risk involved. Nobody has proposed that pigs used for xenotransplantation carry a greater risk of escape, but failures in confinement are always possible.

Critics have also raised concerns about the ethics of genetically modifying animals for use in such procedures. For instance, in commenting on the antithrombin goats, the Humane Society of the United States argued, “It is a mechanistic use of animals that seems to perpetuate the notion of their being merely tools for human use rather than sentient creatures” (Pollack, 2009). There are also questions about the welfare of the pigs used in such procedures, including concerns both about suffering and positive welfare (such as the opportunity for social interaction and the freedom to move around) and whether, in the case of pigs created for lung research, the genetic modifications themselves cause suffering.

Lastly, many are concerned that people will not wish to receive transplants from a different species, and so it may not be worth creating these animals at all. In surveys, people have expressed an unwillingness to accept xenotransplantations, though they are much more willing to accept medicine derived from animal sources

(Prather, Shen, & Dai, 2008; Prather, 2013). It would make little sense to develop the technology if it will not be used.

1. **Suppose you are asked to take charge of devising guidelines to govern the development of xenotransplantation of organs, including (but not limited to) lungs, from pigs to humans. Would you agree to devise these guidelines? If not, explain why not. If you would agree to devise the guidelines, what social, environmental and other ethical concerns would you take into account? What are the main risks about which you would be concerned?**

2. **Would you yourself accept an organ transplant from a pig (assuming that no human alternative was available, and that your need for a transplant was reasonably urgent, although you are not at imminent risk of dying)? Give reasons for your answer.**

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Recommended Readings

- Bendixen, E. K., Danielsen, M., Larsen, K., & Bendixen, C. (2010). Advances in porcine genomics and proteomics—A toolbox for developing the pig as a model organism for molecular biomedical research. *Briefings in Functional Genomics* , 9, 208–219.
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- Sykes, M., D'Apice, A., & Sandrin, M. (2003). The ethics of xenotransplantation. *Xenotransplantation*, 10, 194-203.
- Walters, E. M., Agca, Y., Ganjam, V., & Evans, T. (2011). Animal models got you puzzled?: think pig. *Annals of the New York Academy of Sciences*, 1245, 63–64.
- Vàzquez-Salat, N., Salter, B., Smets, G., & Houdebine, L. M. (2012). The current state of GMO governance: are we ready for GM animals? *Biotechnology Advances*, 30, 1336–1343.
- Verma, N., Rettenmeier, A.W., & Schmitz-Spanke, S. (2011). Recent advances in the use of Sus scrofa (pig) as a model system for proteomic studies. Proteomics, 11, 776–793.

Online Resources

1. EPA Guidelines for Containment of GM Animals: https://www.epa.ie/pubs/advice/gmo/Guidelines%20on%20containment%20measures%2 .
2. National Swine Resource and Research Center: http://nsrrc.missouri.edu/.
3. Organ Procurement and Transplantation Network: http://optn.transplant.hrsa.gov.
4. Genetically Engineered Animals: General Q&A [archived webpage].

Notes

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