



LIGERS, TIGONS, AND SPLICE: HUMAN-ANIMAL HYBRIDS

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When the great naturalist Joseph Kolreuter painstakingly and methodically cross-pollinated hundreds of plants in the 18th century, he could not have foreseen the 21st century version of hybrids: human-animal (HA) hybrids. HA hybrids confront us with a technology which eludes a ready-made ethical conclusion. In “doing bioethics,” particularly with emerging technologies, we find that it takes time to understand, consider and reach an ethical conclusion. An open bioethics conversation among those who share our Judeo-Christian commitments also means that we may be uncertain about preliminary observations as well as ultimate conclusions. HA hybrids is one of those situations. In this column, I’ll address just one aspect of HA hybrids: the insertion of human neurons into animal brains. But first, what are we talking about?

Understand the biotechnology. In the popular understanding, “hybrids” includes three biotechnologies: chimeras, hybrids, and cybrids. Chimeras are entities created by mixing cells of different animals, usually two different species; each cell retains its original genetic identity. Think of a graft, such as replacing an aging human heart valve with one grown in a pig. Other chimeras are created at a much earlier stage by mixing two embryos, changing the appearance of the new organism. While the centaur is a mythological version, unusual animal hybrids exist, for example, the liger (a combination of a male lion and female tiger), the tigon (offspring of a male tiger and female lion), and the beefalo, a bison/cattle breed designed for beef production.

Splice, a 2010 summer movie release, tells the dark tale of Dren, a half-human, half-animal lab-created chimera that unpredictably grows and terrorizes people. Actual human chimeras may not raise the same fears. Their new heart valve does not acquire human DNA. Nor does it change their fundamental humanness.

True hybrids are created by integrating some genetic material from one species into an animal of a different species, perhaps by fertilizing the egg of the former with sperm from the latter. Human “cybrids” are hybrids created by a cloning process: human

DNA is inserted into a non-human egg that has been enucleated (the animal nucleus has been removed), usually from a cow or rabbit. Cybrids contain more than 99% human DNA; the rabbit or cow mitochondrial DNA in the cytoplasm surrounding the nucleus remains. The United Kingdom, one of few places to permit cybrid research, requires the cybrid embryo to be destroyed after fourteen days. Chinese scientists apparently created a human-animal hybrid by inserting human DNA into rabbit eggs for the purpose of extracting the embryonic stem cells.¹

HA hybrids are produced for a variety of purposes: to observe how transplanted cells differentiate in the host (*What kinds of cells do they become?*), to test human cells (*Are these early cells pluripotent?*), to find out what cells will do (*Will these become cancerous?*), to reveal how these cells are affected by different control systems, to test new drugs for medical treatment, and to grow replacement tissues or organs for xenotransplantation. As the Chinese have claimed, embryonic stem cells might be harvested from cybrid embryos. Their research, which has not been proven elsewhere, would produce human embryos in bulk, to create made-to-order tissues for patients.²

Identify potential benefits and risks. HA hybrids might be used to study the causes and development of diseases such as cystic fibrosis, Parkinson’s, AIDS and heart disease, pointing toward new therapies. Genetically engineered mice hybrids with human DNA inserted can generate antibodies to treat cancer that will not be rejected by the human recipient’s body. Researchers may also develop HA hybrids to test new drugs.

Despite their significant research potential, HA hybrids carry some risks. The lessons of history warn of the risk of zoonotic infection. That is, diseases which have been confined to the animal kingdom may cross over to humans. We have witnessed the worldwide calamities triggered by the introduction of HIV, avian virus, and H1N1 influenza (swine flu). A single genetic or protein fragment might be sufficient for crossing the species boundary, causing diseases such as cancer, leukemia, and mad cow disease.



Additional risks include the creation of human diseases and the reality that no one knows how the HA hybrids will develop. When animal viruses cross the species barrier, new strains can emerge which may be carried only by human hosts. Furthermore, while many animal hybrids are sterile, closely related species, such as a mule and a donkey, have been known to reproduce. The “what if” allure of inseminating a primate, such as a chimpanzee, with human sperm may be irresistible. The sensationalized attempt of an early 20th century Soviet scientist to create “humanzees” dramatically illustrates this potential.

Ethical observations. Ethical inquiry often begins with questions about consequences. As HA experiments proceed, what would be the moral status of these new creatures? Are they protected by animal welfare regulations, or do they deserve human subject research protection? Are there limitations on how much human DNA can be inserted into an animal? How are the risks of zoonotic infection controlled? Would this open the door to using primates to grow donor-specific replacement organs, as did the mad scientists in Robin Cook’s *Chromosome 6*?

While consequences are important considerations, our ultimate concern should involve a deeper level of ethical analysis. Three moral and theological questions immediately come to mind: species boundaries, bodily integrity, and human identity. All of these are aspects of our human dignity. We will explore species boundaries, and touch upon human identity with respect to one specific technology. Although it is easier to state categorically that no human female should be inseminated with animal sperm and vice versa, or that cloning with a rabbit ovum and human nucleus is wrong, other HA possibilities are not clear cases of impermissible mixing of species. One of these is the insertion of human brain cells into animal brains.

It is obviously difficult to study the development of the human central nervous system in human subjects, but it is possible

to transplant human brain cells into embryonic, fetal or adult animals, typically mice. Researchers can then track and observe how these cells develop and interact. These HA hybrids are technically chimera, because the human cells do not acquire the mouse DNA; they remain distinct and traceable.

Does this cross a boundary between the human species and the animal? If so, what is the criterion or basis for that boundary? Most people believe that there is a difference, a qualitative difference, between a human being and a tortoise, or even a circus-trained chimpanzee. Christians in the US would describe this as “human dignity.” In the UK, “full moral status” is more commonly used. Both expressions signal that human beings are exceptional, distinct from other creatures.

Human exceptionalism is a difficult problem for biologists who are nominalists. Nominalist theory concludes that only concrete things exist, and that abstract ideas, such as “species,” do not. To illustrate: the nominalist biologist points out that there is no single, universal DNA sequence among human beings; there is no conclusive standard for determining the species of an organism based on its DNA sample. Or, they tout the evolutionary connection of human beings with a common ancestor. According to this perspective, human beings are nothing more than dust and ashes, a particularly clever architecture of molecules and cells.

Science cannot answer why any biological organism is of greater value than another. Admittedly, “species boundary” is a difficult problem, particularly from a biological perspective, but the mere fact of difficulty does not mean that species identities and boundaries do not exist. Think about it: it is hard to define the precise boundary between night and day, but that imprecision does not imply that night and day do not exist. Therefore, while Christian ethicists can and do disagree about where to locate the boundary line in these matters, boundaries do exist, and it is an important part of ethical reflection to strive to discern them.

Matter causes brain causes mind? The nominalist presupposes that the human mind derives only from the brain, which is composed solely of matter, and that the mind is the basis for possessing human dignity. The nominalist would be concerned about a change in the *structure* of the brain that might cause a change in its *function*. When an undefined threshold is reached, that is, a critical number of neurons have been inserted and have integrated themselves into the mouse brain, the mouse brain might demonstrate human-like cognitive characteristics. For the nominalist, this is the threshold of unease, if not outright certainty, that a species or moral barrier has been breached.

If unease is based on “humanlike” cognition alone, it appears to condition species membership and our concomitant moral worth on mental abilities. If we stop to consider a radical, logical extension of this ethical position, the ramifications are chilling. Those with significantly impaired cognitive function—the uncle in a persistent vegetative state, the daughter with serious developmental delays, the elderly grandmother with dementia, the anencephalic newborn boy—are judged to have less moral worth than the Rhodes scholar or moral philosopher. What is respected here is not human *dignity*, but human *cognition*. While cognitive capacity is one evidence of our singularity, it is not the basis of the ontological reality, the truth about our status as creatures made in the image of God. There are many other capacities which are distinctively human, for example, humor, preservation of history, artistic creativity, imagination, self-awareness. No single human being fully expresses all mental capacities, and some humans lack one or more entirely. Yet, it would be wrong to conclude they are not human beings with dignity.

Some advocates of human dignity are concerned about transplanting human neurons into animal brains on different grounds. Because of the brain’s intimate connection with personal *identity*, on this view, brain transplantation—a theoretical possibility for now—would be clearly immoral. The insertion of human cells into an animal brain could be problematic in two ways. The first concerns the origin of the cells: bone marrow stem cells might not be problematic, but neuronal progenitor cells, which raise the “possibility of humanlike connections between the neurons,” are troubling.³ The second concern has to do with the potential of the inserted cells to change the architecture of the brain, that is, its weight, shape, and size. It is not clear what percentage of human neurons constitutes a “significant” alteration. Thus, prudence counsels that we *not* engage in a procedure which potentially alters identity.

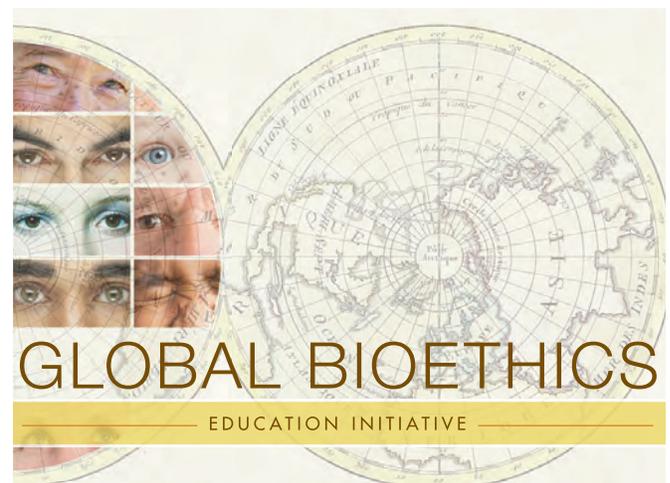
It is important to note that not all HA hybrid research may violate species boundaries. Inserting a small fragment of human DNA into a mouse to develop a cancer-fighting drug, for example, might not implicate human dignity. Growing a human-tolerant pig valve for a heart patient is therapeutic, not threatening.

Thus, we have two different arguments against integrating human DNA into animal brains, one based on nominalist grounds, and the other on dignitarian grounds. A whole host of ethical concerns remain. What about concerns for animal

welfare? The host animal and its offspring may suffer terribly. Could “human dignity” apply to HA hybrids? Are they human, or actually something else? In addition to neurons, are there other types of cells that raise specific concerns, such as gametes, or organs, such as the uterus? Does it matter at what stage of biological development the species mixing occurs? It could be at fertilization, at the embryonic stage, or somewhat later. How is this relevant?

Humanzees or Dren from *Splice* may be fanciful creations. The mass production of human-animal embryos may not. Somewhere in between we may find the highest and best purposes of research, those therapeutic goals that do not violate ethical standards. We still lack a Christian consensus on all aspects of the HA hybrid question, but we must persevere and continue the difficult work of thinking through ethical issues, principles, and their application. A premature conclusion may initially satisfy, but ultimately prove to be a barrier to both encouraging ethical research and respecting human dignity in all its stages, ages, and variations.

- 1 Sharrie Gossett, “Chinese Scientists Create First Human-Animal Embryo.” <http://archive.newsmax.com/archives/articles/2003/8/14/153902.shtml> (accessed Sep. 22, 2010).
- 2 David Derbyshire, “Experiments fail: Controversial human-animal hybrid embryos ‘will not deliver medical benefit.’” <http://www.dailymail.co.uk/sciencetech/article-1134483/Experiments-fail-Controversial-human-animal-hybrid-embryos-deliver-medical-benefit.html> (accessed Sep. 22, 2010).
- 3 Tara L. Seyfer, “An Overview of Chimeras and Hybrids,” *The National Catholic Bioethics Quarterly* (Spring 2006): 37-49, 47.



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