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2,848 words

Human – Animal Chimeras: What are we going to do?

What is a Chimera?

In Greek mythology a chimera was a monster composed of multiple parts of different animals with a goat's body, a lion's head and a serpent's tail. The monster was a terrifying creature and was related to monsters like Cerberus and Hydra. Outside of Greek mythology and over the course of many years a chimera was thought to be only something of fantasy. That was, until recent studies in biotechnology for stem cells has been focused on human-animal chimeras or in other words, the fusing of animal and human cells or tissues. In stem cell research chimeras are "organisms containing cells from two or more zygotes or the imperfect equivalents thereof" (Hyun et al). Human-animal chimera research involves "the transfer of multi-potent or pluripotent human stems cells into animals in embryonic, fetal, or postnatal stages of development to study stem cell behavior" (Hyun et al).

In present day, a chimera can also be something defined as very controversial. While many who study in the field view human-animal chimera research as beneficial for discovering cures to the most prominent of diseases, others feel that we may be crossing the boundaries of nature by this practice. Biotechnologists feel that their research is humane, justified, within the boundaries of nature and doesn't call for new ethical standards. However their thoughts on the subject do not diminish the views of many people who do in fact believe that we are crossing the boundaries of nature and need new ethical standards. By taking a look into dignity, ethics, and the types of practices for the subject at hand, most biotechnologists share the same beliefs. They feel that they should not be limited in their research and their beliefs contrast greatly from those of bioethicists and the public. However they do present information to let the public know what they should be aware of and what to do if research drifted out of scope.

Scientists, for the most part, believe that there is no threat to human dignity. The opinions on ethics are the same, they believe that nothing needs to be done ethically, but some practices need to be more monitored than others. They feel that opposing parties are holding back humans and should reconsider.

The advent of the human-animal chimera poises the basic question, "Is it wrong?" Stem cell human animal chimera research has garnered opposition over the recent years so that we do not "risk disturbing fragile ecosystems, endanger health, and affront species integrity" (Mott,2005). Well, according to History we've always been exchanging biological matter with different species, whether it is through natural or artificial conventions, on purpose or not.

What the People Fear

There are lists of things that people fear when it comes to human-animal chimeras. Some of the main fears are: the crossing of nature's boundaries; the creation of new hybrid species; stem cells becoming biologically deterministic agents; and the loss of "human dignity." These fears are reasonable and predictable for a topic of such magnitude.

The first of the aforementioned fears comes from the idea that people feel that humans and animals should stay separate entities. It also comes from the thought that some of the scientists doing the research cannot be trusted and may not know where to draw the line. One biotechnology activist Jeremy Rifkin, writer of *Who Should Play God* and a well-known economist, is opposed to crossing species boundaries because he feels "animals have the right to exit without being tampered with or crossed by other species" (Mott, 2005). Rifkin in an interview with National Geographic said, "There are other ways to advance medicine and human health besides going out into the strange, brave new world of chimeric animals." He also stated that "sophisticated models could substitute for experimentation on live animals" (Mott, 2005).

David Magnus, director of Stanford Center for Biomedical Ethics, believes that the main concern is whether chimera research will be put to good use and not utilized in a way that would be problematic or dangerous. His belief ties in with the second and third fears that people have of human-animal chimeras of a creation of a new hybrid species. People fear that if not monitored properly, that scientists could develop hybrid species. They also fear that tampering with genes and cells will change the whole biological structures of not only humans but other species. People fear that scientists will determine what exists in the future and how it is composed.

If new human-animal hybrids species were to be created people have already speculated how to handle the situation. People have thought about ideas such as what should be considered human, how these new species should be treated in society, what rights these hybrids have, and what subhuman combination should be produced and for what purpose. One more thing that people question is if we are respecting animals. Those ideas along with other give people the notion that new ethical standards must be developed.

The last of the major fears is the loss of human dignity. Cynthia Cohen believes that a ban on chimera stem cell research should be put into place similar to how it is in Canada. She believes that "by mixing human and animal gametes or transferring reproductive cells it diminishes human dignity" (Mott, 2005). People believe that they have something distinctive and valuable about them that needs to be protected and honored. They feel that losing our dignity would not only be losing our identity but it would also be over-exerting power over nature.

Human-Animal Chimeras from the Scientist's Perspective

Different practices of chimeras should be handled and viewed differently. One of the first points that researchers in the field make is that there is a difference between mixing tissues and mixing genes. They say that mixing tissues in usually a well-accepted practice and the mixing of genes is the source of great fears. Insoon Hyun and his colleagues explain this in great detail. They went over this by mentioning the famous ear-mouse experiment in which an ear was grown on the back of a mouse. They said that "iconic image of the human ear on the back of a mouse owes much to an engineering of scaffolds and nothing to an engineering of genes." The Scientists who conducted that experiment created a mold for a human ear on mouse's back and used the blood flow from the mouse to help the ear stem cells grow. There were no mixing of genes at all.

"History shows that humans and animals have always been exchanging bits of their biological matter, intentionally or by chance, naturally or through artificial aids of various sorts. Yet unlike stem cell chimera research, the majority of these encounters do not elicit fear or opposition." (Hyun et al) The simplest example of this is digestion. Humans accept the entry of animal products in their daily metabolism and diet influences the body both genetically and epigenetically. The very manner in how the human race has evolved from generation to generation has been greatly influenced by diet. For instance, the "effect of certain classes of nutrients on the methylation level of our DNA (one of the most meaningful types of epigenetic modification) is the best defined example of the enduring effect of our diet. On our genetic networks" (Hyun et al). It is also possible for this effect to be transmitted by hereditary.

Medicine has come a long way thanks to research in the human animal chimeras. We've been transplanting animal organ into humans with the replacement of nonfunctioning human heart valves with those from pigs and cows in the process known as xenotransplantation. This has effectively given us human-animal chimeras already, and one that is widely considered to be humane and acceptable in our society. Scientists have added human genes to bacteria and farm animals for years (Mott, 2005). Research in the chimera has given us vaccines as well (Hyun et al).

To the researchers, human-animal crossing is not wrong and is a persistent feature of human society as shown with the diet example. To them, stem cell or chimeras are not exceptional cases because "neither stem cells nor genes can be handled priori as biologically deterministic agents independent of their context." If some cells are more "context independent" than others then ethical framework needs to be placed on the utilization of those cells instead of the field as a whole.

Biotechnologists believe that "the threat to human dignity argument" is severely flawed. The mixing of human and animal matter is neither new nor problematic. People fear that transferring human stem cells may cause uniquely psychological functions to develop in the tested animals. Or in others, the tested animals will develop cognitive function and become aware of itself and its environment. Scientists say that since the animals being tested are generally mice, the chances of that happening is "so improbable as to obviate the need for experimental limitations beyond those normally in place for other types of animal experimentation" (Lensch et al). Therefore they believe that human-to-animal chimera research is not morally wrong.

Robert Strieffer stated the following in response to the concerns regarding human dignity in "At the Edge of Humanity: Human Stem Cells, Chimeras, and Moral Status":

> "Human dignity is not a property of human cells. It is a property of human beings. While recognizing and valuing human dignity, it is important to avoid the mistaken reductionist view that would enshrine human dignity in stem cells and specialized tissues rather than human beings. Of course, humans are part of a vast evolutionary web including many species with "human-like" properties, including varying degrees of cognition, emotive capacity, and social interdependence. Therefore, while it is important to reiterate that chimera research, like all research on non-chimeric animal species, should be governed by animal welfare principles, it is also important that those principles are sufficiently developed to protect animal subjects of research of human-like mind, were such an outcome in fact to emerge regardless of the goal of the research.".

Moral Status and Human Dignity from Bioethics Philosophers

Bioethics philosophers agree with the public on moral status and dignity. They feel there is a threat to both. James Robert and Francois Baylis argue that human animal chimeras would "introduce inexorable moral confusion in our existing relationships with nonhuman animals and in our future

relationships with part-human hybrids and chimeras" (2004,9). They argue that chimeras would cause confusion by making the boundary between beings with a large gap in social status, under the assumption that *humans have higher moral status than nonhuman animals*. What moral status is given to nonhumans is basically reliant on human perception; humans on the other hand give their own value of human life. We value apes more than mice because they display more human-like qualities.

Robert and Baylis say, "In the case of human beings, moral status is categorical insofar as humanness is generally considered a necessary condition for moral standing. In the case of nonhuman animals, though, moral status is contingent on the will off regnant beings." Our devalued opinion of other creatures' moral status has given way to animal testing. It makes more sense for us to test the human central nervous through lab mice by genetically engineering mice with human neural cells that "differentiate into specific neuronal subclasses, and execute neuronal functions" than to test on human subjects (Behringer). Otherwise it would ironically be inhumane. The idea of another identifiable or relatable species scares the mass public.

What though makes us human, and thus have higher moral status then those "lesser" life forms that Robert and Baylis define? Cynthia Cohen in her commentary on Robert and Baylis asks for an explanation of "what it is to be human, even if only sketchily, if we are to claim that human beings have full moral standing." This really puts into question what it is to be human as there is life out there that has similar characteristics to us. Ultimately though, Homo sapiens as a species are just a branch off of the evolutionary tree, and its relationship with other life is just a matter of biology.

Cohen's concern with a human-animal chimera doesn't reside within our genes and how they compare, but rather the phenotypic traits that she sees as inherently human. She gives us this example: "we consider self-consciousness and the ability to use language in speech more important to being human in most contexts than being left-handed or having a good olfactory system."(Cohen 2003,4). This is why Cohen believes chimeras with human characteristics to be a threat to human dignity. Cohen defines humans to have full moral standing based on certain cognitive capacities. What would we classify the moral status of earlier hominids, our closest relatives? Would those of them with the cognitive abilities of a modern child, would be considered of lesser moral status? Not all of humanity inhibits cognitive capacities that are present in Homo sapiens as Degrazia points out. People, by Cohen's thinking, would consider a person less of a moral standing if he or she weren't a cognitively functional human being (Degrazia, 2007,312).

What Biotechnologists say we should do Ethically

Scientists, for the most part, believe we should use our existing ethical standards to deal with animal research and chimeras unless something in stem cell really drives the need for new ethical standards. However they do propose rules and guidelines for reassurance. One is that "for in vitro chimera studies, no in vitro cultures of animal stem cells into human embryos be allowed to develop for longer than 14 days or until the formation of the primitive streak. Also no products of research involving transferred human cells be implanted into a human or nonhuman primate uterus" (Hyun et al). Another is that no chimera study is to involve transferring human sperm to a primate uterus or vice versa.

Most scientists agree in one way or another that "each kind of proposed experiment may need to be evaluated separately in a manner that seeks to uphold both the highest standards of animal welfare and truly beneficial scientific advances" (Cobbe). Evaluations will ensure that no chimera experiments will be

taken out of scope. Hyun lists over nine different recommendations on how to build new ethical standards for human-animal chimera research.

"The transfer of human cells into postnatal, adult recipients is likely the least contentious due to a low probability that human cells introduced at such a late developmental stage may integrate appreciably into existing structures" (Lensch). With that being said, according to the researchers, the only type of chimera study that needs to be monitored and may lead to new ethical standards involve only in vitro experiments into embryos or injection of human cells into animal cytoplasm. Prolonged development from those methods could arise in problems but is still very unlikely. Some scientists do oppose that in vitro chimeras be killed within fourteen days because they feel that "live chimeric animal models would be more valuable as a research tool" (Cobbe). They also believe that it is holding us back from finding why diseases behave in a certain manner and how we can eliminate them. They say it is safer to test it on animals or chimeric animals instead of letting humans continue to die or even worse let humans be the test subjects.

What Now?

Irv Weissman, director of Stanford University's Institute of Cancer/Stem Cell Biology and Medicine, said in an interview with National Geographic , "Anybody who puts their own moral guidance in the way of this biomedical science, where they want to impose their will—not just be part of argument—if that leads to a ban or moratorium…they are stopping research that would save human lives" (Mott, 2005). Weissman shares the feelings of many others in his field. The majority feel that they should not be restricted in their work because doing so would not help the human race. They feel that ethically there is nothing to worry about and that researchers are responsible enough to keep everything under control. While the public would like to believe everything is under control, it is difficult because there have been countries that have banned human-animal chimera research but still have scientists secretly doing the research; the most recent of those countries being Canada. Situations like that have caused the public to lose trust in the scientists, express many fears and thrive for more regulation. Scientist's in the field are going to have to prove that their research is greatly benefitting humans to regain the public's trust.

Only time will tell what new code of ethics will be derived from this field or if any will be at all. If human-animal chimera were introduced to society what affect would it have on what constitutes humanity? Would chimeras be considered our equals alive, dead, or intelligent? The prospect of a side species to homo-sapiens scares the majority of people. One thing is for sure, we will continue to see more issues related to ethics as the human-animal chimera stem cell technology grows.

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