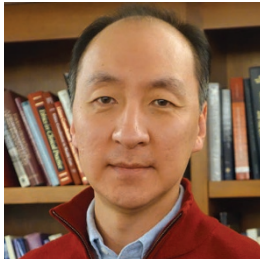


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## Illusory fears must not stifle chimaera research

Human–animal embryos have great biomedical potential — but scientists will have to quell public alarm if funding for such work is restored, says **Insoo Hyun**.

After more than a decade of controversy, the United States is nudging towards approving research on human–animal embryos. Last week, the National Institutes of Health (NIH) closed a month-long public consultation on ‘chimaera research’, and is widely expected to lift a moratorium that forbids federal funding for such work. Human–animal chimaeras are essentially research animals that contain transplanted human cells. Such biologically mixed animals have long been used as staple experimental systems in biomedical studies, including cancer and AIDS research. But, for some, adding human stem cells to animal embryos is a step too far — which is why the NIH imposed the moratorium, in 2015. Before then, it funded chimaeric embryo studies as long as they did not use primate blastocysts.

Chimaeric-embryo research has a vital role in basic and translational stem-cell science, so for the NIH to restore funding would be encouraging. The transfer of human stem cells into animal hosts can advance our understanding of human development and disease, and could eventually lead to the growth of transplantable human organs in livestock.

Still, the availability of federal funds does not guarantee that the research will proceed. Several states — including my own, Ohio — have raised the prospect of laws to ban such research. Institutional stem-cell review boards could still block projects, and hostile public opinion could again place future federal funds in jeopardy. Indeed, there are already signs that the NIH consultation has led to renewed protests against the research.

For these reasons, it is important for scientists to make the case for chimaera research, and to understand why opponents do not want it to proceed. Critics are especially uneasy about studies that could result in chimaeric animals with human cellular and functional modifications to the central nervous system. They argue that the transfer of human cells into animal embryos, or into the central nervous systems of animal hosts, elevates chimaeras to something approaching, or equaling, human moral status. This conflation of the biological humanization of chimaeric animals with their moral humanization is fallacious. The moral status of humans is not automatically assured by our genetic composition or the physical arrangement of our cells. Rather, it is sustained by a complex of mental traits that are fully realized only within what the Swiss philosopher Jean-Jacques Rousseau referred to as the “bosom of society”.

The moral-humanization concern distracts from what is most important in the chimaera debate. The central ethical distinction is not some ancient philosophical division between man and animal; instead, it lies in knowing the right and wrong ways to treat sentient beings according to the complexities of their attributes. The NIH has proposed that its internal steering committee could assess

chimaera-research proposals by focusing on considerations such as the characteristics of the host animal, the physical and behavioural changes likely to be caused by human-cell transfers, and incremental research monitored to determine the effects of chimaerism.

This regulatory approach is consistent with new professional guidelines for stem-cell research offered by the International Society for Stem Cell Research. Its current standards for chimaera research are based on an advisory report drafted by me and other members of its ethics committee. We urged regulators to build on animal-welfare principles in a stem-cell-specific manner, and to avoid unwarranted ‘stem-cell exceptionalism’, whereby research would be restricted by a hazy concern about the possibility of ‘morally significant’ human characteristics in chimaeric animals. The NIH and other decision-makers should heed this call.

Grounding the ethics and regulation of human–animal chimaera research in anything other than animal welfare would invite practical and philosophical difficulties. For example, one argument used against the transfer of human stem cells into early animal embryos is that this research is not overseen by animal-research committees when it is limited to experiments *in vitro*.

The challenge for these critics, then, is to explain why animal embryos containing human cells deserve serious consideration of their moral status — enough to potentially rule out their use — when standard human embryos can be used in other projects. Chimaera studies that involve sentient animals are already tightly regulated by the US Animal Welfare Act — the first federal law governing the use of animals in

research, passed 50 years ago last month — and by other national and international research policies. Under these strictures, animal-welfare principles remain the regulatory focus for all species permitted for scientific use. Because the transfer of human stem cells could have unpredicted effects on a chimaeric animal’s capacity to suffer, it is crucial that qualified veterinary staff and researchers monitor experiments for deviations from normal behaviours and species-typical functioning, and use clear criteria for humane interventional euthanasia.

The NIH’s planned approach does this, and could provide useful information on human stem cells’ possible developmental effects on animal systems, thereby aiding future oversight efforts. Such an arrangement has worked well in monitoring transgenic and knockout-animal models. It can work well for stem-cell chimaera research, too. ■

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