

“Part-Human Chimeras: Worrying the Facts, Probing the Ethics” (2007), by Françoise Baylis and Jason Scott Robert

In 2007, Françoise Baylis and Jason Scott Robert published “Part-Human Chimeras: Worrying the Facts, Probing the Ethics” in *The American Journal of Bioethics*. Within their article, hereafter “Part-Human Chimeras,” the authors offer corrections on “Thinking About the Human Neuron Mouse,” a report published in *The American Journal of Bioethics* in 2007 by Henry Greely, Mildred K. Cho, Linda F. Hogle, and Debra M. Satz, which discussed the debate on the ethics of creating part-human chimeras. Chimeras are organisms that contain two or more genetically distinct cell lines. Both publications discuss chimeras with DNA from different species, specifically in response to studies in which scientists injected human brain cells into mice. “Part-Human Chimeras,” contributes to a chain of ethical and scientific discussion that occurred in the mid-2000s on whether people should be able to conduct research on chimeras, especially in embryos.

Chimerism is a condition in which a single organism has at least two genetically distinct cell lines. That means that any individual cell has a certain set of DNA, the material that makes up genes, but that there are at least two fully distinct sets of DNA present in different cells in the organism's body. Chimeras, organisms which experience chimerism, can occur naturally or through laboratory manipulation. Chimerism has been documented occurring naturally in species such as humans. Scientists believe that happens when two fertilized eggs fuse at an early stage of development, producing a single fetus with cells from two different, genetically distinct sources. Chimeras can also be created in a laboratory setting, including the case discussed in the report by Greely and colleagues and in the response by Baylis and Robert. Both sets of authors discuss a proposed experiment in which researchers would implant human brain stem cells into mice. The resulting mice would be interspecies chimeras because they would have both human and mouse genes. The creation of chimeras, especially those using human cells, has been a source of controversy and debate, of which “Part-Human Chimeras” is a part.

A common argument in favor of part-human chimeras is how they could be used to improve research about and provide medical resources for humans. One example is the creation of non-human animals that could grow human organs, allowing many more people to get potentially life-saving organ transplants. Another is the creation of part-human animals to be used as an assay system, or a simplified system which researchers can use to study the effects of something, like a drug. Both Baylis and Robert and Greely and colleagues write about that kind of research in regards to putting human brain cells into mice. Studying the human brain is often difficult because of human's ethical status, meaning that people think it is unethical to experiment on living humans. Researchers cannot dissect a human brain to, for example, see the effects of a drug. One solution is to cultivate human neural cells in a lab. However, that is not ideal because cells typically behave differently inside and outside of a body. The purpose of the proposed human-mouse chimera, therefore, would be to put human brain cells in an environment where they would still be inside a body, but one that has fewer ethical restrictions and is easier to manipulate.

The authors of “Part-Human Chimeras” both worked within the fields of ethics at the time of article's publication. In 2007, Baylis was a professor and Canada Research Chair in bioethics and philosophy at Dalhousie University in Halifax, Nova Scotia. Her research focused on the intersection of bioethics and policy. In 2007, Robert was working as a professor in the School of Life Sciences at Arizona State University in Tempe, Arizona, and had previously worked at Dalhousie University.

The pair had collaborated on numerous articles, many of which they reference in "Part-Human Chimeras." They wrote their article in response to "Thinking About the Human Neuron Mouse," by Greely and colleagues. In that article, Greely and colleagues discuss the benefits, risks, costs, and further recommendations of part-human chimera research, particularly in the context of adding human brain cells into mouse brains. Baylis and Robert disagreed with the content of that report, prompting them to respond with "Part-Human Chimeras" later on in 2007.

The authors split "Part-Human Chimeras," into six sections. In the first section, an untitled introduction, the authors outline why they decided to respond to the Greely report with their commentary, which was to correct their errors and provide what they called a more comprehensive account of the debate. Then, in a section titled Science, they correct some of Greely's proposed science that they perceived as inaccurate within that report. In the third section, Law and Policy, Baylis and Robert amend some of the claims Greely and his team made about policies preventing chimera research in both Canada and the United States, further claiming that Greely's interpretation could mislead readers about Canadian research rules. Furthermore, from both an American and Canadian perspective, Greely's team does not offer critique on regional ethical oversight into the debate, and Baylis and Robert suggest joint national oversight. In their fourth section, Ethics, they argue that Greely and his team misrepresented a previous article Baylis and Robert had published. Within the fifth and sixth sections, Comments on the Recommendations and Conclusion, Baylis and Robert make recommendations for future discussion on chimera research, stating that approaching such a topic from a purely utilitarian standpoint will not adequately account for the deeper philosophical complications raised by the part-human chimera debate.

In the first section, Baylis and Robert state their goals and purpose in writing the article. In 2003, four years prior to the publication of "Part-Human Chimeras," Baylis and Robert published one of the first articles on the ethics of transplanting human stem cells into non-human embryos, in which they argued that hang-ups over crossing species boundaries should not prevent part-human chimeras. They state that that article stimulated a debate within the scientific community, which was further compounded by a research proposal from biologist Irving Weissman, who initially suggested transplanting human brain cells into a mouse. Several years later, in 2007, Greely and colleagues published "Thinking About the Human Neuron Mouse," in which they considered the ethical and legal issues of chimera research, using Weissman's proposed experiment as a case study. Baylis and Robert state that they published "Part-Human Chimeras" in response to Greely's report, asserting that they have two goals with their commentary. The first goal was to document and correct some of the science, ethics, and politics about part-human chimeras they claim Greely and colleagues had presented incorrectly. Their second goal was to review and comment upon the report's recommendations, with which Baylis and Robert disagree.

In the second section of their commentary, titled Science, Baylis and Robert state that the Greely report failed to understand and contextualize the relevant biology behind part-human chimeras. First, the authors state that the Greely report did not define chimeras accurately, stating that the given definition was biologically misleading as it did not encompass all types of chimerism. Specifically, Greely and his team defined chimeras as creatures with cells, tissues, or organs from individuals from two different species. However, Baylis and Robert state that Greely's definition only encompassed interspecies chimeras, or chimeras formed by two different species of organism. For example, a human-mouse chimera would fall into that category, but a chimera formed by two twins fusing *in vitro* would not. Baylis and Robert suggest a corrected definition that accounts for both chimeras that form from individuals of the same species and individuals from different species.

In the same section, the authors then state that the Greely report inappropriately used the terms chimera and hybrid interchangeably. Whereas a chimera is composed of two or more genetically distinct cell lines from organisms of the same or different species, a hybrid always has one cell line containing combined DNA from different species. Typically, hybrids are created with an egg from one species and a sperm cell from another to form a single embryo that contains the combined genetic material of the two species. For example, mules are hybrids created by breeding horses and donkeys, and they have both horse and donkey genes in every cell in their body. Baylis and Robert provide an example of the misnomer Greely used, citing his use of the word hybrid to describe a mouse that scientists had injected tumor cells into. They state researchers should instead refer to

such an organism as a part-human chimera.

Also in the second section, the authors question the examples of chimera research that the Greely report used. Greely included an example of scientists transplanting human brain cells into vervet monkeys and another example of human stem cells transplanted into sheep. Baylis and Robert state that neither example was recent, and that the latter example was poorly communicated. Therefore, they argue that neither example serves as a robust point of comparison for the human neuron mice. They insinuate that more recent research may have yielded different interpretations by Greely and colleagues and suggest the report should have focused on a more in-depth look at specific examples of human embryonic or brain cell transplantation into non-human hosts. Baylis and Robert also state that Greely and colleagues misstated the biology of engineered chimeras, and that this misunderstanding may have affected their ethical arguments, making them irrelevant.

In the third section of their article, titled Law and Policy, Baylis and Robert clarify some of the claims made within the Greely report about the laws and policies regulating chimera research in Canada and the United States. First, Baylis and Robert assert that Greely and colleagues made incomplete claims about the state of research affairs within Canada that could confuse a reader. They explain that, at the time of the article's publication in 2007, there were laws and policies in place expressly prohibiting any sort of chimera research within Canada. Such restrictions were not as absolute within the United States, where researchers could approach such research through policy loopholes. Furthermore, Greely and colleagues advocate for the use of Embryonic Stem Cell Research Oversight, or ESCRO, committees for chimera research. The National Academy of Sciences originally suggested ESCRO committees in 2005 to offer a singular oversight option for issues pertaining to the use of stem cells within research. Since debates on part-human chimeras sometimes broach the topic of using human embryos, that research could potentially fall under ESCRO committee oversight. However, Baylis and Robert state that the debate at hand is much larger and would require a joint, national approach to assessing the debate surrounding part-human chimeras.

Baylis and Robert then seek to correct what they allege was a misrepresentation of an earlier publication of theirs in the article's fourth section, titled Ethics. Within the Greely report, Greely and colleagues cite another article from Baylis and Robert, "Crossing Species Boundaries," from 2003. The authors of the Greely report claim that Baylis and Robert argued for caution in creating part-human chimeras in the future. However, Baylis and Robert state that their goal with that article was not to take a position on whether or not chimeras should be created, but rather to review and critique objections to crossing species through chimera research, and to suggest that further research was needed.

Then, Baylis and Robert make three recommendations for improvement to the Greely report in their article's fifth section, Comments on the Recommendations. First, the authors suggest that Greely and colleagues consider extending their perceptions on the debate of part-human animal research to review deeper philosophical questions. They state that the report only showed a harms and benefits analysis in terms of its ethical investigation and propose that they should consider deeper philosophical questions about what it means to be a human. Then, Baylis and Robert argue that Greely and colleagues should correct how they refer to a mouse injected with human brain cells. In the original report, Greely and colleagues call a mouse injected with human brain cells a mouse. However, Baylis and Robert suggest that they should instead refer to it as a part-human animal. They state that by referring to the organism as a part-human animal, it may satisfy those who believe the organisms have a higher moral status than non-chimeric laboratory animals. This references another recurring argument in the broader discussion of part-human chimeras, that part-human animals have higher moral status than other, entirely non-human animals.

In the final section of their article, Conclusion, Baylis and Robert note that there have been many new articles and perspectives on whether scientists should or should not do chimera research. While they do not make a specific recommendation, the authors do state that scientific justifications for the research are scarce, and ethical arguments for doing such research are underdeveloped.

Greely and his team responded to Baylis and Robert's article in a 2007 commentary response published in *The American Journal of Bioethics* called "Response to open peer commentaries on 'Think-

ing about the human neuron mouse.” Greely and colleagues argue that Baylis and Robert only pointed out things they believed to be errors or ways they would have written the article themselves, rather than offering a substantive response. Greely and his team also imply that Baylis and Robert misconstrued their original perception of the pair’s 2003 article. The team does concede that they made a mistake by referring to a chimera as a hybrid once, and thank Baylis and Robert for their correction.

As of 2021, Baylis and Robert’s article has been cited over thirty times, primarily in other articles on the ethics and politics of part-human chimeras. The debate on the use of human cells, especially stem cells, in chimera research remains active, and experts continue to discuss whether scientists should proceed with such research, and what its legal and ethical implications would be.

Sources

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