Neural Organoid and Chimera Research: Regulatory Pathways

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Disclosure

- None

Conceptual Map: Regulatory Pinch Points

Funding

Request for Public Comment on the Proposed Changes to the NIH Guidelines for Human Stem Cell Research and the Proposed Scope of an NIH Steering Committee's Consideration of Certain Human-Animal Chimera Research

Notice Number: NOT-OD-16-128

Key Dates

Release Date: August 4, 2016
Response Date: September 6, 2016 ~~September 4, 2016~~

Related Announcements

NOT-OD-16-132
NOT-OD-15-158

Issued by

National Institutes of Health (NIH)

Purpose

The National Institutes of Health (NIH) is requesting public comment on a proposal to amend Section IV and Section V of the NIH Guidelines for Human Stem Cell Research, and on the proposed scope of certain human-animal chimera research that will be considered internally by an NIH steering committee to provide programmatic input to the director of the relevant NIH Institute(s) or Center(s) or equivalent NIH officials responsible for funding decisions.

Background

On July 7, 2009, NIH issued the NIH Guidelines for Human Stem Cell Research ("Guidelines") 74 FR 32170 (July 7, 2009) to implement Executive Order 13505 (March 9, 2009), as it pertains to NIH-funded stem cell research, to establish policy and procedures under which the NIH will fund such research, and help ensure that NIH-funded research in this area is ethically responsible, scientifically worthy, and conducted in accordance with applicable law.

Provenance

- Consent
  - Biomaterials without Consent (e.g. pathology)?
  - De-identification?
  - Broad vs. Specific Consent?
  - Consent to Governance Regime?
- Remuneration
  - Payment for Tissue?
  - Financial Benefit Sharing?
- International Coordination

Research

- Guardrails (aka Prohibitions)
  - Timing
    - 14 day
    - 20 Week
    - International Comparisons
  - Kinds of Experiments
- Oversight
  - Institutional vs Governmental
  - ISSCR Guidelines

Research

Table 1.
International legislation and commentary on part-human chimeric embryos.

Jurisdiction	Legislation, guidelines, and commentary
Australia	The Prohibition of Human Cloning for Reproduction Act prohibits the creation of chimeric embryos via the introduction of animal cells into human embryos, but not via the introduction of human cells into animal embryos.[16]
Canada	The Assisted Human Reproduction Act 2004 prohibits the creation of chimeras, which are defined as (human) embryos into which cells from other animals or humans have been introduced; it does not prohibit the creation of chimeric embryos by introducing human cells to animal embryos.[17] However, the main agencies responsible for funding scientific research in Canada expressly prohibit the creation of either form of chimeric embryo, effectively blocking any such research.[18]
USA	Although federal laws do not restrict the creation of part-human chimeras, the National Institutes of Health has issued a moratorium on federal funding for human-animal chimera research as it considers ethical issues associated with the introduction of human stem cells to animal embryos.[19] The National Academy of Sciences has recommended subjecting part-human chimera research to specialized review in cases where there is a significant possibility that human pluripotent stem cells will contribute to neural or gametic cells and tissues,[20] while bills introduced (but not passed) in Senate in 2005[21] and in House in 2016[22] would have prohibited the creation of several kinds of part-human chimeras, including chimeras whose neural tissues are predominantly human.
UK	The Human Fertilisation and Embryology Act 2008 prohibits (inter alia) keeping a human admixed embryo for longer than 14 days or beyond the appearance of the primitive streak, as well as placing a 'human admixed embryo' in an animal to develop. 'Human admixed embryos' include human embryos altered by the introduction of one or more animal cells, as well as embryos containing both human and animal DNA in which the animal DNA is not predominant.[23] The Academy of Medical Sciences has recommended subjecting some categories of chimera research to additional review by an expert body (including research that would make brain function, behavior, or physical appearance more 'human-like') while rejecting some categories of research outright (including research involving the creation of
	human–nonhuman primate chimeras with 'human-like' brain function or the breeding of animals with human-derived germ cells).[24]
Japan	Under Japanese law human-animal chimeric embryos may only be cultured until the appearance of the primitive streak; they may not be transferred into a human or animal uterus.[25] The Japanese Expert Panel on Bioethics has recommended repealing these prohibitions and proscribing a narrower range of practices, such as the generation of human brains in human–nonhuman primate chimeras.[26]
Germany	The Embryo Protection Act 1990 prohibits the creation of chimeras via introducing animal cells to a human embryo or fusing human and animal embryos.[27] The German Ethics Council has recommended prohibiting some additional kinds of chimera research (including the creation of chimeras capable of forming human gametes) and placing additional restrictions on the creation of human-animal brain chimeras, particularly where such research involves nonhuman primates.[28]
France	French law prohibits the creation of chimeric human embryos. However, it is arguably unclear whether the law bans the introduction of human cells to animal embryos, or whether it bans only the introduction of animal cells to human embryos.[29]
Switzerland	Swiss law on assisted reproduction forbids the creation of most kinds of chimeras, including chimeras created by introducing human embryonic stem cells to an animal embryo. However, because the Swiss law did not anticipate the possibility of creating chimeras by introducing human iPS cells to animal embryos, this technique falls within a loophole of the existing legislation.[30]
International guidelines	The International Society for Stem Cell Research (ISSCR) Guidelines for Stem Cell Research and Clinical Translation recommend that part-human chimera research should not be pursued if it involves breeding part-human chimeras with the potential to form human gametes.[31] The guidelines also hold that research involving chimerism of either the central nervous system or germ line should be subject to specialized research oversight to address possible animal welfare issues.[32]

From Julian J Koplin & Julian Savulescu, Time to Rethink the law on Part-Human Chimeras, Journal of Law and the Biosciences, Volume 6, Issue 1, October 2019, Pages 37–50, https://doi.org/10.1093/jlb/lsz005

Outputs

- Data Sharing
- Clinical Trials/Human Subjects Research
- FDA
- USDA/EPA
- Patent Law
- International Harmonization