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Public Attitudes toward Human-Animal Chimera Research May Be More Complicated than They Appear

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In "The American Public Is Ready to Accept Human-Animal Chimera Research" (2020), Andrew Crane and colleagues report findings from a Mechanical Turk (mTurk) survey of 430 Americans' opinions on human-animal chimeric embryo (HACE) research and its medical applications (Crane et al., 2020). We applaud Crane et al.'s investigation into public attitudes about HACE research. We have comments regarding two areas: methodology and sample representativeness on the one hand, and science communication regarding the presentation of the study's findings on the other.

Unlike the Sawai et al. (2017) study from which their study was adapted, Crane and colleagues did not survey a representative sample of their target population with respect to age, geography, or gender. The authors surveyed a smaller sample of participants that skewed young and well educated, with 51% of respondents holding at least a bachelor's degree, compared to 17% of the American population, according to Census data reported in the supplementary materials. Background knowledge of science, which may be an important mediating variable regarding attitudes toward new biotechnologies and research with animals, was not measured (Pew Research Center, 2018). Men, who may be more open than women to research involving animal biotechnologies (Pew Research Center, 2018), were overrepresented, and those with a religious affiliation were underrepresented. Questions remain regarding the associations between acceptance of HACE research and age, education level, religious affiliation, and gender, and their implications should be further examined before broad conclusions about public opinion are drawn.

As Crane and colleagues note, getting quality data from mTurk surveys is difficult. We are concerned that the exclusion criteria they used may not have been sufficiently robust to protect their results. When we examined the raw data provided in the study's supplementary materials, we noticed that 5% of the sample responded to the primary outcome question in a way that appears logically contradictory. In answering the question, "What steps of this research are you willing to accept according to your personal feelings?", 22 participants checked a box to indicate that no steps of translational HACE research were acceptable to them, while simultaneously checking at least one box to indicate that some steps along the translational process were acceptable to them. This suggests that a non-trivial number of participants may not have adequately engaged the survey content.

Crane et al. did use quality control measures, including an attention check and a minimum time requirement. We agree with these measures being taken. However, the 100 s minimum required for inclusion may have been too permissive. With over 30 questions to consider, many of which had multiple parts, a minimum time of under 2 minutes may have kept participants in the sample who did not sufficiently read through the materials and render considered judgments.

In a field as heterogeneous as chimera research, public attitudes are likely to be heterogenous as well, depending on the application. Crane and colleagues focused on HACE research using human induced pluripotent stem cells (iPSCs) as part of a 3-stage research process that starts with creating a human-pig chimeric embryo and that ends with transplanting a human-compatible organ from pig to human. We appreciate the study authors' targeted approach of ascertaining public opinion for a concrete application. It is a strong feature of the study. However, survey responses may have been different if the survey had been about research involving the insertion of human iPSCs into the brains of non-human primates to model human diseases or the use of iPSCs to create neural organoids that are transplanted into other non-human animals. The title of the article, a claim that has been repeated in several media reports, implies support for an area of research that is much broader than the survey's remit.

Moreover, we question the extent to which the approval of 59% of a small, non-representative sample speaks to the American public's readiness to accept research in a given area. While 59% constitutes a simple majority, it also indicates that 41% of the sample did not support the full process required to achieve the human health benefit of this line of research. It is important to take seriously those who oppose the research and understand the reasons for their opposition. The strength of those opinions also bears on social acceptance of critical research. Some public



concerns may be ameliorated with further engagement and science education, while others call for serious consideration about how and to what extent particular moral concerns should be integrated into the governance and public funding of human-animal chimera research. While praising Crane and colleagues' important work, we also affirm the importance of careful measurement, analysis, and communication regarding the public's opinions of innovative research.

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