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Federation of American Societies for Experimental Biology

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April 14, 2026

Lyric Jorgenson, PhD
Associate Director for Science Policy
National Institutes of Health
6705 Rockledge Drive
Bethesda, MD 20817

RE: Response to Request for Information on Reducing Reliance on Human Embryonic Stem Cells in NIH-Supported Research (NOT-OD-26-031)

Transmitted electronically via online form.

Dear Dr. Jorgenson,

The Federation of American Societies for Experimental Biology (FASEB) appreciates the opportunity to provide feedback on the Request for Information on Reducing Reliance on Human Embryonic Stem Cells in NIH-Supported Research (NOT-OD-26-031), which seeks input on the utility of human embryonic stem cells (hESCs) in biomedical research. FASEB is a coalition of 20 scientific societies representing over 100,000 individual biological and biomedical researchers, many of whom utilize hESC lines in their research programs. Given the ever-changing nature of biomedical and biological science research, our community acknowledges the importance of continuously assessing available methodologies to maximize available resources.

Below, FASEB offers comments addressing questions 1 and 4. These comments recommend that NIH resume review of new hESC lines for inclusion in the Human Embryonic Stem Cell Registry. The Federation also highlights several research areas for which additional investments could bolster the development, validation, and application of hESC alternatives.

Question 1: Research areas in which currently approved hESC lines sufficiently meet the needs of the research community as well as research areas for which new hESC lines are needed

The last decade marked a shift in the use of stem cells in biomedical research from hESC lines to increased use and reliance on induced pluripotent stem cells (iPSC), prompted in part by federal policies that limited the use and development of hESC lines. Despite considerable progress toward meeting the utility of hESCs with iPSCs, important differences exist between hESCs and iPSCs that prevent total interchangeability. Currently, existing hESC lines sufficiently meet the needs of the research community to assess new iPSC pluripotency; however, given ongoing uncertainty surrounding the definition of distinct pluripotent states, FASEB recommends that NIH lift the current pause on the registration of new hESC lines to ensure lines available through the registry reflect technological advancements and scientific potential. FASEB also encourages NIH to establish clear scientific criteria to determine when the registration of new hESC lines is necessary. Such criteria should highlight why a new hESC line is necessary to elucidate scientific insights and address specific research questions that cannot be pursued through existing hESC lines, iPSC models, or other validated systems.

Question 4: Research areas in which additional investments should be made to bolster validated models to replace use of hESCs

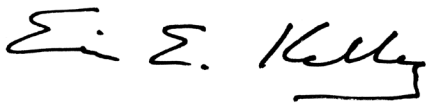
As the research community continues to make progress toward the development of models to replace hESCs, there are several areas for which targeted investments should be prioritized:

1. Additional funding for infrastructure to support iPSC standardization and quality control, including benchmarking genetic stability and differentiation, is critical as the field moves toward widespread adoption of iPSC methodologies. Such investments will support the agency's continued efforts to bolster rigor and reproducibility.
2. Support for the establishment of large, well-annotated iPSC reference panels and banks of patient-derived and disease-specific lines that are linked with whole-genome databases to enable population-scale and ancestry-aware studies that accelerate research examining human rare diseases, common diseases for which diverse populations are differentially susceptible, population variants in infectious disease susceptibility, and population-based medicine.
3. Additional investments in iPSC-based embryoid and organoid models to support the replacement of hESC use in embryology and organogenesis. NIH should also consider developing clear guidance for the use of hESCs and iPSCs in developmental biology research.
4. Additional support to develop validated lineage-restricted cell systems, including trophoblast and organ-specific progenitors, will strengthen methodologies that may more accurately reflect *in vivo* biology.

FASEB appreciates the opportunity to comment as policies surrounding hESC development and registration are revisited. In our comments, we recommend that NIH resume registration of new hESC lines and highlight several areas for which additional investment will support development of alternative methodologies to complement knowledge gained through studies using hESCs.

Please do not hesitate to contact me should you have any questions related to our comments.

Sincerely,



Eric E. Kelley, PhD
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