



April 23, 2026

On behalf of the Society for Neuroscience (SfN), thank you for the opportunity to respond to the National Institutes of Health (NIH) Request for Information (RFI) on reducing reliance on human embryonic stem cells (hESCs) in NIH-supported research. As the world's largest organization dedicated to advancing the understanding of the brain and central nervous system, SfN is committed to advancing biomedical research that drives innovation, improves public health, and maintains the United States' global leadership in scientific discovery. SfN appreciates NIH's efforts to assess research areas suitable for modernization and the role of emerging biotechnologies in advancing biomedical research.

### **Executive Summary**

From a neuroscience perspective, hESCs remain an essential and, in some contexts, irreplaceable research tool, especially in cell replacement therapies for Parkinson's Disease and spinal cord injuries. hESCs serve as the gold standard for human pluripotency and provide unparalleled utility for studying human neural development, neurodevelopmental disorders, and neurodegenerative diseases. While alternative platforms such as induced pluripotent stem cells (iPSCs), adult stem cells, organoids, and computational models have expanded the neuroscience toolkit, none are yet biologically equivalent to hESCs or a suitable wholesale replacement.

Additionally, hESCs contribute to the development of new approach methodologies (NAMs), underscoring the continued necessity of maintaining access to hESCs. Prematurely limiting NIH-supported hESC research risks impeding progress in understanding human brain development, modeling complex neurological diseases, and translating discoveries into therapies for conditions such as Alzheimer's Disease, Parkinson's disease, epilepsy, spinal cord injury, and neurodevelopmental disorders.

Based on the current state of the science, the available evidence does not yet support reducing reliance on hESCs, especially in neuroscience research. The study of human brain development and neurological disease continues to require access to well-characterized human pluripotent stem cells, for which hESCs remain the gold standard. Although alternative approaches have expanded the range of experimental tools available, these systems remain complementary and continue to rely on hESCs. The responses below to the specific RFI questions reflect a neuroscience-based assessment of where hESCs remain necessary to ensure scientific rigor, reproducibility, and progress toward effective treatments for neurological disorders.



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 hESC lines currently approved by NIH support many types of neuroscience research. Researchers routinely use them to make brain cells for learning and memory, Parkinson’s Disease, Amyotrophic Lateral Sclerosis (ALS), spinal cord injuries, and vision. However, neuroscience research continues to evolve, and new hESC lines may be needed in the future. For example, some studies require cells that remain stable over long periods to model brain aging or slow neurodegenerative diseases, and new lines may better represent genetic diversity, which is important for studying differences in disease risk or treatment response for disorders such as Alzheimer’s disease and Parkinson’s disease. Because future research needs cannot be fully predicted, it is important to preserve a pathway for adding new hESC lines when scientifically justified.

2. *Research areas for which hESCs are the gold standard and could not be pursued if hESCs were unavailable.*

hESCs are the “gold standard” for human pluripotency in all areas of research, including basic, applied, and clinical translation research. If hESCs were unavailable, numerous lines of inquiry in basic and clinical research would be significantly hindered or not possible.

#### **Studying early human brain development**

hESCs are uniquely suited to studying how the human brain forms at its earliest stages. These early steps—such as how brain regions are specified and how immature brain cells mature into different types of neurons—are very sensitive to small biological differences. hESCs provide the most reliable model for these questions.

#### **Understanding neurodevelopmental disorders**

Conditions such as autism spectrum disorder, some forms of epilepsy, and intellectual disability often begin during early brain development. hESC-based models allow researchers to study these early processes directly, which is difficult to do using adult cells that have been reprogrammed.

#### **Developing treatments for neurological disease**

hESC-derived brain cells are being tested in clinical trials for neurological conditions, including Parkinson’s disease, ALS, epilepsy, and vision loss. These trials rely on the long history of careful testing and characterization unique to hESCs.

#### **Role of hESCs in Developing and Validating New Approach Methodologies (NAMs) for Neuroscience**

SfN supports the development and appropriate use of New Approach Methodologies (NAMs) to improve human relevance, enhance reproducibility, and, where scientifically justified, reduce



reliance on animal models. As SfN has emphasized in prior comments to NIH, the successful integration of NAMs in neuroscience requires careful validation, realistic expectations, and alignment with the biological complexity of the nervous system.

hESCs play a critical role in this process. hESCs serve as a foundational human reference standard for NAM development, particularly for in vitro models of the nervous system. Many neuroscience-relevant NAMs—including neural cell cultures and brain-region-specific organoids—depend on pluripotent stem cell–derived neural cells. Because hESCs represent naturally occurring, unmodified human pluripotency, they are uniquely suited for validating whether NAMs accurately capture key features of human neural development and function. Importantly, continued access to hESCs supports, rather than conflicts with NIH and FDA goals to advance NAMs. hESC-derived neural models have already contributed to human-relevant platforms that are difficult to assess in animal models. Limiting access to hESCs could undermine efforts to responsibly advance NAMs in neuroscience by removing a key reference point needed for validation and confidence in these approaches.

SfN supports a complementary strategy that emphasizes integration rather than replacement—using hESCs alongside NAMs and animal models, as appropriate, to strengthen scientific rigor and translational relevance. At the present time, hESCs remain essential to ensuring that NAMs used in neuroscience research are reliable, biologically meaningful, and capable of advancing treatments for neurological disease.

*3. Research areas in which the robustness of emerging biotechnologies such as induced pluripotent stem cells, adult stem cells, etc., can replace the use of hESCs.*

At present, no alternative technology can replace hESCs as none has been demonstrated to be fully biologically equivalent. A scientifically responsible strategy would be to strengthen complementary technologies such as iPSCs, organoid systems, and genomic stability monitoring while maintaining access to hESCs.

**Induced pluripotent stem cells (iPSCs)**

iPSCs are useful for studying diseases in cells derived from individual patients, such as rare genetic movement disorders or seizure disorders. While iPSCs have substantially expanded the field of stem cell research and provide a cell source for certain applications, they often do not fully replicate the features of hESCs. Consequently, iPSCs cannot yet be considered functionally equivalent to hESCs, particularly for early developmental neuroscience and translational applications.

**Organoids and computer models**

Brain organoids and computer-based models are promising tools for studying brain organization and activity; however, they lack full cellular and structural complexity, depend on stem cells whose



behavior has been defined using hESCs and cannot yet fully predict human brain development or disease. Sophisticated models are in their infancy, with computational models of animal development only just emerging. At present, these models have little predictive value because they are not sophisticated enough to model most aspects of cell biology. Computational modeling and AI-assisted methods offer potential for future research directions, but do not represent a replacement for research using hESCs.

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

Rather than replacing hESC research, additional investments should help improve and validate complementary approaches, such as directly comparing brain cells made from hESCs and iPSCs under the same conditions; following clinical trial outcomes to understand when different stem-cell sources perform better or worse; improving ways to measure whether lab-grown neurons truly behave like human brain cells; and using experimental data from hESC-based systems to improve computational brain models. All these efforts require continued access to hESCs as a reference standard.

**Conclusion**

From a neuroscience standpoint, hESCs remain essential to understanding the human brain and treating neurological disease. Although emerging technologies have expanded research possibilities, none yet provide the biological equivalence or reliability required to replace hESCs. Continued NIH support for hESC research—alongside strategic investment in complementary approaches—is critical to sustaining progress in basic, translational, and clinical neuroscience.

SfN urges NIH to maintain access to approved hESC lines, preserve pathways for the review of new scientifically meritorious lines, and ensure that neuroscience researchers can continue to use the most appropriate and rigorously validated tools available. Thank you in advance for your consideration, and please contact SfN's Director of Advocacy and Training, Adam M. Katz, at [akatz@sfn.org](mailto:akatz@sfn.org), with any questions.

Sincerely,

A handwritten signature in cursive script that reads "Diane Lipscombe".

Diane Lipscombe, PhD  
Chair, Government and Public Affairs Committee, SfN