

NIH QUESTION: Suggested title to describe your idea:

PETA Answer:

Establish national centers for human-based complex cellular models. NIH Common Fund resources should be used to establish multiple national centers dedicated to advancing human-based *in vitro* research. These centers should accelerate the continued improvement and validation of complex cellular models and provide *in vitro* resources as well as associated education and technical support to scientists throughout the U.S.

NIH QUESTION: A critical challenge or exciting emerging opportunity in biomedical/behavioral research

Critical challenge: Translating basic science and preclinical research into meaningful, affordable outcomes for patients

Despite decades of effort and billions of dollars invested in animal-based models of human biology and disease, effective treatments for the most common and deadly human diseases remain elusive. The “translation gap” between data emerging from basic science research and treatments for human disease is due in part to the limitations of animal models. Species differences in anatomy, physiology, gene expression, developmental trajectories, metabolism, immune responses, and disease susceptibility make translating data from an animal experiment into a human-relevant preventive measure, treatment, or cure extremely difficult. Additionally, animal models are often oversimplified and artificial versions of a complex human behavior, trait, or pathology, with targets that may be meaningful in an animal laboratory but are ultimately inadequate for humans. The failure of animal-based models and assays is contributing to the increased costs of drug development, and the public is declining to trust this type of science.

Emerging opportunity: Increase the availability of complex cellular models of human organs and systems to more researchers

Motivated by both the ethical concerns surrounding animal-based experimentation and testing as well as the limited translatability of animal-based data, advances in complex, 3-D cellular models, such as microphysiological systems, organoids, spheroids, and 3-D bioprinted structures derived from human cell lines and based in human biology have expanded in the past decade. Many of these models simulate human physiology and disease more accurately than traditional *in vivo* models using animals do. Currently, these tools are accessible to researchers working directly on their application and development. However, given their potential to improve preclinical and basic research as well as ongoing advances in their design, it’s essential that investigators with knowledge or access gaps still have the opportunity to take advantage of these cutting-edge *in vitro* methods.

Establishing national centers for innovative and human-based *in vitro* models would help overcome the challenge of translational failure. They would allow many more researchers to have access to cutting-edge *in vitro* technology and increase the amount of human-applicable research being conducted in the U.S. Ideally, these centers would serve as concentrated hubs of technological advancement and expertise and as resources for researchers interested in using these tools. These centers could also serve as a biobank of cell lines, organoids, and

microphysiological systems derived from humans of all ages, sexes, genders, SES status, and racial backgrounds as well as from different patient populations. These centers should be able to offer a full range of support for various types of “omic” technology and gene-editing tools for external researchers using the center’s *in vitro* models.

Resources, tools, or knowledge that are needed to address the important challenge or opportunity

The relative novelty and rapid advancement of human-based cellular models make it challenging for researchers who aren’t immersed in these tools to develop the needed expertise to use them independently. Numerous researchers at all levels lack access to the training or resources they need.

Additionally, many of the technological advances in human-derived 3-D cellular models are occurring outside traditional academic settings, which inherently limits data and technology sharing among investigators and institutes. NIH-funded *in vitro* models that are accessible to all investigators would help foster their advancement, validation, and applicability as well as collaborations among experts in this technology, clinical researchers, and researchers currently relying on inadequate animal models.

National advanced cell culture centers would ideally do the following:

- Bring together experts in the *in vitro* fields as research collaborators, rather than individual competitors.
- Help standardize, expand, and improve *in vitro* methods.
- Provide educational resources to external investigators.
- Accelerate the acceptance, familiarization, mastery, and use of these tools throughout the biomedical community.
- Reduce costs associated with the current fragmented development and validation of these models.
- Expedite the transition away from ethically problematic animal models.

Scientific advancements or other factors that make addressing the important challenge or opportunity particularly timely

The failure to translate data from “bench to bedside” is well known within the science community and by the general public. Regulators, taxpayers, patients, and funding oversight committees are frustrated by the lack of meaningful progress in developing new treatments for prevalent diseases such as cancer, strokes, neuropsychiatric conditions, and neurodevelopment and neurodegenerative disorders. Additionally, as more details about the complexity of nonhuman animals emerge, society is becoming increasingly uncomfortable with using them in experiments—especially if they involve limited resources unlikely to result in health benefits for humans. Pressure for NIH to produce treatments and cures will continue to mount, as will discomfort with the use of sentient animals.

Innovations in complex, human-derived models have the potential to solve both the translational and ethical problems associated with animal-based research. It’s critical to ensure that the entire scientific community can capitalize on the most innovative non-animal, human-relevant *in vitro*

tools. This approach would help make NIH-funded research more accurate, relevant, and efficient—and, therefore, more acceptable to government oversight committees and the public.

Other comments or input you wish to provide.

Establishing cutting-edge *in vitro* centers to support researchers around the U.S. would achieve the goals that the Common Fund is expected to accomplish. These centers would be all of the following.

- **Transformative:** Improving the translatability of preclinical and basic science research by investing in human-derived cellular models and increasing their accessibility to all researchers would dramatically affect biomedical and behavioral research over the next decade.
- **Catalytic:** These centers should be part of the high-impact goal of reducing or replacing the use of ineffective animal models and replacing them with more effective and accurate human-based research.
- **Synergistic:** All NIH ICs and the research they fund would benefit from the increased use and availability of human cell-based models.
- **Cross-cutting:** These centers would help multiple NIH ICs achieve their goals, as these tools are being used to study multiple diseases and conditions. Establishing these centers and coordinating their subsequent resources would require a coordinated, trans-NIH approach.
- **Unique:** The NIH Common Fund is the agency's only funding source that could successfully establish and manage these centers.

Most importantly, these centers would help NIH achieve the last part of its mission, “to enhance health, lengthen life, and reduce illness and disability.”