

NIH Common Fund Solicitation of Ideas for NIH-wide Challenges and Opportunities

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NIH Laboratory Transition Program

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

NIH is increasingly supporting the development and validation of human-relevant methods, but a critical implementation gap remains between the availability of these approaches and their adoption in established research programs. Currently, NIH lacks a coordinated mechanism to help laboratories replace experiments on animals with non-animal methods. Investigators may be prepared and willing to make this change but unable to absorb its immediate costs, including redesigning research programs, acquiring new expertise or collaborations, retraining personnel, purchasing equipment, and temporarily disrupting publication and grant-submission timelines.

The Common Fund should establish a laboratory transition program that provides structured financial, technical, and institutional support to investigators who commit to ending defined experiments on animals and replacing them with human-based approaches. Unlike programs centered on developing new methods, this initiative would address the implementation barriers that prevent existing methods from changing routine research practice. By testing this approach across disciplines and institutions, the program would generate a scalable model that every NIH Institute and Center could subsequently use.

The program would address an NIH-wide scientific and implementation challenge. Increasing the availability of human-based approaches will not necessarily produce corresponding reductions in experiments on animals unless investigators have a viable pathway for replacing established workflows.

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

The program should include the following coordinated mechanisms:

1. Transition-planning awards to help investigators identify appropriate methods and standardized protocols, assess laboratory needs, establish milestones, and develop budgets and timelines;
2. Laboratory transition awards supporting protected time, personnel retraining, technical collaborations, equipment, access to human tissues and data, access to validation resources, and establishment of new workflows;
3. Institutional transition agreements protecting participating investigators from professional penalties during the transition; and
4. Shared technology hubs to provide scientific, engineering, computational, clinical, and implementation expertise.

Awards should require investigators to identify the experiments on animals that will end, specify the approaches replacing them, establish completion dates, and report progress.

Through this program, NIH would negotiate binding agreements with participating institutions to ensure investigators are not penalized for undertaking a transition.

Institutions should adjust tenure, promotion, productivity, training, and other expectations when necessary. They should protect investigators from losing laboratory space, institutional support, or professional standing because transition work temporarily changes publication or grant-submission timelines. These protections should be conditions of the award and not responsibilities left to individual investigators or institutions.

The program should also identify barriers that could be especially difficult for smaller teams to navigate, including access to human samples or data, access to technical expertise, procurement, and intellectual property issues.

The program should strategically select laboratories across diverse biomedical research areas to determine what successful transitions require in different scientific contexts and institutional settings. This would generate broadly applicable evidence and resources rather than isolated examples of individual laboratory transitions.

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

The capabilities and availability of human tissues, organoids, organs-on-chips, advanced imaging, computational modeling, artificial intelligence, and large human datasets have expanded. At the same time, NIH has begun prioritizing human-based research, creating a timely opportunity to address the implementation gap between the availability of these approaches and their adoption in established research programs. The immediate challenge is increasingly whether investigators can integrate these resources into their established research programs to replace the use of animals.

Laboratories conducting experiments on animals may have years of specialized training, equipment, personnel, collaborations, and institutional investment tied to those practices. This scientific and institutional lock-in cannot be overcome by declaring non-animal methods eligible for funding. Without a mechanism focused specifically on transition, increased investment in human-based methods may not translate into corresponding reductions in experiments on animals. Investigators need a viable pathway for changing methods without jeopardizing their careers or laboratories.

This Common Fund program could establish that pathway, determine what laboratory transitions require in different disciplines, and create reusable models for successful transition.

Please include other content the submitter wants to add to the submission

The program should promise to deliver:

- A national cohort of laboratories that have transitioned away experiments on animals;
- Standardized, scalable transition templates, budgets, milestones, and institutional agreements, including models for repurposing equipment and infrastructure and retiring or rehoming animals;
- Shared technical assistance and training resources;
- Evidence on transition costs, timelines, barriers, research outputs, and long-term durability; and
- Recommendations for transition requirements and incentives for future NIH funding opportunities.

Success should be measured by completed transitions and sustained discontinuation of the identified experiments on animals. The primary product of this program would be an efficient, NIH-wide mechanism for producing gold standard science, as well as meeting the goals of the administration and the public in prioritizing human-based research and reducing NIH-funded experiments on animals.

Grand Challenge for Combinatorial NAMs

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

Many major diseases arise through interactions among neural, immune, vascular, endocrine, metabolic, reproductive, and other human biological processes. Existing research programs often examine these processes separately, limiting the ability to explain disease heterogeneity, progression, treatment response, and interactions across organs.

The Common Fund should establish a network to use human-based methods to answer defined questions in neuropsychiatric disease, neurodegenerative disease, immunology and related critical illness (e.g. sepsis), women's health, cancer, and other areas where medical progress has

been stalled and experiments on animals are poorly translatable. Examples include why sepsis trajectories differ among patients, why neurodegenerative diseases progress at different rates and are largely human-specific, how immune and vascular processes contribute to neuropsychiatric disease, why patients respond differently to cancer treatments, why clinical trials in these areas most often result in failure, and more.

The network should integrate human tissues, experimental systems, clinical information, and computational models around these biological questions. Supported projects should use exclusively human-based and computational approaches and should not include experiments on animals.

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

The network should organize multidisciplinary teams around specific questions that cannot be answered through a single model or dataset. Each team should connect experimental human biology with patient-level information and produce resources usable beyond its initial disease area.

Shared resources should include:

- Diverse, well-characterized human cells, tissues, biospecimens, and longitudinal clinical data;
- Experimental platforms that incorporate relevant combinations of neural, immune, vascular, endocrine, reproductive, stromal, and/or tumor components;
- Interoperable clinical, imaging, genomic, multi-omic, spatial, and experimental datasets;
- Computational models connecting biological measurements with disease trajectories and treatment responses;
- Common standards for metadata, quality control, reproducibility, and model characterization;
- Reference datasets and benchmarks for determining which systems are appropriate for defined scientific questions;
- Secure systems for linking experimental findings with patient data; and
- Shared expertise in clinical research, engineering, computational science, experimental biology, and patient engagement.

The network should prioritize resources that can be transferred, reproduced, and used across institutions. Protocols, datasets, analytical tools, reference materials, and model-characterization information should be publicly available wherever legally and ethically possible.

The purpose would be to connect human-based systems and data into an interoperable research infrastructure capable of investigating complex human disease.

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

Human organoids, organs-on-chips, bioprinting, advanced imaging, multi-omics, spatial biology, artificial intelligence, and patient-derived models can now provide complementary information about human disease. Large clinical and population datasets create additional opportunities to connect laboratory findings with patient experiences and outcomes.

Many of these advancements are currently fragmented across laboratories, institutions, diseases, technologies, and NIH Institutes and Centers. Individual projects are generating sophisticated models, but they rarely establish the shared standards or interoperable infrastructure needed to examine interactions across biological systems.

The Common Fund is positioned to coordinate a challenge-driven network spanning diseases and Institutes and Centers. Its cross-cutting structure could connect existing scientific capabilities, reduce duplication, establish common standards, and create integrated platforms individual investigators or disease-specific programs can use to further gold standard science.

Please include other content the submitter wants to add to the submission

The network should promise to deliver:

- Integrated human-based platforms addressing defined questions in neuropsychiatric disease, neurodegenerative disease, immunology and sepsis, women's health, cancer, and other complex conditions;
- Public reference datasets linking experimental findings with clinical phenotypes, disease trajectories, and treatment responses;
- Cross-disease models of neural, immune, vascular, endocrine, reproductive, metabolic, and tumor interactions;
- Standardized protocols, metadata, reference materials, and quality control measures;
- Benchmarks for assessing model reproducibility, applicability, and performance for defined research questions;
- Interoperable computational tools and shared data infrastructure; and
- A tested and sustainable framework through which additional diseases and research communities can use the network. This framework should include how to design and integrate human-based research systems around complex biological questions, include

standards for selecting complementary experimental systems, and connect experimental and clinical data.

Progress should be evaluated according to the biological questions answered, the reproducibility and adoption of shared resources, and the extent to which the platforms enable further human-based research. The network would establish a new paradigm centered on integrated human biology while expanding NIH's capacity to investigate disease without experiments on animals.

Modernizing Research through Portfolio Analysis

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

NIH has extensive mechanisms for identifying new scientific opportunities but lacks a systematic, transparent process for identifying where experiments on animals most often fail to translate to human health and should cease being supported. NIH-funded animal experimentation grants have been continuing through established funding programs, infrastructure, breeding systems, training pipelines, peer review expectations, and institutional incentives even when better approaches are available or the experiments have provided limited benefit for understanding human health.

This creates a portfolio-level challenge that cannot be addressed solely by developing or funding additional human-based methods. NIH also needs a systematic way to identify existing categories of animal experimentation that should be discontinued and determine how the associated resources can be redirected.

This Common Fund initiative would identify priority areas for animal model discontinuation and create evidence-based roadmaps for phasing them out. The initiative would examine categories of funding rather than adjudicate individual applications. Its central purpose would be to give NIH a repeatable portfolio-management process for deciding where the public receives low returns on investment, how funds should be redirected, and how implementation should be measured.

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

This initiative would create a standardized framework for evaluating categories of experiments on animals across NIH. That framework should incorporate:

- Analyses of spending on animal experimentation grants, breeding programs, infrastructure, training, resource centers, and development of new animal models;
- Systematic reviews of animal experiments' human translation, reproducibility, duplication, and contributions (or lack thereof) to subsequent clinical or scientific advances;
- Assessments of which questions can be investigated using or reframed to use human cells, tissues, participants, imaging, clinical data, computational approaches, or combinations of these resources;

- Identification of peer-review practices, funding policies, and institutional incentives that perpetuate the identified experiments on animals;
- Transparent criteria for prioritizing areas for review and recommending discontinuation;
- Conflict-of-interest standards for participants in evidence reviews and roadmap development;
- Methods for classifying projects that combine experiments on animals and non-animal methods and making this classification system transparent and publicly available; and
- Publicly accessible baseline measures and annual indicators for tracking changes in funding.

Reviews should examine the full funding ecosystem supporting a category of experiments on animals, not only the direct research grants. The existence of long-standing infrastructure, specialized expertise, or routine use within a field should not in itself justify continued funding.

NIH should select initial areas that cross multiple Institutes and Centers so that the resulting process is applicable to the entire agency.

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

The availability of human tissues, clinical data, organoids, organs-on-chips, advanced imaging, artificial intelligence, computational modeling, and population-level resources has expanded the questions that can be investigated directly through human biology.

At the same time, increasing support for non-animal methods does not necessarily reduce spending on experiments on animals. New initiatives can be added while established funding, infrastructure, and training continue unchanged. Because federal research resources are finite, maintaining lower-value approaches diverts investment from scientifically and ethically superior human-based work.

NIH therefore needs a mechanism that complements technology development by identifying existing expenditures that should end. Common Fund coordination is particularly appropriate because similar experimental practices, infrastructure, and funding assumptions appear across diseases and Institutes and Centers.

The timing is particularly important as NIH considers how to implement its growing emphasis on human-based research. A portfolio-level evaluation mechanism would allow NIH to move beyond parallel investment in new and established approaches and instead identify where resources can be deliberately redirected toward research grounded in human biology.

Please include other content the submitter wants to add to the submission

For each selected area, the initiative should produce a public discontinuation roadmap specifying:

1. The category of experiments on animals recommended for discontinuation;
2. The scientific, translational, ethical, and funding evidence supporting that recommendation;
3. The human-based resources available to address the relevant questions;
4. Any defined capability gaps that must be resolved before discontinuation;
5. A timeline for reducing and ending NIH support;
6. Required changes to funding opportunities, peer review instructions, training programs, and research resource support;
7. Plans for ending associated breeding programs and repurposing infrastructure;
8. Safeguards against shifting discontinued activities into different funding categories or renaming them;
9. Responsibilities and implementation milestones for relevant Institutes, Centers, and Offices; and
10. Public measures for tracking changes in dollars, grant categories, infrastructure, and scientific activity.

The initiative should also design the structure, institutional obligations, eligibility standards, and outcome measures for future funding opportunities that help laboratories and institutions implement the roadmaps. Those subsequent awards could be issued by the relevant Institutes and Centers rather than duplicated within this initiative.

This program should deliver an NIH-wide funding baseline, a repeatable evaluation framework, several completed roadmaps, Institute- and Center-specific implementation plans, proposed changes to NIH funding and review policies, and public reports showing whether and how the recommendations changed the research portfolio.