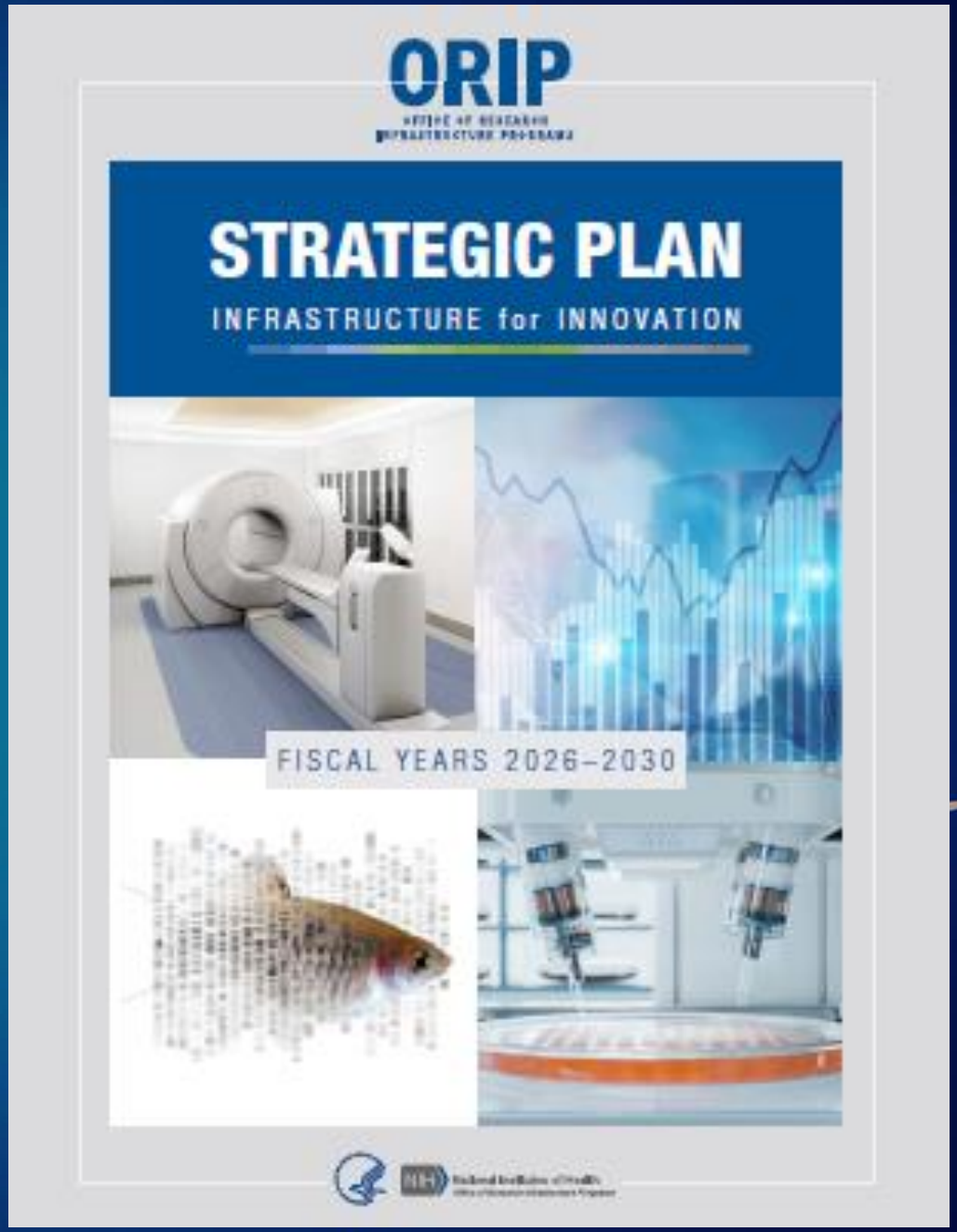
Development of Models, New Approach Methodologies, and Biological Materials for Studying Human Health and Diseases

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OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS



Concept Clearance

Concept Clearance: Reissue

Development of Models, New Approach Methodologies (NAMs), and Biological Materials for Studying Human Health and Diseases (R21)

Objective: Encourage innovative research to develop, characterize, improve or preserve research models and related biological materials; develop or improve technologies, including NAMs, for studying human health and diseases; and improve the identification and control of factors that could confound or interfere with the use of research models

Funds Available and Anticipated Number of Awards: Contingent upon NIH appropriations and the submission of meritorious applications

Award Project Period: 2 years

Council Action: Vote for approval of the concept for "Development of Models, New Approach Methodologies, and Biological Materials for Studying Human Health and Diseases (R21 Clinical Trial Not Allowed)"

Background

- Research Models R21 Program was established by NCRR and has continued to evolve since 2012 under ORIP's administration
- Meets demand for research models that are more predictable and accessible for biomedical research
- Addresses need for technological advancements for developing research models, such as NAMs, genomics, gene editing, and informatics
- Aligns with ORIP's mission on supporting research resources and infrastructure

NOFO	Time Period	# of Applications	# of Awards	Award Rate
PA-16-141	03/18/2016 to 09/08/2019	192	35	18%
PAR-19-369	09/09/2019 to 03/17/2021	85	19	22%
PAR-21-167	03/17/2021 to 11/15/2024	184	48	26%
PAR-25-273	11/15/2024 to 01/08/2028	111	11	Ongoing

Progress and Impacts

Publications from Awards Under the Past 3 Completed NOFOs

- Average award rate (# of awards/# of applications) was approximately 20%
- Most applications and awards were on model development, with the primary model being mouse followed by fly and zebrafish
- Major cross-cutting themes included genome engineering, disease modeling, imaging tools and technologies, and regeneration
- Percentage of awards with one or more publications is about 75%
- Approximately 290 publications are linked to 102 awards since 2017
- These publications have been cited around 5,725 times in total

Other Metrics Under the Past 3 Completed NOFOs

- 9 granted US patents cited 3 publications from 4 awards
- Examples of patents:
  - Robotic platform for high throughput injections into intact tissue
  - Systems, methods, and compositions for site-specific genetic engineering

Impact of R21 Projects

Exploratory/Developmental Research

- Address major gaps or solve long-standing issues in technology and resource development
  - Transgenic methods for stable genetic modification of sea urchins
  - Resources for studying apical extracellular matrix structure and biogenesis in worms
  - Cryopreservation of fly strains
  - High-throughput microinjection for fly embryos
  - Low temperature adapted gene editing tools in Xenopus
  - High throughput generation of mitochondrial disease models in zebrafish and mouse
  - Hematopoietic humanized mouse model to study CAR-T therapy
  - Organoids for studying T cell development and HIV/SIV infection

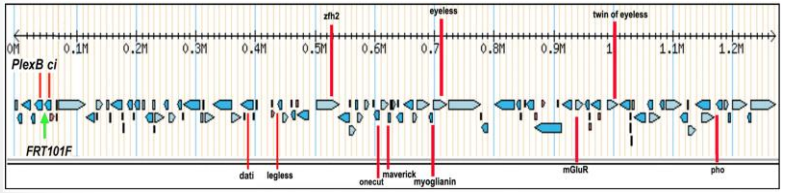
Impact on Research Projects and Resource Development

- Shared new technologies and resources with broad research communities
- Led to R01 research projects or large-scale R24 research resource projects

Large Scale Resource Development Example

R21OD024794
Awarded in 2017

- Resource for marking clones on the fly 4th chromosome
- Gap: 4th chromosome was largely ignored due to a lack of recombination in *Drosophila*
- Grant cited in 8 publications



https://doi.org/10.1093/g3journal/jkag077

R24OD028242
Awarded in 2020

- Comprehensive resource for fly 4th chr
  - UAS.fly cDNA and UAS.human homolog cDNAs
  - Gene trap mutants and protein traps
  - Stocks for meiotic and mitotic recombination
  - Stocks for mutagenesis of each 4th chr gene for marking single-cell clones
- Generated >400 stocks for ~80 coding genes
- Diseases: macular degeneration, cancer, heart disease, neurological syndromes
- Grant cited in 13 publications
- Deposited in stock centers and ordered >1,200 times

Purpose of the Reissuance

- **ORIP Strategic Plan 2026-2030:**
  - ORIP advances the NIH mission by supporting resources and infrastructure for innovation
  - ORIP empowers and expands existing programs and develops new initiatives to support NIH at the forefront of the scientific progress
  - Priority 1 focuses on developing and expanding access to model resources to advance the study of human diseases
- **R21 Program encourages innovative research for human health and diseases by:**
  - Developing, characterizing, improving or preserving research models and biological materials
  - Developing or improving technologies, including NAMs
  - Improving the identification and control of factors that could confound or interfere with the use of research models in biomedical research
- **To align with ORIP's NIH-wide mission, proposed projects must:**
  - Have broad application to multiple NIH Institutes and Centers
  - Explore multiple body systems or evaluate diseases that impact multiple body systems

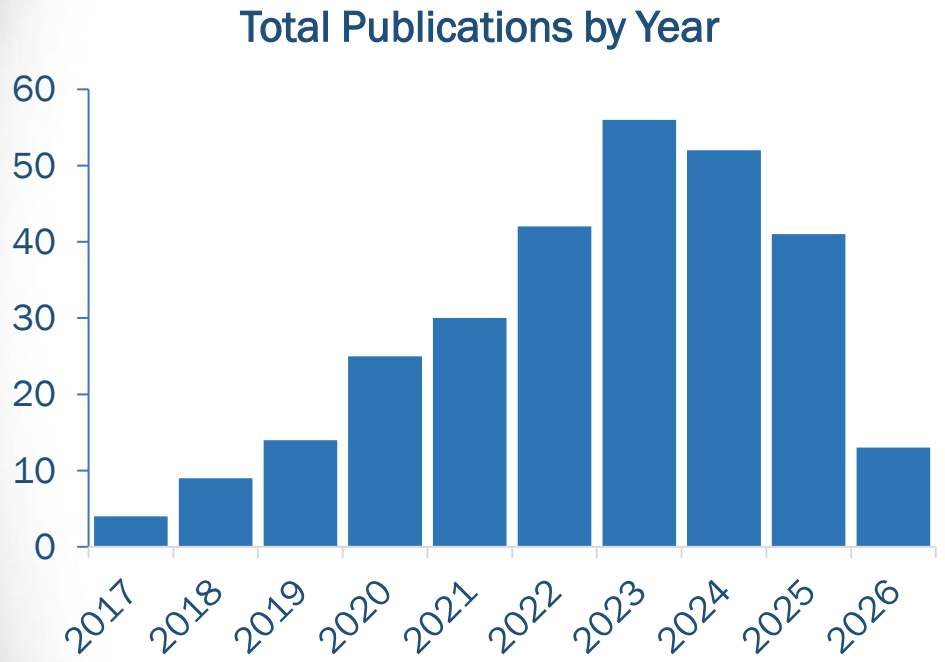
Concept Clearance

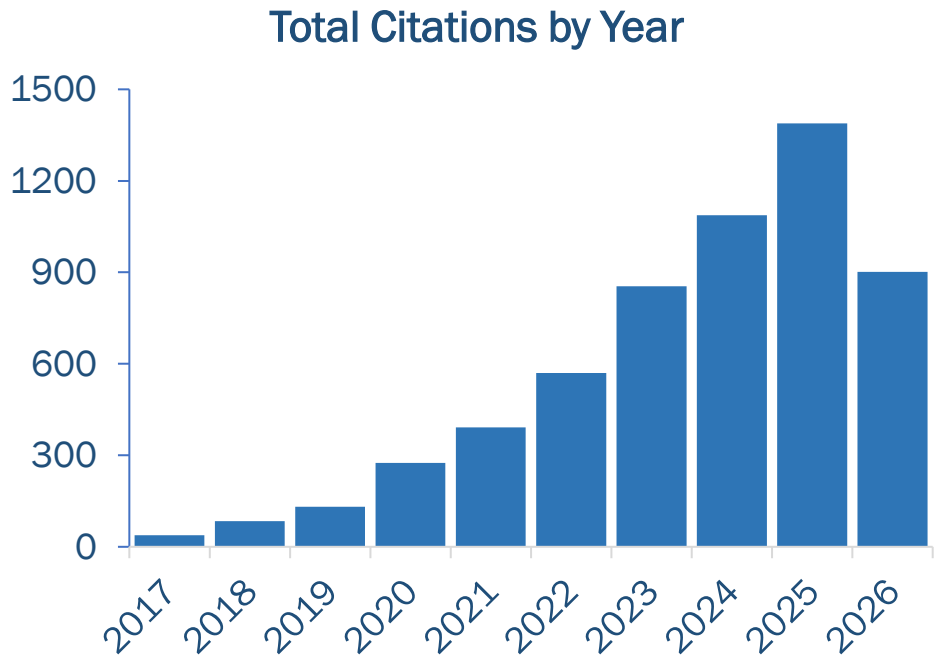
Vote for approval of the concept for "Development of Models, New Approach Methodologies, and Biological Materials for Studying Human Health and Diseases (R21 Clinical Trial Not Allowed)"

Additional Materials

Progress and Impacts

Under The Past Three Completed NOFOs

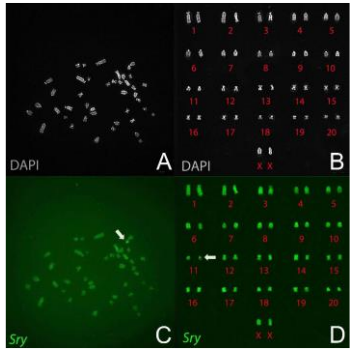




R21 Project Leading to R01 Grant Example

R21OD026560
Awarded in 2018

- Sry transgenic rats for investigation of XX vs. XY differences in phenotypes
- Gap: Lack of rigorous and reproducible rat models to study sex differences in disease incidence or progression
- Grant cited in 9 publications



https://pmc.ncbi.nlm.nih.gov/articles/PMC9934672/

R01OD030496
Awarded in 2021

- Transformative rat models to study sex differences in disease
  - Phenotype characterization of Sry transgenic rats at molecular and developmental level
  - Studies of sex differences in diverse models of physiology and disease, i.e., women's health, cardiovascular and renal function, metabolic disorders, addiction, and autoimmune disorders
- Grant cited in 5 publications

NIH National Institutes of Health
Office of Research Infrastructure Programs