

Concept Clearance – Reissue of Development of Animal Models and Related Biological Materials for Research (R21)

A major theme of the [ORIP Strategic Plan 2021-2025](#) is to facilitate the development and ensure the availability of the highest quality and most useful animal models and related resources for the advancement of research on human disease. As part of ORIP's NIH-wide emphasis, ORIP seeks to improve and disseminate the best animal models that are of interest to multiple NIH Institutes and Centers (ICs). Thus, ORIP has developed an Animal Models R21 Program to encourage innovative research to develop, characterize, and improve animal models, biological materials, and novel technologies to better understand human health and disease as well as to seek projects aimed at improving the diagnosis and control of diseases that interfere with animal use for biomedical research. Proposed R21 projects must have broad application to multiple NIH ICs and explore multiple body systems or evaluate diseases that impact multiple body systems. This R21 Program was established in 2007 by the National Center for Research Resources and has continued to evolve under ORIP's administration since 2012. To align with ORIP's mission on awarding grants to support research resources, such as animal models of human disease, this R21 program meets the demand for animal models that are more predictable and accessible for biomedical research and addresses the need for technological advancements for developing animal models.

ORIP has issued 4 funding opportunity announcements (FOAs) for the Animal Models R21 Program since 2013, which are [PA-13-145](#) (2013-2016), [PA-16-141](#) (2016-2019), [PAR-19-369](#) (2019-2021), and [PAR-21-167](#) (2021-2024). For [PA-13-145](#), 29 of 154 applications were funded, and for [PA-16-141](#), 35 of 187 applications were funded at a similar award rate of 19%. During the two-year period for [PAR-19-369](#), 19 of 76 applications were funded (25% award rate). Applications continue to be accepted and awards made under [PAR-21-167](#).

The R21 grant mechanism is intended to encourage exploratory/developmental research by providing support for the early and conceptual stages of project development for up to 2 years, with the combined direct costs of \leq \$275,000. On average, the combined total costs of R21 awards supported by ORIP are \sim \$410,000. ORIP's Animal Models R21 program has made significant progress and impacts. Awards under [PA-13-145](#) and [PA-16-141](#) resulted in 114 and 87 publications, respectively, with \sim 80% of these awards having at least one publication. Publications associated with [PA-13-145](#) and [PA-16-141](#) have been cited 2,165 and 796 times, respectively, as of March 2022. The higher publication and citation numbers for [PA-13-145](#) are due to its earlier release date compared to [PA-16-141](#). Although [PAR-19-369](#) ended only last year, three publications have been reported under this FOA so far.

Most R21 applications and awards in this Animal Models Program were focused on animal model and technology development, with the primary model being the mouse followed by the fly and the zebrafish. A number of these high-risk, high-reward studies led to the development of novel techniques, methodologies and applications that will impact biomedical research. One such example is an award titled "Resolving Complex Systemic Endogenous Expression Patterns into Subcellular High-Resolution Location" to Baylor College of Medicine, which resulted in 6 publications. One of these publications was on methods and genetic stocks for efficient generation of transgenic flies with multiplexed drug-based single-step selection and counterselection ([Cell Rep. 2021;36\(11\):109700](#); cited 2 times as of March 2022). Stocks generated from this project have been deposited to the Bloomington *Drosophila* Stock Center for distribution. Another award titled "CHD5 Dosage in Epigenetic Control of Cancer, Infertility, and Autism" to Cold Spring Harbor Laboratory led to 8 publications. One of the resulting publications was on the development of Chromodomain helicase DNA binding protein 5 (Chd5) mutant mice and the understanding of the role of Chd5 in mediating chromatin remodeling during sperm development ([Nature Communications 2015; 5: 3812](#); cited 49 times). A third example is an award titled "Gene Targeting in Zebrafish: Building Models to Assay Disease Genes" to the University of Utah, which led to 2 publications, with one publication on precise gene editing of the zebrafish genome and efficient recovery of recessive and phenotypically silent conditional mutations ([Dev Cell 2016;36\(6\):654-67](#); cited 107 times).

Based on the recent successes of the Animal Models R21 Program and the demand for better animal models for biomedical research, ORIP requests concept clearance from the Council of Councils to continue support for the "Development of Animal Models and Related Biological Materials for Research (R21)".