National Institutes Office of Research Infrastructure Programs

2019 Marmoset Community White Paper

The core mission of the Office of Research Infrastructure Programs (ORIP) within the Office of Director (OD) is to advance the NIH mission by supporting research infrastructure and research-related resource programs and by coordinating NIH's science education efforts. Specifically, ORIP's Strategic Plan supports the NIH-Wide Strategic Plan by funding the "scientific human and physical resources that will help to ensure the Nation's capability to prevent disease." ORIP awards grants to support research resources, such as animal models of human disease and state-of-the-art biomedical instrumentation. ORIP plans, organizes, and conducts workshops, both independently and in collaboration with NIH Institutes and Centers, to identify and pursue scientific opportunities. ORIP supports research-training opportunities for veterinary scientists to capitalize on their distinct perspective and expertise based in a deep understanding of comparative medicine and insight into animal models of human diseases. In the last several decades, the mouse system has been a powerful model for medical research due to, in large part, an array of sophisticated gene-editing techniques to manipulate the mouse genome and strategies for cell-type specific, inducible, or spatiotemporal regulation. However, considerable anatomical, physiological, cognitive, and behavioral differences between mice and humans limit the degree to which insights from mouse models shed light on human diseases. This is reflected in the high number of failed clinical trials for drugs that were effective in treating mouse models of human disease. Thus, non-human primates (NHPs) may serve as better models for studying human disease with the macaque being the traditional choice. However, the common marmoset (*Callithrix jacchus*) has emerged recently as a complementary species with advantageous characteristics that expand the types of studies that can be performed in a nonhuman primate. First, marmosets share with other primates, including humans, many aspects of physiology, a complex brain organization, and sophisticated social and cognitive behaviors. For example, like humans, marmosets are diurnal and housed in social groups consistent with the size and composition of groups in the wild. This is particularly important because the range of sophisticated social and cognitive behaviors that emerge naturally within social groups can be effectively studied under more controlled laboratory conditions. Second, marmosets are among the shortest-lived NHPs with small body size and strong reproductive power, making them highly economical and scalable for housing and generating the number of marmosets needed for preclinical evaluation. Third, in contrast to rhesus macaques, marmosets are free of Herpes B viruses, making the species safer to work with. Finally, technologies for generating genetically modified marmosets have already been developed, and their short generation time represents a distinct advantage for creating and expanding transgenic lines over larger nonhuman primate species.

Breadth of Current Research. Ongoing research in the marmoset is focused on modeling various human diseases and investigating in a wide range of systems and multiple levels of analysis, including aging, Alzheimer's disease, Parkinson disease, Huntington's disease and multiple sclerosis. Furthermore, the marmoset has been used

to develop a model system to evaluate various gene-editing approaches and strategies for therapy. Efforts are also ongoing to characterize the effects of pharmacological and life-style interventions on health span in the marmoset.

The Future. ORIP can play an essential role in addressing numerous resources issues that impede the progress in using marmosets as a biomedical model. Here are some examples. First, one of major bottlenecks in using marmosets to model human disease is the extreme short supply of marmosets available for sale to research community. Second, the genetic diversity of marmoset population in this country is largely unknown. The information is critical in better maintaining high population diversity and modeling human disease. For example, it will be extremely informative to know the divergence and frequency of marmoset alleles relevant to human mutations such as major risk factors ApoE and Trem2 for AD. Third, it is not known if immunological reagents and protocols for analytic experiments in the marmoset are available. Database for these reagents and, if needed, developing these reagents will become critical for the success of modeling human disease. Fourth, it is critical to develop genetic viral tools that work in the marmoset. Finally, ORIP can offer workshop to advance above endeavors and disseminate the resulting resources.

Author
Kuo-Fen Lee