

U.S. Department of Health and Human Services National Institutes of Health Division of Program Coordination, Planning, and Strategic Initiatives Office of Research Infrastructure Programs Division of Comparative Medicine

## Validation of Animal Models and Tools for Biomedical Research Session V. Validation of Non-Mouse Models for Preclinical Research

Thursday, December 10, 2020 Virtual Meeting

**Workshop Report** 

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### **Executive Summary**

The fifth of 10 sessions of the Virtual Workshop on Validation of Animal Models and Tools for Biomedical Research was held on December 10, 2020. This workshop is intended as a venue to discuss the status of and needs for the validation of animal models used in biomedical research. Session V focused on the validation of non-mouse models and tools for preclinical research. Animals highlighted in the discussion included rabbits, naked mole rats, guinea pigs, ferrets, rats, and hamsters. During the session, the participants spoke on the benefits of non-traditional small mammal models, noting their usefulness in modeling human diseases physiologically (i.e., compared with mice) at a relatively low cost (i.e., compared to larger animal models and human challenge models). They emphasized that investigators should recognize the advantages and limitations of their chosen model; cooperative efforts would allow integration between different models to fill knowledge gaps. Several participants emphasized the importance of developing models based on physiological and cellular applicability. They also noted that data variation represents a challenge for investigators; the biological drivers of variability should be considered. During the meeting, the following needs were identified: (1) resources to support the generation and distribution of non-mouse rodent models, (2) assistance in developing molecular tools and reagents (e.g., specific antibodies) for model validation, (3) support for genome sequencing and annotation, as well as other -omic assessments (e.g., proteomics), (4) public support services for investigators, (5) support for model standardization, and (6) facilitation of collaborative efforts.

#### **Session Co-Chairs**

Mary Dickinson, Ph.D., Baylor College of Medicine Kent Lloyd, D.V.M., Ph.D., University of California, Davis

#### Presenters

Rochelle Buffenstein, Ph.D., Calico Life Sciences John Engelhardt, Ph.D., The University of Iowa Renzhi Han, Ph.D., The Ohio State University Johan Neyts, Ph.D., Katholieke Universiteit Leuven, Belgium Rebecca Shansky, Ph.D., Northeastern University Hailey Weerts, Ph.D., Walter Reed Army Institute of Research

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#### **Organizing Committee**

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### **Workshop Report**

#### **Opening Remarks**

Stephanie Murphy, V.M.D., Ph.D., Director, Division of Comparative Medicine, ORIP Sige Zou, Ph.D., Coordinator, Program Official, ORIP

Drs. Stephanie Murphy, Director, Division of Comparative Medicine, ORIP, and Sige Zou, Coordinator, Program Official, ORIP, welcomed the participants and offered thanks to the Organizing Committee and Session Chairs for their efforts in organizing the event. Dr. Zou explained that the meeting is the fifth in a series of 10 sessions. They also acknowledged the support of several National Institutes of Health (NIH) Institutes: the National Heart, Lung, and Blood Institute (NHLBI); National Institute on Aging (NIA); National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); National Institute of General Medical Sciences (NIGMS); and National Institute of Neurological Disorders and Stroke (NINDS). Dr. Murphy reminded the participants that validation of animal models and tools is a critical part of ORIP's trans-NIH efforts. She offered thanks for the participants' input. Dr. Mary Dickinson, Co-Chair, emphasized the importance of developing and testing models that replicate the disease state in humans. She thanked the participants for their engagement. Drs. Dickinson and Kent Lloyd, Co-Chair, introduced the speakers.

#### A Rabbit Model of Duchenne Muscular Dystrophy for Preclinical Therapeutic Testing

Renzhi Han, Ph.D., The Ohio State University

Dr. Renzhi Han presented on the use of a rabbit model for Duchenne muscular dystrophy (DMD). He explained that DMD is one of the more than 7,000 rare diseases that collectively affect about 8% of the U.S. population. About 80% of rare diseases are genetic, and 50% affect children. Fewer than 5% of these diseases, however, have treatments that are approved by the U.S. Food and Drug Administration. DMD affects about 1 in 5,000 male births and results from a dystrophin gene mutation. The disease is characterized by progressive muscle weakness and wasting, eventually leading to cardiomyopathy and premature death. Several mammalian models (e.g., mice, dogs, pigs) have been developed for DMD. Mice are widely available and inexpensive for research but often fail to present DMD symptoms (e.g., body weight, clinical course, lifespan, age at first symptom, loss of ambulation, muscle wasting, cardiomyopathy, limb muscle fibrosis, muscle regeneration). Rabbits have long been used for biomedical research, although their use has declined over time. Rabbit models offer several advantages: physiological similarity to humans, previous successful use in translational studies, large size, short gestation period and high proliferation, and ease of genetic manipulation. Dr. Han's group created a DMD rabbit model by injection of CRISPR and base editing. These DMD rabbits exhibit signs of muscular dystrophy and cardiomyopathy. Challenges associated with rabbit models include limited resources for model creation, high costs for breeding and maintenance, incomplete genomic DNA sequence coverage and gene annotations, and scarce -omics data (i.e., compared to human and mouse data). Dr. Han proposed the creation of a knockout rabbit consortium to (1) generate and supply genetic rabbit models; (2) phenotype genetic lines; (3) provide training on experimental handling, common surgeries, and reagent administration; (4) annotate the rabbit genome and enhance the coverage and accuracy of current genome sequences; and (5) facilitate collaborations between academia and industry.

# Breaking the Mol(e)d: The Naked Mole-Rat—A Long-Lived Animal Model of Exceptional Biogerontological Interest

Rochelle Buffenstein, Ph.D., Calico Life Sciences

Dr. Rochelle Buffenstein spoke on the use of the naked mole rat as a model for research on human diseases and aging. She emphasized that the selection of an appropriate model organism requires complex consideration of many factors to balance ease of use with biological relevance. Additionally, experimental

research designs should be species appropriate. Most biomedical research on aging focuses on four standard organisms: yeast, nematode worms, fruit flies, and mice. These organisms are supported by a myriad of experimental tools and share several common features with humans, including loss of health with aging. An alternative approach, however, is to identify species that over the course of their evolution have developed mechanisms to resist a specific biomedical problem (e.g., resistance to such lifestyle diseases as osteoporosis, type 2 diabetes, and ischemia/reperfusion injury) or overcome specific health constraints (e.g., tissue regeneration). Naked mole rats have gained public attention for their considerable longevity, which is about six times greater than their predicted lifespan-determined by their body sizeand for their lack of Gompertzian-associated age-dependent mortality hazards. Additionally, naked mole rats display several unique characteristics directly pertinent to defying the harmful effects of specific diseases: (1) hypoxia and hypercapnia tolerance; (2) imperviousness to acid burn and other painful stimuli; (3) hypo-functioning pain signaling associated with osteoarthritis; (4) unusual immune cell populations; (5) resistance to cancer and cardiovascular diseases; (6) resistance to plaques, tangles, and neurodegeneration associated with beta-amyloid and tau in the brain; and (7) abrogated aging. Unlike other mammals, the naked mole rat's risk of dying does not increase with age after sexual maturity. Despite the high energetic costs of continuous reproduction, breeding females live longer than subordinates in the colony, in defiance of the disposable soma theory of aging. Additionally, breeding females do not undergo menopause or exhibit reduced fertility with age. Moreover, this species appears to resist common aging phenotypes (e.g., reduced bone mineral density, reduced cardiovascular health) and ultraviolet-induced skin tumorigenesis. Naked mole rat cells can be transformed, providing a novel resource for assessing mechanisms of *in vivo* cancer resistance. Dr. Buffenstein highlighted resources needed for naked mole rat research: public support services for investigators, establishment of a tissue bank or animal stock center, development of species-specific antibodies, and molecular and genomic tools (e.g., CRISPR). Recent advancements in -omics studies (e.g., RNA sequencing, CRISPR) are suitable for nontraditional models. These tools-together with a multispecies comparative biology approach-would allow investigators to compare molecular differences in response to various challenges and determine the disparate mechanisms employed. Currently, some technologies routinely used in mice are unavailable for naked mole rats, and the creation of transgenic mole rats remains a challenge for investigators. Advancements in high-throughput phenotyping (e.g., metabolic chambers, cell painting and imaging, image analyses through machine learning), however, represent new opportunities in this area.

#### Use of Guinea Pig Models to Assess the Efficacy of Enteric Countermeasures

#### Hailey Weerts, Ph.D., Walter Reed Army Institute of Research

Dr. Hailey Weerts presented on her work with guinea pig models and enteric countermeasures. The focus of her work is *Shigella* infection and pathogenesis, which has a low infectious dose (i.e., 10–100 bacteria) and is characterized by invasion of the mucosa epithelium, intracellular replication, and intercellular spread. In humans, hallmarks of Shigella infection are neutrophils in stool, bloody and mucoidal stools, inflammation, and tissue damage and ulceration. Animal models that mimic human disease are essential tools for studying Shigella pathogenesis and product efficacy. Efforts toward validated models have included the following: (1) objective, rather than subjective, disease scoring criteria; (2) technical adaptations resulting in disease that closely mimics human disease; and (3) overall increased reproducibility. Mouse models are highly accessible but often insufficiently represent the disease in humans. Controlled human infection models and nonhuman primate models, in contrast, are challenging and costly to perform. Dr. Weerts' group uses two guinea pig models-keratoconjunctivitis and rectocolitis-for Shigella infection. They have used alternative methodologies and refinement of the keratoconjunctivitis model (e.g., anesthetic treatment, objective scoring and measures, reduction in inoculum) to meet their objectives for validation. Refinements to the rectocolitis model (e.g., catheter placement, inoculum volume, disease scoring system) have enabled the use of older animals with more developed immune systems, leading to more consistent outcomes. Additional parameters included objective (e.g., weight loss, blood, mucous) and subjective (e.g., fecal grade, peri-anal inflammation) measures. Scores from each category are combined to calculate a composite disease score. Disease

measures for this model are characteristic of human disease. Dr. Weerts emphasized that the models mimic human disease on a cellular level; intrarectal challenge induces a reproducible disease that mimics human disease at a cellular and system level. Furthermore, human and guinea pig models share similar disease characteristics. She stated that both models have advantages and drawbacks for research. Barriers for model validation include technical challenges (e.g., target dose, lack of reagents) and scientific limitations (e.g., higher challenge dose, objective scoring parameters, lack of disease spectrum). Dr. Weerts emphasized that standardization of disease scoring across challenge models is crucial for validation.

# Genetic Modeling in the Ferret to Study Disease Pathophysiology, Stem Cell Biology, and Genetic Therapies

John Engelhardt, Ph.D., The University of Iowa

Dr. John Engelhardt discussed his research on genetic modeling in ferrets using cystic fibrosis as a disease example. Seven model species have been identified for cystic fibrosis (i.e., zebrafish, mouse, rat, rabbit, sheep, pig, ferret), a disease that affects lung, liver, intestine, and pancreatic tissues. Ferret and pig models spontaneously develop lung and pancreatic disease that is characteristic of cystic fibrosis in humans, whereas rodent models have not reproduced this phenotype. His group has developed CRISPRmediated approaches (e.g., non-homologous end-joining and homology-directed repair) to engineer ferret zygotes and create ferret models that are assisting in understanding the anatomical and cellular variation responsible for phenotypic disease disparity among model species. Differences in the airway cellular anatomy should be considered when comparing disease phenotypes between species. Cell types in the major proximal airway differ between ferrets and mice; the ferrets more closely represent human anatomy. Heterogeneity in cystic fibrosis transmembrane conductance regulator ( $\overline{CFTR}$ ) expression is present in epithelial cell types that vary in abundance across model species. Dr. Engelhardt's group found that ionocytes influence anion current in polarized tracheal epithelia from ferrets but not mice. New ferret genetic models may inform ionocyte functions. His group generated three genetic ferret models (ROSA-TG Cre reporter, FOX11-Cre<sup>ERT2</sup>, CFTR<sup>L/L</sup> conditional knockout) for ionocyte lineage tracing and conditional CFTR knockout in ionocytes. They are using conditional and cell-specific CFTR knockouts to address CFTR function in ionocytes and its role in cystic fibrosis disease progression. Dr. Engelhardt explained that the same approach could be applied to other cell types when Cre drivers are generated. Additionally, the generation of human CFTR mutations in the ferret has provided information for prenatal and postnatal treatments to prevent disease progression. Genetic models also have provided insight into stem cell compartments that participate in regeneration of the proximal airways following injury. Mouse models have been used to establish stem cells within airway submucosal glands that are limited to the proximal trachea, but ferrets and humans have submucosal glands throughout the extrapulmonary and intrapulmonary cartilaginous airways. Transgenic ferrets capable of lineage tracing these glandular stem cells were generated, and the team found that these cells contribute to airway repair following injury. Single-cell analysis of this stem cell compartment demonstrates previously unappreciated cell subtypes within ferrets and help to validate their existence in humans. Single-cell analysis also will inform the pathways that control cell lineage commitment toward surface airway basal cells, providing a geneediting target for cystic fibrosis therapeutics. Additionally, work in cystic fibrosis ferret models has demonstrated phasic changes to endocrine pancreatic function; these results are consistent with recent clinical findings. Transgenic ferrets are being used to lineage-trace stem cell compartments in the pancreas involved in postnatal islet regeneration; these appear to be similar to those in mouse during limited to stages of pancreatic development. These processes cannot be studied in cystic fibrosis mice because they do not develop pancreatitis, even though lineage tracing in mice has framed most knowledge on pancreatic progenitors. Challenges for non-mouse models include the "orphan status" of many genomes and reagents for validation (e.g., antibodies). Dr. Engelhardt emphasized that most knowledge on regenerative stem cell biology is framed in mice using fate mapping and conditional genetics; mobilization of these technologies to other species will aid in model validation.

#### The Promise and Pitfalls of Rodent Models of Psychiatric Disease

Rebecca Shansky, Ph.D., Northeastern University

Dr. Rebecca Shansky spoke on rodent models for psychiatric disease. She explained that rodent and human brains share a striking homology in neural circuitry. Thus, these species are ideal models for mental illness and neurological diseases. Dr. Shansky pointed out that historically, neuroscientists have studied male rodents nearly six times more frequently than females. She emphasized that this disparity represents a public health challenge. Most mental illnesses occur in both men and women but are expressed at different ratios between sexes. The sex-specific factors for susceptibility are not understood fully. In the past, neuroscientists were reluctant to study female rats because the estrous cycle might introduce variability. Recent studies, however, have shown that this degree of data variability does not differ significantly between the sexes in rodents. In 2016, the NIH introduced the Sex as a Biological Variable (SABV) initiative, which requires NIH-funded investigators to consider sex as a biological variable in their experimental design. Investigators should apply male-validated paradigms to female subjects or provide scientific justification if only using one sex. The inclusion of females might require new considerations for interpretation. For example, female expression of anxiety in elevated maze testing does not map onto human epidemiology. Additionally, female rat behavior is characterized primarily by motor activity, whereas male rats are driven by sex and anxiety. Furthermore, Pavlovian fear conditioning focuses on male-biased behaviors; new metrics for this response are needed. Machine-learning tools allow unbiased identification of behavioral phenotypes and novel fear responses. Many drugs were developed using only male animals; consideration of females could help investigators identify drugs that were overlooked previously and provide a better understanding of brain function.

# A SARS-CoV-2 Hamster Infection Model to Study the Effect of Vaccine Candidates and Antivirals Johan Neyts, Ph.D., Katholieke Universiteit Leuven, Belgium

Dr. Johan Neyts presented a hamster model for SARS-CoV-2 infection, which can be used for studies of vaccine candidates and antivirals. He explained that hamsters represent the infection more effectively than mice. Using microcomputed tomography, Dr. Nevts' group demonstrated that a COVID-19-like disease is present in the hamster lungs following infection. They found that signal transducer and activator of transcription 2 (STAT2) signaling restricts viral dissemination but drives severe pneumonia in SARS-CoV-2-infected hamsters. They reported several symptoms of severe COVID-19 (e.g., peri-bronchial inflammation, perivascular inflammation, bronchopneumonia, perivascular edema, apoptotic bodies in bronchi walls, necrotizing bronchitis). Heat maps indicate variation in gene expression between wild-type and transgenic mice with infection. Next, the group validated a SARS-CoV-2 vaccine candidate, based on the YFV17 vaccine as a vector, in hamsters. Protection was conferred with one dose, suggesting a strong immune response. Dr. Neyts explained that investigators currently lack the tools for cell-mediated immunity in hamsters; this deficiency represents an area for future development. Gene expression changes were observed after vaccination. They performed a transmission study, demonstrating the protective effects of vaccination within groups of animals. Dr. Neyts' group also validated antiviral therapeutics in this model; they demonstrated that favipiravir reduces SARS-CoV-2 replication, but hydroxychloroquine, combined with azithromycin, does not. Additionally, favipiravir protects against SARS-CoV-2 transmission. They further demonstrated that ultrapotent human antibodies provide protection against SARS-CoV-2. Dr. Nevts concluded that the hamster model provides a valuable tool to study COVID-19 pathogenesis and therapeutics. He stated that this model represents an ideal approach for vaccine studies.

#### **Group Discussion**

Mary Dickinson, Ph.D., Baylor College of Medicine Kent Lloyd, D.V.M., Ph.D., University of California, Davis

In response to a question from Dr. Peter Nghiem, Dr. Han explained that he had created two mutant dystrophin lines. In the first line, CRISPR was used to generate random mutations. In the second line, base editing was used to create a nonsense mutation. Dr. Nghiem wondered how the rat and rabbit models for DMD differ, and he asked about measurement of functional outcomes in the models.

Dr. Dickinson asked the panelists to discuss the applicability of model systems across different diseases. Dr. Han noted that the challenges of recapitulation in mice span many human diseases, including other muscular dystrophies. He stated that rabbits are promising models for cardiovascular research because rabbit cardiac function (e.g., action potentials in cardiomyocytes) is comparable to that of humans. He added that few disease models have been generated in rabbits to date.

Dr. Douglas Wallace noted that viral transcription did not appear to be inhibited in the hamster models; he asked whether this might result from differences in peptides between species. Dr. Neyts responded that this question requires further investigation but agreed that the protein likely is unrecognized.

Dr. Marco Brotto stated that rabbits might be useful models for aging. He added that an ongoing need exists for surgical models, such as models with bone gene mutations generated by CRISPR; rabbits could provide a valuable service in this area. Dr. Han agreed about the advantages of rabbit models; he added that rabbits are less costly and more accessible than alternative models.

Dr. Art Arnold commented on his group's work in deleting the sex-determining region Y gene and transferring it to an autosome, resulting in experimental control of the animal's gonad development. Using this approach, investigators can determine the effect of biological sex on disease phenotype.

Dr. Dickinson asked about the cost and logistical challenges that limit larger sample sizes. Dr. Engelhardt suggested that SABV be addressed in a study section but noted that readjustment of expectations is needed for studies using larger animal models, given that animal numbers are more limited in such studies than in mouse studies. Dr. Wallace asked what biological factors drive sex differences in neurologic disorders; he noted that mitochondrial-associated processes appear to play a role. Dr. Shansky replied that more data in this area are needed. Dr. Zoe Donaldson noted that sex differences represent variability; the underlying causes of variability represent a new area for exploration.

Dr. Gary Lewin commented that in naked mole rats, susceptibility to disease is dependent on an animal's social ranking; sociality effects should be considered as a contributing biological factor in research.

Dr. Steven Rowe commented on correlates between human physiology and specific disease models. He stated that investigators should confirm the model's ability to mimic cellular physiology of a disease state of interest by organ. This approach would help facilitate the identification of molecular reagents for research. Dr. Engelhardt agreed but noted that coordination across species would be challenging from a cost standpoint.

Dr. Engelhardt commented that a new study section focused on larger animal models could benefit the field of animal model validation, because mouse-heavy study sections often have expectations that are difficult to align with larger animal studies and their fiscal limitations. Dr. Engelhardt suggested this was a topic that needed discussion at a higher level.

Dr. Hugo Bellen added that Session IX will focus on vertical integration approaches. Dr. Keith Cheng spoke on the need for a mechanism to connect human pathology data to the effects of therapeutics. He

also highlighted the need for comparisons of radiology and pathology across various models and humans for various diseases (COVID-19, intestinal diseases, muscular dystrophy). He added that Session VII will focus on technologies, phenotyping, and data science.

Dr. Nghiem stated that investigators should recognize both the values and limitations of their chosen animal models. Collaborative efforts could help address limitations in specific models. He asked Dr. Han to speak on his group's DMD model. Dr. Han explained that models are created in different countries; importing animals for research often is challenging. Thus, his group produced its model in the United States and made the resource widely available to the research community. Dr. Han added that his group is developing new tests to measure muscle functional testing. Dr. Nghiem replied that he is developing a similar approach for assessments in dogs.

#### **Additional Comments**

In the Zoom chat, Dr. Rowe asked about examples of how an understanding of a specialized feature in an organism has result in the identification of molecular targets applicable to human disease. He asked whether certain organs, physiological features, or molecular traits are more likely to be translatable.

Dr. Lewin commented that many long-lived species (e.g., primates, whales, bats) are highly social. The naked mole rat is unique as a model that is highly social in a laboratory environment. Dr. Buffenstein commented that these examples of social animals are difficult to maintain in the laboratory, highlighting the usefulness of the naked mole rat as a social species in this regard. Dr. Lewin added that laboratory maintenance enables access to tools for cell physiology, stem cell biology, and genetics; knowledge of underlying molecular processes is important for mechanistic studies.

Dr. Jessica Bolker asked whether the MoSeq tool can be used across different species and whether rabbits are suitable for other categories of disease; Dr. Shansky responded that mice and rats have been used thus far, but it is intended to be made broadly applicable. Dr. Bolker noted that body size is critical in diseases that involve fluid flow.

Dr. Bolker wondered whether a *Shigella*-like pathogen is native to guinea pigs. She also wondered whether the basis for the broad spectrum of disease variability is understood. Dr. Brotto wondered how the participants are approaching the issues and drivers of data variability. Dr. Martha Delany commented that variability in human diseases (e.g., COVID-19) should be considered.

Dr. Buffenstein stated that the effect of the estrus cycle should be considered in studies with female specimens. Drs. Leslie Leinwand and Shansky countered that cardiac and neurological data do not vary significantly between sexes. Dr. Buffenstein responded that hormonal variation is likely to introduce variation in other physiological situations. Animals might be at different stages of their cycle; this effect could contribute to the noise around the data. Dr. Shansky agreed but noted that similar sources of variability appear to exist in male specimens. She shared an opinion article on the topic:

• Shansky RM. Are hormones a "female problem" for animal research? *Science*. 2019:364(6443);825–826. doi.org/10.1126/science.aaw7570.

Dr. Arnold highlighted a new rat model that allows the investigator to discriminate between gonadal hormonal and sex chromosomal factors that cause sex differences in any disease or phenotype.

#### **Summary and Suggestions**

Non-mouse models can play an essential role in biomedical research when other more traditional and commonly used species are inappropriate or lack sufficient human disease relevance. Because many of these systems have limited utility due to the costs associated with the animals and their care, efficient strategies for resource and data sharing are highly encouraged. The participants discussed and provided the following areas that require new or continued support from ORIP and the NIH:

- Resources to support the generation and distribution of non-mouse models
- Molecular tools and reagents (e.g., specific antibodies) for model validation
- Support for genome sequencing and annotation
- Public resources or services for investigators
- Support for model standardization
- Facilitation of collaborative efforts

## **Appendix A: Meeting Agenda**

#### Session V. Validation of Non-Mouse Models for Preclinical Research 2:00–4:00 p.m. EST December 10, 2020

#### Chairs

Mary Dickinson, Ph.D., Baylor College of Medicine Kent Lloyd, D.V.M., Ph.D., University of California, Davis

2:00–2:05 p.m.	Opening Remarks
	Stephanie Murphy, V.M.D., Ph.D., Director, Division of Comparative Medicine, Office of Research Infrastructure Programs (ORIP)
	Sige Zou, Ph.D., Coordinator, Program Official, ORIP
2:05–3:30 p.m.	Presentations
	Renzhi Han, Ph.D., The Ohio State University A Rabbit Model of Duchenne Muscular Dystrophy for Preclinical Therapeutic Testing
	Rochelle Buffenstein, Ph.D., Calico Life Sciences Breaking the Mol(e)d: The Naked Mole-Rat—A Long-Lived Animal Model of Exceptional Biogerontological Interest
	Hailey Weerts, Ph.D., Walter Reed Army Institute of Research Use of Guinea Pig Models to Assess the Efficacy of Enteric Countermeasures
	John Engelhardt, Ph.D., The University of Iowa Genetic Modeling in the Ferret to Study Disease Pathophysiology, Stem Cell Biology, and Genetic Therapies
	Rebecca Shansky, Ph.D., Northeastern University The Promise and Pitfalls of Rodent Models of Psychiatric Disease
	Johan Neyts, Ph.D., Katholieke Universiteit Leuven, Belgium A SARS-CoV-2 Hamster Infection Model to Study the Effect of Vaccine Candidates and Antivirals
3:30–4:00 p.m.	Group Discussion

### **Appendix B: Discussants List**

#### Session V. Validation of Non-Mouse Models for Preclinical Research 2:00–4:00 p.m. EST December 10, 2020

Kristine Abraham, Ph.D., National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Lola Ajavi, Office of Research Infrastructure Programs (ORIP) Art Arnold, Ph.D., University of California, Los Angeles Hugo Bellen, Ph.D., Baylor College of Medicine Jessica Bolker, Ph.D., University of New Hampshire Marco Brotto, Ph.D., The University of Texas at Arlington Elizabeth Bryda, Ph.D., University of Missouri Paul Buckmaster, D.V.M., Ph.D., Stanford University Rochelle Buffenstein, Ph.D., Calico Life Sciences Michael Chang, Ph.D., ORIP Keith Cheng, M.D., Ph.D., The Pennsylvania State University Miguel Contreras, Ph.D., ORIP Martha Delaney, D.V.M., Ph.D., University of Illinois at Urbana-Champaign Mary Dickinson, Ph.D., Baylor College of Medicine Zoe Donaldson, Ph.D., University of Colorado Boulder John Engelhardt, Ph.D., The University of Iowa Craig Franklin, D.V.M., University of Missouri Glenn Gerhard, M.D., Temple University Amelie Gubitz, Ph.D., National Institute of Neurological Disorders and Stroke (NINDS) Renzhi Han, Ph.D., The Ohio State University Barbara Horowitz, M.D., Harvard Medical School Erik Jorgensen, Ph.D., The University of Utah Duncan Lascelles, Ph.D., North Carolina State University Leslie Leinwand, Ph.D., University of Colorado Boulder Gary Lewin, Ph.D., Max Delbrück Center for Molecular Medicine Lisa Schwartz Longacre, Ph.D., National Heart, Lung, and Blood Institute Kent Lloyd, D.V.M., Ph.D., University of California, Davis Stephanie Murphy, V.M.D., Ph.D., ORIP Johan Neyts, Ph.D., University of Leuven, Belgium Peter Nghiem, D.V.M., Ph.D., Texas A&M University John Postlethwait, Ph.D., University of Oregon Crystal Rogers, Ph.D., University of California, Davis Rebecca Roof, Ph.D., NINDS Steven Rowe, M.D., Ph.D., Johns Hopkins University School of Medicine Rebecca Shansky, Ph.D., Northeastern University Leonard Shultz, Ph.D., The Jackson Laboratory Lilianna Solnica-Krezel, Ph.D., Washington University in St. Louis Douglas Wallace, Ph.D., Children's Hospital of Philadelphia Zhongde Wang, Ph.D., Utah State University Hailey Weerts, Ph.D., Walter Reed Army Institute of Research Michael Yeager, Ph.D., University of Colorado Denver Xiaoli Zhao, Ph.D., National Institute of General Medical Sciences Sige Zou, Ph.D., ORIP