Advancing Disease Modeling in Animal-Based Research in Support of Precision Medicine

A Workshop of the Roundtable on Science and Welfare in Laboratory Animal Use with support from the Office of Research Infrastructure Programs, National Institutes of Health

October 5-6, 2017
2100 C Street NW, Washington, DC
Historic National Academies of Sciences Building
Fred Kavli Auditorium

An ad hoc planning committee will plan and conduct a public workshop to explore the potential of ongoing and future research in animal models with implications for precision medicine. This workshop will bring together experts on the use of state-of-the-art technologies and technological advances to explore:

- How the design, creation, and analysis of current and next-generation animal models can inform the practice of precision medicine;
- Reproducibility concepts to improve the clinical relevance of animal-based validation experiments and pre-and co-clinical trials in the context of precision medicine;
- Welfare and regulatory considerations of current and especially next-generation animal models that would inform the design of targeted, personalized therapies.

According to the National Institutes of Health, precision medicine “is an approach for disease treatment and prevention that takes into account individual differences in lifestyle, environment, and biology1.” During the next two days state-of-the-art animal-based research and its relevance to precision medicine will be presented and discussed. The workshop’s sessions will explore ways with which in vivo “precision modeling”, next-generation animal models and phenotyping platforms can catalyze and accelerate the advent of precision medicine. Complementary in vitro and in silico approaches to advance the Three Rs and means to ensure reproducibility of methods and data will be prominent features of the sessions and discussions.

1 https://allofus.nih.gov/about/about-all-us-research-program
Thursday, October 5

8:00 - 9:00am  Registration

9:00  Where We Are Today in Precision Medicine

Moderator: Kent Lloyd, University of California, Davis (Organizing Committee Co-Chair)
This session will provide the historical context and roots of Precision Medicine; present the current definitions and framework of the field; discuss the anticipated goals and outcomes of the Precision Medicine Initiative; and expand on the hurdles to achieve these goals. It will also provide an overview of the regulatory framework and the ethical and welfare challenges relating to the use of animals in precision medicine.

The evolution and foundations of precision medicine -
India Hook-Barnard, University of California, San Francisco

The vision and goals of the All of Us Research Program -

The regulatory landscape of precision medicine -
Robert M. Califf, Duke University School of Medicine
(Organizing Committee Member)

Ethical and welfare considerations regarding precision animal modeling -
Elizabeth Heitman, University of Texas Southwestern Medical School

10:15  Coffee Break

10:30  Defining “Precise”: Translation and Human Relevance of Current Animal Models

Moderator: Melissa Haendel, Oregon Health and Sciences University (Organizing Committee Member)
In their most classic use, animal models express phenotypic alignment rather than biological relevance at the molecular level. Do precise animal models currently exist? What characteristics should a precise animal model embody to be relevant in the context of precision medicine? This session will explore the translatability, alignment and relevance of current animal models to the human condition.

Elements of precision in the design, creation, use, and data analysis of current animal models -
David Valle, Johns Hopkins University

Comprehensive phenotyping of the mouse genome -
Steve Brown, Medical Research Council, United Kingdom

Functional analysis of genes essential for life -
Mary Dickinson, Baylor College of Medicine

Exploring genetic variability using precision pathology in animals -
Keith Mansfield, Novartis
12:10  **Lunch** (will not be provided. There is a cafeteria in the basement of the National Academies of Sciences, Engineering, and Medicine.)

1:00  **Applying “Precise”: New Ways of Modeling Diseases in Animals**

*Moderator: Robert M. Califf, Duke University School of Medicine*

*Improving the relevance of animal models to human diseases is at the heart of preclinical and translational research. Focusing on the application of precision, this session will explore new approaches to disease modeling, e.g., can modeling platforms improve the clinical relevance of current animal models, and what lessons have we learned from transformative uses of animals to support human clinical trials?*

**The great contributions of the mouse**

*Genetic modeling using CRISPR/Cas9 in mice -*

*Improving diagnostics and therapeutics for Mendelian diseases using precision mouse models -*

Robert Burgess, Jackson Labs

*Co-clinical trials of mice and human patients -*

J. Sean Clohessy, Beth Israel Deaconess Medical Center

**New approaches to disease modeling**

*Developing new “non-model” model systems -*

Jennifer Maier, University of Illinois

*Making connections between human and animal phenotypes -*

Melissa Haendel, Oregon Health and Sciences University

**The Animal Rule: A holistic approach to “precision” -**

3:00  **Coffee Break**

3:40  **Improving Predictivity in Precision Medicine Experimentation - Reproducibility Considerations**

*Moderator: Cory Brayton, Johns Hopkins University School of Medicine (Organizing Committee Member)*

*This session will begin with an overview of the essential elements that uphold and strengthen the reproducibility of study design. Subsequent presentations will examine ways with which reproducibility can be sustained in the context of precision modeling.*

**The translational potential of animal models -**

Ulrich Dirnagl, Charité, Berlin, Germany

**Systematic reviews, meta-analysis, and reproducibility -**

Merel Ritskes Hoitinga, Nijmegen University

**Biomedical computing, large databases, and reproducibility -**

Arjun Kumar Manrai, Harvard Medical School
Reproducibility in the alignment of the individual human patient and the "precise" animal model -
Jonathan Kimmelman, McGill University

5:30  Adjourn for the Day
The National Academies of
SCiences • Engineering • Medicine
Approaches to integrating evidence from animal and human studies in chemical assessments -
Kristina Thayer, United States Environmental Protection Agency

12:10pm  **Lunch** (will not be provided. There is a cafeteria in the basement of the National Academies of Sciences, Engineering, and Medicine.)

1:00  **Precision Medicine Around the World**
*Moderator:*
The speakers of this session will present a number of national approaches and strategies to creating precision medicine initiatives. The session will provide a platform to highlight the rationales, expected outcomes and possible convergence of these different approaches. The speakers will also address how central animal-based research is or can be to these initiatives, and strategies to sharing the data generated at a global scale.

  **The UK’s 100,000 Genomes Project** -
  Damian Smedley, Genomics England, United Kingdom

  **The French Plan for Genomic Medicine** -

  **Japan’s Initiative on Rare and Undiagnosed Diseases** -
  Kenjiro Kosaki, Keio University School of Medicine, Japan

  **The World Economic Forum’s Precision Medicine Effort** -
  Genya Dana, Center for the Fourth Industrial Revolution, World Economic Forum

2:20  **Linking Animal-Based Research to Precision Medicine: The Patient’s Perspective**
*Moderator:*
Patients are powerful supporters and advocates for sustaining research to improve care and treatment. How do patient advocacy groups understand the relevance of animal-based research in the era of precision medicine? How could researchers explain new approaches to research with and without the use of laboratory animals?

  **Patient advocacy in the context of precision medicine** -
  Daryl Pritchard, Personalized Medicine Coalition

  **Pets with naturally occurring tumors - A natural model for improving cancer care and treatment** -
  Amy K. LeBlanc, National Cancer Institute

  **Using precision medicine to help patients with Parkinson’s Disease** -
  Brian Fiske, The Michael J. Fox Foundation for Parkinson’s Research

  **Community advisory boards and research in precision medicine** -
  Richard Sharp, Mayo Clinic
What Can We Expect from Integrating Precision Animal Modeling Into the Precision Medicine Paradigm?

The speaker will discuss a possible future in which animal precision models are integral to fulfilling the promises of precision medicine for improving human health.

Kent Lloyd, University of California, Davis

Adjourn Meeting