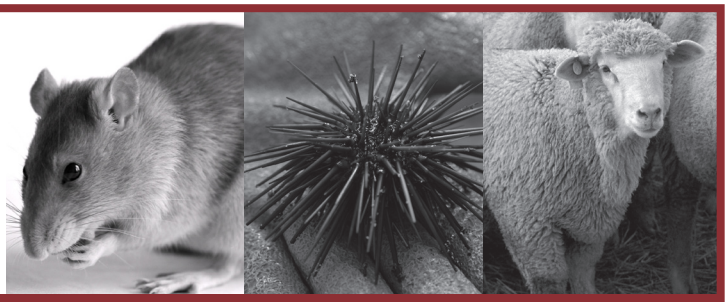
ILAR Roundtable



Gene Editing to Modify Animal Genomes for Research - Scientific and Ethical Considerations

A Workshop of the Roundtable on Science and Welfare in Laboratory Animal Use

December 7-8, 2015

500 5th Street NW, Washington DC 20001
National Academies of Sciences, Engineering, and Medicine
Keck Center, Room 100

This public workshop will examine scientific, policy and ethical challenges from the widespread use of gene editing technologies affecting the use of animals in scientific research. Invited speakers will address the applications of these technologies in various animal species; regulatory and other policy issues in the U.S. and international contexts; and broad ethical and welfare issues stemming from using gene editing in animals. A rapporteur-prepared summary of the presentations and discussions of the workshop will be published.

Monday, December 7

7:30 - 8:45am **Registration**

8:45 **Opening Remarks**
Rhonda Wiler, Genentech - Planning Committee Co-Chair
Lida Anestidou, National Academy of Sciences - Roundtable Director

9:00 **The Age of Editing - Trends and Techniques in Animal Transgenesis**
Mankind has been changing the germ line of animals for millennia. For a long time this was accomplished via selective breeding, a slow process driven by chance, low efficiency and unpredictable outcomes. In relatively recent times - the last few decades - different techniques of genetically modifying animals in a more-or-less directed way were developed. Initially this was accomplished using transgenic constructs, followed by the use of gene targeting and embryonic stem cell technologies. Though both techniques have transformed the generation and use of all laboratory animals, their use has mainly been limited to rodents, especially mice. Lately the introduction and rapid and wide acceptance of genome editors, such as Zinc finger nucleases, TAL effector nucleases and CRISPR/Cas9 has changed this, and precision genome editing has been demonstrated for many different species. As a result, additional species are becoming available for scientific research that could not be used before, or at least not at the required level of precision. Clearly, these developments will have ethical consequences. In his talk, Peter Hohenstein will discuss if, and if so why,

genome editing is a game-changer for scientific research, how genome editing techniques work, what the pros and cons of these new techniques are, and how their introduction might affect the ethics of the use of animals in research.

Peter Hohenstein, The Roslin Institute, University of Edinburgh, United Kingdom

10:00 Break

10:15 **Species-Specific Use of Gene Editing Technologies**

In just a few short years, CRISPR/Cas9 genome editing has had a transformative impact on biomedical research using genetically-altered organisms. The relative technical simplicity, high efficiency, lower cost, and adaptability for inducing genetic modifications to the genome of a variety of animal species beyond the mouse has opened the landscape of opportunity for developing novel and unique animal models, especially those for studying the genetic basis of disease that more precisely recapitulate the human condition. This session provides an overview of applying CRISPR/Cas9 technology in a variety of animal species, and what scientific and ethical issues are confronted to day and can be foreseen in the future using this technology across species.

Animals in Biomedical Research
Zebrafish - Monte Westerfield, University of Oregon

Rodents - Carlisle Landel, Transposagen Biopharmaceuticals, Inc.

Swine - Angelika Schnieke - Technische Universität München, Germany

Nonhuman Primates - Marina Emborg, University of Wisconsin - Madison

Agricultural Animals
Polled Cattle - Scott Fahrenkrug - Recombinetics

12:45 **Q&A Session with all Species-Specific Presenters**

1:15 **Lunch** (will not be provided. There is a cafeteria on the third floor of the Keck Center.)

2:30 **Regulatory Governance of the Use of Gene Editing Technologies in Animals**

Government policies and regulations on the development and use of genetically-modified animals were established to protect human and animal health and to better understand the impact of these animals on the environment. In the United States, regulations have been established through multiple government agencies including the Food and Drug Administration (FDA), Department of Agriculture (USDA), Environmental Protection Agency (EPA), and the National Institutes of Health - Office of Biotechnology Activities (NIH-OBA). Much of the U.S. governmental policy was consolidated under the Coordinated Framework for the Regulation of Biotechnology, first established in 1986 and updated in 1992. International regulation of policies on the use of genetically-modified animals vary from more or less stringent than those in the U.S. The development of more efficient gene-editing methods and their use in a much

broader species range has prompted the need to revisit current regulations and policies. Speakers from the U.S. and international government agencies will discuss current regulations/policies and the challenges in keeping these current.

Regulatory Considerations for Genetically Engineered Animals at the U.S. Food and Drug Administration
Malini Wileman, U.S. Food and Drug Administration

Regulation of Genetically Modified Animals in Argentina
Yanina Petracca, Ministry of Agriculture, Argentina

Responsible Oversight Strategies for Genetic Editing Technology in Agricultural Animals in the United States
Bhanu Telugu and Susan Harper, U.S. Department of Agriculture

Environmental Assessment of Animals Developed via Biotechnology in Canada
James Louter, Environment Canada

3:50 **Q&A Session with afternoon speakers**

4:20 **Summation of Workshop Day 1**
David Kurtz, National Institute of Environmental Health Sciences - Planning Committee Member

4:45 **Adjourn**

Tuesday, December 8

8:30 **Welcome and Focus of the Day**
Kent Lloyd, University of California, Davis - Planning Committee Co-Chair

8:40 **General Introduction to the Ethical Issues Surrounding Gene Editing in Laboratory Animals**
Ethical and governance issues surrounding the creation of novel animal species are the focus of the second day of this workshop. Spurred by the fast pace of gene editing using the CRIPSR/Cas9 methodology, ethical considerations are now more urgent that ever, while the obligation to safeguard the welfare of these animals spreads beyond the research laboratory. At the same time, oversight regulations need to adapt to the changing landscape of research and ethics to ensure the continuity of excellence in science while maintaining the highest standards for the care and use of research animals. Within the framework set by the first two presenters, specific cases of genetically modified animals will be discussed followed by a session on present and future oversight issues.

Arthur Caplan, Langone Medical Center, New York University - Planning Committee Member

8:55 **Overview of the Ethical Issues of Germ Line Modification in Animals**
Alison Van Eenennaam, University of California, Davis

9:20 **Case Studies on the Ethics of Germ Line Modification to Create Novel Animals**

AquAdvantage Salmon: Food for Thought
Ron Stotish, AquaBounty

GloFish: Ethical Considerations Related to the First Widely Available Biotech Animal
Alan Blake, Yorktown Technologies

What Went Right? Lessons from the Approval Process for the Release of Genetically Edited Moths
Carolyn Plunkett, New York University

Ethics of Germ Line Editing in Non-Human Primates
Mildred Cho, Stanford School of Medicine (via webex)

10:40 **Q&A Session with Speakers**

11:15 **Break**

11:30 **Adequacy of Oversight of Germ Line Engineering in Research Animals**

The History and Lessons Learned from Regulating GMOs
Andrew Torrance, University of Kansas School of Law

Value- and Risk-Based Governance for Genetically Engineered Organisms - Finding Middle Ground
Jennifer Kuzma, North Carolina State University

Future Possibilities for Governance of Gene Editing Technologies in Research Animals
Henry Greely, Stanford University

12:45 **Q&A Session with Speakers**

1:30 **Summation of Workshop Day 2**
Arthur Caplan, Langone Medical Center, New York University - Planning Committee Member

1:45 **Overview of Workshop**
Saverio "Buddy" Capuano III, University of Wisconsin-Madison - Planning Committee Member

2:00pm **Adjourn**