
NEW ACD WORKING GROUP

**CATALYZING THE DEVELOPMENT AND USE OF
ALTERNATIVE METHODS TO ADVANCE BIOMEDICAL
RESEARCH**

Howard Chang

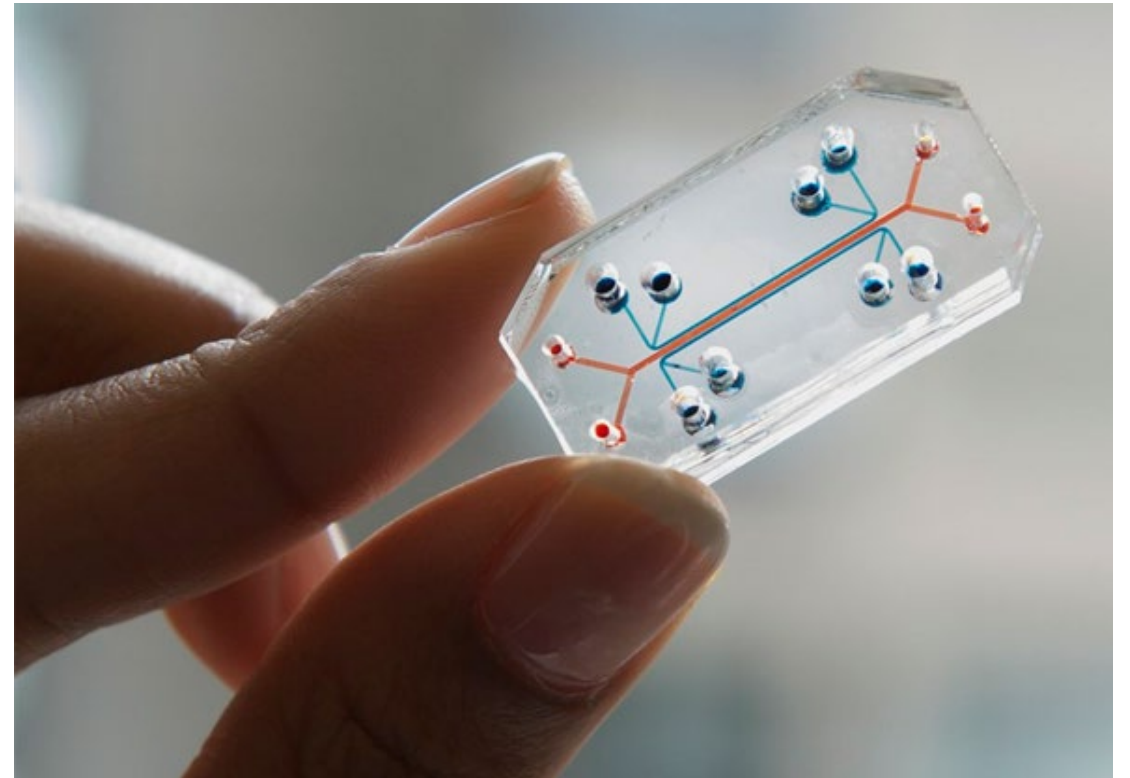
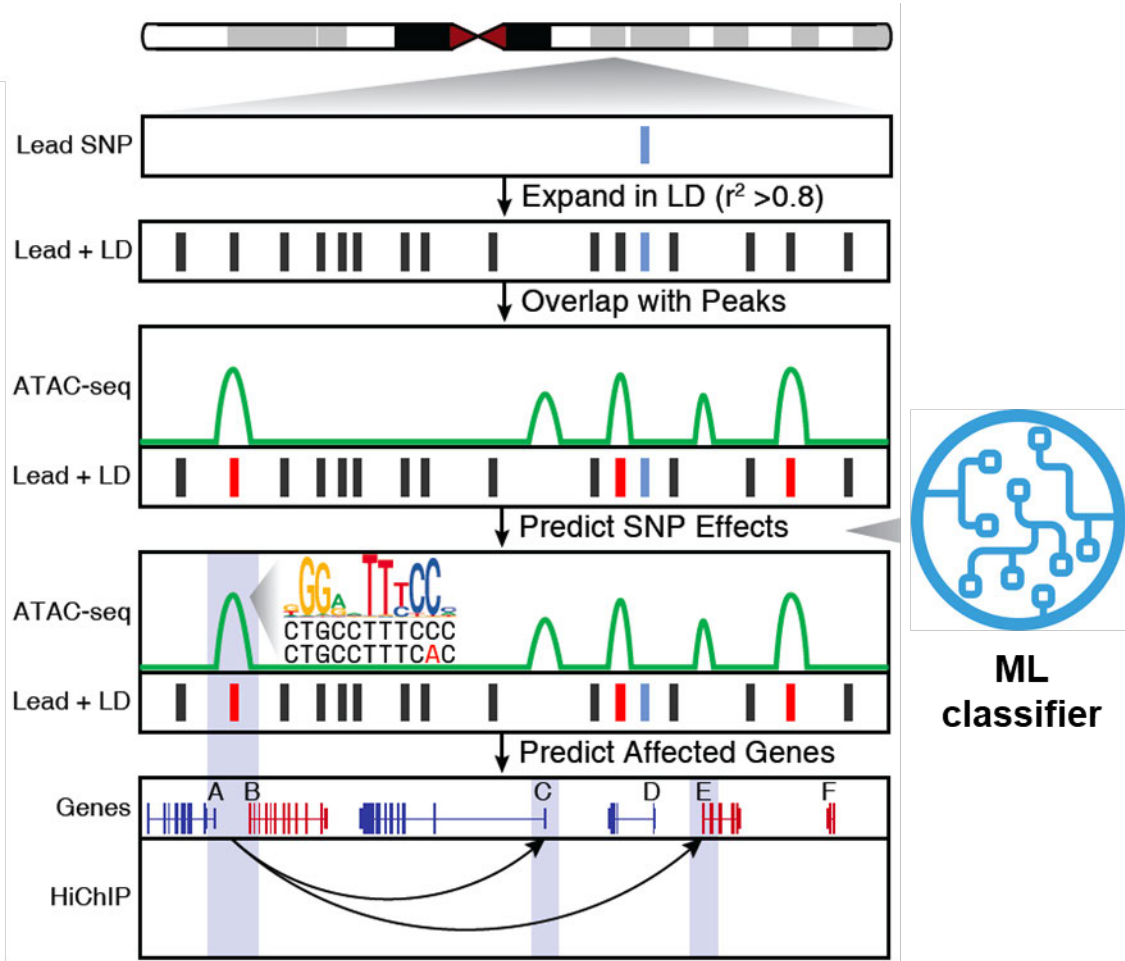
Virginia and D.K. Ludwig Professor of Cancer Research and
Professor of Dermatology and Genetics, Stanford University

Lyric Jorgenson

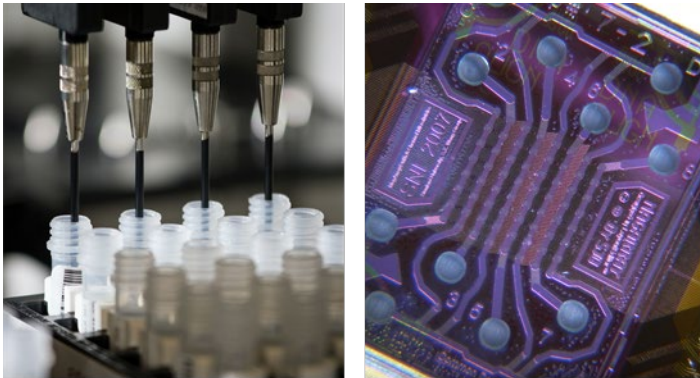
Acting NIH Associate Director for Science Policy & Acting
Director of the Office of Science Policy
National Institutes of Health

December ACD Meeting
December 8, 2022

INNOVATIVE TECHNOLOGIES CREATE TREMENDOUS SCIENTIFIC OPPORTUNITY



TECHNOLOGY DRIVEN, COMPLEMENTARY APPROACHES TO ANIMAL MODELS



in Chemico

- Cell-free methods
- Epigenetics
- Biochemical pathways
- Chemical genetics

in Vitro

- Cultured cell methods
- Induced Pluripotent Stem Cells (iPSC)
- Microphysiological Systems (MPS)

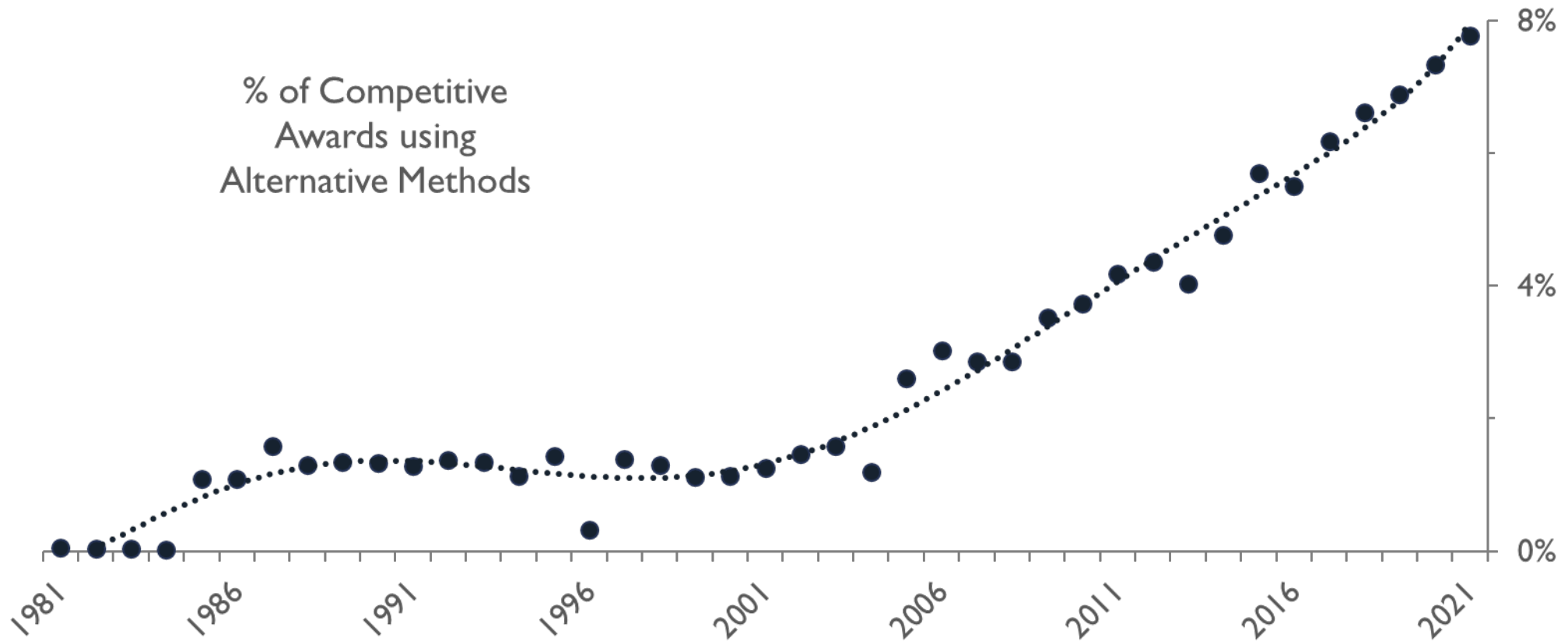
in Silico

- Computational methods
- Artificial intelligence, deep learning, machine learning
- Mathematical modeling and simulations



NIH INVESTMENT IN ALTERNATIVES

CAPITALIZING ON TECHNOLOGICAL OPPORTUNITIES

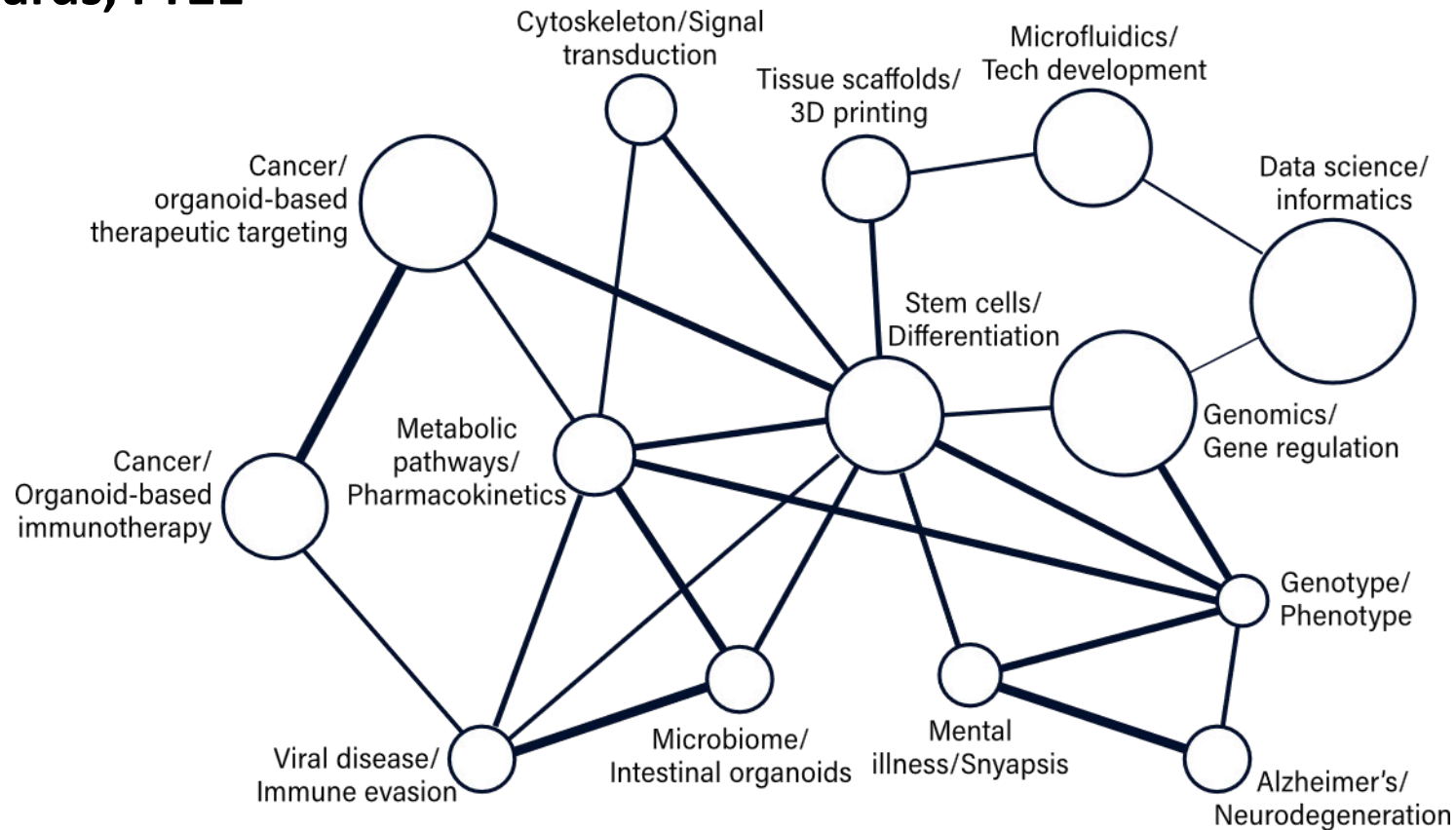


**Does not include clinical research*

NIH INVESTMENT IN ALTERNATIVES

SPURRING ADVANCES ACROSS BIOMEDICAL RESEARCH AREAS

Relative # Awards, FY21



NIH INVESTMENT IN ALTERNATIVES

FOSTERS COMMITMENT TO RESPONSIBLE RESEARCH

The principles of the 3R in animal research



Research with animals

Replace

Achieve a research objective by avoiding or replacing the use of animals.

Reduce

As many experiments as necessary, but as few laboratory animals as possible.

Refine

Minimize the potential suffering and stress of laboratory animals and enhance their wellbeing.

WHY NAMS ARE VALUABLE DIVERSIFYING THE TOOLKIT

The use of any given approach is predicated on need, in terms of scientific appropriateness & relevance for the research inquiry



EXPERIMENT DETERMINES THE APPROACH
WHEN ARE ALTERNATIVE METHODS MOST VALUABLE?



Toxicology

Uses more standardized approaches

Availability of historical data

Consistency of aims



Research Dependent on Animal Models

Reliance on animal models in some research areas

Studies of biological differences

Alternatives can lead to need for use of animal models



Rigor, Transparency, and Translatability

Development of new methods outpaces standards

Authentication of cell lines

Validation of computer simulations



Regulatory Considerations

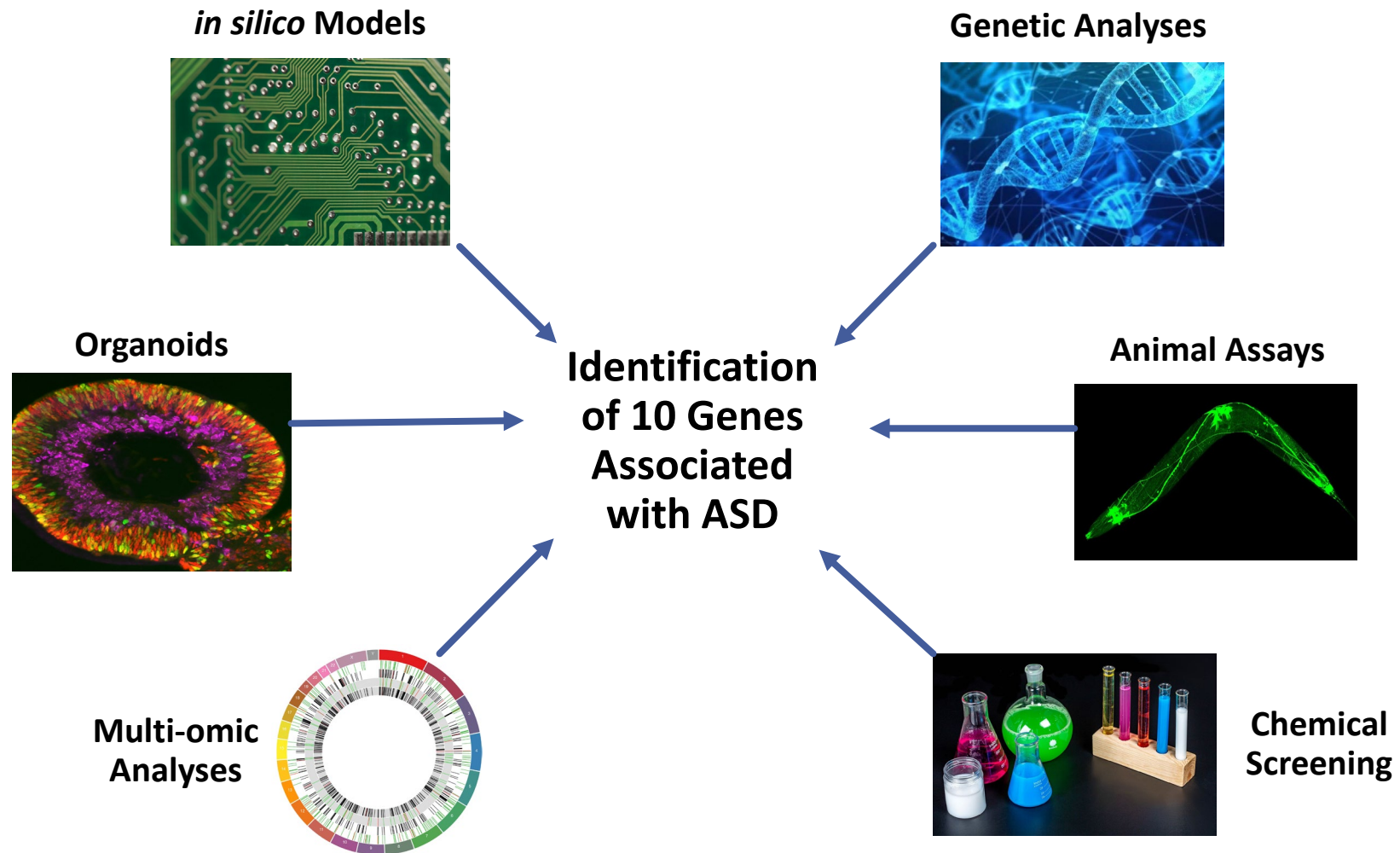
Animal Rule

Public trust

Scientific limitations

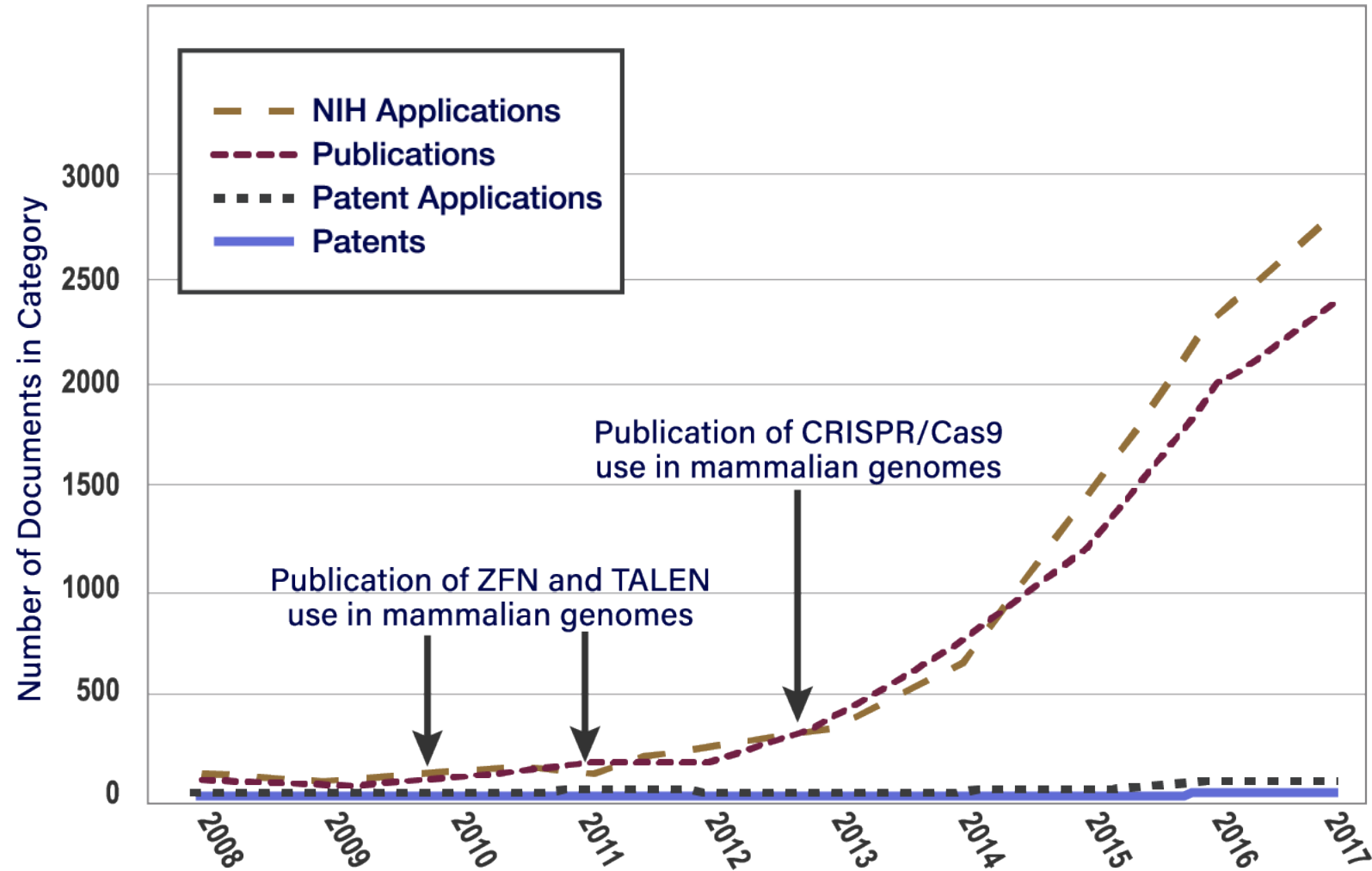
LESSONS FROM AUTISM

COMPLEMENTARY APPROACHES TO SOLVE COMPLEX CHALLENGES



LESSONS FROM GENE EDITING

IMPROVED TECHNOLOGIES CAN REVOLUTIONIZE SCIENCE



LESSON FROM ACD

HIGH-LEVEL GROUP ON NON-ANIMAL MODELING SYSTEMS

ACD WORKING GROUP ON
ENHANCING RIGOR,
TRANSPARENCY, AND
TRANSLATABILITY IN ANIMAL
RESEARCH

Alternative approaches may:

- enable more efficient (e.g., in time or cost) mechanistic investigation that could precede/complement/replace animal studies
- answer mechanistic question less amenable to complex modeling platform or when a translationally relevant animal model is lacking
- share some similar questions regarding rigor, reproducibility, transparency, and but also come with their own sources of variance and uncertainty

**POWER IN
NUMBERS
SYNERGISTIC
EFFORTS**



NIH INVESTMENT IN ALTERNATIVES

CATALYZING THE NEXT WAVE OF OPPORTUNITY

An Honest Assessment of Scientific Opportunity

- Enhance the rigor and translatability of animal studies (ACD rec)
- Identify where alternatives can have the biggest scientific impact

Proactive & Strategic Shaping of NIH Portfolio

- Where use of alternatives can catalyze new scientific discoveries
- Areas ripe for innovation to spur new research approaches

NEW WORKING GROUP CHARGE!

NOVEL ALTERNATIVE METHODS (NAMS)

1. Identify the types of alternative methods being developed for use in biomedical research and assess their general strengths and weaknesses for studying human biology, circuits, systems, and disease states
2. Characterize the types of research, condition, or disease for which alternative methods are most applicable or beneficial
3. Articulate high-priority areas for NIH investment in the use and development of novel alternative methods with human applicability to:
 - Advance progress into understanding specific biological processes or states
 - Augment the tools and capabilities for biomedical research to complement and/or potentially replace traditional models

NEW WORKING GROUP ROSTER!

NOVEL ALTERNATIVE METHODS (NAMS)

Howard Chang, MD, PhD (*co-chair*)
Stanford University

Lytic Jorgenson, PhD (*co-chair*)
National Institutes of Health

Antonio Banes, PhD
NC Central University/University of
North Carolina

Szczepan Baran, DVM
Verisym Life

Wendy Chapman, PhD
University of Melbourne

Myrtle Davis, DVM, PhD
Bristol-Myers Squibb

Linda Griffith, PhD
Massachusetts Institute of Technology

Ranu Jung, PhD
University of Arkansas

Arnold Kriegstein, MD, PhD
University of California, San Francisco

Nancy Lane, MD
University of California, Davis

Kelly Metcalf Pate, DVM, PhD
Massachusetts Institute of Technology

Sergiu Pasca, MD
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Gordana Vunjak-Novakovic, PhD
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Maureen Gwinn, PhD
Environmental Protection Agency

Danilo Tagle, PhD
National Institutes of Health

EXECUTIVE SECRETARIES

Brittany Chao, DPhil
National Institutes of Health

Jessica Creery, PhD
National Institutes of Health

NEW WORKING GROUP PROCESS!

NOVEL ALTERNATIVE METHODS (NAMS)

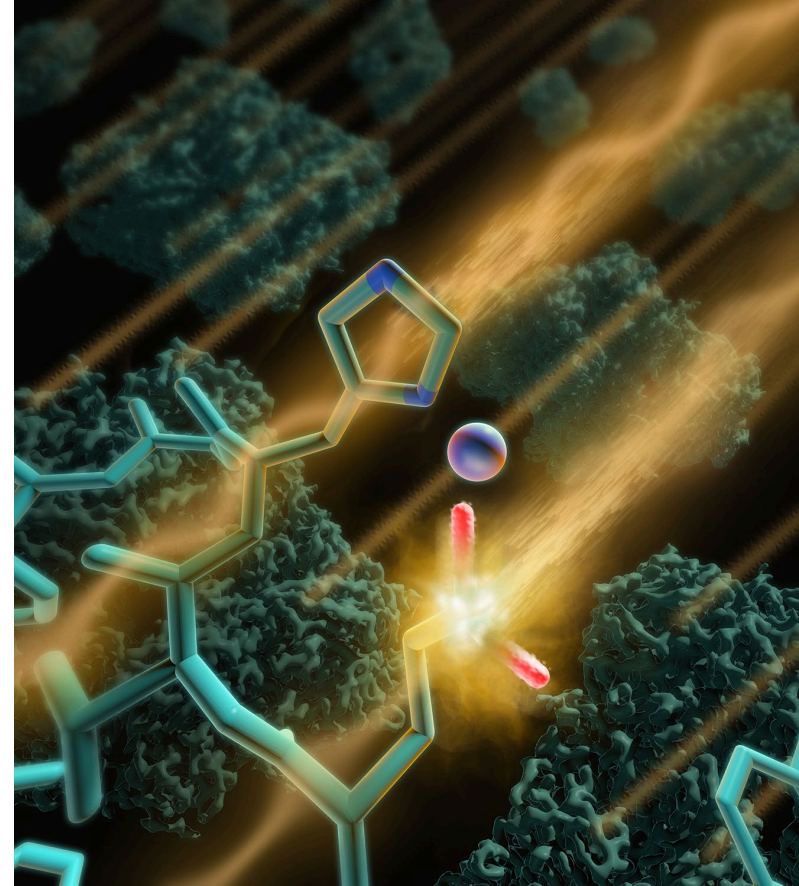
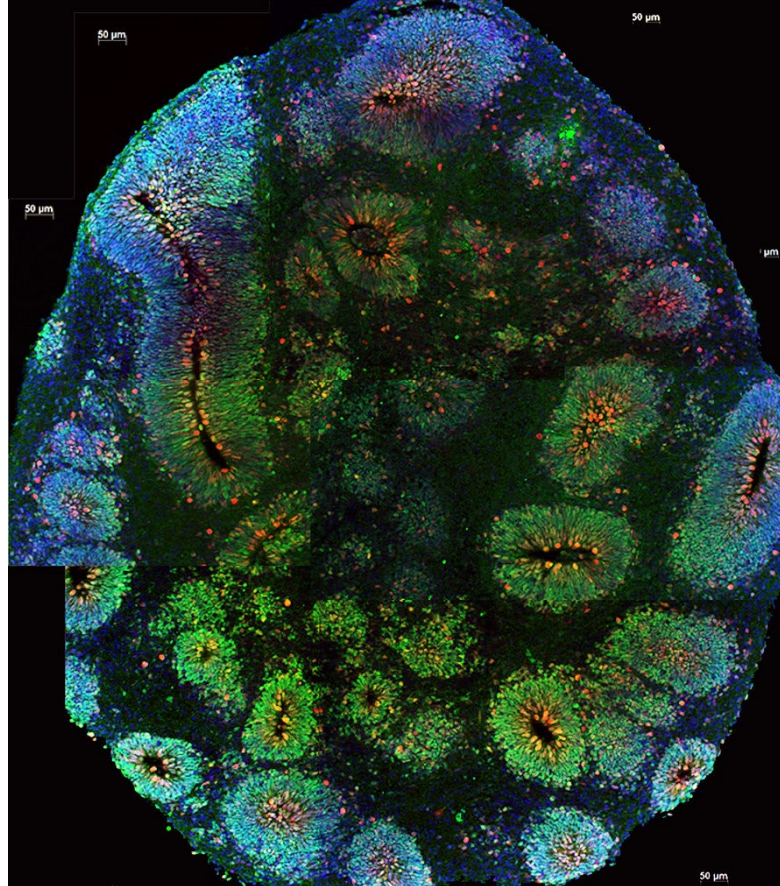


We will:

- Seek input broadly from the scientific community
- Include perspectives from those with experience in different relevant fields
- Hold open meetings and workshops on specific topics as needed

TIMELINE OF NEXT STEPS

- ~~Announce planned WG~~ *(November 2022)*
- **Update ACD and discuss workplan** *(December 2022)*
- **Work!** *(January–May 2023)*
- **Present preliminary findings to ACD** *(June 2023)*
- **Stakeholder engagement** *(June–November 2023)*
- **Final report with recommendations** *(December 2023)*



DISCUSSION