Introduction to the Pilot Centers Program for Precision Disease Modeling

Oleg Mirochnitchenko, Ph.D.
Program Director, Division of Comparative Medicine/ORIP
Precision medicine is the expansion of the concept of personalized medicine, where therapeutic strategies are precisely tailored to each patient’s requirements.”
Precision Medicine

Animal-based studies will be essential for precision medicine

Lloyd KC, Robinson PN, MacRae CA. 2016. Sci Transl Med 8(352):352ed12

Brain Storming Meeting Agenda

“Next generation animal models targeting personalized disease phenotypes”

DCM/ORIP/DPCPSI/OD,
September 6, 2012
6701 Democracy Blvd.
Room 989
Bethesda, MD 20892

14 invited guests, 12-15 NIH staff
Next Generation of Precision Animal Models

- Understanding the relationship between gene and phenotype
- Stratification of diseases into subtypes according to their underlying biological mechanisms
- Testing complex genetic variations in relevant biological systems
- Improvement of the disease simulation process, with recapitulation of molecular mechanisms
- Clinical trial “like” animal model testing and clinical/model iterations
- Rigorous evaluation of predictability and validity
Pilot Centers for Precision Disease Modeling (U54)

Integrated Data Collection/Bioinformatics Section
- Medical records
- Patient's genetics
- Patient's omics

Human/animal Genetic/omics databases

GWAS Disease databases/Animal models

Phenotypes/ontologies

Training/Education

Disease Modeling Unit
- Rare and Common Diseases
- Biospecimens (tumors, iPSCs)
- Tissue/organ engineering
- GM animals
- Humanized animals

Human disease-associated variations in “patient-specific” environment

Coordination Core

Translational/Co-Clinical Section
- Use model system to guide clinical application

Biomarker’s development
- Drugs/therapeutics development
- High-throughput screening
- Toxicity, safety studies
- Identification of resistant and sensitive population
- Preventive care development

Use model system to guide clinical application

Genetics/Omics/Disease Mechanism-Based Clinical Trials
Pilot Centers for Precision Disease Modeling (U54)

PAR-14-280, application due date October 1, 2014

3 Centers funded in Summer 2015

The Jackson Laboratory Center for Precision Genetics: From New Models to Novel Therapeutics
Robert Burgess, Jackson Laboratory, ME

A New Disease Platform Leveraging Complex Drosophila and Mammalian Models
Ross Cagan, ICAHN School of Medicine at Mount Sinai, NY

MSKCC Pilot Center for Precision Disease Modeling
Scott Lowe, Sloan-Kettering Institute for Cancer Research, NY

Pilot Centers for Precision Disease Modeling PIs Introductory Meeting occurred on March 29, 2016 (Bethesda, MD)
The Jackson Center for Precision Genetics

Clinical Collaborations:

- Cedars-Sinai Medical Center, Los Angeles, CA
- Duke University, Durham, NC
- UCSD, La Jolla, CA
- UCSF, San Francisco, CA
- The Research Institute at Nationwide Children's Hospital, Columbus, OH
- Columbia University, New York, NY
- University of Massachusetts Medical School, Worcester, MA
## The Jackson Center for Precision Genetics

<table>
<thead>
<tr>
<th>Disease Modeling Unit</th>
<th>Principal Investigator(s)</th>
<th>Preclinical Partner(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charcot Marie-Tooth Peripheral Neuropathy</td>
<td>Robert Burgess</td>
<td>Scott Harper, NCH, Steven Gray</td>
</tr>
<tr>
<td>Intractable Epilepsies</td>
<td>Wayne Frankel</td>
<td>David Goldstein, Stephen Traynelis, Daniel Lowenstein</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis</td>
<td>Cat Lutz</td>
<td>Robert Baloh</td>
</tr>
<tr>
<td>Human Autoimmune Diseases</td>
<td>Dave Serreze, Lenny Shultz</td>
<td>Dale Greiner, Sally Kent</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>Ron Korstanje</td>
<td>Adrzej Krowlewski</td>
</tr>
<tr>
<td>Age-related Macular Degeneration</td>
<td>Patsy Nishina</td>
<td>Jonathan Lin, Stephen Tsang</td>
</tr>
</tbody>
</table>
A New Disease Platform Leveraging Complex Drosophila and Mammalian Models

Icahn School of Medicine at Mount Sinai, New York, NY

Administrative Core
Bioinformatics Core
Preclinical/Co-clinical Section
Pathology Core
External Advisory Committee
Four Projects
A New Disease Platform Leveraging Complex Drosophila and Mammalian Models

Icahn School of Medicine at Mount Sinai, New York, NY

Administrative Core
Bioinformatics Core
Preclinical/Co-clinical Section
Pathology Core
External Advisory Committee
Four Projects
A New Disease Platform Leveraging Complex Drosophila and Mammalian Models

- Project 1: Complex colorectal cancer, RASopathy fly models
- Project 2: Polypharmacology drug development
- Project 3: Noonan iPSCs to Model Hypertrophic Cardiomyopathy
- Project 4: Patient-Derived Xenografts from Tumor Initiating Cells (PDX-TIC): A Novel Platform for Discovery and Validation of Therapeutic Targets, Colorectal Cancer

Project I: Ross Cagan

Project II: Arvin Dar

Project III: Bruce Gelb

Project IV: Carlos Cordon-Cardo
Memorial Sloan Kettering Cancer Center, New York, NY

**PI: Scott Lowe, Ph.D.**

Chair of the Cancer Biology and Genetics Program at Memorial Sloan Kettering Cancer Center

Chairman of the Geoffrey Beene Cancer Research Center

Professor, Weill Cornell Graduate School of Medical Sciences