Director’s Report

NCATS Advisory Council and CAN Review Board

CHRISTOPHER P. AUSTIN, M.D.
DIRECTOR, NCATS
SEPTEMBER 15, 2016
We would like to save trees, but please let us know in advance of next Council if you would like the Activity Summary document printed
Translational Innovation Highlights

• **Early-stage translation**
  - Drug repurposing for Zika
  - Chaperone therapeutics for rare and common disease

• **Mid-stage translation**
  - Gene therapy innovations

• **Late-stage translation**
  - Rare disease patient videos
  - Adherence research - AiCure SBIR
  - Community engagement research at CTSAs
Early-stage translational highlights

**Zika drug repurposing**

- **Background**
  - Zika infection reported in 60 countries
  - Associated with neurological disorders including microcephaly in babies of infected mothers, Guillain-Barré in adults
  - No effective drug treatments or vaccines
  - Zika virus (ZIKV) infects human embryonic cortical neural progenitor cells (hNPCs)
  - ZIKV infection leads to increased cell death of hNPCs

- **NCATS project**
  - DPI rapidly established collaborative team, identified approved and investigational drugs as starting points for drug development to treat Zika infection
  - Generalized paradigm applicable to public health emergencies, used previously in Ebola

**Graphical Abstract**

**Authors**
Hengli Tang, Christy Hammack, Sarah C. Ogden, ..., Peng Jin, Hongjun Song, Guo-ji Ming

**Correspondence**
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**In Brief**
The suspected link between ZIKV infection and microcephaly is an urgent global health concern. Tang et al. report that ZIKV virus directly infects human cortical neural progenitor cells with high efficiency, resulting in stunted growth of this cell population and transcriptional dysregulation.

**Tang et al., Cell Stem Cell 18: 1, 2016**
Zika drug repurposing

- **Collaborators**
  - Hongjun Song and Guoli Ming, Johns Hopkins University
  - Hengli Tang, Florida State University

- **Assays**
  - Zika infection-induced caspase 3/7 activation
  - Zika infection-induced cell death
  - Zika virus live titer, RNA, protein
  - 3D human forebrain organoid cultures

- **Compounds**
  - NCATS Pharmaceutical Collection (approved drugs): 2800
  - Investigational drugs and bioactive compounds: 3200

- **Results**
  - Emricasan: investigational pan-caspase inhibitor
    - Also protected human cortical neural progenitors from cell death
  - Niclosamide: FDA-approved antihelminthic
    - Also inhibited ZIKV replication
  - Ten structurally unrelated inhibitors of cyclin-dependent kinases
    - Also inhibited ZIKV replication

- **Combination of neuroprotective and antiviral drugs**
  - Combination of emricasan and CDKi further increased protection of human neuronal progenitors from Zika virus induced cell death
Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen

Miao Xu1,2,16, Emily M Lee3,16, Zhexing Wen1,7,16, Yichen Cheng3, Wei-Kai Huang7,8, Xuyu Qian7,9, Julia TCW10, Jennifer Kouznetsova1, Sarah C Ogden3, Christy Hammack3, Fadi Jacob7,11, Ha Nam Nguyen7,12, Misha Itkin1, Catherine Hanna3, Paul Shinn1, Chase Allen3, Samuel G Michael1, Anton Simeonov1, Wenwei Huang1, Kimberly M Christian7,12, Alison Goate10, Kristen J Brennand13, Rui Li Huang1, Menghang Xia1, Guo-li Ming7,9,11,12,14,15,17, Wei Zheng3,17, Hongjun Song7,9,11,12,15,17 & Hengli Tang5,17

In response to the current global health emergency posed by the Zika virus (ZIKV) outbreak and its link to microcephaly and other neurological conditions, we performed a drug repurposing screen of ~6,000 compounds that included approved drugs, clinical trial drug candidates and pharmacologically active compounds; we identified compounds that either inhibit ZIKV infection or suppress infection-induced caspase-3 activity in different neural cells. A pan-caspase inhibitor, emricasan, inhibited ZIKV-induced increases in caspase-3 activity and protected human cortical neural progenitors in both monolayer and three-dimensional organoid cultures. Ten structurally unrelated inhibitors of cyclin-dependent kinases inhibited ZIKV replication. Niclosamide, a category B anthelmintic

All screening results have been deposited in Pubchem database for community use
Zika drug repurposing publicity

Treating Zika Infection: Repurposed Drugs Show Promise

NIH collaboration helps advance potential Zika treatments
Zika drug repurposing publicity

Various compounds may help advance Zika treatments

NCATS research team identifies compounds for potential treatment against Zika virus
Zika drug repurposing publicity

NIH-LED TEAM IDENTIFIES 3 COMPOUNDS THAT WORK AGAINST ZIKA VIRUS-LINKED BRAIN CELL DEATH

Drugs Used to Fight Hepatitis, Worm Infections Might Stop Zika
Zika drug repurposing publicity

**Miami Herald**
FSU study: Drugs may stop Zika from replicating, damaging fetal brains

**THE BALTIMORE SUN**
Drug to treat parasites, liver disease shows promise for Zika

**MNT**
Zika treatable with existing drugs, says breakthrough study
Zika drug repurposing publicity

Scientists Identify Existing Drugs That Can Kill Zika

Potential Zika Virus Therapies Identified by Researchers
Several candidates found from among 6,000 drugs already commercially available or undergoing clinical trials

Team of researchers inch closer to Zika treatment
Drug development for treatment of Zika virus infection

**Next Steps**

- **Evaluation of in vivo efficacy of identified compounds**
  - Mouse models of Zika infection (collaborator at Florida State)
  - Mouse neuronal models for neuronal protections against Zika virus infection (collaborators at Johns Hopkins)

- **Chemistry optimization**
  - Niclosamide prodrug development to improve oral bioavailability and reduce toxicity
  - Analog development to improve potency, and increase blood-brain-barrier penetration

- **A new high-throughput ZIKV NS-1 assay developed**
  - To perform a new round of drug repurposing screen for identifying more compounds with different mechanism of action
  - To carry out genome-wide siRNA screen for identification of potential new drug targets
“Chaperone” drugs
A widely applicable therapeutic modality
Glucocerebrosidase chaperones for Gaucher Disease (GD) and Parkinson’s Diseases (PD)

Collaborators: Ellen Sidransky, NHGRI/NIH; Dimitri Krainc, Northwestern; Frank Schoenen and Steven Rogers, Univ Kansas

Gaucher Disease (GD)

Rare hematologic and neurologic disorder caused by mutations in gene encoding the enzyme glucocerebrosidase, characterized by intracellular accumulation of lipid in lysosomes of macrophages and/or neurons.

Parkinson’s Disease (PD)

Common neurologic progressive disorder characterized by dysfunction/death of brain dopamine-producing neurons, which show intracellular accumulations called Lewy bodies containing alpha-synuclein.
Glucocerebrosidase chaperones for Gaucher Disease (GD) and Parkinson’s Diseases (PD)

- GD and PD are, remarkably, related
  - Patients with GD have an increased risk of PD
  - Patients with PD have a high prevalence of glucocerebrosidase mutations

Multicenter Analysis of Glucocerebrosidase Mutations in Parkinson’s Disease


- Therapeutic hypothesis
  - Interventions that correct glucocerebrosidase defect will reduce intracellular accumulations in GD (lipids) and PD (alpha-synuclein) and reverse disease pathology and symptoms both diseases
Translational principle result #1
Disease-mimicking cellular models are critical

- Chaperones developed in non-disease relevant cell types (cell lines or patient fibroblasts) did not translate

- Macrophages created from Gaucher patient blood monocytes or iPSCs, and neurons created from Gaucher iPSCs show disease phenotype
  - Reduced GCase activity
  - Reduced lysosomal GCase
  - Pronounced lipid accumulation

- Aged iPSC-derived neurons from Gaucher patients with parkinsonism and Parkinson’s patients without GCase mutations accumulate alpha-synuclein
Translational principle result #2
Chaperones that don’t inhibit are critical

- Chaperones bind to their target proteins and can inhibit, activate, or neither
  - Most inhibit

- Chaperones that are noninhibitory or even activate can be found but require innovative testing systems to find them
Translational principle result #3

Treatments for common diseases can come directly from rare diseases but requires a dedicated strategy

- Treatment with NCATS-developed GCase chaperones correct disease phenotype in Gaucher patient iPSC-derived macrophages and neurons
- GCase chaperones also cleared alpha-synuclein from neurons from both GD-Parkinsonism and PD patients
- Potential treatment for Gaucher Disease with Parkinsonism (enzyme replacement ineffective)
- Novel treatment modality for Parkinson’s disease
- Approach generalizable to other lysosomal storage and neurodegenerative diseases
A glucocerebrosidase chaperone to ward off Parkinson’s disease

Ian Martin

*Author Affiliations*

DOI: 10.1126/scitranslmed.aaa5492
Gene Therapy at NCATS

- NCATS is interested in platform approaches that can be readily adapted to multiple diseases.

- Gene therapy (GT) is such a platform approach and relevant to the treatment of rare genetic diseases.

- NCATS supports GT development through several programs.
Gene Therapy: The View from NCATS

Philip J. Brooks,¹,* N. Nora Yang,² and Christopher P. Austin³

¹Division of Clinical Innovation and Office of Rare Diseases Research, and ²Division of Preclinical Innovation, ³Office of the Director, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, Bethesda, Maryland.

Commentary published in January 2016
TRND Gene Therapy Learning Collaborative

• Platform focusing on building GT toolbox for treating rare genetic diseases
• Pilot projects addressing common GT translational issues:
  ➢ Tissue-specific delivery
  ➢ Vehicle and cargo design
  ➢ New technology for large scale vector manufacturing and characterization
  ➢ Long term safety and efficacy
• Uses hallmark NCATS collaborative model:
  ➢ Partnerships between foundations, companies, academia, and NCATS
## TRND Gene Therapy Portfolio

<table>
<thead>
<tr>
<th>Disease</th>
<th>Collaborator</th>
<th>Target Tissue</th>
<th>Addressing GT Challenges</th>
</tr>
</thead>
</table>
| Pompe Disease                                | Duke University Medical Center    | Liver         | • Immunomodulatory therapy  
• Systemic delivery  
• Liver expression                                           |
| Aromatic L-amino acid decarboxylase (AADC) Deficiency | Agilis Biotherapeutics            | CNS – putamen | • CNS local delivery  
• Delivery to newborns  
• Global regulatory approval for ultra-rare diseases |
| Duchenne Muscular Dystrophy (DMD)            | Solid GT, Solid Biosciences       | Striated Muscles | • Largest tissue by body mass; widely distributed throughout the body  
• Lack of scalable manufacturing technology to support phase III testing and commercialization  
• Re-dosing                                           |
GT for AADC Deficiency

- **Collaborators**
  - Agilis Biotherapeutics, Taiwan Natl U

- **Background**
  - Rare CNS disorder arising from a reduction in the enzyme, aromatic L-amino acid decarboxylase (AADC)
  - Deficits in major neurotransmitters: dopamine, norepinephrine, epinephrine, serotonin, and melatonin

- **Goals**
  - First CNS gene therapy approved worldwide
  - Develop new devices for GT delivery in infants
  - Global regulatory approval strategy for ultra rare diseases
Megan O’Boyle tells the story of her daughter, who has Phelan-McDermid syndrome

https://www.youtube.com/watch?v=VOMSq1D24Fc
The cost of medication nonadherence and patient behavior is significant.

**$40 billion**
**CLINICAL RESEARCH LOSSES**
Over-recruitment, delayed launches, and litigation.

**$300 billion**
**NEGATIVE HEALTH OUTCOMES**
Hospitalizations, adverse events, and death.

“The economic impact of behavior modification in healthcare has been estimated to be “indefinitely large.”

Courtesy AiCure
Medication adherence drops across all therapeutic areas over time

By the end of the first year of treatment, 50 to 90% of patients stop taking their prescribed therapies.

*Adherence rate ranges were averaged.  Source: Various sources; A.T. Kearney analysis

Largest economic costs derive from high-risk patients who are non-adherent

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Impact</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient misses one dose of Hepatitis C treatment</td>
<td>x2 course of therapy</td>
<td>$50,000-$90,000 additional cost</td>
</tr>
<tr>
<td>Stroke patient stops Xarelto®</td>
<td>↑30% hospitalization risk</td>
<td>$50,000 to $100,000 inpatient services</td>
</tr>
<tr>
<td>Schizophrenia discontinues treatment with Risperdal</td>
<td>↑25% hospitalization risk</td>
<td>Avg. $60,000 inpatient stay</td>
</tr>
<tr>
<td>30-50% of CNS trials fail because of subject nonadherence.</td>
<td>↓ statistical power</td>
<td>$5,000 to $20,000 cost per patient</td>
</tr>
</tbody>
</table>

5% of patients cause 50% of US healthcare costs. Current interventions such as text messages or electronic medication packaging have shown limited effect on both adherence and health outcomes (Checchi et al, JAMA, 2014; de Jongh et al, Cochrane Database Systemic Review, 2012).
SBIR support of a technology solution

• AiCure is a small company based in NYC
  ➢ Focused on medication adherence solutions based on artificial intelligence

• SBIR Phase I and Phase II awards
  ➢ Supported development and initial testing of app
  ➢ Supported validation of technology against blood levels of medications and showed that the app improves adherence rates in schizophrenia and stroke clinical trials (study publication expected late 2016)

• SBIR support from NCATS, NIMH, and NHLBI have now allowed company to attract VC financing

Watch a short video about AiCure at https://www.aicure.com
Importance of capturing accurate dosing patterns

Clinical trials: “Need for measures of adherence that do not solely rely on self-reporting and that are not easily manipulated by participants.” (Marrazzo et al, NEJM, 2015)

Population health: “providers usually have had to rely on the patient for information about his/her use of the medication, even though such information is subject to problems of recall and various barriers to candor.” (Blaschke et al, 2012)

Courtesy AiCure
AiCure uses Artificial Intelligence (AI) to visually confirm medication ingestion

The platform has been clinically validated against blood levels.

<table>
<thead>
<tr>
<th>FACIAL RECOGNITION</th>
<th>IDENTIFY MEDICATION</th>
<th>CONFIRM INGESTION</th>
<th>ANTI-FRAUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIPAA-compliant identification of the patient.</td>
<td>Verify that the medication and/or the blister pack is correct.</td>
<td>Ensure ingestion for oral medications in real-time.</td>
<td>Identify duplicate enrollment and other types of fraudulent activity.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>NO VIDEO REVIEW</th>
<th>BYOD OR PROVISIONED</th>
<th>REAL-TIME ANALYTICS</th>
<th>PATIENT ENGAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>The software replaces the need to perform manual review of video.</td>
<td>Downloadable onto any iOS or Android device or provision devices.</td>
<td>Access accurate data in real-time allowing for pre-emptive intervention.</td>
<td>An assistive technology that provides reminders, instructions and site contact.</td>
</tr>
</tbody>
</table>

Courtesy AiCure
Quantifiable impact: reducing drug development time and preventing hospitalizations

The platform has been clinically validated against blood levels.

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Improvement vs No Monitoring

Cumulative blood concentration levels

50% Improvement vs No Monitoring

Peer-reviewed publications:
Hanina A, Shafner L. Using Artificial Intelligence (AI) to monitor adherence on mobile devices. SIRS (Schizophrenia International Research Society), poster presentation
Bain EE, et al. Use of an Artificial Intelligence Platform on Mobile Devices to Assess Dosing Compliance in a Phase 2 Schizophrenia Study. ISCTM (The International Society for CNS Clinical Trials and Methodology), poster to be presented
Labovitz D, et al. Using Artificial Intelligence to measure and optimize adherence on anticoagulation therapy. Connected Health Symposium, poster to be presented

Courtesy AiCure
CTSA Program Update

Petra Kaufmann will present shortly
Community Engagement is a critical component of the CTSA Program

- Community Engagement (CE) section in most recent CTSA Program Funding Opportunity Announcement (PAR-15-304)
  - Defines communities broadly
  - Addresses CE as a scientific problem
  - Integrates CE into leadership, research and communication at hubs
  - Integrates CE across translational spectrum
  - Acknowledges CE in academic policy and culturally competent training for staff fosters innovation, disseminate best practices
Rockefeller CTSA
Community-Engaged Research Navigation (CEnR-Nav) Program

Background

Rockefeller University Center for Clinical and Translational Science (RU-CCTS) has partnered with Clinical Directors Network (a PBRN) to create a community-engaged research navigation (CEnR-Nav) Program
Community-Engaged Research Navigation (CEnR-Nav) Program

- Provides model for basic scientists to engage communities, community clinicians, patients and other stakeholders
- Develops and conducts collaborative study protocols
- Incorporates principles of CE, team science and community-engaged participatory research
- Involves clinical scholar trainees, early-career physician-scientists, faculty, students, postdocs
- Led by an academic navigator and a practice-based research network (PBRN) navigator
Community-Engaged Research Navigation (CEnR-Nav) Program

- 23 approved protocols and 2 substudies
  - 19 identified community partners
  - Nine named community partners as coinvestigators
  - 2/3 focused on T1-T2 translational aims
  - Seven secured external funding
  - 11 disseminated results through presentations or publications
    - Five included a community partner as a coauthor

http://journals.lww.com/academicmedicine/Abstract/publishahead/Helping_Basic_Scientists_Engage_With_Community.98512.aspx
Helping Basic Scientists Engage With Community Partners to Enrich and Accelerate Translational Research

Rhonda G. Kost, MD, Andrea Leinberger-Jabari, MPH, Teresa H. Evering, MD, MS, Peter R. Holt, MD, Maija Neville-Williams, MPH, Kimberly S. Vasquez, MPH, Barry S. Collier, MD, and Jonathan N. Tobin, PhD

Abstract

Problem
Engaging basic scientists in community-based translational research is challenging but has great potential for improving health.

Approach
In 2009, The Rockefeller University Center for Clinical and Translational Science partnered with Clinical Directors Network, a practice-based research network (PBRN), to create a community-engaged research navigation (CEnR-Nav) program to foster research pairing basic science and community-driven scientific aims. The program is led by an academic navigator and a PBRN navigator. Through meetings and joint activities, the program facilitates basic science–community partnerships and the development and conduct of joint research protocols.

Outcomes
From 2009–2014, 39 investigators pursued 44 preliminary projects through the CEnR-Nav program; 25 of those became 23 approved protocols and 2 substudies. They involved clinical scholar trainees, early-career physician–scientists, faculty, students, postdoctoral fellows, and others. Nineteen (of 25; 76%) identified community partners, of which 9 (47%) named them as coinvestigators. Nine (of 25; 36%) included T3–T4 translational aims. Seven (of 25; 28%) secured external funding, 11 (of 25; 44%) disseminated results through presentations or publications, and 5 (71%) of 7 projects publishing results included a community partner as a coauthor. Of projects with long-term navigator participation, 9 (of 19; 47%) incorporated T3–T4 aims and 7 (of 19; 37%) secured external funding.

Next Steps
The CEnR-Nav program provides a model for successfully engaging basic scientists with communities to advance and accelerate translational science. This model's durability and generalizability have not been determined, but it achieves valuable short-term goals and facilitates scientifically meaningful community–academic partnerships.
<table>
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<tr>
<th>Year</th>
<th>Status</th>
<th>Area of inquiry</th>
<th>Subject group</th>
<th>Origin</th>
<th>Extent</th>
<th>Location of protocol-specific aims on translational continuum</th>
<th>Community partner identified in protocol (as coinvestigator)</th>
<th>External funding since CEnR-Nav (directly related)</th>
<th>No. of presentations, no. of publications (no. with community coauthors)</th>
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<td>FQHC patients</td>
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<td>Study of virulence factors and MRSA recurrence</td>
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<td>FQHC clinicians (no)</td>
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<td>2011</td>
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<td>Mechanism and pathobiology of keloid formation</td>
<td>Minority patients with keloid</td>
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<td>FQHC patients</td>
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<td>PERN FOHC clinicians (yes)</td>
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</table>
Community-Acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) Project (CAMP1) Surveillance Network

**Goals**

1. Define incidence of CA-MRSA in New York area Community Health Centers (CHCs)
2. Insure that CHCs clinicians have the training to provide optimal care to patients with CA-MRSA
3. Identify substrains of MRSA responsible for infections
4. Assess relationship between the MRSA colonizing a patient’s nose and the MRSA causing the clinical infection
5. Build a respectful, enduring, bidirectional partnership and network infrastructure for conducting and disseminating future studies
Policy and Legislative Updates
FY 2017 Budget

- February 9, 2016: President’s budget request
  - NCATS’ request is $685.417 million (same as FY 16)

- Appropriation bills
  - Each House and Senate Appropriation committee passed a Labor, HHS, and Education bill
  - Neither bill was voted on by the full chamber

- Continuing Resolution likely - *stay tuned!*
  - Senate vote possible next week
  - If passed, it would:
    - Extend government funding through Dec. 9 at FY16 levels
    - Include funding for Zika
Congressional Authorizing Activity

• House - 21st Century Cures (H.R. 6, 7/10/15)
  - NIH “Innovation Fund” - $8.75 billion over five years

• Senate - Innovations for Healthier Americans
  - Held hearings to discuss potential bills for inclusion, but no complete bill released yet
    - Mandatory funding for NIH is main sticking point

• Status
  - Rep. Fred Upton (Chair, House E&C) and Senator Lamar Alexander (Chair, Senate HELP) have indicated that President will have bill on desk by end of September
Presidential Transition

- **At Administration level**
  - Obama administration has convened:
    - White House Transition Coordinating Council (WHTCC)
    - Agency Transition Directors Council (ATDC)
- **At NIH level**
  - NIH has begun developing briefing materials for the new Administration

### Pre-Election
- Designation of “Acting”
- Preparation of materials

### Post-Election
- Agency Review Teams arrive
- Selection of incoming Presidential Appointees begins

### Post-Inauguration
- Inauguration and onboarding of new Political Appointees begins
NCATS Strategic Plan

*Timeline*

https://ncats.nih.gov/strategicplan

- **Fall 2015**
  - Launch Strategic Plan Website
  - Publish Request for Information (RFI)
  - Hold Town Hall Webinars

- **Winter 2016**
  - Update NCATS Advisory Council & CAN Review Board
  - Analyze Stakeholder Comments & Suggestions

- **Spring - Fall 2016**
  - Update NCATS Advisory Council & CAN Review Board
  - Draft and Publish NCATS Strategic Plan
NCATS Strategic Plan

Stakeholder Engagement

- **Internal**
  - NCATS employees engaged to provide perspectives and develop strategic principles

- **External**
  - **Council/CAN RB**
    - Series of focus groups were created including internal staff and Council/CAN RB members
      - Identified priorities and challenges in overarching translational areas
    - Provided additional input at Open Session of Sept. 2015 Council
  - **Request for Information (RFI) & Webinars**
    - Public RFI was published and a series of four “town hall”-style webinars were held in late Fall-Winter 2015
    - Identified areas of opportunity and research needs in translational science space
NCATS Strategic Plan

Strategic Goals

1. Conduct and support innovative research that uncovers fundamental scientific and operational principles of translational science to catalyze the development and dissemination of novel medical interventions

2. Advance translational team science by fostering innovative partnerships and collaborations with a strategic array of stakeholders

3. Develop and foster innovative translational training and a highly skilled, creative and diverse translational science workforce

4. Enhance good stewardship of public funds by promoting and employing efficient and effective management practices
Enhancing NIH Stewardship of Clinical Trials

New initiatives progressed by the NIH Clinical Trial Stewardship Reforms Task Force

• Single IRB for Multi-site Studies
  - Policy regarding domestic sites of NIH-funded multi-site studies will use a single IRB
  - Policy was released in June 2016, effective May 2017

• Clinical Trials Registration and Results Submission
  - Developing the requirements for clinical trial registration and results submission to CT.gov and the final NIH policy
  - Will be published in Sept

• Clinical Trial Specific FOAs
  - NIH policy requiring all clinical trials to be submitted to specific FOAs (i.e., clinical trial-specific FOA template)
  - Will be published in NIH Guide in Sept; tentatively effective ~Sept 2017

• Good Clinical Practice Training for Investigators
  - Policy establishing expectation that NIH-funded investigators will be trained in GCP
  - Will be published in NIH Guide in Sept; effective Jan 2017

• Clinical Trial Protocol Template
  - NIH-FDA joint initiative; electronic format of template will be available early 2017 and electronic tool in late 2017
NIH-FDA Joint Leadership Council

**Biomarkers Taxonomy**

- **Co-Chairs:** Rob Califf (FDA) & Pamela McInnes (NIH) & Mike Pacanowski (FDA)
- **Goal:** Ensure consistent use of terminology and further explore opportunities for biomarker infrastructure development
- **Updates:**
  - Biomarkers, EndpointS, and other Tools (BEST) resource published as NCBI eBook
  - Published JAMA article
NIH-FDA Joint Leadership Council

*Clinical Trial Protocol Template*

- **Co-Chairs:** Petra Kaufmann (NIH) & Peter Marks (FDA)
- **Goal:** Develop a clinical trial protocol template to be used by NIH investigators submitting protocols to FDA
- **Updates:**
  - Published NIH Guide notice and gathered public comments via a request for information (RFI) on draft protocol template
  - Analyzed RFI responses
  - Incorporating suggested changes with trans-NIH-FDA group
  - Working with TransCelerate to make templates consistent
International Rare Diseases Research Consortium (IRDiRC)

- Global coordination and cooperation to stimulate and maximize output of rare disease research efforts
  - Members from Europe, North America, Asia, Australia, Middle East
  - Each funder supports its own research
- Initial focus on developing common scientific and policy frameworks
- 2011-2016 objectives: 200 new therapies for rare diseases & means to diagnose most rare diseases by 2020
IRDiRC

Background

- 2009 - Idea for IRDiRC precipitated from meeting between Dr. Ruxandra Draghia-Akli (EC) and Dr. Francis Collins (NIH)
- October 2010 - European Commission and NIH announced IRDiRC at workshop in Reykjavik
- April 2011 - IRDiRC established with Dr. Draghia-Akli elected as Chair at workshop in Bethesda
- October 2011 - Gathered for workshop with private and public organizations in Montreal
- January 2013 - Dr. Paul Lasko (Canadian Inst. of Health Research) elected as new Chair
- April 2013 - First IRDiRC Conference for researchers, clinicians, patient groups and representatives of public and private organizations in Dublin
- November 2014 - Second IRDiRC Conference in China
- March 2015 - Task Forces established to tackle specific areas of importance
- February 2016 - Dr. Chris Austin (NIH/NCATS) elected as new Chair
IRDiRC

NCATS Representation

- **Chris Austin** - Chair of Consortium Assembly
- **Steve Groft** - Member of Interdisciplinary Scientific Committee
- **Petra Kaufmann** - Member of Interdisciplinary Scientific Committee; member of Automatable Discovery and Access, Patient-Centered Outcome Measures, and Participant Unique Identifiers for Research Data Sharing Task Forces
- **Noel Southall** - Member of Steering Committee of Data Mining/Repurposing Task Force
• Five year celebration
• All stakeholders - investigators, policy makers, opinion leaders, critical thinkers, young investigators, patient advocates - active in the area of RD are invited to join
• Celebrate achievements in the field, identify future milestones and goals, and work toward bringing diagnoses and therapies to all RD patients
• Registration will open shortly: www.irdirc.org/conference-2017
New Global Preclinical Collaborative

• Global collaborative effort among national/regional organizations to accelerate preclinical translational science:
   European Infrastructure for Translational Medicine (EATRIS)
   Canadian Centre for Drug Research and Development (CDRD)
   Therapeutic Innovation Australia (TIA)
   UK Medical Research Council Technology (MRCT)
   US National Center for Advancing Translational Sciences (NCATS)

• Emphases on
   Communicating common messages on importance of TS
   Training platforms and resources
   Sharing best practices
   Sharing complementary capacities on projects
Discussion