THE ROLE OF PATIENT ADVOCATES IN NCATS AND THE RARE DISEASE CLINICAL RESEARCH NETWORK

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EVERYLIFE FOUNDATION
NCATS Mission

To catalyze the generation of **innovative methods and technologies** that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.
NCATS Scientific Initiatives

- **Clinical Translational Science**
  - Clinical and Translational Science Awards
  - Rare Disease Clinical Research Network
  - New Therapeutic Uses program

- **Preclinical Translational Science**
  - NIH Chemical Genomics Center
  - Therapeutics for Rare and Neglected Diseases program
  - Bridging Interventional Development Gaps program

- **Re-engineering Translational Sciences**
  - Toxicology in the 21st Century
  - Microphysiological Systems (Tissue Chip) program
  - Office of Rare Diseases Research
RDCRN: Background Information

• Established in 2003 by Office of Rare Diseases Research (ORDR) in response to a Request for Application (RFA).
  ➢ 10 consortia a central Data Management and Coordinating Center (DMCC)
• Expanded in 2009 to 17 consortia and a DMCC
• RDCRN 3rd cycle (Renewed - 2014), an ORDR, NCATS Initiative 22 Consortia and a DMCC
• Each RDCRN Consortium: multiple diseases/investigators/sites collaborative clinical research Involving Patient Advocacy Groups (PAGs).
• These are 5 year cooperative agreement (U54) awards.
• Each awardee (Consortium) receives no more than $1.25 M total cost/year.
Goals of the RDCRN

• Facilitate clinical research in rare diseases by:
  – Creation of Consortia focused on related diseases
  – Cost-sharing research infrastructures
  – Establishing uniform protocols for data collection
  – Making meaningful large-scale studies possible
    • Longitudinal cohorts, pilot projects, and randomized trials
    • Natural History studies *required* in each consortium
• Train new investigators in rare diseases research
• Directly engage patients and their advocates
The Data Management and Coordinating Center

Dystonia Coalition

Brain Vascular Malformation Consortium

Rare Kidney Stone Consortium

Rare Lung Diseases Consortium

Lysosomal Disease Network

The Frontotemporal Lobar Degeneration Clinical Research Consortium

Inherited Neuropathies Consortium

Nephrotic Syndrome Study Network

Developmental Synaptopathies Associated with TSC, PTEN and SHANK3 Mutations

RDCRN

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Autonomic Disorders Consortium

Sterol and Isoprenoid Diseases Consortium

Clinical Research in ALS & Related Disorders for Therapeutic Development

Autonomic Disorders Consortium

Sterol and Isoprenoid Diseases Consortium

Clinical Research in ALS & Related Disorders for Therapeutic Development

Clinical Research in ALS & Related Disorders for Therapeutic Development

Chronic Graft Versus Host Disease

Porphyria Rare Disease Clinical Research Consortium

North America Mitochondrial Diseases Consortium

Primary Immune Deficiency Treatment Consortium

Brittle Bone Disorders Consortium

Urea Cycle Disorders Consortium

Brain Vascular Malformation Consortium

Genetic Disorders of Mucociliary Clearance

Consortium of Eosinophilic Gastrointestinal Disease Researchers

Rett, MECP2 Duplications and Rett-Related Disorders Consortium

Patient Advocacy Group (PAG)

Coalition of Patient Advocacy Groups (CPAG)
RDCRN Steering Committee Organization

Review, facilitate and establish all Network procedures and functions

- NIH Institutes’ Project Scientists
- CPAG Chairperson
- Consortia PIs
- NCATS Program Coordinator for RDCRN (From ORDR)
- DMCC PI
Impact of Patient Advocacy Group Collaboration

• Focus on specific disease
• Patients
  ➢ US and international
• Pilot funding to leverage our investment
• Knowledge
• Reality check
• Inspiration
By the numbers

- RDCRN is studying 200 rare diseases in natural history and clinical trials at 240 clinical sites located in the US and 14 other countries.
- More than 90 active protocols.
- 30,630 patients have enrolled in clinical studies.
- There have been 208 trainees.
- There are 2,290 collaborative members.
- More than 100 PAGs as research partners.

http://rarediseasesnetwork.epi.usf.edu/
Re-engineering Translational Sciences

**NCATS Chemical Genomics Center**

- Founded as part of Molecular Libraries Program
- Currently > 200 collaborations with investigators worldwide
- Assay development, HTS, chemical informatics, medicinal chemistry: “target to lead”
- Focus is unprecedented targets, rare/neglected diseases
- **Mission**
  - Chemical and siRNA probes/leads
  - New technologies/paradigms to improve efficiency and success rates of target-to-lead stage of drug development
  - Chemical genomics: general principles of siRNA action, small molecule-target interactions
Partnering with Disease Foundations to Speed Drug Discovery

NCATS’ postdoctoral fellows with disease expertise receive training in early drug discovery.
Identification of Drug Modulators Targeting Gene-Dosage Disease CMT1A

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ABSTRACT: The structural integrity of myelin formed by Schwann cells in the peripheral nervous system (PNS) is required for proper nerve conduction and is dependent on adequate expression of myelin genes including peripheral myelin protein 22 (PMP22). Consequently, excess PMP22 resulting from its genetic duplication and overexpression has been directly associated with the peripheral neuropathy called Charcot-Marie-Tooth disease type 1A (CMT1A), the most prevalent type of CMT. Here, in an attempt to identify transcriptional inhibitors with therapeutic value toward CMT1A, we developed a cross-validating pair of orthogonal reporter assays, firefly luciferase (FLuc) and β-lactamase (βLac), capable of recapitulating PMP22 expression, utilizing the intronic regulatory element of the human PMP22 gene. Each compound from a collection of approximately 3,000 approved drugs was tested at multiple titration points to achieve a pharmacological end point in a 1536-well plate quantitative high-throughput screen (qHTS) format. In conjunction with an independent counter-screen for cytotoxicity, the design of our orthogonal screen platform effectively contributed to selection and prioritization of active compounds, among which three drugs (fenretinide, olvanil, and bortezomib) exhibited marked reduction of endogenous Pmp22 mRNA and protein. Overall, the findings of this study provide a strategic approach to assay development for gene-dosage diseases such as CMT1A.
Giant Axonal Neuropathy (GAN)

Hannah’s Hope

Lori Sames, founder of Hannah’s Hope Fund, and her daughter Hannah, who has giant axonal neuropathy, a progressive neurological condition. (Lori Sames Photo)

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Patient-driven science

Collaborations between patient organizations and NCATS Intramural scientists

- **Patient organizations contribute**
  - Disease-specific scientific knowledge
  - Sponsor fellowships for postdoctoral researchers

- **NCATS contributes**
  - Scientific expertise
    - High throughput screening
  - Training

Division of Preclinical Innovation: Dr. Anton Simeonov anton.simeonov@nih.gov
Translational Science Spectrum

- Public Health
- Basic Research
- Clinical Implementation
- Clinical Research
- Pre-Clinical Research

Patient Involvement

NIH National Center for Advancing Translational Sciences

NCATS
Stephen Groft, Champion of Rare Diseases Research, Retires

A Distinguished Career

Stephen C. Groft, Pharm.D.

Posted February 2014
Kaufmann Appointed Head of NCATS’ Office of Rare Diseases Research

On Sept. 3, 2015, NCATS Director Christopher P. Austin, M.D., named Petra Kaufmann, M.D., M.Sc., as director of the Center’s Office of Rare Diseases Research (ORDR)
Questions?

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RARE CLINICAL DISEASES RESEARCH NETWORK

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