RDCRN: A Model for Collaborative Rare Diseases Research Efforts

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GENE THERAPY: CHARTING A FUTURE COURSE
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NIH, BETHESDA
Stimulates and coordinates research on rare diseases

- Rare Diseases Clinical Research Network (RDCRN)
- Scientific Conferences
- NIH Clinical Center Bench to Bedside Research Program with Intramural/Extramural Research Investigators partnership
Rare Diseases: Background

- Prevalence < 200,000 people in the USA
- Estimated 6%-8% of Population has a Rare Disease
- > 7000 Genetic and Acquired Rare Diseases
- ~ 18-25 million people in the United States are affected

- Exact Prevalence Unknown
- Global Distribution of Patients
Challenges for Rare Diseases Research

• Disease often not well characterized or defined
• Rarity means:
  - Recruitment for clinical studies is usually quite difficult
  - Study populations become widely dispersed
  - Few expert centers for diagnosis, management, and research
• Often little high-quality evidence available to guide treatment
The Rare Diseases Clinical Research Network (RDCRN)
1) RDCRN (Background)

To facilitate clinical research

• Established in 2003: by the Office of Rare Diseases Research, six NIH Institutes & Centers (ICs) collaborated: 10 Rare Diseases Clinical Research Consortia (RDCRC) and 1 Data Management Coordinating Center (DMCC)

• Expanded in 2009: initially to 19 RDCRC and 1 DMCC (eight collaborating ICs)

• Each RDCRC: multiple diseases/investigators/sites collaborative clinical research Involving Patient Advocacy Groups (PAGs)

• Cooperative agreement (U54) awards for 5 years

• 3rd cycle in planning stage
  - Renewal is planned - open competition
Goals of the RDCRN

• Facilitate clinical research by:
  - Creating multi-site Consortia focused on minimum three related diseases
  - Making meaningful large-scale clinical studies possible
    - Longitudinal studies, pilot projects and Clinical Trials, Natural History Studies are required)
    - Establishing uniform protocols for data collection
    - Cost sharing infrastructure

• Collaborate with patients advocacy groups (as research partners)

• Train new investigators

• Provide Website resource for education and research in rare diseases
Requirements for each RDCRC

- Two clinical studies (one longitudinal study, 2\textsuperscript{nd} can be a clinical trial)
- Pilot projects program
- Career development program (training of investigators)
- Collaboration with PAGs
- Collaboration with DMCC and NIH scientific staff
About the RDCRN

- 225 clinical sites world-wide, collectively studying more than 200 diseases
- 17 Consortia & DMCC
- 86 Accruing protocols
  - 17,188 patients enrolled in studies
  - Natural History studies, clinical trials, Genotype/Phenotype
- 2,290 consortium members
- 95+ patient advocacy groups
- 174 trainees

http://rarediseasesnetwork.epi.usf.edu/
RDCRN is supported by

- ORDR/NCATS
- NINDS
- NICHD
- NIDDK
- NIAID
- NIDCR
- NIAMS
- NHLBI
- NCI
Coalition of Patient Advocacy Groups (CPAG)

Dystonia Coalition

Genetic Disorders of Mucociliary Clearance Consortium

Porphyria Rare Disease Clinical Research Consortium

Vasculitis Clinical Research Consortium

Lysosomal Disease Network

Inherited Neuropathies Consortium

Urea Cycle Disorders Consortium

Salivary Gland Carcinomas Consortium

Sterol and Isoprenoid Diseases Consortium

Autonomic Rare Diseases Clinical Research Consortium

Chronic Graft Versus Host Disease Consortium

North America Mitochondrial Diseases Consortium

Primary Immune Deficiency Treatment Consortium

Rare Kidney Stone Consortium

Nephrotic Syndrome Rare Disease Clinical Research Network

Angelman, Rett and Prader-Willi Syndromes Consortium

Brain Vascular Malformation Consortium

The Data Management and Coordinating Center

DHHS-NIH
ORDR/NCATS, NINDS, NIAMS, NICHLD, NHLBI, NIDDK, NIDCR, NIAID, NCI
Value of PAGs as Research Partners

Since 2004 Many PAGs within RDCRN are involved in more than one of the following expanded roles as research partners:

- Recruit patients for clinical studies, encourage participation in NHS
- Identify cohorts of patients with range of phenotypic expression
- Provide financial support for research and training programs of RDCRC (consortia) and patient registries
- Educate patients, public, media and health care providers
- Identify research efforts and translate research results to communities
- Organize and fund research based Scientific conferences and meetings for patients/families/caregivers
- Provide financial support for travel clinics to facilitate patient access to investigators and studies
- Establish global partnership
RDCRN Steering Committee Organization

Review, facilitate and establish all Network procedures and functions
## RDCRN Protocols

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RDCRN International Sites

- Australia (INC)
- Belgium (DC)
- Canada (BVMC, DC, LDN, MCC, NAMDC, NEPTUNE, PIDTC, RKSC, STAIR, UCDC, VCRC)
- England (DC, INC)
- France (DC, RKSC)
- Germany (DC, INC, RKSC, UCDC)
- Iceland (RKSC)
- India (DC)
- Italy (DC, INC, RKSC)
- Netherlands (DC, RKSC)
- Scotland (DC)
- Spain (RKSC)
- Switzerland (UCDC)
RDCRN Data Management and Coordinating Center (DMCC)

• Supports RDCRN by providing technologies, tools to collect clinical research data and support of study design and data analysis

• On-line protocol management system
  - Web-based patient enrollment (recruitment and referral)
  - Data entry and collection with data standards
  - Adverse event reporting

• Provides protocol training for research staff

• Works with the individual NIH Institutes’ Data and Safety Monitoring Boards to establish protocols for Adverse Events notification and reporting
Responsibilities of DMCC (Cont.)

- Monitor Network protocol adherence, data collection and data submission
- Coordinates site visits for auditing individual consortia sites
- Provides a user-friendly web resource site for the public, research scientists, and clinicians; involvement of PAGs
- Maintain members’ website, documentation and database
- Oversees and maintains RDCRN Patient Contact Registry
RDCRN Website
http://rarediseasesnetwork.org

- Portal to websites for each Consortium
  ➢ Contact PI's for collaboration

- Portal to members' website

- Portal for patient advocacy groups

- RDCRN Contact Registry

- RDCRN Media Center
RDCRN Contact Registry (2004)
(U.S. Geographic Distribution of Contact Registrants)

- Enrollment open to patients with diseases under study by Consortia
- Provides international on-line system for communication, recruitment, research
- more than 12000 Registrations
- 180 Diseases represented in 67 countries
World Geographic Distribution of Contact Registrants
Data Sharing and ORDR DataRepository

- The DMCC also coordinates with NIH program staff including registration with and data uploading of appropriate RDCRN studies to ORDR-governed data repository
- Through dbGaP, a database for genotypes and phenotypes (NCBI, National Library of Medicine)
- Data transfer to dbGaP occurs on regular basis
- RDCRN Data Access Committee (DAC)
Urea Cycle Disorders Consortium (PI- Dr. Mark Batshaw)

- They are developing adeno-associated viral gene therapy for *Ornithine Transcarbamylase (OTCD) deficiency* in neonates.
- They have a candidate vector and are ready to move into clinical trials.
1) Dr. Notarangelo (co-PI of the PIDTC) has an active protocol for gene therapy for XSCID using a lentiviral vector.

- It’s a collaborative study with several other PIDTC institutions in the US as well as in France and the UK.

2) The group is doing the pre-clinical studies necessary for an IND for Artemis-deficient SCID (SCID A)
Team Work!

- Clinical Sites
- Principal and co-investigators and The DMCC
- Trainees
- Study Coordinators
- Patient Advocacy Groups (PAGs)
- Pharmaceutical industry
- NIH ORDR and ICs staff (program officers and project scientists)
- Patients

RDCRN: Working model for collaborative, multi-site clinical studies in an inexpensive way!

RDCRN consists of ~225 sites, 97 PAGs and conducts research on 200 rare diseases
RDCRN Request For Applications (RFA)

- Current U54 awards end in 2014
- Plan to reissue the RDCRN RFA
- Timeline - similar to last RFA
- NIH ICs as collaborators

Contact:
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Thank you for your attention

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