Rare Diseases: Challenges and Opportunities – NIH Perspective

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Conflicts of Interest

None to Report
Meeting the Challenges – Expanding Knowledgebase of Rare Diseases

- Increase Understanding of Rare Diseases Through Training Programs
- Participate in Patient Registries (GRDR), Natural History (RDCRN, CC), and Epidemiological Studies
  - Provide Fundamental Characterization and Delineation of Heterogeneity in Populations
  - Establish Reliable Data on Prevalence of Rare Diseases
  - Identify Severity of Diseases in All Age Groups Throughout the Lifespan
- Develop Standards of Care With and Without Available Interventions and for Emergency and Critical Care Treatments
- Organize Research Based Conferences
  - Expand Long Distance Learning Opportunities for Diagnosis, Treatment, Training, and Research Capabilities
  - Increase Participation at Scientific Conferences and Workshops to Scientific and Patient Communities Around the World and Extend Knowledge of Outcomes
Meeting the Challenges – Expanding Knowledgebase of Rare Diseases

- Globalization of Industry and Expanded Rare Diseases Emphasis by Pharmaceutical, Biotechnology and Medical Devices Industries with Increased Interest in Niche Markets

- Recognition of Genetic Differences in Patients
  - Molecular Diagnosis with Whole Genome Sequencing and Analyses Capabilities
  - Identify Cohorts of Patients with Range of Genotype and Phenotype Expression
  - Genetic Predictors of Patient Responders
  - Rare Diseases Can Inform About Common Diseases
Meeting the Challenges – Patient Recruitment

- Global Distribution of Patients Requires Global Linking of Protocols, Patients, Families, Health Care Providers, and Patient Advocacy Groups
- Establish Partnership(s) with Patient Advocacy Groups and Professional Specialty Societies to Improve Recruitment
- Expand Roles of Patient Advocacy Groups - Genetic Alliance, NORD, Children’s Rare Diseases Network, and Disease Specific Organizations - Around the World
- For Some Diseases, Patients Have Difficult Choices with Increased Number of Clinical Trials
- Increased Development of Genetic and Diagnostic Tests (Whole Genome Sequencing and Analyses)
- Understand Cultural, Ethical, Legal, and Social Issues Related to Data Gathering and Sharing from Multiple Populations.
Meeting the Challenges - Research Investigators

- Recruit Critical Mass of Investigators Willing to Share Data and Publications
- Convince Scientific Community of the Need for and Value of Patient registries, Biospecimen repositories and Natural History Studies
- Access to Annotated Biospecimen Samples
- Utilize Central IRB Approval for Multiple Site Studies with Common Protocols
Meeting the Challenges - Research Investigators

- Identify and Utilize Existing Research Infrastructure of Consortia, Research Networks (RDCRN, CTSA, NeuroNExT, NBSTRN) and Grant and Contract Resources

- Foster International Research Collaborations on Grant Applications

- Limited Resources for Studies of Rare Diseases; Must Use the Existing Grant and Contract Resources from Private and Public Sectors
Meeting the Challenges - Research Emphasis

- Expanding Federal, National, and International Interest and Support Has Led to the Development of More Directed Research Agendas with Focus on Interventions and Diagnostics

- Increased Federal Government Emphasis on Rare and Neglected Diseases
  - National Center for Advancing Translational Sciences (TRND, BrIDGs)
  - Cures Acceleration Network
  - NIH Institute Translational Research Programs (NCATS, NINDS, NIAID, NICHD, NHLBI, NCI)
  - FDA Expanded Emphasis on Rare Diseases and Orphan Products Development
  - NIH-PhRMA Collaboration on Repurposing of Products
  - NIH-DARPA-FDA Collaboration - Better Ways to Predict Drug Safety and Efficacy
Meeting the Challenges - Research Emphasis

- Respond to Increasing Scientific Opportunities with Limited Funding Resources

- Encourage Pharmaceutical, Biotechnology, and Medical Device Industries to Identify Chemical Libraries, Compounds or Products Available for Research and Development.

- Establish Better Definitions of Patient Responders with Development of Appropriate Biomarkers and Clinical and Surrogate Endpoints for Safety and Efficacy

- Develop Animal and *In Vivo* and *In Vitro* Models representative of human diseases.
International Rare Diseases Research Consortium (IRDiRC) Goals

- Dr. Ruxandra Draghia-Akli, Chair Interim Executive Committee
- Mission - Foster International Collaborative Research on Rare Diseases
- Goal of 200 Therapies for Rare Diseases by 2020
- Develop Diagnostic Tools (or means) for Most Rare Diseases
- Annual Meeting Dublin, Ireland, April 16-17, 2013

Scientific Committees
- Therapies
- Interdisciplinary (Horizontal) with Working Groups
  - Genomic Analysis, Animal Models and *In Vitro* Systems, Ontologies/Disease Classification/Natural History Studies, Biomarkers and Clinical Endpoints Development and Validation, Patient Registries and Biospecimen Repositories, Preclinical Research and Clinical Trials, Communication/Publication Policy/Information Sharing/IPR/Data Sharing Policy
- Diagnostics and Sequencing Characterization

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Turning Discovery Into Health
Question 1. Participation in patient registries and natural history studies
(a.) Will not provide delineation of disease heterogeneity in patients.
(b.) Can identify severity of diseases across the lifespan.
(c.) Will help develop standards of care only when treatment interventions are available.
(d.) Will not help to establish useful prevalence data for rare diseases.

Question 2. The research community finds
(a.) Limited roles exist for patient advocacy groups and professional societies participation in recruitment of patients and study participants for rare diseases clinical studies.
(b.) Public and Private Sector initiatives continue to de-emphasize research on rare diseases.
(c.) Public and Private Sector emphasis on rare diseases research has led to a more directed research agenda with a focus on development of interventions and diagnostics.
(d.) Participation of a critical mass of research investigators has no impact on the completion of rare diseases clinical studies.