Translational Science of Rare Diseases 5 (2020) 97–98
DOI 10.3233/TRD-211000
IOS Press

Editorial

The general status of rare disorders

Alan K. Percy, MD and Rashmi Gopal-Srivastava, PhD
Co-Editors-in-Chief

In this issue, the thorough review by a consensus panel details the current status, realistic goals, and future research priorities in Down syndrome (Opportunities, barriers, and recommendations in Down syndrome research) in response to an NIH/National Institute of Child Health and Human Development (NICHD) initiative in 2020 to update research plans in this disorder. This report represents a joint effort of the National Down Syndrome Society and the LuMind IDSC Foundation with additional input from other Down syndrome organizations including the Lejeune Foundation and the National Task Force on Intellectual Disabilities and Dementia Practices. By itself, this document provides a way forward for this relatively rare disorder. During the past forty or more years, survival of individuals with Down syndrome has increased dramatically, bringing additional issues of importance to clinicians, researchers, families, and society in general. Important areas requiring further study include natural history exploration, advanced diagnostics, outcome measure development, multisystem disability (language and communication skills, intellectual decline, multiple system issues), biomarker development, and access of appropriate controls. The exploration of these issues is balanced with identified gaps in understanding and suggested routes of study to close these deficiencies.

Yet, the overall message resonates far beyond Down syndrome. Similar issues exist for most, if not all, of the more than 7,000 rare disorders. While natural history studies have been or are being conducted in a variety of these disorders including metabolic (lysosomal, urea cycle, or fatty acid oxidation, neurocutaneous (neurofibromatosis, tuberous sclerosis), or neurodevelopmental disorders (Angelman, Prader-Willi, or Rett syndromes), many others still lack concerted efforts. Even with the disorders noted above, similar gaps in knowledge are notable. Diagnostic methodology is lacking for many. Advances in whole genome and exome sequencing offer important advances, but these methodologies must be applied broadly and wisely to be effective. Expansion of natural history studies across the age spectrum is crucial. A thorough approach to direct and indirect involvement of all organ systems is essential. Development of sensitive, valid, and reliable outcome measures and biomarkers will be important as new therapeutic interventions are assessed. For many of these disorders, the creation of appropriate, valid animal models is critical. While rodent models are currently most prevalent, they may not reflect the human disorder precisely and lack the higher cortical features that may be critical to more precise modeling. This may require models in other species including non-human primates. Finally, inclusion of industry sponsors and the FDA is an important step in ensuring that the planned studies meet the goals and standards of these crucial partners.

Such efforts require strong input form the NIH. The Office of Rare Diseases (ORDR), Genetic and Rare Diseases Information Center (GARD), and the Clinical Translational Science Awards (CTSA) Program within the NIH National Center for Advancing Translational Sciences (NCATS) and several institutes at NIH are important partners in the global studies of rare disorders.

However, the breadth and depth of new research ventures require involvement not only of the NIH, but also private foundations, disorder-specific foundations, industry, and other federal agencies such as the Center for Disease Control and Prevention (CDC), the National Science Foundation, and the FDA. Solving any single rare disorder will necessitate the broad involvement of many organizations. Recognition of this requirement is essential.