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EXECUTIVE SUMMARY

The Intellectual and Developmental Disabilities (IDD) Branch, formerly the Mental Retardation and Developmental Disabilities Branch, within the Center for Developmental Biology and Perinatal Medicine of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), has a longstanding history of providing support for a diverse portfolio of research projects, training programs, and research centers dedicated to promoting the well-being of individuals with intellectual and developmental disabilities. When the Institute was created at the National Institutes of Health (NIH) in 1962 at the request of then-President John F. Kennedy and with the support of congress, one if its primary charges was to encourage investigations in human development throughout the lifespan, with an emphasis on understanding developmental disabilities, including intellectual disabilities (historically referred to as mental retardation). The mission of the IDD Branch is to:

- Develop and support research and research training programs in IDD;
- Administer a program of support for centers for research in IDD;
- Coordinate with university-affiliated programs for IDD with respect to integration of research, training, and service activities; and
- Partner with other federal agencies, organizations, and advocacy groups to advance efforts toward the prevention, diagnosis, treatment, and management of IDD that will improve the quality-of-life for these individuals and their families.

Since its last report to the National Advisory Child Health and Human Development (NACHHD) Council, the Branch has continued its mission through with a variety of mechanisms, grants, and contracts. The Branch has also added breadth to its portfolio by expanding traditional efforts to address quality-of-life issues for individuals with IDD, while increasing multidisciplinary and translational research to facilitate the movement of basic research from the bench to the clinic and beyond. The Branch's expanded newborn screening program and the growth of certain cooperative research centers reflect such opportunities.

This report highlights advances from Branch-sponsored research, emphasizes major Branch initiatives from the past four years, and outlines areas of future expansion in the field of IDD research.

Branch activities are organized into topical research initiatives, with some areas of programmatic overlap. These initiatives will be the focus of subsequent sections of this report:

- Eunice Kennedy Shriver IDD Research Centers (IDDRCs)
- Program on Fragile X syndrome (FXS) and associated disorders
- Rare Disease Cooperative Research Consortia (RDCRCs)
- Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers
- Chromosome abnormalities, genetic/genomic syndromes, and epigenetic disorders
- Biochemical and metabolic research
- Research on Autism Spectrum Disorders (ASDs)

- Newborn screening
- Research resources
- Branch-supported Training Initiatives

The next several sections focus on major accomplishments within each of the areas listed above, with an emphasis on areas for which the Branch has employed collaborative approaches to improve coordination and leverage of resources.

The report concludes with an overview of possible *Future Directions for the Branch* in IDD research. The section describes the discussions of an expert panel of IDD researchers and clinicians assembled as part of the Institute's continued efforts to improve strategic planning and transparency for its components. The expert panel and Branch members gathered to discuss the Branch's existing research portfolio as a way to address the following issues: opportunities in prenatal, perinatal, and postnatal identification of infants and children at risk for developing cognitive impairment; areas, such as adolescent brain development, obesity, and health disparities, in which IDD research has lagged; and promotion of training initiatives. Branch staff and members of the expert panel also discussed a de-emphasis on individual disorders with concomitant support for groups of conditions with common pathways or shared elements as a way to facilitate the ambitious but necessary goal of developing drugs and other cognitive and behavioral interventions to improve the lives of individuals with IDD and their families. The potential to guide the IDD field toward translational applications is enormous and potentially transformative, making this a very exciting time in IDD research.

Biosketches of Branch personnel are listed in *Appendix A*. Funding Opportunity Announcements (FOAs), which reflect areas of programmatic emphasis, released by the Branch during the last four years are listed in *Appendix B*. *Appendix D* lists expert panel members. *Appendix E* describes the various conferences and meetings the Branch supported since the Branch's last report to the National Advisory Child Health and Human Development (NACHHD) Council.

INTRODUCTION TO THE BRANCH

Intellectual and developmental disabilities (IDD) represent a significant source of morbidity and mortality among the pediatric population. Intellectual disability is characterized by significant limitations in intellectual functioning and adaptive behavior as expressed in conceptual, social, and practical adaptive skills. These limitations originate before age 18 years. The American Association on Intellectual and Developmental Disabilities describes developmental disabilities more broadly as severe chronic disabilities that can be cognitive, physical, or both, that generally appear before age 22 years, and that are likely to be lifelong. The etiology of IDD is complex, and more than 500 genetic diseases (most individually rare) contribute to this condition; chromosomal disorders, such as Down syndrome, are estimated to account for 5 percent to 19 percent of all IDD cases (Yeargin-Allsopp, et al, 2007). The prevalence of severe intellectual disability is estimated as 3 to 4 per 1,000 children and adults, while mild intellectual disability is much more common. IDD significantly impacts the physical, emotional, and financial health

and well-being of the affected individuals and their families. Approximately 17 percent of children in the United States have some type of disability, and about 2 percent of children will require lifelong care for their disability; the associated economic costs of these disabilities are significant (Boyle and Cordero, 2005).

Although "mental retardation" and "intellectual disability" are technically synonymous, intellectual disability is the preferred term among many professional organizations, advocacy groups, and government agencies. This language is considered to be less offensive to persons with IDD, to be more consistent with internationally used terminology, and to align with current professional practices that focus on supports tailored to enhance individuals' functioning (Schalock et al, 2007). To reflect the field's move away from the term "mental retardation" and toward the broader term IDD, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) changed the name of the Branch from the Mental Retardation and Developmental Disabilities Branch to the IDD Branch. Similarly, this document uses the term IDD, not "mental retardation" to describe the relevant conditions. Branch reports and other documents published prior to September 2009 use the older Branch name and terminology.

This change in the Branch name also necessitated a change in its functional statement to better reflect the Branch's growing number of partnerships with other federal agencies, organizations, and advocacy groups. The revised mission of the IDD Branch is to:

- Develop and support research and research training programs in IDD;
- Administer a program of support for centers for research in IDD;
- Coordinate with university-affiliated programs for IDD with respect to integration of research, training, and service activities; and
- Partner with other federal agencies, organizations, and advocacy groups to advance efforts toward the prevention, diagnosis, treatment, and management of IDD that will improve the quality-of-life for these individuals and their families.

The revised mission also better reflects the Branch's longstanding goals toward prevention, diagnosis, treatment, and management of IDD to improve the quality-of-life for those with IDD and their families.

In fiscal year 2008, the Branch supported IDD research with a total budget of $106.4 million, which represents a stable investment of approximately $106 million during the four-year reporting period, as well as a decrease in actual or constant dollars when corrected for inflation for that same time period (Figure 1). Among the 236 total Branch-supported projects for fiscal year 2008, most (just less than 50 percent) were research project grants (e.g., R01, R03, R13, R15, R21, and R37 mechanisms), the "bread and butter" of National Institutes of Health (NIH) awards (see Figure 2 and Table 1). One-quarter of Branch funds supported Research Centers grants (P30 and P50 mechanisms), and 13.5 percent of the portfolio supported Program Project grants (P01 mechanism) for multi-investigator projects. Three percent of the Branch's portfolio is devoted to training initiatives, including training programs (Ts), fellowships (Fs), and research career development program awards (Ks). Small business awards (Small Business Innovative Research awards and Small Business Technology Transfer awards), contracts, and cooperative

Syndrome to coordinate NIH efforts on Down syndrome research. IDD Branch staff chair the Taskforce, which includes representatives from NIA, NINDS, the National Eye Institute, NIDCD, NIAMS, the National Human Genome Research Institute (NHGRI), NCI, the National Heart, Lung, and Blood Institute, and the National Institute of Allergy and Infectious Disease, among others. The Trans-NIH Taskforce met three times, once with members of the Taskforce on Down Syndrome organized by the National Down Syndrome Society. Three additional meetings resulted:

- Gatlinburg Conference, March 2007, *Down Syndrome: Genes, Brain and Behavior*
- Trans-NIH Taskforce Meeting, July 2007, *Down Syndrome and Cognition* (funded by the NICHD Office of the Director)
- R13 conference, September 2007, *The Biology of Chromosome 21 Genes: Toward Genotype/Phenotype Correlations in Down Syndrome*

This effort resulted in the issuance of the *NIH Research Plan on Down Syndrome* in October 2007. Table 3 lists the matrix of research objectives from the Plan; the full Plan is available at http://www.nichd.nih.gov/publications/pubs/upload/NIH_Downsyndrome_plan.pdf. This research agenda will address, within the next five to ten years, topics such as:

- Aging and family dynamics
- Measures of cognitive function in Down syndrome throughout the lifespan
- Issues involving medications and clinical trial participation
- Use of Alzheimer disease research to inform potential therapeutics
- Transitions to independent or assisted living for adults
- Comorbid psychiatric and medical conditions throughout the lifespan
- Improving and expanding availability and studies in animal models
- Health disparities in survival and access to care

In 2009, NICHD issued an RFA, *Factors Affecting Cognitive Function in Adults with Down Syndrome* (RFA HD 09-028). Applications in response to that RFA were reviewed in August 2009; final decisions are pending.

Other advances in the realm of Down syndrome research include:

- An assessment of gastrointestinal anomalies by sex, race, and ethnicity;
- Identification of modifier genes located on other chromosomes that impact variability in Down syndrome features;
- Evidence from animal models of specific genes involved in craniofacial and brain development and in reduced solid-tumor formation; and
- Identification of specific genes that are candidates for the constant features of Down syndrome.

Other ongoing activities include efforts to develop clinical trials, in humans and animal models, for agents that ameliorate or improve intellectual development and cognitive performance and to

- Postdoctoral Training in Mental Retardation Research, University of Wisconsin, Madison, Wisconsin (2005, 2006, 2007, 2008)
- Postdoctoral Research in Neurodevelopmental Disorders, University of North Carolina, Chapel Hill, North Carolina (2005, 2006, 2007, 2008)
- Research Training in Mental Retardation, University of Notre Dame, Indiana (2006, 2007, 2008)
- Postdoctoral Training in Developmental Disabilities Research, Children's National Medical Center, Washington, DC (2006, 2007, 2008)