Towards Targeted Therapy for Neurodevelopmental Disorders Symposium

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Neurodevelopmental disorders include autism spectrum disorder (ASD), developmental delay/intellectual disability, and childhood epilepsy syndromes, which, broadly defined, affect approximately 15% of the population in the USA and represent a major public health problem. Such conditions are thought to be caused by disruption of normal developmental processes due to genetic and/or environmental factors. A greater understanding of the cause of such disorders offers a window into basic mechanisms of brain development and function and could lead to improved therapies or cure.

Recent advances in genetic testing have driven spectacular progress in the ability to diagnose the underlying cause of many neurodevelopmental disorders. This has led to an increased understanding of the genetic architecture of the neurodevelopmental disorders, insights into disease mechanisms, and the identification of potential new molecular targets for therapeutic manipulation. Such progress has been met by the parallel emergence of ex-

perimental approaches such as gene therapy or use of antisense oligonucleotides to specifically target the underlying cause of such disorders.

This special issue of *Developmental Neuroscience* includes a series of review articles and commentaries based on the proceedings of the 1-day symposium “Towards Targeted Therapy for Neurodevelopmental Disorders,” held online, on July 31, 2020. This symposium brought together 1,004 registrants from around the world to discuss advances in the field of neurodevelopmental disorders. Participants included clinicians, basic scientists, and representatives from the industry; staff from the National Institute of Neurological Disorders and Stroke (NIH NINDS); and members of patient advocacy groups. Three keynote lectures (Drs. Guoping Feng, Arnold Kriegstein, and Beverly Davidson) and 4 minisymposia (Human Genetics to Inform Treatment Targets, Targeted Therapy for Neurodevelopmental Disorders, Mechanisms of Neurodevelopmental Disorders, and Mechanisms of/Treatment for Ion Channelopathies) featured leaders in the field, while over 30 short talk/virtual poster sessions provided opportunities for graduate students, postdoctoral fellows, and junior investigators to present their work. Speakers covered a range of topics, including epilepsy,

ASD, developmental delay/intellectual disability, mitochondrial disorders, and related conditions, using a variety of approaches from genomic diagnostics in human patients, experimental model systems, to basic mechanisms, as well as the development and application of emerging therapeutic strategies.

Part I of the issue (Models and Mechanisms) focuses on advances in the generation and application of experimental model systems to investigate pathomechanisms of neurodevelopmental disorders. Several articles discuss the use of mouse models as well as neurons and organoids from induced pluripotent stem cell lines generated from human patients with neurodevelopmental disorders, to study disease mechanisms. This section includes insightful reviews of the mechanisms and potential approaches towards treatment of a range of neurodevelopmental syndromes including mTORopathies, KCNQ-related neurodevelopmental disorders, Pitt-Hopkins syndrome, and mitochondrial encephalopathies, and the roles of dendritic integration, cerebral cortex GABAergic interneuron diversity, and cerebellar development in the pathogenesis of neurodevelopmental disorders.

Part II (Therapeutic Strategies) highlights advances in human genetics, and provides targets for therapeutic modulation and development of novel treatment strategies. Articles discuss the identification of new genetic mechanisms of neurodevelopmental disorders such as poison exons (Carvill and colleague), advances in gene therapy for specific forms of genetic diseases, potential

use of antisense oligonucleotide therapy to treat developmental and epileptic encephalopathies, and treatment of genetic causes of epilepsy and ASD with gene transfer therapy and CRISPR/Cas9-based approaches.

This special issue will be of great interest to clinicians and basic and translational scientists in the fields of neurodevelopment, neurogenetics, and neurodevelopmental disorders, and those engaged in emerging attempts at targeted therapy.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

E.M.G. drafted and revised the work critically for important intellectual content, approved the version to be published, and agreed to be accountable for all aspects of the work; and A.T. drafted and revised the work critically for important intellectual content, approved the version to be published, and agreed to be accountable for all aspects of the work.