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Preface

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This is the inaugural volume in a series entitled *The Year in Human and Medical Genetics*, one of a growing number of annual review series in different subject areas published within the Annals of the New York Academy of Sciences. Most academic libraries have online access to the Annals, so most of academia has convenient and full online access to the reviews in this volume and the series, just as it has to the rest of the scholarly journals, courtesy of local academic libraries.

The first chapter in this volume presents some of the highlights of the year. Additional contributions to this volume cover a broad range of topics, including developmental defects, malformations and dysmorphology, enzyme deficiency and neurobehavioral disorders, and epidemiology. Authors have included current information on aspects of embryogenesis, genome architecture, chromatid formation, gene regulation, and structure and function of ion channels.

Dale Dorsett and Ian Krantz review Cornelia de Lange syndrome and cohesin structure and function. Their studies have shed light on the large number of proteins involved in sister chromatid cohesion and on the genetic heterogeneity of Cornelia de Lange syndrome. They also present exciting evidence on the roles played by these proteins in regulation of gene expression.

Philip Giampietro and colleagues review advances in our understanding of molecular embryology and genetics of vertebral development and etiology of malformations of the spinal column. They provide a fascinating description of gene action and the segmentation clock that controls somitogenesis in the embryo. Also included in their review is a discussion of environmental factors that interact with genetic factors in the pathogenesis of specific vertebral anomalies.

Reviews of Cornelia de Lange syndrome and vertebral anomalies provide examples of the importance of studies of other organisms in generating information required to promote our knowledge of the pathogenesis of human malformation syndromes.

Abnormalities of sexual development are discussed in two contributions, in the paper by Michele Ramsay and colleagues, and in the review of highlights of the year. Michele Ramsay and colleagues present cases of true hermaphroditism and the molecular studies they carried out that led to diagnosis of XX/XY chimerism. They present an interesting analysis of the mechanism of the origin of chimerism.

Izelle Smuts and colleagues present a case study of the lysosomal storage disorder mucolipidosis type III, and they include a brief review of the molecular defects in the mucolipidoses. The case they present is striking in its revelation of the degree to which function and behavior in a child are influenced by pain and how alleviation of that pain may lead to dramatic improvement in these areas. The problem of recurrence of symptoms in this case lurks ominously. Cases such as these spur on our endeavors to search for successful therapeutic interventions with long-term effects.

Neurobehavioral disorders, including autism and schizophrenia, are addressed in several papers in this volume. Roos and colleagues describe epidemiology and characteristics of schizophrenia in the Afrikaner population in South Africa, and they

compare this to characteristics of schizophrenia within the United States. The Afrikaner population represents a genetic isolate. Population isolates are considered particularly advantageous for the study of genetically complex and polygenic disorders. The theoretical basis for advantage is the proposition that specific allelic variants predisposing to complex disorders may be more readily identified because the overall range of allelic variation is less than in an outbred population.

The roles of structural genomic variation and copy number variation in schizophrenia are discussed in my own article on the highlights of the year. Also discussed in that article are new data on the role of microRNA in brain development, functioning of the mature nervous system, and information on microRNA abnormalities in schizophrenia. In an article on autism by my colleagues and me, we review evidence that alterations of gene dosage and structure influence neurodevelopment and synaptic function and lead to manifestations of that disorder. We also consider the roles of mitochondrial abnormalities and nuclear mitochondrial interaction in autism pathogenesis.

Jay Gargus presents a review of the physiology and molecular genetics of ion channels, particularly the calcium ion channels. There is evidence that channelopathies play important roles in the etiology of specific monogenic disorders and in complex diseases, including seizures, migraine, and neurobehavioral disorders such as autism and bipolar disorder.

Availability of the human genomic sequence and of platforms for microarray analysis has dramatically altered our ability to analyze structural variation in the human genome and our approaches to diagnosis of cytogenetic abnormalities. Lisa Edelmann and Kurt Hirschhorn review these topics in their paper.

Advances in epigenetics and epigenomics are briefly considered in my paper summarizing the highlights the year. That contribution ends in a revisiting of the Duffy blood group antigen. The gene that encodes this antigen was the first gene mapped to a human autosome by Victor McKusick's research group 40 years ago. Recent research demonstrated that Duffy antigen functions as a cytokine receptor and that this receptor plays important roles in response to Plasmodium vivax malaria and HIV/AIDS.

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