Carol A. Wise · Jonathan J. Rios *Editors*

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Carol A. Wise
Sarah M. and Charles E. Seay Center for Musculoskeletal Research
Texas Scottish Rite Hospital for Children
Dallas
Texas
USA

Jonathan J. Rios
Sarah M. and Charles E. Seay Center for Musculoskeletal Research
Texas Scottish Rite Hospital for Children
Dallas
Texas
USA

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The editors thank the patients and families with pediatric orthopaedic disorders who have participated in research studies and furthered our understanding of their conditions.

Preface

Pediatric orthopaedic practice typically centers around a diverse array of heritable disorders. At one extreme end of the heritability spectrum are completely penetrant Mendelian disorders such as brachydactyly, where unaffected parents never have affected offspring. Described by Farabee in 1905, brachydactyly was the first published description of autosomal dominant inheritance of a human malformation (1). Even earlier, however, Galton described the concept of traits such as height that, although often lacking a clear transmission pattern in families, are still heritable to some degree (2). We of course now appreciate that there are significant genetic underpinnings in many non-traumatic childhood orthopaedic disorders, such as idiopathic scoliosis and talipes equinovarus (clubfoot), and that the care of such complex diseases typically represents the majority of pediatric orthopaedic practice. Finally, at the other extreme of the heritability spectrum is the startling discovery that completely non-heritable malformations such as macrodactyly, paradoxically, have genetic origins. Disease gene discovery for these disorders began, for all practical purposes, in the late 1980's and has since moved ahead with dizzying speed, driven in large part by technological advances. Such discoveries are enabling a new biochemical understanding of disease processes and, more importantly, informing the design of new treatments, as for example therapies that target the signaling pathways causing the troubling manifestations in neurofibromatosis (3).

The purpose of this volume is to update the pediatric orthopaedic community—clinicians, surgeons, geneticists, and researchers—on recent genetic developments relevant to the diverse presentations in these patients. We begin with an introduction to "next-generation" technologies that are enabling rapid gene discovery. We also present chapters describing post-gene discovery advancements for neurofibromatosis, various disorders of the joints, and basic bone development. Almost half of the volume is devoted to the complex disorders scoliosis and clubfoot and describes their classification, genetic contributions, and the exciting breakthrough in understanding genetic and environmental interactions. Finally we present the very recent discoveries of the mutations causing somatic, non-heritable, and all too devastating overgrowth malformations.

New insights into each of these areas are no doubt waiting in the wings, given the pace of discovery today. Our goal in this volume is to provide pediatric clinicians,

surgeons, geneticists, and researchers with a resource for understanding these emerging new developments as a means to advance the care of affected children.

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Contributors

Susan H. Blanton Department of Human Genetics, University of Miami, Miami, FL, USA

Sally L. Dunwoodie Developmental and Stem Cell Biology, Victor Chang Cardiac Research Institute, Sydney, NSW, Australia

Marybeth Ezaki Department of Orthopaedics, Texas Scottish Rite Hospital for Children, Dallas, TX, USA

Jerry Jian Q. Feng Biomedical Sciences, Baylor College of Dentistry, Dallas, TX, USA

Jacqueline T. Hecht Department of Pediatrics, University of Texas Health Science Center—Medical School and School of Dentistry, Houston, TX, USA

Mateusz Kolanczyk Campus Virchow Institut für Medizinische Genetik und Humangenetik, Neurofibromin in Skeletal Development, Charité Universitätsmedizin, Berlin, Germany

Shuxian Lin Biomedical Sciences, Baylor College of Dentistry, Dallas, TX, USA

Jonathan J. Rios Sarah M. and Charles E. Seay Center for Musculoskeletal Research, Texas Scottish Rite Hospital for Children, Dallas, TX, USA

Stephen P. Robertson Department of Women's and Children's Health, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand

Duncan B. Sparrow Developmental and Stem Cell Biology, Victor Chang Cardiac Research Institute, Sydney, NSW, Australia

David A. Stevenson Department of Pediatrics, Division of Medical Genetics, University of Utah, Salt Lake City, UT, USA

Peter D. Turnpenny Clinical Genetics, Royal Devon & Exeter Hospital, Exeter, UK

Katelyn S. Weymouth Department of Pediatrics, University of Texas Medical School, Houston, TX, USA

Carol A. Wise Sarah M. and Charles E. Seay Center for Musculoskeletal Research, Texas Scottish Rite Hospital for Children, Dallas, TX, USA

Departments of Orthopaedic Surgery, Pediatrics, and McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center, Dallas, TX, USA