
Preface

I was delighted when asked by John Walker whether I would be interested in editing a volume on the Wilms' tumor gene (WT1), for the distinguished Methods in Molecular Biology Series. However my first thought was to question whether a single gene would cover sufficient ground for a complete volume. I was heartened by the fact that similar successful volumes in the series had been compiled on other genes, notably p53. Also on further consideration I realized WT1 would be ideal. It is a multifunctional protein, mutations in which may lead to a variety of disorders in humans, including the eponymous pediatric kidney cancer, leukemia, gonadal dysgenesis, and occasionally diaphragmatic hernia and heart disease. WT1 is a key regulator of the development of a number of tissues, particularly those involving switches between mesenchymal-epithelial switches; in addition to the kidney, gonads, and heart it has been shown to mark and regulate stem/progenitors for visceral fat. Beyond its role in development, WT1 has been shown to be required for the homeostasis of a number of adult tissues and to be activated in tissue repair. WT1 is a zinc finger protein that clearly in part regulates all these cellular processes by functioning as a transcription factor. However an increasing body of evidence suggests that WT1 also regulates post-transcriptional processes by binding to RNA. What is more, two major WT1 splice isoforms differing by only three amino acids appear to have different relative roles in transcription and post-transcriptional processes. Finally, as WT1 is expressed in a number of adult epithelial tumors but not the healthy tissue counterparts immune cancer therapies against the protein are being trialed. All these facets ensure that WT1 is a rich source for methods chapters. The volume starts with three review chapters to set the scene. These cover the involvement of WT1 in pediatric cancer, kidney disease, and tissue development and homeostasis. These are followed by methods chapters, firstly on tools for studying developmental and cellular processes. These include chapters on cell marking and lineage tracing, epicardial cell methodology, colony forming assays for bone marrow stem cells, isolation of adipocyte progenitors using Fluorescence Activated Cell Sorting, methods for studying angiogenesis, and multiphoton imaging of lipids. All these chapters deal exclusively with mice and mouse tissues/cells. Zebrafish provide another valuable organism for studying Wt1 biology and function, so there is an overview of Wt1 in zebrafish followed by two valuable methods chapters on immunohistochemistry in zebrafish and isolation of kidney podocytes. The remaining methods chapters cover some of the latest tools in Genomics, Molecular Biology, and Biochemistry. These begin with methods for dissecting transcription factor function in cell-free systems and for measuring the binding constants of protein-nucleic acid interaction. These are followed by chapters on ChIP-Seq to identify transcriptional targets and methods for identifying WT1-interacting RNA and proteins. The final methods chapter describes bioinformatic approaches for analyzing Next Generation Sequence data. To round the volume off there is a chapter on Cancer Immune Therapy

based on antibodies to WT1. This is a combination of overview and some methodological detail. All the chapters are by experts in the field and I was delighted when everyone approached agreed to write a chapter. I thank the authors and editors and do hope the readers find this volume helpful.

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Methods and Protocols

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