

# Preface

Tremendous strides have been made in recent years in unraveling the aberrant biology driving renal carcinomas. These discoveries have led to unparalleled shifts in the treatment paradigm of this once devastating disease, historically known for its unrelenting progression of metastatic disease and high incidence of drug resistance and fatality. Rapidly emerging new therapeutic strategies that have the ability to neutralize this cancer have now engendered hope and optimism. In many instances, the speed of advances in clinical management has outpaced the biology, and observations made in the clinic using new therapeutics have fueled scientific discovery. In this way, renal cell carcinoma has truly served as a paradigm tumor type in the rapid flux of discovery from bench to bedside and back to the bench.

This textbook reviews and examines this enormously productive period with chapters touching on every major topic area in the modern era of renal carcinoma biology and treatment. Beginning with the discovery of the von Hippel Lindau (*VHL*) gene in 1993, we now understand on a more fundamental level the association of *VHL* mutation and the resultant HIF family stabilization as well as the intimate relationship this axis plays in the development of clear cell renal cell carcinoma. The unique and intricate genetics of this cancer are highly distinct from most other tumors, and the advances made in this cancer beyond *VHL* biology have been intrinsically driven by discoveries from familial renal cell carcinomas linked with newer large-scale genomic efforts in sporadic disease. The remarkable parallels of sporadic and familial diseases have enabled the elucidation of critical pathways in the renal tumorigenic process. These genetic findings fuel strategies to analyze and define sporadic tumors for greater accuracy in prognosis and prediction of response to therapy, the latest of which will be detailed in this text. Completing the circle, major new therapeutic strategies harness these biological discoveries, in particular angiogenic, energy metabolism, chromatin remodeling, tumor microenvironment, and classical signaling pathways. Many of these therapies have moved beyond management of metastatic disease to arenas in combination with surgical approach to advance the opportunities for durable remission or cure. This text will bring all of these avenues of investigation together for readers interested in understanding the

dynamics of this field in the last decade and anticipating a continued steep trajectory in advancements toward the cure of this disease in its many manifestations.

The field does continue to evolve at an enormously rapid pace. In addition to placing each of these major advances in historical context, the chapters in this textbook take a critical look forward to consider the future advances in each topic. The goal of this textbook is to educate the reader regarding the state of the art in renal cancer biology and therapeutic strategies as well as to engage readers as participants in an ongoing and exciting period of discovery and translation to advance the care of patients with renal cell carcinoma.

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