

# Preface

Androgens play an important role in the development and progression of prostate cancer, which is the most frequently diagnosed cancer and is the second leading cause of cancer death in US males. Androgen deprivation therapy (ADT) was developed by Dr. Charles Huggins in the 1940s and remains the standard treatment for metastatic prostate cancer. Unfortunately, patients treated with ADT eventually relapse with castration-recurrent or -resistant prostate cancer (CRPC), most within 2 years after ADT. The current treatment for CRPC includes docetaxel combined with prednisone, abiraterone, MDV3100, and enzalutamide. However, these treatments can only prolong the survival of patients by 3–5 months on average. There is an urgent need for new approaches to prevent and/or treat CRPC. The activation of androgen signaling in prostate tumor cells in patients on ADT is a key step leading to castration resistance. Understanding the mechanisms of androgen action and the roles of androgen signaling at different phases of prostate carcinogenesis and progression has significant clinical implications.

Androgen action is mediated through the androgen receptor (AR), a member of the nuclear steroid hormone receptor superfamily, which is an androgen-dependent transcription factor that regulates the expression of androgen-responsive genes. Identification and characterization of androgen-responsive genes and investigation of the mechanisms of their regulation by AR have enriched our understanding of androgen action at the molecular and cellular levels.

With this book, we hope to provide readers with up-to-date information on the regulation, function, and clinical relevance of androgen-responsive genes. Internationally recognized experts have summarized their current research in this volume. Several chapters address the mechanisms regulating the expression of androgen-responsive genes by AR, AR co-regulators, and cell signaling. These chapters also address the importance of androgen-responsive elements, AR binding, chromatin structure, and the dynamic interactions between AR and the nucleosomes. Another important topic in this book concerns the mechanisms of androgen-independent induction of androgen-responsive genes, and the role of AR overexpression and AR splicing variants. In addition, this book addresses the mechanisms of androgen regulations of cell signaling, cell–cell interactions,

epithelial–mesenchymal transition, and prostate cancer cell invasion. This book also describes the application of powerful technologies, such as RNAseq, microarray, and ChIPseq, in the identification and characterization of androgen-responsive coding and noncoding transcripts. Finally, this volume discusses the potential application of androgen-responsive genes in prostate cancer management.

The research on androgen-responsive genes in prostate cancer is moving rapidly, which makes it difficult to provide a comprehensive overview. This book is intended to provide a snapshot of the current status of research of androgen-responsive genes and provide the basis for further exploration of the role of androgen-responsive genes in prostate cancer.

Understanding of androgen signaling in prostate carcinogenesis remains incomplete, despite significant progresses in recent years. Many important questions need to be further addressed. For example, how does androgen stimulate prostate cancer cell proliferation? What are the genes mediating this important process? What are the alterations in androgen signaling during prostate carcinogenesis? Androgens are known to stimulate prostate luminal epithelial cell proliferation via a paracrine mechanism in the normal prostate. However, androgens stimulate prostate cancer cell proliferation by an intracrine mechanism mediated by AR within the prostate cancer cells. What are the mechanisms leading to the transition of androgen action from the paracrine mechanism in the normal prostate to the intracrine mechanism in prostate cancer? The information provided in this book will likely facilitate future research aimed to resolve these questions.

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