PREFACE

Androgens are widely recognized as essential elements for development and maintenance of the male phenotype. Over the years it has been demonstrated how androgen receptor (AR) mediates the physiological actions of androgens in distinct cells and tissues. However, novel perspectives are continuously being added to this field of study, with the identification of new AR variants, discovery and development of natural and synthetic AR-agonists and antagonists, and the extension of a myriad of target-genes composing the AR-gene network, as well as, with the disclosure of additional peculiarities of AR structure and signaling pathways.

The majority of information on AR functions and mechanisms of action has been produced and systematically organized in mammals. However, non-mammalian vertebrates present a greater diversity in the number of *AR* genes and type of AR ligands. The first chapter of this book discusses the gene and protein structure, mechanism of action, ligands, tissue distribution and physiological effects of AR in fish, birds, amphibians and reptiles comparatively with the information available in mammals, highlighting for the changes that have occurred across vertebrate evolution.

The molecular biology of AR complies the existence of variants generated by alternative splicing mechanisms, which have been essentially characterized in pathological conditions, such as prostate cancer and androgen insensitivity syndromes. Recently, naturally occurring variants of AR were identified, which could have a profound impact in AR signaling mechanisms under non-pathological conditions as revealed in Chapter 2.

The next three sections of the book explore the structural and functional aspects of AR in the context of disease. The AR has been defined as a major therapeutic target in androgen-related diseases and the elucidation of crystal

structures of AR ligand-binding domain harboring natural or synthetic androgens opens new windows to modulate the mechanism of action of AR in a tissue- or disease-specific manner (Chapter 3). Overexpression of AR protein, the existence of AR mutations and the presence of alternatively spliced forms of AR are common events associated with prostate cancer onset and progression. On the other hand, detailing the AR signaling pathways and identifiying the genes downstream of AR transcriptional activity are crucial aspects to disclose the role of AR in prostate cancer, providing valuable clues for development of alternative and more effective therapeutic options (Chapters 4 and 5).

Untranslated regions regulate the life-time, location and translation rate of mRNA molecules and thus, common motifs and putative regulatory regions should be found in proteins that function in a common network. Chapter 6 starts pointing the role of AR untranslated regions defining the AR-gene network in diseases such as spinal and bulbar muscular atrophy, androgen insensitivity and cancer, as well as, in brain and sexual development.

Although extensive scientific reports exist establishing the role of androgens and AR in male physiology, actually it is also accepted that androgens may regulate female reproductive function as is demonstrated in the last chapter of this book.

It is expected that the present book will be a valuable resource for those interested in understand the AR molecule and the mechanisms underlying its action in the context of normal physiology and disease. Acknowledging to all of the authors for contributing their time and expertise, it is also aspired that this publication will support the progress of scientific research in this field throughout the foreseeable future.