
Preface

The thyroid hormone receptors (TRs) are important regulators of a large number of biological processes in animal and human physiology. They play a major role in brain development, in the development of hearing, in maturation of bone growth, in amphibian morphogenesis, in the regulation of metabolic rate, in the differentiation of the intestine, in the control of heart rate, and in development of vertebrate photoreceptors and color vision. Aberrant functions of TRs induce tremendous defects in these pathways, including the human disease of Resistance to Thyroid Hormone, which is a genetically autosomal dominant inherited syndrome that is caused by mutations in the gene encoding the TR β . The TRs are hormone-controlled intracellular regulators and thus the analyses of their mechanisms of action will contribute to our understanding of their physiology on the molecular level.

The aim of *Thyroid Hormone Receptors: Methods and Protocols* is to cover the major area of TR research and to offer an overview, as well as practical experimental details, of the major methods in the field for both newcomers and experienced researchers. The book will cover the up-to-date methodology for the diverse topics of TR research. Hereby, an introduction to each topic precedes several methods associated with the analysis of the specific research area. The topics include the analysis of heart rate, amphibian morphogenesis, and transcriptional regulation by TRs in cell-free systems, as well as in living cells. Also, the isolation of TR-regulated protein complexes, the functional role of TRs in vertebrates, and the analysis of the oncogene *v-erbA* in blood cell differentiation are described in this book. Additionally included are target gene analysis in brain and liver by various approaches, among them being detailed methods for microarray chip analysis to identify TR-target genes in liver.

The large spectrum of methods described here includes the generation of knockout mice, transgenic mice, transgenic *Xenopus*, and the use of the *Xenopus* system for analyses on the molecular and chromatin levels. Furthermore, microarray chip analysis, *in situ* hybridization, the *in vitro* transcription system, chromatin immunoprecipitation, baculovirus expression system, and various DNA transfer methods for cells and cell lines are described. In addition, methodology is presented for the isolation of *in vivo* protein complexes

involved in TR-mediated gene control, the analysis of regulated chromatin and its hormonal regulation, the use of retroviral systems and primary blood cell culture, and heart rate measurements. Furthermore, the generation of null-mutant, transgenic mice and of *Xenopus*, the identification of mutant TRs from patients with RTH syndrome, and the functional analyses of these TRs are described. All these methods are provided, as in other Humana Press Methods in Molecular Biology titles, in a richly detailed manner including a Notes section.

Thus, *Thyroid Hormone Receptors: Methods and Protocols* covers all major topics and includes all the important methods of up-to-date research on thyroid hormone receptor biology. TRs play a most diverse role in animal physiology, one that is correlated with a nearly incomparable spectrum of approaches. Therefore, the various TR functions are being analyzed in different systems for a variety of purposes by both scientists and medical doctors. Subsequently, each specific system and approach to analyze TR functionality is associated with a specific spectrum of various methods. Therefore, to fulfill the reader's expectation of a book covering all major TR research topics with their corresponding methodology, our book is structured with sections devoted to specific topics. Each chapter provides an overview of a specific topic and the system analyzed, discussion of its potential to gain new insights into TR functionality, and, in great detail, the associated spectrum of methods. Therefore, the particularity of this book is that each chapter describes several specific methods required to analyze TR function within a specific TR-regulated biological process.

Thyroid Hormone Receptors: Methods and Protocols is suitable for both basic and applied researchers, including physicians, pharmacologists, technicians, and pathophysiologists working in the field of molecular endocrinology and TR-action. Since thyroid hormone receptors are members of the large supergene-family of nuclear hormone receptors, the methodology provided here may be of great value also to the investigation of other members of these hormone-controlled regulators.

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