
Preface

The past decade has ushered in enormous changes in how we perceive and study changes in gene expression in the heart. Early in the 1990s, the human genome project was just getting underway and establishing methods with the sensitivity to measure changes in the expression of genes with low copy number was an accomplishment. We all experienced some trepidation when the first news of microarrays arrived espousing the ability to measure changes in expression of hundreds to tens of thousands of genes (the whole genome) at once. This high throughput method was an astonishing jump in our approach to biological science. At the same time Steve Fodor and Pat Brown published papers describing two completely different approaches to measuring the expression changes of large numbers of genes at the same time. Thus began the microarray era and as a consequence the beginning of an era with a host of new approaches in pursuit of understanding the role and regulation of gene expression in cell biology and pathology including driving forward the field of bioinformatics.

The array, no pun intended, of contributions contained in *Cardiac Gene Expression: Methods and Protocols* an edition of Humana's Methods in Molecular series, address both new and established methods that researchers in the cardiac field will certainly find useful as a reference for the development of projects and training. Our aim in this compilation was to provide insight and details for a comprehensive range of methods that will serve both startup and sophisticated users alike. Sections cover expression profiling by microarray Section I, targeted analysis of gene expression (Section II), transcription factor DNA binding and regulation of promoter activity (Section III), *in silico* approaches to identifying functional *cis* regulatory elements and regulation of cardiac gene expression (Section IV), *in silico* and mass spectrometry methods to identify sequence nucleotide polymorphisms (SNPs) (Section V), and to bring findings from the above studies to the next level overexpression of genes *in vivo* and isolated myocytes and cardiac-specific targeted gene deletion (Section VI).

Section I, Cardiac Gene Expression Profiling: the Global Perspective. Five chapters describe several different approaches to examining and identifying changes in gene expression in the transcriptome as well as analytic approaches. Methods and analysis have improved significantly as many investigators have strived to increase array reliability and reproducibility. Section II, Cardiac Gene Regulation: Gene-Specific mRNA Measurement in the Myocardium, follows accordingly with chapters outlining more sensitive and gene targeted expression methods that are more conducive for follow up studies to verify and fur-

ther characterize those important findings from array experiments or those of your favorite gene. Underlying mechanisms of gene regulation can be studied using methods that focus on the interaction of transcription factors with their cognate *cis* binding elements and how these *cis* elements impact overall promoter activity in Section III, Cardiac Gene Regulation: Promoter Characterization in the Myocardium. Changes in gene expression reflect the combined effects of transcriptional enhancers and repressors that serve to precisely control the level of expression of thousands of genes from conception to death. Studies that focus on how the interaction between transcription factors and their cognate *cis* DNA elements regulate gene expression were provided some assistance recently with the completion of the Human Genome Project in 2003 in addition to several other genomes with more coming available at a rapid pace. New analytical approaches to decipher the functional elements buried in the 3 billion nucleotides of the human genome and other model genomes are described in Sections IV, *In Silico* Assessment of Regulatory *cis*-Elements and Gene Regulation, and V, Cardiac Single Nucleotide Polymorphisms. One important aspect of understanding the importance of available sequence is being able to sift through sequence and reliably identify and distinguish functional regulatory elements from nonfunctional elements. Pennachio and colleagues at Lawrence Livermore Labs have simplified this task by using a comparative approach. By using available genome sequence for several different species across evolution this approach was able to reliably predict the functionality of elements according to their evolutionary conservation. Resources for the analysis of gene regulation data and SNPs will provide essential functionality for the understanding of changes in gene expression and effects of SNPs on gene function and expression. With the identification of exciting new targets one begins to think of the functional aspects and begins to plan experiments to validate hypotheses. Section VI, Gene Overexpression and Targeting in the Myocardium, highlights methods that facilitate overexpression or cardiac specific targeted deletion of your favorite gene in the heart

Thus, this array of contributions provides an array of methods that will take the investigator through screening, analysis, characterization, and functional confirmation of novel genes or old genes with a new function serving as a template for a solid research program.

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Cardiac Gene Expression

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