



Gene Discovery for Disease Models

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This book provides readers with new paradigms on the mutation discovery in the post-genome era. The completion of human and other genome sequencing, along with other new technologies, such as mutation analysis and microarray, has dramatically accelerated the progress in positional cloning of genes from mutated models. In 2002, the Mouse Genome Sequencing Consortium stated that “The availability of an annotated mouse genome sequence now provides the most efficient tool yet in the gene hunter's toolkit. One can move directly from genetic mapping to identification of candidate genes, and the experimental process is reduced to PCR amplification and sequencing of exons and other conserved elements in the candidate interval. With this streamlined protocol, it is anticipated that many decades-old mouse mutants will be understood precisely at the DNA level in the near future.” The implication of such a statement should be similar to the identification of mutated genes from human diseases and animal models, when genome sequencing is completed for them. More than five years have passed, but genes in many human diseases and animal models have not yet been identified. In some cases, the identification of the mutated genes has been a bottleneck, because the genetic mechanism holds the key to understand the basis of the diseases. However, an integrative strategy, which is a combination of genetic mapping, genome resources, bioinformatics tools, and high throughput technologies, has been developed and tested. The classic paradigm of positional cloning has evolved with completely new concepts of genomic cloning and protocols. This book describes new concepts of gene discovery in the post-genome era and the use of streamlined protocols to identify genes of interest. This book helps identify not only large insertions/deletions but also single nucleotide mutations or polymorphisms that regulate quantitative trait loci (QTL).

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