



Gene Knockout Protocols (Methods in Molecular Biology)

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Following the completion of the mouse and human genome sequences, a major challenge is the functional characterization of every mammalian gene and the deciphering of their molecular interaction network. The mouse offers many advantages for the use of genetics to study human biology and disease, unmatched among other mammals. Its development, body plan, physiology, behavior, and diseases have much in common, based on the fact that 99% of the human genes have a mouse ortholog. The investigation of gene function using mouse models is based on many years of technological development. In the two decades since gene targeting in murine embryonic stem (ES) cells was first described by Mario Capecchi and colleagues, more than 3000 predesigned mouse mutants have been developed. To date, a variety of mouse mutagenesis techniques, either gene- or phenotype-driven, are used as systematic approaches. The availability of the genome sequence supports gene-driven approaches such as gene-trap and targeted mutagenesis in ES cells, allowing efficient and precise gene disruption. In combination with the use of site-specific DNA recombinases, in particular the Cre/loxP system, gene disruption can be directed to specific cell types in conditional mouse mutants. Furthermore, chemical and transposon mutagenesis of the mouse genome enables us to perform phenotype-driven screens for the unbiased identification of phenotype-genotype correlations involved in models of human disease. Over the next several years, the mouse genome will be systematically altered, and the techniques for achieving predesigned manipulations will be constantly developed further and improved. The second edition of Gene Knockout Protocols brings together distinguished contributors with extensive experience in the gene targeting and mouse genetics fields.

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