

**Methods in Molecular Biology™**

**VOLUME 195**

# **Quantitative Trait Loci**

*Methods and Protocols*

*Edited by*

**Nicola J. Camp  
Angela Cox**



**HUMANA PRESS**

# Quantitative Trait Loci Methods And Protocols

**Jeff Braman**



## **Quantitative Trait Loci Methods And Protocols:**

**Quantitative Trait Loci** Nicola J. Camp,Angela Cox,2008-02-03 In *Quantitative Trait Loci Methods and Protocols* a panel of highly experienced statistical geneticists demonstrate in a step by step fashion how to successfully analyze quantitative trait data using a variety of methods and software for the detection and fine mapping of quantitative trait loci QTL Writing for the nonmathematician these experts guide the investigator from the design stage of a project onwards providing detailed explanations of how best to proceed with each specific analysis to find and use appropriate software and to interpret results Worked examples citations to key papers and variations in method ease the way to understanding and successful studies Among the cutting edge techniques presented are QTDT methods variance components methods and the Markov Chain Monte Carlo method for joint linkage and segregation analysis *Quantitative Trait Loci (QTL)* Scott A. Rifkin,2012-05-09 Over the last two decades advances in genotyping technology and the development of quantitative genetic analytical techniques have made it possible to dissect complex traits and link quantitative variation in traits to allelic variation on chromosomes or quantitative trait loci QTLs In *Quantitative Trait Loci QTLs Methods and Protocols* expert researchers in the field detail methods and techniques that focus on specific components of the entire process of quantitative trait loci experiments These include methods and techniques for the mapping populations identifying quantitative trait loci extending the power of quantitative trait locus analysis and case studies Written in the highly successful *Methods in Molecular Biology*™ series format the chapters include the kind of detailed description and implementation advice that is crucial for getting optimal results in the laboratory Thorough and intuitive *Quantitative Trait Loci QTLs Methods and Protocols* aids scientists in the further study of the links between phenotypic and genotypic variation in fields from medicine to agriculture from molecular biology to evolution to ecology **Methods in Molecular Biology: Quantitative trait loci: methods and protocols** John M. Walker,1984 **Quantitative Trait Loci** Nicola J. Camp,Angela Cox,2002-04-26 In *Quantitative Trait Loci Methods and Protocols* a panel of highly experienced statistical geneticists demonstrate in a step by step fashion how to successfully analyze quantitative trait data using a variety of methods and software for the detection and fine mapping of quantitative trait loci QTL Writing for the nonmathematician these experts guide the investigator from the design stage of a project onwards providing detailed explanations of how best to proceed with each specific analysis to find and use appropriate software and to interpret results Worked examples citations to key papers and variations in method ease the way to understanding and successful studies Among the cutting edge techniques presented are QTDT methods variance components methods and the Markov Chain Monte Carlo method for joint linkage and segregation analysis *In Vitro Mutagenesis Protocols* Jeff Braman,2008-02-05 Hands on researchers with proven track records describe in stepwise fashion their advanced mutagenesis techniques The contributors focus on improvements to conventional site directed mutagenesis including a chapter on chemical site directed mutagenesis PCR based mutagenesis and the modifications that allow high

throughput mutagenesis experiments and mutagenesis based on gene disruption both in vitro and in situ based Additional methods are provided for in vitro gene evolution for gene disruption based on recombination transposon and cassette mutagenesis and for facilitating the introduction of multiple mutations Time tested and highly practical the protocols in In Vitro Mutagenesis Protocols 2nd Edition offer today s molecular biologists reliable and powerful techniques with which to illuminate the proteome

**Superantigen Protocols** Teresa Krakauer, 2008-02-05 Leading researchers in the biological chemical and physical investigation of superantigens describe in step by step detail their best experimental techniques to assess the physical characteristics and biological effects of superantigens Their protocols range from those for investigating the interactions of superantigens with cellular receptors to those for the analysis of their immunological and biological effects including methods for using BIOcore to determine binding kinetics and establishing various lymphocyte cell culture systems There are also accounts of such methods as the RNase protection assay cytokine ELISA FACS analysis and cytokine production at the single cell level

**DNA Methylation Protocols** Ken I. Mills, Bernie H. Ramsahoye, 2008-02-05 DNA Methylation Protocols offer a set of readily reproducible protocols of the analysis of DNA methylation and methylases These powerful methods provide the tools necessary for studying methylation at both the global level and the level of sequence and include many techniques for identifying genes that might be aberrantly methylated in cancer and aging Additional methods cover genome wide analysis of abnormal DNA methylation and the isolation and measurement of demethylases and related proteins

**MHC Protocols** Stephen H. Powis, Robert W. Vaughan, 2008-02-05 The aim of MHC Protocols is to document protocols that can be used for the analysis of genetic variation within the human major histocompatibility complex MHC HLA region The human MHC encompasses approximately 4 million base pairs on the short arm of chromosome 6 at cytogenetic location 6p21.3 The region is divided into three subregions The telomeric class I region contains the genes that encode the HLA class I molecules HLA A B and C The centromeric class II region contains the genes encoding the HLA class II molecules HLA DR DQ and DP In between is the class III region originally identified because it contains genes encoding components of the complement pathway The entire human MHC has recently been sequenced and each subregion is now known to contain many other genes a number of which have immunological functions The study of polymorphism within the MHC is well established because the region contains the highly polymorphic HLA genes HLA polymorphism has been used extensively in solid organ and bone marrow transplantation to match donors and recipients As a result large numbers of HLA alleles have been identified a process that has been further driven by recent interest in HLA gene diversity in ethnic populations The extreme genetic variation in HLA genes is believed to have been driven by the evolutionary response to infectious agents but relatively few studies have analyzed associations between HLA genetic variation and infectious disease which has been difficult to demonstrate

**Biostatistical Methods** Stephen W. Looney, 2008-02-03 Leading biostatisticians and biomedical researchers describe many of the key techniques used to solve commonly occurring data analytic problems in molecular

biology and demonstrate how these methods can be used in the development of new markers for exposure to a risk factor or for disease outcomes Major areas of application include microarray analysis proteomic studies image quantitation genetic susceptibility and association evaluation of new biomarkers and power analysis and sample size

**Calcium-Binding Protein Protocols** Hans J. Vogel, 2008-02-04 Calcium plays an important role in a wide variety of biological processes This divalent metal ion can bind to a large number of proteins by doing so it modifies their biological activity or their stability Because of its distinct chemical properties calcium is uniquely suited to act as an on off switch or as a light dimmer of biological activities The two books entitled Calcium Binding Protein Protocols Volumes I and II focus on modern experimental analyses and methodologies for the study of calcium binding proteins Both extracellular and intracellular calcium binding proteins are discussed in detail However proteins involved in calcium handling e.g. calcium pumps and calcium channels fall outside of the scope of these two volumes Also calcium binding proteins involved in bone deposition will not be discussed as this specific topic has been addressed previously The focus of these two books is on studies of the calcium binding proteins and their behavior in vitro and in vivo The primary emphasis is on protein chemistry and biophysical methods Many of the methods described will also be applicable to proteins that do not bind calcium Calcium Binding Protein Protocols is divided into three main sections The section entitled Introduction and Reviews provides information on the role of calcium in intracellular secondary messenger activation mechanisms Moreover unique aspects of calcium chemistry and the utilization of calcium in dairy proteins as well as calcium binding proteins involved in blood clotting are addressed

**Transgenesis Techniques** Alan R. Clarke, 2008-02-05 The past decade has witnessed a spectacular explosion in both the development and use of transgenic technologies Not only have these been used to aid our fundamental understanding of biologic mechanisms but they have also facilitated the development of a range of disease models that are now truly beginning to impact upon our approach to human disease Some of the most exciting model systems relate to neurodegenerative disease and cancer where the availability of appropriate models is at last allowing radically new therapies to be developed and tested This latter point is of particular significance given the current concerns of the wider public over both the use of animal models and the merits of using genetically modified organisms Arguably advances of the greatest significance have been made using mammalian systems driven by the advent of embryonic stem cell based strategies and more recently by cloning through nuclear transfer For this reason this new edition of Transgenesis Techniques focuses much more heavily on manipulation of the mammalian genome both in the general discussions and in the provision of specific protocols

**Epithelial Cell Culture Protocols** Clare Wise, 2008-02-05 There have been significant advances in research involving the isolation and culture of epithelial cells in the past decade and many new techniques have been developed Monolayer cultures can be used to evaluate the nature and behavior of cells while the use of epithelial cells in model systems has allowed a deeper understanding of cellular and molecular mechanisms and interactions The aim of this book is to provide a comprehensive step by step guide to many

techniques for epithelial cell culture combining in one volume the more commonly used protocols along with many that are more specialized Epithelial Cell Culture Protocols should help those who are new to this field and want to learn the basic culture techniques as well as those needing to use more wide ranging and specific protocols It should be a useful resource on its own and also complement the other volumes that have been written about cell culture in the Methods in Molecular Biology series Epithelial Cell Culture Protocols covers a wide variety of protocols mostly aimed at the researcher but also a few aimed at clinicians The establishment and maintenance of primary cultures derived from many different tissues and different species is covered Particular emphasis has been placed on protocols needed to further analyze and assess epithelial cells for example by looking at apoptosis and integrins and by measuring membrane capacitance and confluence Using different coculture techniques it is possible also to develop models to investigate many different systems in vitro

**Functional Genomics** Michael J. Brownstein, Arkady Khodursky, 2008-02-03 This collection of robust readily reproducible methods for microarray based studies includes expert guidance in the optimal data analysis and informatics On the methods side are proven techniques for monitoring subcellular RNA localization en masse for mapping chromosomes at the resolution of a single gene and for surveying the steady state genome wide distribution of DNA binding proteins in vivo For those workers dealing with massive data sets the book discusses the methodological aspects of data analysis and informatics in the design of microarray experiments the choice of test statistic and the assessment of observational significance data reduction and clustering

**PCR Cloning Protocols** Bing-Yuan Chen, Harry W. Janes, 2008-02-05 PCR Cloning Protocols Second Edition updates and expands Bruce White's best selling PCR Cloning Protocols 1997 with the newest procedures for DNA cloning and mutagenesis Here the researcher will find readily reproducible methods for all the major aspects of PCR use including PCR optimization computer programs for PCR primer design and analysis and novel variations for cloning genes of special characteristics or origin with emphasis on long distance PCR and GC rich template amplification Also included are both conventional and novel enzyme free and restriction site free procedures to clone PCR products into a range of vectors as well as state of the art protocols to facilitate DNA mutagenesis and recombination and to clone the challenging

uncharacterized DNA flanking a known DNA fragment **Capillary Electrophoresis of Carbohydrates** Pierre Thibault, Susumu Honda, 2008-02-03 A collection of cutting edge techniques for using capillary electrophoresis CE to analyze complex carbohydrates These readily reproducible protocols provide methods for sample preparation analysis of mono and oligosaccharides glycoproteins and glycoconjugates A useful appendix describes the structures of the most commonly encountered carbohydrate residues and oligosaccharides from mammalian and bacterial origins Each protocol contains detailed information on reagents apparatus notes comments and tips on procedures

**Cardiac Cell and Gene Transfer** Joseph M. Metzger, 2008-02-03 Heart disease is the leading cause of death in developed countries Recent experimental advances featuring cellular molecular and genetic tools and technologies offer the potential for new therapeutic strategies



directed toward remediation of inherited and acquired heart diseases Whether these recent basic science advances will ultimately translate to clinical efficacy for patients with heart disease is unknown and is important to ascertain Cardiac Cell and Gene Transfer Principles Protocols and Applications is designed to provide the reader with up to date coverage of a myriad of specific methodologies and protocols for gene and cell transfer to the myocardium Each chapter features a Notes section that provides useful how to problem solving insights that are often left unstated in standard published protocols Cardiac Cell and Gene Transfer Principles Protocols and Applications addresses principles and applications of cell and gene transfer to the heart including protocols for vector production and purification Detailed step by step methods and applications for first second generation adenoviral vectors adeno associated vectors gutted adenoviral vectors and lentiviral vectors are included Additionally detailed methods for cardiac cell grafting and transplantation are provided and these chapters highlight the prospects of cell based therapies for cardiac repair The book also covers specific in vivo techniques for cardiac gene transfer and specifies subsequent cellular and organ level physiological assessment techniques and protocols Accordingly this book is designed for basic science and clinical researchers in the academic pharmaceutical and biotechnology sectors of the cardiovascular community **GTPase Protocols** Ed Manser, Thomas Leung, 2008-02-03

In the last 10 years researchers have firmly established key roles for Ras related GTPases in almost every aspect of cell biology In the 1980s the proto oncogene Ras itself was the focus of interest though in the 1990s this shifted to the increasing variety of Ras related proteins In this new decade much yet needs to be done to establish the role for all the small GTPases now uncovered by the human genome project In particular these GTPases need to be understood in the appropriate biochemical and cellular contexts In the process of trying to uncover the role of these versatile proteins a variety of novel techniques and methodologies has been developed These now enable investigators to move easily within a diversity of fields ranging from structural studies to real time in vivo analysis of a GTPase In recognition of the need for access to key background methodologies GTPase Protocols The Ras Superfamily is devoted to techniques that are presently widely used and that will continue to be the standard for researchers worldwide Each chapter is aimed at supplying detailed methodologies to allow reproduction in any laboratory while also providing the general principles on which the methods are based Some of the techniques grouped in the first section apply broadly to small GTPases whereas others in Part II are more applicable within each GTPase subfamily

**Tumor Suppressor Genes** Wafik S. El-Deiry, 2008-02-03 It has become clear that tumors arise from excessive cell proliferation and a corresponding reduction in cell death Tumors result from the successive accumulation of mutations in key regulatory target genes over time During the 1980s a number of oncogenes were characterized whereas from the 1990s to the present the emphasis shifted to tumor suppressor genes TSGs It has become clear that oncogenes and tumor suppressor genes function in the same pathways providing positive and negative growth regulatory activities The signaling pathways controlled by these genes involve virtually every process in cell biology including nuclear events cell cycle cell death

cytoskeletal cell membrane angiogenesis and cell adhesion effects Tumor suppressor genes are mutated in hereditary cancer syndromes as well as somatically in nonhereditary cancers In their normal state TSGs control cancer development and progression as well as contribute to the sensitivity of cancers to a variety of therapeutics Understanding the classes of TSGs the biochemical pathways they function in and how they are regulated provides an essential lesson in cancer biology We cannot hope to advance our current knowledge and to develop new and more effective therapies without understanding the relevant pathways and how they influence the present approaches to therapy Moreover it is important to be able to access the powerful tools now available to discover these genes as well as their links to cell biology and growth control

Protein Sequencing Protocols Bryan John Smith, 2008-02-02 Determination of the protein sequence is as important today as it was a half century ago even though the techniques and purposes have changed over time Mass spectrometry has continued its recent rapid development to find notable application in the characterization of small amounts of protein for example in the field of proteomics The traditional chemical N terminal sequencing is still of great value in quality assurance of the increasing number of biopharmaceuticals that are to be found in the clinic checking processing events of recombinant proteins and so on It is joined in the armory of methods of protein analysis by such techniques as C terminal sequencing and amino acid analysis These methods are continually developing The first edition of Protein Sequencing Protocols was a snapshot of methods in use in protein biochemistry laboratories at the time and this the second edition is likewise Methods have evolved in the intervening period and the content of this book has similarly changed the content of some chapters having been superseded and replaced by other approaches Thus in this edition there is inclusion of approaches to validation of methods for quality assurance work reflecting the current importance of biopharmaceuticals and also a guide to further analysis of protein sequence information acknowledging the importance of bioinformatics

### **Molecular Cytogenetics**

Yao-Shan Fan, 2008-02-05 The new techniques of molecular cytogenetics mainly fluorescence in situ hybridization FISH of DNA probes to metaphase chromosomes or interphase nuclei have been developed in the past two decades Many FISH techniques have been implemented for diagnostic services whereas some others are mainly used for investigational purposes Several hundreds of FISH probes and hybridization kits are now commercially available and the list is growing rapidly FISH has been widely used as a powerful diagnostic tool in many areas of medicine including pediatrics medical genetics maternal fetal medicine reproductive medicine pathology hematology and oncology Frequently a physician may be puzzled by the variety of FISH techniques and wonder what test to order It is not uncommon that a sample is referred to a laboratory for FISH without indicating a specific test On the other hand a cytogeneticist or a technologist in a laboratory needs from case to case to determine which procedure to perform and which probe to use for an informative result To obtain the best results one must use the right DNA probes and have reliable protocols and measures of quality assurance in place Also one must have sufficient knowledge in both traditional and molecular cytogenetics as well as the particular areas of medicine for which the



test is used in order to appropriately interpret the FISH results and to correlate them with clinical diagnosis treatment and prognosis

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