Statistical Genetics: Gene Mapping Through Linkage and Association

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This book was conceived at the 2005 methodology workshop in Boulder, Colorado. Its purpose was to provide background reading and a working text for students and researchers being introduced to the principles and practice of linkage and association analysis in the context of twin and family studies of complex traits, including behavioral and psychological traits. It is edited by four of the most interesting and dynamic young researchers in the field, and authored by them and a roster of 25 additional world class experts in statistical, behavioral, and psychiatric genetics.

The methodology workshops are part of a series that began in Leuven, Belgium, in 1987, and are now regularly held in Boulder, Colorado, supported by a grant from the US National Institute of Mental Health. These workshops have resulted in the publication of two textbooks and two special editions of the journal Behavior Genetics, one following the inaugural workshop and emphasizing the analysis of twin data (Martin, Boomsma, & Neale, 1989), and one focusing on variance components methods for quantitative trait loci (QTL) analysis (Cherny, Sham, & Cardon, 2004). The first workshop textbook, Methodology for genetic studies of twins and families (Neale & Cardon, 1992), written by the faculty, focused on biometrical genetics and structural equation modeling and became the standard reference in the area. A recent revision (Neale & Maes, 2004) is downloadable free of charge at http://ibgwww.colorado.edu/workshop2006/cdrom/HTML/BOOK.HTM

The new book, *Statistical Genetics: Gene mapping Through Linkage and Association*, has its own supporting web site at http://www.genemapping.org/. The contents of the 22 chapters correspond to a full curriculum on human linkage and association studies: 1. Introduction, 2. The basics of DNA and genotyping, 3. Introduction to biometrical genetics, 4. Introduction to statistics, 5. Statistical power, 6. Population genetics and its televance to gene mapping, 7. Principles of linkage Analysis, 8. IBD estimation, 9. Regression methods for linkage analysis, 10. Variance components linkage Analysis for quantitative traits, 11. Extensions to univariate linkage analysis, 12. QTL Detection in multivariate data from sibling pairs, 13. Factors affecting Type I error and power of linkage analysis, 14. Introduction to association, 15. Single-locus association models, 16. Genome-wide association, 17. Haplotype estimation, 18. Multi-locus association models, 19. linkage disequilibrium and tagging, 20. Haploview, 21. Factors affecting Type I error and power in association, and 22. Resampling approaches to statistical interference.

Each chapter is written by specialists to give an overview of the topic, as well as hands-on guidance and program scripts where appropriate. The first six chapters provide an orientation to the subject, including the basic information about DNA and genotyping, biometrical genetics, statistics, power, and population genetics, that underlies the study of QTL. These background chapters are followed by seven chapters on linkage methods, and then eight chapters on association methods, with a final chapter on statistical inference that uses randomization or permutation tests as a more flexible alternative to traditional parametric tests. Together these chapters provide a thorough introduction to both the theory and practice of statistical genetic analysis for complex traits in human families. The style throughout is didactic and pitched at a level that anyone serious about wanting this information will find accessible. Because the authors are practicing researchers in the field, and in many cases have written the analysis packages that are being discussed, the tone of the chapters is relaxed but authoritative. Topics are not necessarily treated exhaustively, but rather the reader is given enough information to get started, and enough guidance to have a grasp of the kinds of pitfalls and errors that he or she might encounter along the way. This is a book that will stimulate readers to want to explore the subject more, and to apply the methods learned to their own research. To help with this, there is additional guidance on further reading and web based resources, including software and program scripts. And, of course, there is always the opportunity to attend one of the workshops. Information about the workshops can be found at http://ibgwww.colorado.edu/workshop2008/.

In sum, this book is well organized and is written and edited by enthusiastic experts. It will be a great starting place for anyone who wants to understand and, hopefully, get involved with research on the genetics of human complex traits.