

“Computational Genomics in the GWAS Era”

Marylyn Ritchie, PhD

Associate Professor, Molecular Physiology & Biophysics
Director, Program in Computational Genomics
Center for Human Genetics Research
Vanderbilt University

The identification and characterization of susceptibility genes for common complex human diseases is a difficult challenge. One primary difficulty is that many susceptibility genes exhibit effects that are partially or solely dependent on interactions with other genes. In addition, the focused study of one or a few candidate genes alone limits our ability to identify novel genetic effects associated with disease. Whole-genome association has been proposed as a solution to these problems; however, the analysis of whole genome data is problematic because we must separate the one or a few true, but modest, signals from the extensive background noise.

Recent technological advances enable genotyping hundreds of thousands of human single-nucleotide polymorphisms at the population level. Because strategies for analyzing these data have not kept pace with the laboratory methods that generate the data it is unlikely that these technological advances will immediately lead to an improved understanding of the genetic contribution to common human disease. Currently, no single analytical method can extract even a reasonable portion of the total available information from a whole-genome association study. In fact, no single method can be optimal for all datasets, since the genetic architecture for diseases varies substantially and in unknown ways. Therefore, an integrative platform is needed that accommodates multiple analytical methods to maximize our information extraction and thus maximize our chances of dissecting complex genetic architectures. We propose a system for the analysis of genome-wide association data that will incorporate multiple analytical approaches as filters to allow a scientist to choose whatever analytical methods they wish to apply. This is crucial due to the number of novel methods being developed and the current inability to integrate these methods in a cohesive manner.