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101 Biochemistry

Understanding the biochemical effects of nonsynonymous SNPs and mutations

Research in the Mooney Laboratory

We are developing computational methods for automatically annotating genomic data with information that is useful to researchers for understanding how variation (genetic differences between individuals) affect molecular and clinical phenotypes and disease. Single nucleotide polymorphisms (SNPs) are the most common form of genetic variation, and the distribution and function of SNPs is an important area of current research. There are now more than five million validated SNPs in the human genome, and many more pending validation. As linkage disequilibrium and genome wide approaches become more common for genetic association, understanding the biochemical effects of SNPs becomes increasingly important. SNPs can give rise to many molecular effects, including changes in gene expression, splicing and protein product function. Currently, the most effort has been spent characterizing the SNPs that result in an amino acid substitution. This is primarily because mutations in human proteins cause a wide spectrum of diseases and phenotypes and many of these mutations have been studied extensively. We now understand many of the basic biochemical functions these mutations disrupt, thereby leading to a clinical observation. Understanding within the context of a specific patient how a mutation causes biochemical changes that lead to a disease is a formidable problem that will require years, perhaps decades, to unravel. In this talk, I will give an overview of our efforts to develop and apply bioinformatics methods to identify functional sites in proteins and to hypothesize the disruption of protein structure and function of both inherited and somatic mutations in human diseases. I will also include some discussion of our efforts to build informatics systems to enable translational approaches such as genetic, pharmacogenetic, and gene therapy studies.

References

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