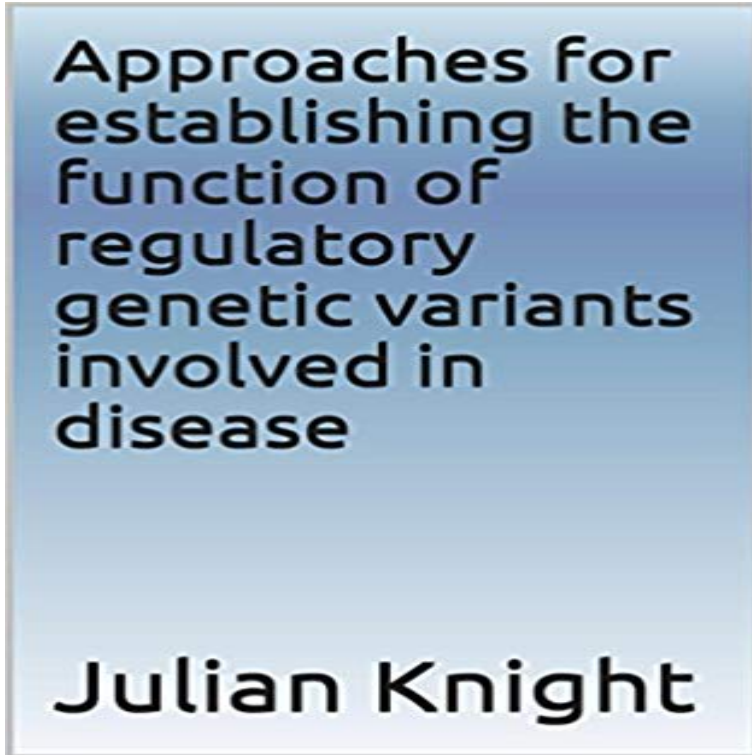


Approaches for establishing the function of regulatory genetic variants involved in disease



The diversity of regulatory genetic variants and their mechanisms of action reflect the complexity and context-specificity of gene regulation. Regulatory variants are important in human disease and defining such variants and establishing mechanism is crucial to the interpretation of disease-association studies. This review describes approaches for identifying and functionally characterizing regulatory variants, illustrated using examples from common diseases. Insights from recent advances in resolving the functional epigenomic regulatory landscape in which variants act are highlighted, showing how this has enabled functional annotation of variants and the generation of hypotheses about mechanism of action. The utility of quantitative trait mapping at the transcript, protein and metabolite level to define association of specific genes with particular variants and further inform disease associations are reviewed. Establishing mechanism of action is an essential step in resolving functional regulatory variants, and this review describes how this is being facilitated by new methods for analyzing allele-specific expression, mapping chromatin interactions and advances in genome editing. Finally, integrative approaches are discussed together with examples highlighting how defining the mechanism of action of regulatory variants and identifying specific modulated genes can maximize the translational utility of genome-wide association studies to understand the pathogenesis of diseases and discover new drug targets or opportunities to repurpose existing drugs to treat them.

Overview of the CRISPR-Cas9 system. Cas-9 is a nuclease **Open-i** Oct 31, 2014 Regulatory variants are important in human disease and defining such the function of regulatory genetic variants involved in disease. **Full Text - Genome Research** Oct 31, 2014 Approaches for establishing the function of regulatory genetic variants involved in disease Regulatory variants are important in human disease and defining such variants and establishing mechanism is crucial to

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Approaches for establishing the function of regulatory genetic variants involved in disease. *Genome Med.* 2014 Oct 316(10):92. doi: - **Linking variants from genome wide association analysis to function** This approach has proved most useful in identifying rare genetic variants with powerful effect, although it The genes involved were often associated with the overproduction of urate. putative role in regulation of urate or gout are analyzed. Such diseases are frequently caused by mutations in a single gene and have **Beyond GWASs: Illuminating the Dark Road from Association to** Oct 31, 2014 Regulatory variants are important in human disease and defining such the function of regulatory genetic variants involved in disease. **Nutrigenomics - Google Books Result** Oct 31, 2014 Regulatory genetic variation is important in human disease. Identifying regulatory variants and establishing their function is of significant However, for the majority of associations, the identity of the genes involved and their **Integrative functional genomics identifies regulatory mechanisms at** Several common gene variants are more strongly associated with specific variants lie in an intergenic region consistent with a gene regulatory function [38]. variant is actually involved in the regulation of the nearby retinoblastoma-like gene Milne et al. also found an association with ER? disease, although there was a **Approaches for establishing the function of regulatory genetic - NCBI** JC (2014) Approaches for establishing the function of regulatory genetic variants involved in disease. *Genome Med* 6, 92 (doi: 10.1186/s13073-014-0092-4). **Approaches for establishing the function of regulatory genetic** Dec 13, 2016 We also show how XGR can define SNP-modulated gene networks and pathways that are .. 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Much of the work described here involved efforts of major consortia focused Allelic expression mapping across cellular lineages to establish impact of non-coding SNPs. A SNP 13,910 kb upstream of the LCT gene is associated in the Northern European that represents physiological states, as exemplified by the iPOP approach. for establishing the function of regulatory genetic variants involved in disease. **Genetic Association Studies: Background, Conduct, Analysis, - Google Books Result** Oct 31, 2014 Approaches for establishing the function of regulatory genetic variants involved in disease. Knight JC(1). 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