Roles of Regulatory Variants in Complex Diseases

Abstract:

Genome wide association studies (GWAS) are identifying more loci associated with complex disorders. However, the loci cover broad stretches of the genome with many variants, and progress toward understanding disease mechanisms has been limited because of the inherent difficulty of identifying the functional variants within the loci.

In this study, I will present a technology called Massively Parallel Reporter Assay (MPRA) and how we can use this technology for identifying functional genetic variants in regulatory regions such as enhancer, promoter or 3'-untranslated regions (3'UTR). We have also developed an innovative statistical method, we called it MGExA (MPRA-mediated Gene Expression Association Analysis), that combines the results from GWAS with MPRA for identifying causal genes that potentially contribute to a specific trait.

As more MPRA and GWAS datasets continue to be generated, we believe that MGExA will be an important tool to identify potential causal mechanisms in complex diseases, especially those where traditional genetic approaches have yet to provide plausible hypotheses.

Reference:

Allele-specific expression and high-throughput reporter assay reveal functional genetic variants associated with alcohol use disorders.
Rao X, Thapa KS, Chen AB, Lin H, Gao H, Reiter JL, Hargreaves KA, Ipe J, Lai D, Xuei X, Wang Y, Gu H, Kapoor M, Farris SP, Tischfield J, Foroud T, Goate AM, Skaar TC, Mayfield RD, Edenberg HJ, Liu Y.
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