A Bioinformatics Pipeline for Identifying Functional Explanations of SNP-Phenotype Associations on a Transcriptional Level

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Background and Hypothesis: Genome-wide association studies (GWAS) have identified thousands of associations between single nucleotide polymorphisms (SNP) and traits of interest. These associations do not offer biological or functional explanations for differences in phenotype. This study works on filling the gap between these associations and their functional effect on phenotype by identifying variants that are associated due, at least in part, to their effect on a transcriptional level.

Experimental Design or Project Methods: GWAS analysis and RNA-sequencing was run on the post-mortem brain tissue of heavy drinkers and non-drinkers. Genes that were associated with differential transcript production were overlaid with chromatin interaction data to identify potential enhancers. A number of properties of enhancers were used to narrow down the list.

Results: Identified enhancers offer a potential functional explanation for the association between a SNP and trait.

Conclusion and Potential Impact: This new technique offers a powerful tool to identify genetic variants in key regulatory regions. Although here it is used for an alcohol use disorder study, this protocol has the potential to be used in a wide range of statistical genomic settings to find functional explanations for associations between SNP and trait.