The Effect of APOE SNPs on Brain Tissue Specific Gene Expression

Authors: Blessing Ibe (University of Illinois at Urbana-Champaign), Anastasia Gurinovich (Boston University) and Paola Sebastiani (Boston University)

ABSTRACT

The three major Apolipoprotein E (APOE) gene alleles e2, e3, and e4 are derived from genotypic combinations of two single nucleotide polymorphisms (SNPs) rs7412 and rs429358. The e4 allele is a known risk factor for Alzheimer's disease (AD), while the e2 allele has been found to be negatively associated with AD and cognitive decline. The APOE gene, however, may have other significant undiscovered effects on age-associated diseases through its interaction with other genes.

In this project, we investigated the effect of APOE alleles on brain tissue-specific gene expression in hopes of finding highly associated genes that may modify AD risk by interaction. We chose brain tissues because of the previously found link between APOE and AD. We used normalized RNA-seq expression data from 13 different brain tissues, such as the amygdala, hippocampus, etc. The data were obtained from the v7 release of the Genotype-Tissue Expression (GTEx) portal database representing 80 to 154 subjects—depending on the brain tissue site. APOE genotype data were also available for all subjects. With the homozygous e3 allele as a reference factor, we fit logistic regression models using APOE genotype and GTEx-provided covariates as predictors for gene expression in each tissue site. False discovery rate adjusted p-values were used to analyze results at the 30% significance level. For both e2 and e4 alleles, there were no significantly associated genes in the anterior cingulate cortex, cerebellum, cerebellar hemisphere, putamen, and spinal cord. However, there were significant associations found for both alleles on the remaining brain tissue sites. Through literature review, preliminary results show that APOE e2 associated genes have functions including cancer cell modulation and disease pathway interruption.

Our analyses present a new way of looking at the relationship between APOE genotypes and AD risk which could facilitate the discovery of new processes.

Keywords: biostatistics, differential expression, disease