Association Studies of VAV Gene SNPs with Crohn’s Disease

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Abstract

Crohn’s disease is a chronic inflammatory disorder of the gastrointestinal tract of unknown etiology. The prevalence rate of Crohn’s is estimated to be 0.1% in North America. It has been observed that mice deficient in VAV display numerous ulcers in the cecum and colon, which is similar to the Inflammatory Bowel Disease phenotype in humans. 150 Tag SNPs (11 VAV1, 67 VAV2, and 72 VAV3) were selected for the VAV genes, encoded on chromosomes 19, 9, and 1 respectively, and were analyzed for association in a cohort of 282 individuals (146 Crohn’s, 29 Ulcerative Colitis, 2 indeterminate colitis, and 105 control). Based on findings in this test, an additional 35 SNPs (3 VAV1, 30 VAV2, 2VAV3) were typed in the case-control cohort and a separate family based cohort of 715 families (433 Crohn’s and 172 Ulcerative Colitis). Fisher’s Exact test was performed in the case-control cohort while the Pedigree Disequilibrium Test, linkage analysis and haplotype analysis were performed in the pedigree data. Haplotype analysis was conducted with haplotypes composed of two through six nucleotide strings. Replication of the over-transmitted allele in statistically associated SNPs between the case-control data and the pedigree data provide support for association. A VAV2 SNP, rs3780739 was found to be associated with ulcerative colitis and IBD in the non-Jewish families (p= 0.006). The same allele found over-represented in the affected offspring was also over-represented in the cases from the case-control cohorts. This SNP was statistically significant in the ulcerative colitis cohort (p= 0.00048). This SNP is in linkage disequilibrium with several other SNPs also found significant in the family data. The proximal location of rs3780739 to a known Vav2 exon, makes it a likely candidate for involvement in the translation of this exon.