Abstract

Ann Rheum Dis. 2015 Mar;74(3):618-24. doi: 10.1136/annrheumdis-2013-204475. Epub 2013 Dec 10.

FUT2: filling the gap between genes and environment in Behçet's disease?

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Abstract

OBJECTIVES: To identify new susceptibility loci for Behçet's disease (BD), we performed a genome-wide association study (GWAS) using DNA pooling.

METHODS: Two replicate pools of 292 Iranian BD cases and of 294 age- and sex-matched controls were allelotyped in quadruplicate on the Affymetrix Genome-Wide Human SNP Array 6.0. Of the 51 top markers, 47 were technically validated through individually genotyping. Replication of validated single nucleotide polymorphisms (SNPs) was performed in an independent Iranian dataset (684 cases and 532 controls).

RESULTS: In addition to the well-established HLA-B locus, rs7528842 in a gene desert on chromosome 1p21.2, and rs632111 at the 3'UTR of FUT2 were associated in both the discovery and replication datasets (individually and in combination). However, only the FUT2 SNP was associated in a previous GWAS for BD in Turkish people. Fine-mapping of FUT2 in the full Iranian dataset showed additional associations in five coding SNPs (2.97E-06<pcombined<1.34E-04), including the rs601338 nonsense (W143X) variant which, in Caucasians, determines the secretion of the H antigen (precursor of the ABO blood group antigens) in body fluids and on the intestinal mucosa. Meta-analysis with the published Turkish GWAS data strengthened the FUT2 associations (4.78E-09<pmeta<1.66E-07).

CONCLUSIONS: This study suggests for the first time a putative link between a specific gene and environment in the aetiopathogenesis of BD. The non-secretor phenotype affects mucosal glycosylation, which may explain its known association with dysbiosis and altered susceptibility to infections. A different antigenic stimulation in early life and consequent increased propensity for autoimmunity and inflammation may contribute to BD development.

PMID: 24326010 [PubMed - in process]

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