Shared Genetic Basis for Type 1 Diabetes, Islet Autoantibodies, and Autoantibodies Associated With Other Immune-Mediated Diseases in Families With Type 1 Diabetes - DTU Orbit (04/11/2018)

Shared Genetic Basis for Type 1 Diabetes, Islet Autoantibodies, and Autoantibodies Associated With Other Immune-Mediated Diseases in Families With Type 1 Diabetes

Type 1 diabetes (T_{1}D) is a polygenic autoimmune disease that is often present with autoantibodies directed against pancreatic islet proteins. Many genetic susceptibility loci are shared with other autoimmune or immune-mediated diseases that also cosegregate in families with T_{1}D. The aim of this study was to investigate whether susceptibility loci identified in genome-wide association studies (GWAS) of T_{1}D were also associated with autoantibody positivity in individuals with diabetes. Fifty single nucleotide polymorphisms (SNPs) were genotyped in 6,556 multiethnic cases collected by the Type 1 Diabetes Genetics Consortium (T1DGC). These were tested for association with three islet autoantibodies—against autoantibodies to GAD (GADA), IA-2 (IA-2A), and zinc transporter 8 (ZnT8A)—and autoantibodies against thyroid peroxidase (TPOA) in autoimmune thyroid disease, gastric parietal cells (PCA) in autoimmune gastritis, transglutaminase (TGA) in celiac disease, and 21-hydroxylase (21-OHA) in autoimmune hypoadrenalism. In addition to the MHC region, we identify SNPs in five susceptibility loci (IFIH1/2q24, PTPN22, SH2B3, BACH2, and CTLA4) as significantly associated with more than one autoantibody at a false discovery rate less than 5%. IFIH1/2q24 demonstrated the most unrestricted association, as significant association was demonstrated for PCA, TPOA, GADA, 21-OHA, and IA-2A. In addition, 11 loci were significantly associated with a single autoantibody.

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