Autor(en) des Beitrags:

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A strategy for combining minor genetic susceptibility genes to improve prediction of disease in type 1 diabetes

Abstract:
Genome-wide association studies have identified gene regions associated with type 1 diabetes. The aim of this study was to determine how the combined allele frequency of multiple susceptibility genes can stratify islet autoimmunity and/or type 1 diabetes risk. Children of parents with type 1 diabetes and prospectively followed from birth for the development of islet autoantibodies and diabetes were genotyped for single-nucleotide polymorphisms at 12 type 1 diabetes susceptibility genes (ERBB3, PTPN2, IFIH1, PTPN22, KIAA0350, CD25, CTLA4, SH2B3, IL2, IL18RAP, IL10 and COBL). Non-human leukocyte antigen (HLA) risk score was defined by the total number of risk alleles at these genes. Receiver operator curve analysis showed that the non-HLA gene combinations were highly effective in discriminating diabetes and most effective in children with a high-risk HLA genotype. The greatest diabetes discrimination was obtained by the sum of risk alleles for eight genes (IFIH1, CTLA4, PTPN22, IL18RAP, SH2B3, KIAA0350, COBL and ERBB3) in the HLA-risk children. Non-HLA-risk allele scores stratified risk for developing islet autoantibodies and diabetes, and progression from islet autoimmunity to diabetes. Genotyping at multiple susceptibility loci in children from affected families can identify neonates with sufficient genetic risk of type 1 diabetes to be considered for early intervention.