P1-P269

The association between TSHR, IFIH1 and ETV5 polymorphisms with Graves' disease and diabetes mellitus type 1 in children

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Background

Many organs of human body are attacked by autoimmune processes and countless number of genes are involved in their pathogenesis. Diabetes mellitus type 1 (T1DM) attaching pancreas is a common autoimmune disease in childhood. Among autoimmune thyroid diseases (AITD) we can distinguish less frequent in children population- Graves' disease (GD). Thyroid stimulating hormone receptor (TSHR) gene encodes membrane protein responsible for thyroid metabolism. Interferon induced helicase (IFIH1) gene tends to be related to development of many autoimmune diseases. ETV5 transcription factor is considered to be obesity-associated loci.

Objective

Identification of genetic variants enabling differentiation between GD and T1DM in children.

Methods

The study was performed among 170 patients with GD and 194 with T1DM. Three single nucleotide polymorphisms (SNPs): **Rs 179247-TSHR**, **Rs 1990760- IFIH1** and **Rs 7647305- ETV5** were genotyped by TaqMan SNP genotyping using QuantStudio 12 K Flex OpenArray plates.

Results

Table 1. Distribution of alleles and genotypes: rs179247- TSHR in GD and T1DM

Allele/Genotype	GD	T1DM	
A	155 (46%)	149 (39%)	p=0.05 OR=1.35
G	181 (54%)	235 (61%)	
A/A	36 (21%)	23 (12%)	
A/G	83 (49%)	103 (54%)	p=0.02 OR=2.09
G/G	49 (30%)	66 (34%)	

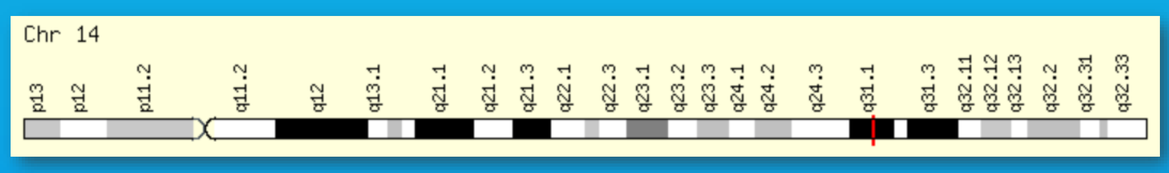
Table 2. Distribution of alleles and genotypes: rs1990760- IFIH1 in GD and T1DM

Allele/Genotype	GD	T1DM	
C	140 (41%)	119 (31%)	p=0.003 OR=1.6
T	200 (59%)	269 (69%)	
C/C	36 (21%)	9 (5%)	
C/T	68 (40%)	101 (52%)	p=0.0 OR=4.99
T/T	66 (39%)	84 (43%)	

Table 3. Distribution of alleles and genotypes: rs7647305- ETV5 in GD and T1DM

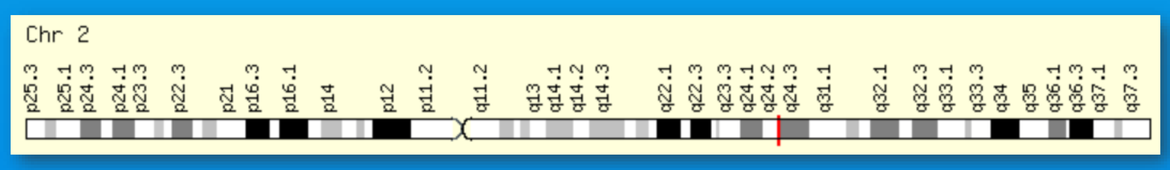
Allele/Genotype	GD	T1DM	
C	254 (76%)	247 (64%)	p=0.0 OR=1.8
T	80 (24%)	141 (36%)	
C/C	91 (55%)	88 (45%)	
C/T	72 (43%)	71 (37%)	p=0.0 OR=8.68
T/T	4 (2%)	35 (18%)	

Fig.1 TSHR gene location



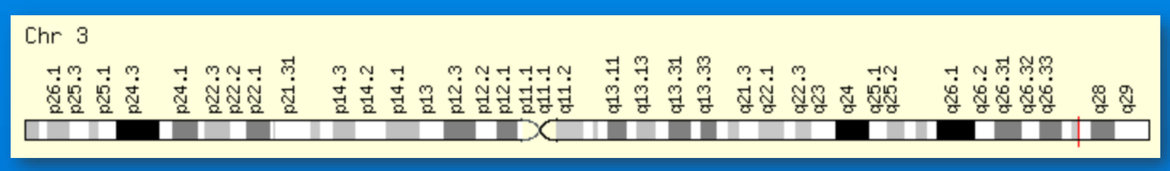
The TSHR gene is located on the long (q) arm of chromosome 14 at position 31.1

Fig.2 IFIH1 gene location



The IFIH1 gene is located on the long (q) arm of chromosome 2 at position 24.2

Fig.3 ETV 5 gene location



The ETV5 gene is located on the long (q) arm of chromosome 3 at position 27.2

Conclusions

When comparing GD with T1DM, Rs179247 A/G, Rs 1990760 C/T and Rs7647305 C/T polymorphisms could contribute to GD development in children. The main risk factor for Rs 179247 is A allele, for Rs 1990760 is C allele and for Rs 7647305 is C allele.

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