Analysis of chosen polymorphisms rs7138803 A/G - FAIM2, rs7093069 C/T - IL-2RA, rs5742909 C/T - CTLA-4 in pathogenesis of Hashimoto's thyroiditis in children

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OBJECTIVES

Autoimmune thyroid diseases are multifactorial diseases with a genetic susceptibility and environmental factors. A potential role of the Fas apoptotic inhibitory molecule 2 (FAIM2) gene, the high-affinity alpha subunit (CD25) of the interleukin-2 receptor (IL-2RA) gene, the cytotoxic T cell antigen 4 (CTLA-4) gene polymorphisms on autoimmune thyroid diseases (AITDs) in children has not been established equivocally yet.

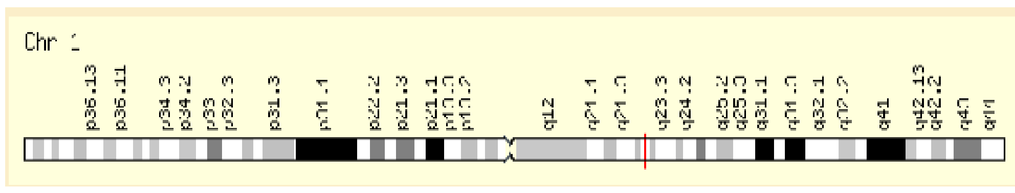
METHODS

The study was performed in 170 patients with GD, 81 with HT and 110 healthy volunteers from two endocrine centers (Białystok, Messina). The three single nucleotide polymorphisms (SNPs): Rs7138803 FAIM2, Rs7093069-IL-2RA and Rs5742909-CTLA-4 were genotyped by TaqMan SNP genotyping assay with platform QuanStudio 12K Flex - OpenArray plates using the real-time PCR

RESULTS

Distribution of genotypes and alleles: rs7138803 A/G - FAIM2 gene (Fas apoptotic inhibitory molecule 2 (FAIM2) gene) in AITD and controls

Group		HT	GD	Controls
Genotype	A/A	16 (20%) *p=0.009 OR=3.5*	34 (20%) *p=0.0075 OR=2.9*	9 (8%)
	A/G	42 (52%)	77 (46%)	54 (50%)
	G/G	23 (28%)	58 (34%)	46 (42%)
Allele	A	74 (46%)	145 (43%) *p=0.019 OR=1.5*	72 (33%)
	G	88 (54%)	193 (57%)	146 (67%)

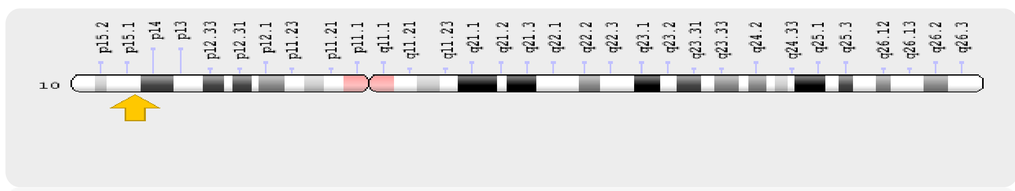


- Rs7138803 A/A genotypes were more frequent in HT and GD patients in comparison to healthy subjects (p=0.009 with OR=3.5; p<0.0075 with OR=2.9, respectively).
- Rs7138803 A alleles were more frequent in GD patients in comparison to healthy subjects (p=0.019 with OR=1.5).

Distribution of genotypes and alleles: rs7093069 C/T - IL-2RA gene in AITD and controls

Group		HT	GD	Controls
Genotype	C/C	47 (61%)	69 (43%)	55 (52%)
	C/T	27 (35%)	81 (50%)	48 (46%)
	T/T	3 (4%)	10 (7%)	2 (2%)
Allele	C	121 (79% *p=0.032 OR=1.6*	219 (68%)	158 (75%)
	T	33 (21%)	101 (32%)	52 (25%)

Molecular Location: base pairs 6,010,694 to 6,062,370 on chromosome 10 (Homo sapiens Annotation Release 109, GRCh38.p12)

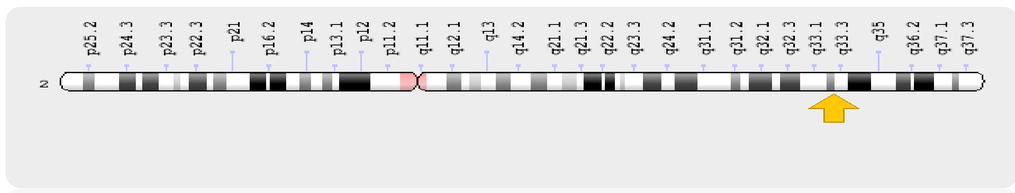


Rs7093069 C alleles were more frequent in HT patients in comparison to healthy subjects (p=0.032 with OR=1.61). That means that risk for development of HT is 1.6 higher for C allele in comparison to T allele.

Distribution of genotypes and alleles: rs5742909 C/T - CTLA-4 gene in GD, HT and controls

Group		HT	GD	Controls
Genotype	C/C	62 (77%)	126 (74%)	73 (66%)
	C/T	17 (21%)	38 (22%)	31 (28%)
	T/T	1 (2%)	6 (4%)	6 (6%)
Allele	C	141 (88% *p=0.045 OR=1.8*	290 (85%)	177 (80%)
	T	19 (12%)	50 (15%)	43 (20%)

Molecular Location: base pairs 203,867,788 to 203,873,960 on chromosome 2 (Homo sapiens Annotation Release 109, GRCh38.p12)



- Rs5742909 C alleles were more frequent in HT patients in comparison to healthy subjects (p=0.045 with OR=1.8).

CONCLUSIONS

- Rs7138803 A/G, Rs7093069 C/T and Rs5742909 C/T polymorphisms could contribute to development of HT in children.
- The main risk factor for rs7093069 and rs5742909 is allele C.
- In case of rs7138803 the main risk factor is allele A for development of both GD and HT.