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Analysis of chosen polymorphisms rs5742909 C/T - CTLA4, rs7522061 C/T – FCRL3, rs7138803 A/G - FAIM2 in pathogenesis of autoimmune thyroid diseases in children.

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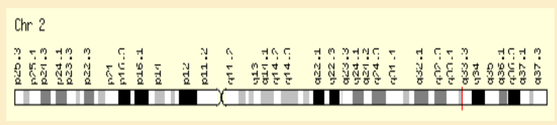
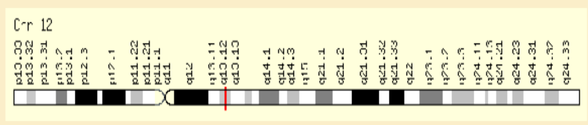
Introduction:

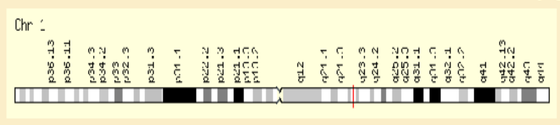
Autoimmune thyroid diseases are multifactorial diseases with a genetic susceptibility and environmental factors. A potential role of cytotoxic T-lymphocyte-associated protein 4 (CTLA4) gene, Fc receptor-like 3 (FCRL3) gene, Fas apoptotic inhibitory molecule 2 (FAIM2) gene polymorphisms on autoimmune thyroid diseases (AITDs) in children has not been established equivocally yet.



CTLA4 gene



FCLR3 gene



FAIM2 gene

Aim of Study:

To estimate the association of polymorphisms of CTLA4, FCRL3 and FAIM2 genes with the predisposition to Graves' disease (GD) and Hashimoto's thyroiditis (HT) in children.

Materials and Methods:

The study was performed in 142 patients with GD, 57 with HT and 160 healthy volunteers. The three single nucleotide polymorphisms (SNPs): rs5742909 – CTLA4, rs7522061 – FCRL3 and rs7138803 – FAIM2 were genotyped by TaqMan SNP genotyping assay using the real-time PCR.

	Graves' disease	Hashimoto thyroiditis	Controls	*p, **p
Female/male (n)	145 (109/36)	87 (74/13)	161 (75/86)	
Age (years)	16.5±2	15.2±2.2	16.3±3	NS, NS
Weight(kg)	55.19±2.39	58±5.28	60.9±7.8	NS, NS
Height (cm)	162.19±2.69	154.26±4.14	160±8	NS, NS
fT4 (ng/dl)	14.18±2.7	1.8±0.63	2.1±0.46	*p<0.001, NS
fT3 (ng/dl)	12.19±2.27	3.08±0.5	3.79±0.18	*p<0.001, NS
TSH (μU/ml)	2.37±2.1	9.87±4.37	3.04±0.72	p<0.01, p<0.025
TRAb (IU/L)	11.56±2.11	0.5±0.32	0.4±0.2	*p<0.001, NS
anti-TGAb (IU/mL)	347.49±86.7	620.98±240.34	91.6±30.46	*p<0.01, **p<0.01
anti-TPOAb (IU/mL)	331.97±58.12	329.91±92.93	66±52.73	*p<0.01, **p<0.01
treatment	Methimazole	L-thyroxine	none	

Table I: Characteristics of groups of patients with autoimmune thyroid disease and controls

Results:

		Rs5742909-	CTLA4		
		All	Male	Female	Significance/OR
GD	C	243 (85%)	59 (86%)	184 (85%)	
	T	41 (14%)	9 (13%)	32 (14%)	
	C/C	106 (74%)	26 (76%)	80 (74%)	P=0,029
	C/T	31 (21%)	7 (20%)	24 (22%)	OR=1,8
	T/T	5 (3%)	1 (2%)	4 (3%)	
HT	C	85 (85%)	16 (88%)	69 (84%)	
	T	15 (15%)	2 (11%)	13 (15%)	
	C/C	35 (70%)	7 (77%)	28 (68%)	
	C/T	15 (30%)	2 (22%)	13 (31%)	
	T/T	0 (0%)	0 (0%)	0 (0%)	
Control	C	258 (80%)	144 (84%)	114 (76%)	
	T	62 (19%)	26 (15%)	36 (24%)	
	C/C	109 (68%)	62 (72%)	47 (62%)	
	C/T	40 (25%)	20 (23%)	20 (26%)	
	T/T	11 (6%)	3 (3%)	8 (10%)	

		Rs7522061-	FCLR3		
		All	Male	Female	Significance/OR
GD	C	117 (41%)	33 (48%)	89 (39%)	P=0,007
	T	165 (58%)	35 (51%)	130 (60%)	OR=1,76
	C/C	18 (12%)	6 (17%)	12 (11%)	
	C/T	81 (57%)	21 (61%)	60 (56%)	P=0,021
	T/T	42 (29%)	7 (20%)	35 (32%)	OR=1,87
HT	C	35 (31%)	6 (30%)	29 (31%)	
	T	77 (68%)	14 (70%)	63 (68%)	
	C/C	6 (10%)	0 (0%)	6 (13%)	
	C/T	23 (41%)	6 (60%)	17 (36%)	
	T/T	27 (48%)	4 (40%)	23 (50%)	
Control	C	44 (28%)	21 (32%)	23 (25%)	
	T	110 (71%)	43 (67%)	67 (74%)	
	C/C	6 (7%)	3 (9%)	3 (6%)	
	C/T	32 (41%)	15 (46%)	17 (37%)	
	T/T	39 (50%)	14 (43%)	25 (55%)	

		Rs7138803-	FAIM2		
		All	Male	Female	Significance/OR
GD	A	126 (25%)	34 (50%)	92 (42%)	
	G	156 (64%)	34 (50%)	122 (57%)	
	A/A	30 (21%)	8 (23%)	22 (20%)	
	A/G	66 (46%)	18 (52%)	48 (44%)	
	G/G	45 (31%)	8 (23%)	37 (34%)	
HT	A	51 (50%)	6 (33%)	45 (53%)	P=0,025
	G	51 (50%)	12 (66%)	39 (46%)	OR=3,57
	A/A	12 (23%)	0 (0%)	12 (28%)	
	A/G	27 (52%)	6 (66%)	21 (50%)	P=0,069
	G/G	12 (23%)	3 (33%)	9 (21%)	OR=1,87
Control	A	57 (35%)	35 (34%)	22 (37%)	
	G	103 (64%)	67 (65%)	36 (62%)	
	A/A	9 (11%)	5 (9%)	4 (13%)	
	A/G	39 (48%)	25 (49%)	14 (48%)	
	G/G	32 (40%)	21 (41%)	11 (37%)	

Distribution of genotypes and alleles rs5742909, rs7522061 and rs7138803 in groups with HT, GD and in healthy controls.

Rs5742909 C alleles were more frequent in GD patients in comparison to healthy subjects (p=0.029 with OR=1,8). It means that risk for development of GD is exactly 1,8 higher for C allele in comparison to T allele. Rs7522061 C alleles were more frequent in GB patients in comparison to healthy subjects (p=0.007, OR=1,76). Rs7138803 A alleles were more frequent in HT patients in comparison to healthy subjects (p=0.025, OR=3,57). Rs7522061 C alleles were also more frequent in GD female patients in comparison to healthy subjects (p=0.021, OR=1,87). In case of HT patients rs7138803 A alleles were also more frequent in females compared to healthy subjects (p=0.069, OR=1,87).

Conclusions:

Rs5742909 C/T, Rs7522061 C/T and Rs7138803 A/G polymorphisms could contribute to development of AITDs in children. The main risk factor of developing GD for rs5742909 and also rs7522061 is allele C. In case of rs7138803 the main risk factor of developing HT is allele A.

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Thyroid

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