Hashimoto's thyroiditis and thyroid peroxidase autoantibody levels share genetic background

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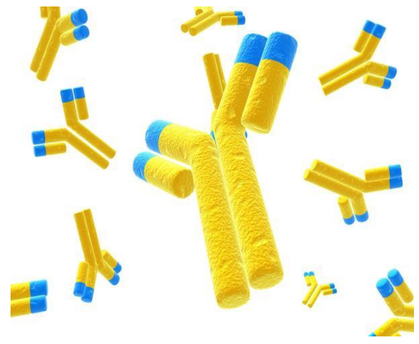
Introduction

Hashimoto's thyroiditis (HT) is the most common form of autoimmune thyroid diseases (AITD) characterised by progressive destruction of thyroid tissue that usually leads to hypothyroidism. High thyroid autoantibodies against thyroid peroxidase (TPOAb) levels are present in 90% of HT patients and serves as a clinical marker for the detection of early AITD/HT.



Genetic factors that contribute to HT development are poorly understood. The main aim of our study was to test if recently identified genetic variants associated with TPOAb levels are also involved in HT development

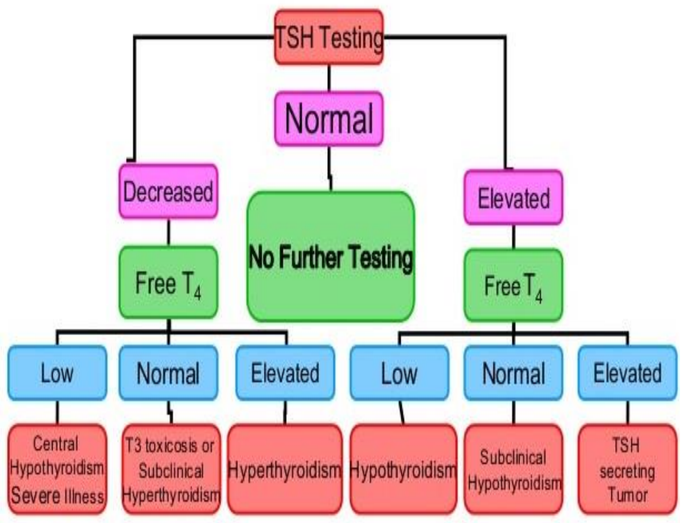
Methods

Design

- We selected and genotyped 14 known TPOAb associated genetic variants.
- Case-control logistic regression model was used to test association of selected genetic variants with HT.
- Additionaly, we tested association of the same genetic variants with thyroid related quantitative traits (TPOAb levels, TgAb levels and thyroid gland volume) using linear regression.

Subjects

- A total of 538 unrelated individuals, including 200 HT patients and 338 controls, were involved in this study.
- Diagnosis of HT cases was based on clinical examination, measurement of thyroid hormones (TSH and fT4) and antibodies (TgAb, TMAb) and ultrasound examination.



Results

- Three genetic variants showed nominal association with HT; rs10774625 in *ATXN2* gene (p=0.0132, OR=0.73, CI=0.57-0.94), rs7171171 near *RASGRP1* gene (p=0.0194, OR=1.43, CI=1.06-1.94) and rs11675434 in *TPO* gene (p=0.0489, OR=1.28, CI=1.01-1.64).
- Two of these SNPs (rs1077462, rs11675434) also showed association with TPOAbs levels (p=0.0434, *β*=-0.39; p=0.0418, *β*=0.40, respectively) and one (rs7171171) was associated with thyroid gland volume (p=0.016, *β*=-0.22).

Table 1. HT disease, TPOAbs, TgAb and thyroid gland volume association analysis results for the 14 genotyped SNPs

			HT			TPOAb			TgAb			Thyroid gland volume		
Genotyped (proxy) SNP	Nearest gene	A1[a]	N	OR	*P* value	N	*β*	*P* value	N	*β*	*P* value	N	*β*	*P* value
rs10774625	*ATXN2*	G	538	0.73	**0.0132**	196	-0.39	**0.0434**	194	0.11	0.52	89	-0.01	0.9163
rs7171171	*RASGRP1*	G	538	1.43	**0.0194**	196	0.26	0.2844	194	0.14	0.5084	89	-0.22	**0.016**
rs11675434	*TPO*	T	538	1.28	**0.0489**	196	0.40	**0.0418**	194	-0.21	0.2435	89	-0.01	0.9757
rs3757247	*BACH2*	A	537	1.22	0.1123	196	-0.37	0.0807	194	0.3	0.1158	89	-0.11	0.1737
rs2839508	*UBASH3A*	C	537	1.20	0.1699	196	0.01	0.9976	194	-0.09	0.6429	89	0.09	0.3304
rs10774577	*SPPL3*	T	538	0.88	0.3263	196	0.12	0.563	194	0.02	0.9322	89	-0.02	0.8267
rs7523492	*FCRL3*	C	464	1.15	0.3381	124	-0.25	0.2712	122	0.1	0.6611	42	-0.12	0.2035
rs2359167	*PHTF1*	T	538	0.89	0.4281	196	0.12	0.6413	194	0.46	0.0536	89	-0.04	0.6628
rs2010099	*KALRN*	T	536	0.91	0.6252	194	0.18	0.5695	192	-0.36	0.1904	87	-0.17	0.1645
rs9344996	*BACH2*	C	538	0.92	0.7004	196	0.02	0.963	194	0.16	0.5786	89	-0.04	0.6959
rs3087243	*CTLA4*	A	536	0.96	0.7422	195	-0.05	0.8255	193	0.15	0.422	88	-0.05	0.5424
rs7574865	*STAT4*	T	538	0.96	0.8008	196	0.13	0.5705	194	0.08	0.7225	89	0.1	0.2525
rs2873413	*FCRL2*	A	538	1.01	0.9511	196	0.38	0.0646	194	-0.11	0.5657	89	0.04	0.5904
rs17005931	*BC045668*	T	537	1.01	0.9861	195	-0.42	0.0728	193	0.23	0.2692	88	0.07	0.3758

[a]Minor allele in all individuals.

OR and all *β* values are calculated for A1. *P* values less than 0.05 are highlighted in bold.

Conclusion

Our findings suggest that variants inside or near *TPO, ATXN2* and *RASGRP1* genes are associated with HT. This is the first report that shows common genetic background of TPOAb levels and HT.