Association of established hypothyroidism associated genetic variants with Hashimoto's thyroiditis

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Aim

Hashimoto's thyroiditis (HT) is a chronic autoimmune disease, with 8 times higher incidence in women. It is the most common cause of hypothyroidism. The main aim of this study was to explore the association of known hypothyroidism-associated single nucleotide polymorphisms (SNPs), discovered by two recent genome-wide association analyses, with HT.

Material and Methods

The case-control dataset included 200 HT cases and 304 controls. We genotyped and analysed 11 known hypothyroidism associated genetic variants in case-control setting using logistic regression model. Additionally, each SNP was tested for the association with thyroid related quantitative traits (TPOAb levels, TgAb levels and thyroid gland volume) in HT cases only using linear regression.

	Genotyped (proxy) SNP	rs10774625	rs7171171	rs11675434	rs3757247	rs2839508	rs10774577	rs7523492	rs2359167	rs2010099	rs9344996	rs3087243	rs7574865	rs2873413	rs17005931
	CHR	12	15	2	6	21	12	1	1	3	6	2	2	1	4
	BP	111910219	38907041	1407815	90957463	43845294	121364324	157637964	114299516	124300257	90929301	204738919	191964633	157737504	123545648
	A1[a]	G	G	T	A	C	T	C	T	T	C	A	T	A	T
HT	N	538	538	538	537	537	538	464	538	536	538	536	538	538	537
	OR (95% CI)	0.73 (0.57-0.94)	1.43 (1.06-1.94)	1.28 (1.01-1.64)	1.22 (0.95-1.56)	1.20 (0.93-1.54)	0.88 (0.68-1.14)	1.15 (0.86-1.53)	0.89 (0.65-1.20)	0.91 (0.62-1.33)	0.92 (0.62-1.38)	0.96 (0.75-1.23)	0.96 (0.72-1.29)	1.01 (0.79-1.29)	1.01 (0.76-1.33)
	P value	**0.01323**	**0.01943**	**0.04892**	0.1123	0.1699	0.3263	0.3381	0.4281	0.6252	0.7004	0.7422	0.8008	0.9511	0.9861
TPOAb	N	196	196	196	196	196	196	124	196	194	196	195	196	196	195
	δ (SE)[b]	-0.3891 (0.1914)	0.2563 (0.2338)	0.4031 (0.1968)	-0.3708 (0.2111)	0.0007 (0.2231)	0.1212 (0.2092)	-0.2469 (0.2234)	0.1226 (0.2627)	0.1752 (0.3076)	0.01512 (0.3257)	-0.04613 (0.2090)	0.1342 (0.2362)	0.3770 (0.2028)	-0.4153 (0.2302)
	P value	**0.04343**	0.2844	**0.04185**	0.08068	0.9976	0.563	0.2712	0.6413	0.5695	0.963	0.8255	0.5705	0.06458	0.07275
TgAb	N	194	194	194	194	194	194	122	194	192	194	193	194	194	193
	δ (SE)[c]	0.1123 (0.1742)	0.1429 (0.2157)	-0.2106 (0.1800)	0.3034 (0.1920)	-0.0936 (0.2016)	0.0162 (0.1904)	0.0963 (0.2190)	0.4555 (0.2346)	-0.3622 (0.2756)	0.1629 (0.2927)	0.1515 (0.1883)	0.0758 (0.2131)	-0.1057 (0.1838)	0.2306 (0.2081)
	P value	0.52	0.5084	0.2435	0.1158	0.6429	0.9322	0.6611	0.05365	0.1904	0.5786	0.422	0.7225	0.5657	0.2692
Thyroid gland volume	N	89	89	89	89	89	89	42	89	87	89	88	89	89	88
	δ (SE)[d]	-0.0072 (0.0685)	-0.2189 (0.0890)	-0.0022 (0.0718)	-0.1123 (0.0819)	0.0881 (0.0901)	-0.0168 (0.0769)	-0.1167 (0.0903)	-0.0422 (0.0965)	-0.1667 (0.1189)	-0.0441 (0.1123)	-0.0468 (0.0765)	0.0950 (0.0825)	0.0401 (0.0743)	0.0693 (0.0778)
	P value	0.9163	**0.01597**	0.9757	0.1737	0.3304	0.8267	0.2035	0.6628	0.1645	0.6959	0.5424	0.2525	0.5904	0.3758

P values less than 0.05 are highlighted in bold; a Minor allele in all individuals; b,c,d Expressed in sd of logarithm transformed TPOAbs levels, TgAb levels and thyroid gland volume, respectively

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

Results

We identified two genetic variants nominally associated with HT: rs3184504 in *SH2B3* gene and rs4704397 in *PDE8B* gene. The *SH2B3* genetic variant also showed nominal association with TPOAb levels and rs4979402 inside *DFNB31* gene was nominally associated with TgAb levels.

Conclusion

Our findings suggest that *SH2B3* and *PDE8B* genetic variants are associated with HT. Identified loci are novel and biologically plausible candidates for HT development and represent good basis for further exploration of HT susceptibility.