A genome-wide association analysis of Hashimoto's thyroiditis

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INTRODUCTION

- Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease characterized by chronic inflammation and reduced function of the thyroid gland.
- HT has never been analyzed on the genome-wide level.
- The aim of our study was to identify genetic variants associated with HT by performing the first genome-wide association analysis of this disease.

METHODS

- Discovery dataset consisted of 430 HT cases and 439 controls while two independent replication cohorts comprised a total of 302 HT cases and 303 controls (Figure 1).
- All HT cases met ETA recommendations and guidelines for Management of Subclinical Hypothyroidism. Study followed the principles of the Declaration of Helsinki.
- Association analysis was performed under the univariate linear mixed model using GEMMA. Binary disease status was treated as quantitative trait, and model was adjusted for age, sex, population stratification and relatedness.

RESULTS

- GWAS resulted with 13 suggestively associated independent SNPs (P-values < 10^{-5}) that were taken for replication
- Meta-analysis of discovery and replication datasets resulted with suggestive association of three SNPs (Figure 2).

CONCLUSIONS

We have identified three biologically plausible candidate genomic regions for HT susceptibility. Variants in these regions were previously suggestively associated with glycosylation of IgG, circulating cytokine eotaxin and Graves' disease. We seek for independent HT cohorts for replication of these results and further GWAS meta-analysis.

Figure 1. Study design

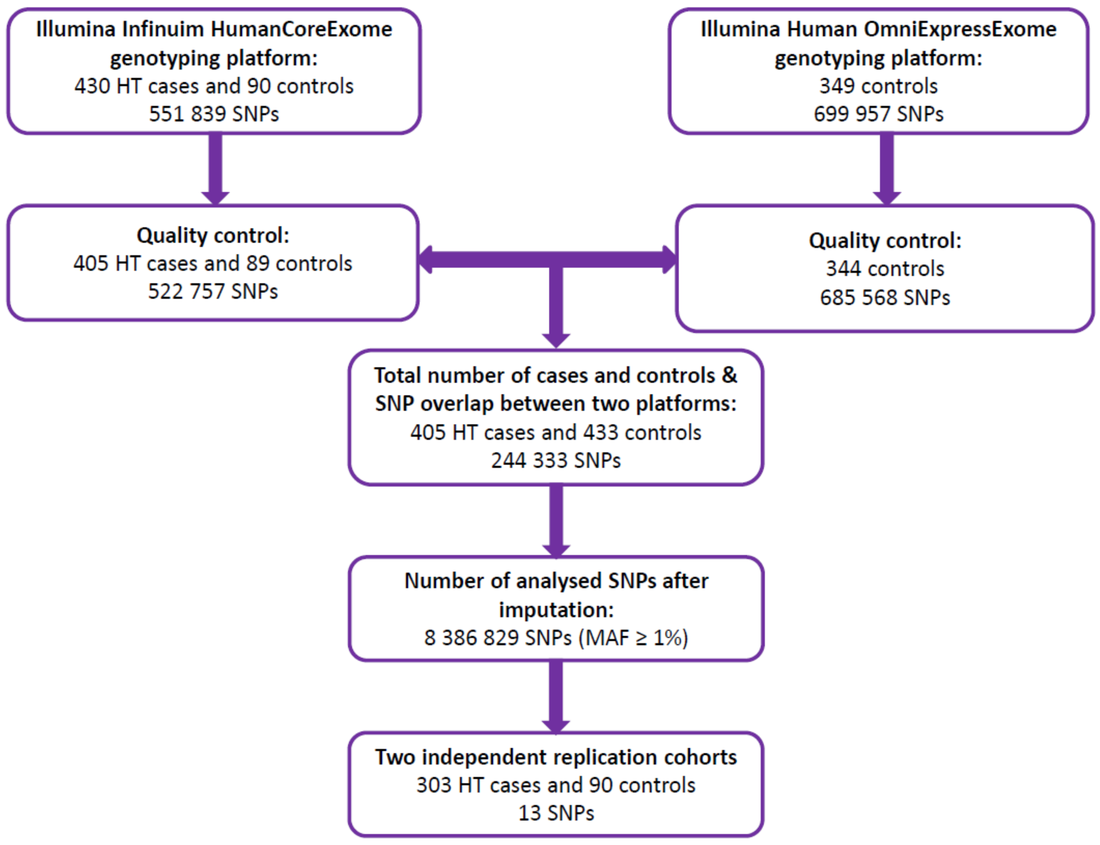

Figure 2. Forest plots and regional association plots of top SNPs