The -112G>A polymorphism of the secretoglobin 3A2 (SCGB3A2) gene encoding uteroglobin-related protein 1 (UGRP1) increases risk for the development of Graves' disease in subsets of patients with elevated levels of immunoglobulin E.

https://arctichealth.org/en/permalink/ahliterature138513

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Source: J Appl Genet. 2011 May;52(2):201-7

Date: May-2011

Language: English

Publication Type: Article

Keywords: Adolescent
Adult
Asthma - genetics
Case-Control Studies
Female
Genetic Association Studies
Genetic markers
Genetic Predisposition to Disease
Genotype
Graves Disease - epidemiology - genetics
Humans
Hypersensitivity - genetics
Immunoglobulin E - blood
Male
Odds Ratio
Polymorphism, Single Nucleotide
Promoter Regions, Genetic
Russia - epidemiology
Secretoglobins
Sequence Analysis, DNA
Uteroglobin - blood - genetics
Young Adult

Abstract: The human secretoglobin 3A2 (SCGB3A2) gene encoding secretory uteroglobin-related protein 1 (UGRP1) resides on the chromosome region 5q31-33 that harbors a susceptibility locus to several autoimmune and inflammatory diseases, including asthma and Graves' disease (GD). Recently, association between the marker rs1368408 (-112G?>A), located in the promoter region of the SCGB3A2 gene, and susceptibility to GD was found in Chinese and UK Caucasians. The study aim was to evaluate whether this polymorphism confers GD susceptibility in a large population cohort comprising 1,474 Russian GD patients and 1,619 controls. The marker rs1368408 was studied using a TaqMan allele discrimination assay. Serum levels of UGRP1 and immunoglobulin E (IgE) were assessed using enzyme-linked immunosorbent assay (ELISA) analyses. Association between the allele A of SCGB3A2 and a higher risk of GD (odds ratio [OR] = 1.33, P = 2.9 × 10(-5)) was shown. Both affected and non-affected carriers of the higher risk genotype A/A had significantly decreased levels of serum UGRP1 compared to the subjects homozygous for G/G (93 ± 37 pg/ml vs. 132 ± 45 pg/ml, P = 0.0011 for GD patients; 77 ± 28 pg/ml vs. 119 ± 33 pg/ml, P = 0.0019 for controls). Serum IgE levels were significantly higher in non-affected subjects homozygous for A/A compared to control individuals homozygous for G/G (153 ± 46 IU/ml vs. 122 ± 40 IU/ml, P = 0.0095). Our data suggest that the carriage of the SCGB3A2 -112A/A variant increases the risk for GD in subsets of patients with elevated levels of IgE, a hallmark of allergic asthma. Therefore, the SCGB3A2 -112G?>A polymorphism may be considered as a likely marker linking susceptibility to allergy/asthma and GD on chromosome 5q31-33.

PubMed ID: 21170691 View in PubMed