



# CTLA4 A49G and C60T genetic polymorphism in Croatian children and young adults with autoimmune thyroid disease



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## OBJECTIVES

Autoimmune thyroid disease (AITD), including autoimmune thyroiditis (AT) and Graves' disease (GD), is a complex autoimmune disease with a strong genetic component. The cytotoxic product of T-lymphocyte antigen-4 (CTLA4) gene, encoding a negative regulator of the T-lymphocyte immune response, was shown to be associated to AITD.

The aim of this study was to investigate the association of A49G and C60T polymorphisms of CTLA4 gene in population of Croatian children and young adults with AITD

## METHODS

The study comprised of 158 unrelated AITD patients (36 males, 122 females) with median age of 12.5 years (4.2-25.9), 127 with AT and 31 with GD.

The control group consisted of 94 unrelated healthy subjects (46 males, 48 females) with median age of 12.0 years (4.6-21.5).

SNP genotyping was performed using TaqMan® probes (rs231775 and rs3087243) in a PCR ABI PRISM 7500 Sequence Detection System (Applied Biosystems by LT).

| CTLA-4 49AG genotype | Genotype  |           |           | OR* (95% CI)     | p    | G allele n (%) | OR* (95% CI)     | p    |
|----------------------|-----------|-----------|-----------|------------------|------|----------------|------------------|------|
|                      | G/G n (%) | A/G n (%) | A/A n (%) |                  |      |                |                  |      |
| <b>AITD</b>          |           |           |           |                  |      |                |                  |      |
| All; N=158           | 31 (19,6) | 66 (41,8) | 61 (38,6) | 1,67 (0,81-3,43) | 0,16 | 128 (40,5)     | 1,15 (0,79-1,66) | 0,47 |
| AT; N=127            | 26 (20,5) | 56 (44,1) | 45 (35,4) | 1,76 (0,84-3,70) | 0,13 | 108 (42,5)     | 1,25 (0,85-1,84) | 0,26 |
| GD; N=31             | 5 (16,1)  | 10 (32,3) | 16 (51,6) | 1,31 (0,42-4,08) | 0,76 | 20 (32,3)      | 0,80 (0,44-1,48) | 0,48 |
| Control group; N=94  | 12 (12,8) | 46 (48,9) | 36 (38,3) |                  |      | 70 (37,2)      |                  |      |

The frequency of genotypes and G allele of CTLA-4 49AG polymorphism in patients with AITD in comparison to the control group.

| CTLA-4 C60T genotype | Genotype  |           |           | OR* (95% CI)     | p     | G allele n (%) | OR* (95% CI)     | p    |
|----------------------|-----------|-----------|-----------|------------------|-------|----------------|------------------|------|
|                      | G/G n (%) | A/G n (%) | A/A n (%) |                  |       |                |                  |      |
| <b>AITD</b>          |           |           |           |                  |       |                |                  |      |
| All; N=158           | 64 (40,5) | 64 (40,5) | 30 (19,0) | 2,23 (1,26-3,95) | <0,01 | 192 (60,8)     | 1,36 (0,95-1,96) | 0,10 |
| AT; N=127            | 54 (42,5) | 49 (38,6) | 24 (18,9) | 2,42 (1,34-4,38) | 0,003 | 157 (61,8)     | 1,42 (0,97-2,09) | 0,07 |
| GD; N=31             | 10 (32,3) | 15 (48,4) | 6 (19,4)  | 1,56 (0,64-3,80) | 0,33  | 35 (56,5)      | 1,14 (0,64-2,03) | 0,65 |
| Control group; N=94  | 22 (23,4) | 56 (59,6) | 16 (17,0) |                  |       | 100 (53,2)     |                  |      |

The frequency of genotypes and G allele of CTLA-4 C60T polymorphism in patients with AITD in comparison to the control group.

## RESULTS

A49G disease associated G/G genotype of CTLA4 gene was detected more frequently in AITD patients (19.6%; OR 1.67, 95% CI 0.81-3.43; p=0.16), in AT patients (20.5%, OR 1.76, 95% CI 0.84-3.70, p=0.13) and GD patients (16.1%, OR 1.31, 95% CI 0.42-4.08, p=0.76) as compared to controls (12.8%), but no statistical significance for associations in none of the groups was found.

Significant associations were found for the C60T disease-associated G/G genotype and AITD (OR 2.23, 95% CI 1.26-3.95; p<0.01), mainly for AT (OR 2.42, 95% CI 1.34-4.38; p=0.003), but not GD (OR 1.56, 95% CI 0.64-3.80; p=0.33).

The risk allele G of both polymorphisms (A49G and C60T) was not significantly associated to AITD (p=0.47 and p=0.10, respectively).

\*for G/G genotype; AITD – autoimmune thyroid disease; AT – autoimmune thyroiditis, GD – Graves disease;

## CONCLUSIONS

Our results do not indicate association of CTLA4 gene G49A polymorphism in the pathogenesis of AITD. However, the C60T polymorphism of CTLA4 gene was found to be associated to the risk of AITD, particularly to AT in our population.

## REFERENCES

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