# Lack of association between estrogen receptor β dinucleotide repeat polymorphism and autoimmune thyroid diseases in Japanese patients


## ABSTRACT

The present results do not support an association between the ERβ microsatellite marker and AITD in the Japanese population. We also suggest that the ERβ microsatellite polymorphism has at most a minor pathogenic importance in predicting the risk of osteoporosis as a complication of GD.


## INTRODUCTION

Background As outlined in a paper we have already published, we analyzed a dinucleotide (TA)n repeat polymorphism lying upstream of the human estrogen receptor (ER) α gene in patients with autoimmune thyroid diseases (AITDs) in normal subjects. Seventeen different alleles were found in 130 patients with Graves' disease (GD), 93 patients with Hashimoto's thyroiditis (HT), and 190 control subjects. There was no significant difference in the distributions of ERα alleles between patients and controls. The pathogenesis of AITDs involves complex interactions between genetic and environmental factors. Susceptibility to AITDs is conferred by genes in the human leukocyte antigen (HLA) and genes unlinked to HLA, including the cytotoxic T lymphocyte antigen (CTLA)-4 gene. The existence of an ERα gene polymorphism has been documented, and its association to some variant ERα genotypes found in breast cancer, hypertension, osteoporosis, generalized osteoarthritis, and some autoimmune diseases such as rheumatoid arthritis has been reported. A gene for a second type of human ER (ERβ) was recently identified. The ERβ is located at human chromosome 14q23-24.1, where the aberration of DNA copy number in bone disorders is frequently found. This locus was close to, but distinct from, a new susceptibility gene (GD-1) on chromosome 14q31. Recently, an association between some ERβ genotypes and osteoporosis has been reported. ER belongs to the nuclear hormone receptor superfamily and modulates the transcription of target genes in response to estrogen, a potent immunomodulatory hormone. Estrogens appear to play a central role in the immune response and immune-mediated diseases. In view of the possible role of estrogens in the pathogenesis of AITDs, we analyzed a dinucleotide (CA)n repeat polymorphism located in the flanking region of ERβ gene in patients with AITDs and in normal subjects. We also studied associaitons of a ERβ gene microsatellite polymorphism with distal radius bone mineral density (BMD) and biochemical markers of bone turnover to determine how this polymorphism might influence the development of osteoporosis as a complication of GD.

## CONCLUSION

Conclusions Our data did not appear to indicate any association between a dinucleotide repeat polymorphism located in the flanking region of ERβ gene and the AITDs analyzed. However, this does not rule out the ERβ gene as a whole; other polymorphisms within the gene could still be associated with AITD. There are also limitations in using microsatellite markers with multiple allleles in case-control studies. Our result might be indicative of a large diversity in the genetic backgrounds of AITDs, although this observation deserves further analysis in a larger group of AITD patients. We also suggest that the ERβ microsatellite polymorphism has at most a minor pathogenic importance in predicting the risk of

osteoporosis as a complication of GD, although further study is warranted to confirm the affects of this polymorphism on BMD and risk of osteoporosis.