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Molecular biology

Sample origin: Saliva

Genetic polymorphisms implicated in various pathways

Result

Deiodinase, iodothyronine, type II

DIO2 (T92A) rs225014	Homozygous wildtype TT

Interpretation

Consequences of the detected genotype:
- no genetic predisposition for a decreased T3 synthesis

General background to the analysed genetic polymorphism

The type II iodothyronine deiodinase (DIO2) is an enzyme which catalyzes the 5' deiodination of thyroxine (T4) to generate an active thyroid hormone (T3). DIO2 is further known to be responsible for catalyzing the local production of T3 in specific tissues such as the developing brain, the anterior pituitary gland, the brown adipose tissue and also in human skeletal muscles. In the human thyroid the selenoprotein DIO2 is abundant at levels 50 to 150 times higher than in placenta and it's especially highly expressed in patients with Graves' disease or with follicular adenomas. Exposure to the thyroxine substrate increases the degradation of DIO2, resulting in decreased DIO2 activity. Missense mutations such as the SNP T to C (rs225014) in the DIO2 gene cause the amino acid substitution Thr92Ala. In vivo studies showed that this substitution is connected to a decreased DIO2 velocity in skeletal muscle and thyroid biopsy samples and is further associated with obesity especially in patients with an additional Trp64Arg mutation in the beta-3 adrenergic receptor (ADRB3). The Thr92Ala substitution may affect ubiquination of DIO2 impairing its ability to increase its activity in the presence of low T4 levels, reducing the ability to maintain homeostasis and increasing dependence on serum T3 as a source of T3 in the brain. Patients on T4 replacement monotherapy with genetic polymorphisms in the DIO2 gene might be affected in their psychological well-being while in comparison to patients on combination therapy with T3/T4 who might show a slightly improved psychological well-being.

Note

Please note: Studies on associations of genetic variants with a certain phenotype or disease or condition have been performed mainly in Caucasian/North American populations. Thus, the interpretation of the results obtained in the present report can not necessarily be extrapolated to other ethnic groups.