Aerodrome Kingsmill Lane
UK - RH154P REDHILL SURREY

Matricule: 19740521000

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Molecular biology

Sample origin: Saliva

Genetic polymorphisms implicated in various pathways

Xenobiotics (phase II detoxification)

Result

Catechol-O-methyltransferase

COMT (V158M) rs4680	Homozygous variant genotype MM

Interpretation

The presence of the homozygous variant genotype MM is associated with a strongly reduced predictive activity of the COMT enzyme compared to carriers of the wild-type. 1) The inactivation capacity of catecholamines by the COMT is strongly reduced. Carriers of this genotype have increased dopamine levels that are associated with advantages regarding the cognitive capacities and a reduced susceptibility to develop eating disorders compared to carriers of the wild-type. With regard to the analyzed polymorphism, these individuals have an increased risk to develop addictions, obsessive compulsive disorders (OCD) or schizophrenia compared to carriers of the wild-type. 2) In the presence of other variations affecting for example the genes CYP1B1 or CCND1 as well as in the case of obesity, postmenopausal syndrome or endometriosis, the relative risk for estrogen-dependent breast cancer is increased compared to individuals that are devoid of these risk factors.

General background to the analysed genetic polymorphism

The catechol-O-methyltransferase (COMT) is an enzyme that catalyzes the transfer of a methyl group from S-adenosylmethionine (SAM) on all compounds that contain a catechol residue. 1) The COMT methylates catecholamine neurotransmitters of endogenous (dopamine, adrenaline, noradrenaline) and exogenous (e.g. L-DOPA) origin and thus leads to their inactivation. Hence, it influences the neurotransmitter levels in the brain. As a consequence, a variability in the level of COMT activity can be associated with cognitive, emotional (e.g. depression, schizophrenia), neurodegenerative (e.g. Parkinson`s disease), eating (e.g. Anorexia nervosa) and behavioral (e.g. obsessive compulsive disorders, OCD) disorders. 2) The COMT is also involved in the metabolism of estrogens, including catechol-estrogens that are generated by hydroxylation of estrogens. Several catechol-estrogens, especially those which are hydroxylated at position 4 and 16, are thought to participate, together with other risk factors, in the genesis of certain tumors (e.g. estrogen-dependent breast cancer). The genetic polymorphism [V158M] consists in the substitution of a valine (V) by a methionine (M) in position 158, which leads to a decreased enzymatic COMT activity.

Homocystein metabolism

Result

5,10-methylenetetrahydrofolate reductase (NADPH)

MTHFR (C677T) rs1801133	Homozygous variant genotype TT
MTHFR (A1298C) rs1801131	Homozygous wildtype AA

Interprétation

The presence of the homozygous variant [C677T] genotype is associated with a highly decreased predictive enzymatic activity and increased serum homocysteine levels. Presence of a genetic predisposition for thromboembolic diseases with regard to the two analyzed polymorphisms. The relative risk for adverse effects to a treatment with methotrexate is increased.

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