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SWISS CENTER FOR GENETICS

Patient:
First-name NAME:
DOB:
Gender: F/M

Analysis requested
By: Dr
Your reference:

Material:
Sample received:
Reporting date:
Lab reference:

GENETIC REPORT OF DETOX PANEL - SAMPLE

This analysis panel detects genetic variations in enzymes that detoxify xenobiotics and free radicals. Detoxification occurs in two phases, where enzymes convert fat-soluble toxins into water-soluble forms for easier excretion. These phases work together to safely process and eliminate harmful substances, minimizing their toxic effects.

Alzheimer/Coronary Artery disease — 100% activity

Lipids Metabolism

APOE | APOE*

Gastrointestinal Tract/Microbiome — 43% activity

Celiac Disease / Vitamin B12 deficiency

FUT2 | FUT2*

Cardiovascular System — 67% activity

Homocysteine Metabolism

MTHFR | MTHFR* | CBS | CBS*

Oxidative Stress

PON1

Nervous System — 65% activity

Serotonin / Dopamine / Noradrenaline / Adrenaline

MTHFR | MTHFR* | COMT | MAOA | MAOB

Liver — 48% activity

Excretion through bile

GSTM1 | GSTT1 | SULT1A1 | SULT1E1 | UGT1A1

Kidney — 51% activity

Elimination of toxins

CBS | CBS* | NAT2 | GSTP1

Hormones — 92% activity

Phase I Detoxification

CYP1A1 | CYP1A2 | CYP1B1 | CYP2C9 | CYP3A4 | PON1

Hormones — 58% activity

Phase II Detoxification

COMT | MTHFR | MTHFR* | GSTM1 | GSTP1 | GSTT1 | SULT1A1 | SULT1E1 | SULT2A1 | UGT1A1

Color Key
- Beneficial properties
- Moderate risk
- High risk

*2 Rs of the same gene

GENETIC ANALYSIS RESULTS of Phase I enzymes

Role: Phase I of detoxification involves the modification of toxins through chemical reactions, such as oxidation, reduction, and hydrolysis. These reactions introduce or expose a functional group (such as a hydroxyl group) on the toxin, making it more reactive.

Key Enzymes*:* Cytochrome P450 enzymes (CYPs): These are the most important Phase I enzymes. They are a large family of enzymes that catalyze the oxidation of organic substances. CYP enzymes, such as CYP1A1, CYP1A2, CYP1B1, CYP2C9, and CYP3A4 play a major role in drug metabolism and the detoxification of various toxins.

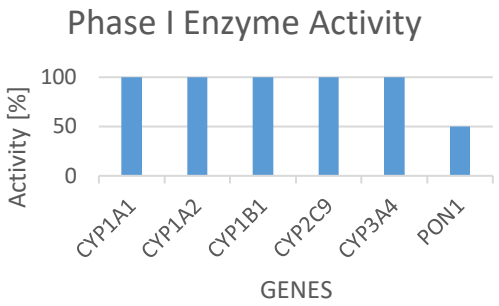
Paraoxonase 1 (PON1) is a phase-I detoxification enzyme involved in the hydrolysis of organophosphate esters. PON1 can be involved in the pathophysiology of various diseases, including kidney failure, neurological disorders, cardiovascular disorders, diabetes, and sleep apnea. PON1 is also known to hydrolyze the metabolites of organophosphorus insecticides.

Those metabolites stemming from PON1 can be used as a marker of environmental exposure. Low levels of PON1 can increase the risk of oxidative damage and atherosclerosis. PON1 is responsible for detoxifying organophosphates, oxidized lipids, and aromatic esters.

Genotypes and acticity of Phase I enzymes

GENES	Genomic Coordinates	Genotype	Zygosity	Enzyme activity
CYP1A1	Chr15: 74719300	AA	Homozygous	100
CYP1A2	Chr15:74749576	CC	Homozygous	100
CYP1B1	Chr2: 38071060	CC	Wildtype	100
CYP2C9	Chr10:94942290	CC	Wildtype	100
CYP3A4	Chr7:99784473	TT	Wildtype	100
PON1	Chr7: 95316772	TA	Heterozygous	50

Global activity: 92%



GENETIC ANALYSIS RESULTS of Phase II enzymes

Role: Phase II detoxification involves Sulphation, Conjugation with glutathione, Glucuronidation, Acetylation, Amino-Acid Conjugation and Methylation to form more stable and water-soluble compounds that can be easily excreted.

Key Enzymes: The UGT1A1 gene encodes UDP-glucuronyl transferase, the main enzyme responsible for the glucuronidation of bilirubin and some other compounds. The UGT1A1 gene is expressed mainly in the liver. Certain genetic variants affecting the production of UDP-glucuronyl transferase are a risk factor for the development of Gilbert's Syndrome. The function of the UGT1A1 gene is to convert estrogens into their conjugates with glucuronic acid. The conjugation process allows the body to metabolize and eliminate toxic forms of estrogen from the body.

Glutathione-S-transferases (GSTs): Catalyze the conjugation of glutathione to reactive intermediates, neutralizing them and making them more water-soluble.

Glutathione S-transferase Pi (GSTP1) is an isozyme encoded by the GST pi gene that plays an important regulatory role in detoxification, anti-oxidative damage, and the occurrence of various diseases. Gene polymorphism reduces the activity of the enzyme, which inhibits phase II xenobiotics, including medicinal derivatives, and detoxification.

Sulfotransferases (SULTs): Transfer sulfate groups to hydroxyl groups on toxins, increasing their water solubility. The sulfotransferase enzymes family (SULT1A1, SULT1E1, SULT2A1) catalyze the sulfate conjugation of many hormones, neurotransmitters, drugs, and xenobiotic compounds.

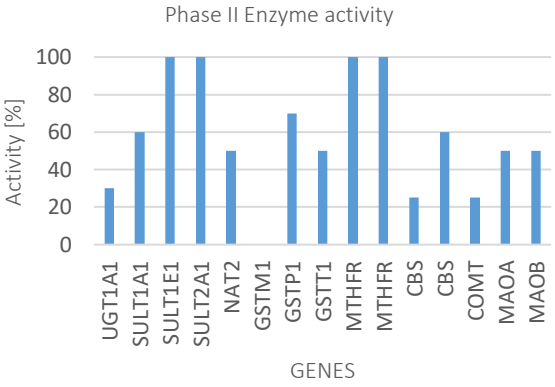
N-acetyltransferases (NATs): Catalyze the acetylation of aromatic amines and hydrazines, which is important in metabolism of drugs and other toxins.

The end products of Phase II detoxification are generally non-toxic, highly water-soluble, and can be readily excreted through urine or bile.

Genotypes and acticity of Phase II enzymes

GENES	Genomic Coordinates	Genotype	Zygosity	Enzyme activity
Glucoronidation				
UGT1A1	Chr2: 233764076	GG	Homozygous	30
Sulphation				
SULT1A1	Chr16:28606193	TC	Heterozygous	60
SULT1E1	Chr4: 69860103	CC	Wildtype	100
SULT2A1	Chr19:47868938	TT	Wildtype	100
Acetylation				
NAT2	Chr8: 18400344	TC	Heterozygous	50
Glutathion Conjugation				
GSTM1	Null Allelle	AA	Homozygous	0
GSTP1	Chr11: 67585218	GA	Heterozygous	70
GSTT1	Null Allelle	TC/AT	Heterozygous	50
Methylation				
MTHFR	Chr1: 11796321	GG	Homozygous	100
MTHFR	Chr1: 11794419	TT	Homozygous	100
CBS	Chr21:43060506	AA	Homozygous	25
CBS	Chr21:43065240	AG	Heterozygous	60
COMT	Chr22: 19963748	AA	Homozygous	25
MAOA	ChrX: 43731789	TT	Homozygous	50
MAOB	ChrX: 43768752	CC	Homozygous	50

Global activity: 58%



GENETIC ANALYSIS RESULTS of Microbiome / Methylation / Methionine cycle

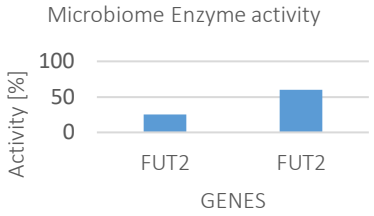
Role: Fucosyltransferase 2 (FUT2) is an enzyme responsible for the synthesis of the H antigen in body fluids and on the intestinal mucosa.

Key Enzymes: A major polymorphism in the Fucosyltransferase 2 (FUT2) gene influences the risk of multiple gut diseases. Common variant in FUT2 gene is associated with levels of vitamin B (12).

Genotypes and acticity of Microbiome enzymes

GENES	Genomic Coordinates	Genotype	Zygosity	Enzyme activity
FUT2	Chr19:48703374	TT	Homozygous	25
FUT2	Chr19:48703417	AG	Heterozygous	60

Global activity: 43%



GENETIC ANALYSIS RESULTS of Alzheimer disease risk assessment

Role: The APOE gene is a known genetic risk factor for dementia, Alzheimer's disease, and cardiovascular diseases.
Key Enzymes: APOE gene alleles modify human aging and the response to diet at many levels with diverse pleotropic effects from gut to brain.

This specific gene is responsible for coding a protein called apolipoprotein E, which performs important biological functions involving lipid and cholesterol metabolism across different tissues and cells. Genetic variations of the APOE gene are linked to variations in blood cholesterol levels, which can lead to increased susceptibility to developing Alzheimer's and cardiovascular diseases.

APOE RISK TABLE

Results	E2/E2	E2/E3	E2/E4	E3/E3	E3/E4	E4/E4
Coronary Artert Disease	Lowest Risk (except for those with hyper-lipo-proteinemia)	No Increase in Risk	No Increase in Risk	No Increase in Risk	Higher Risk	Highest Risk
Alzherimer's Disease	Lowest Risk	Lower Risk	Higher Risk	No Increase in Risk	Higher Risk	Highest Risk (3-4x)

Source: https://rxhometest.com/blog/APOE-Alzheimers-Dementia-CVD

Your result is E2/E2

Brief Explanation of the Functions of the Studied Genes

PHASE I Detoxification Enzymes

Most toxins in our body are fat-soluble substances. Therefore, to eliminate them through urine and bile, the following mechanisms are employed by the liver:

- Oxidation
- Reduction
- Hydroxylation
- Hydrolysis of xenobiotics to active intermediate metabolites
- Dehalogenation

After fat-soluble toxins have been transformed into water-soluble form during Phase I, the liver proceeds to Phase II. Phase I reactions can sometimes produce more toxic intermediates, which need to be further processed by Phase II enzymes.

PHASE II Detoxification Enzymes

At this stage, the liver plays a crucial role in rapidly neutralizing the intensified toxic by-products from Phase I of detoxification. These by-products have become more potent than in the initial phase, emphasizing the need for efficient and rapid elimination. Toxins are prepared for removal from the body through various pathways, including urine and bile.
Reactions of Phase II of detoxification are:

- **Sulphation**, which involves conjugation of toxins with sulphate.
- **Conjugation with glutathione**. Glutathione is a major antioxidant in our body. Through its conjugation, heavy metals, pesticides, and the most dangerous carcinogens are eliminated from the body.
- **Glucuronidation** - the most energy-demanding process of detoxification, as it processes a large amount of toxins. It detoxifies drugs, steroid hormones, preservatives, nicotine, and bilirubin. Genetic defects in this phase can lead to Gilbert's syndrome.
- **Acetylation**, which neutralizes histamine, serotonin, exhaust gases, tobacco, and other substances.
- **Amino-Acid Conjugation –** is particularly common with the phenoxyacetic herbicides like 2,4-D.
- **Methylation –** that occurs in four cycles:
    i. Urea cycle.
    ii. Ammonia cycle.
    iii. Folate cycle.
    iv. Methionine cycle.

Methylation cycle is a fundamental biochemical pathway that governs and supports a wide range of crucial functions in the body, including gene regulation (turning genes on and off), detoxification of external and internal chemical substances and toxins, synthesis of neurotransmitters (dopamine, serotonin, adrenaline), and hormone metabolism (estrogens).

Microbiome / Methylation / Methionine cycle

Fucosyltransferase 2 (FUT2) is an enzyme responsible for the synthesis of the H antigen in body fluids, as well as on the intestinal mucosa.
The FUT2 loss-of-function mutations have often been found to be associated with inflammatory bowel disease.

Alzheimer disease risk assessment

Genetic variations of the APOE gene are linked to variations in blood cholesterol levels, which can cause an increased susceptibility to developing Alzheimer's and cardiovascular diseases.

Method

DNA was extracted from a cheek swab sample in accordance with the kit manufacturer's instructions. Genotyping was performed using Agena's MassARRAY © System. In a first step, raw results were analyzed using the MassARRAY Report software. In a second step, this report was generated using proprietary scripts.

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