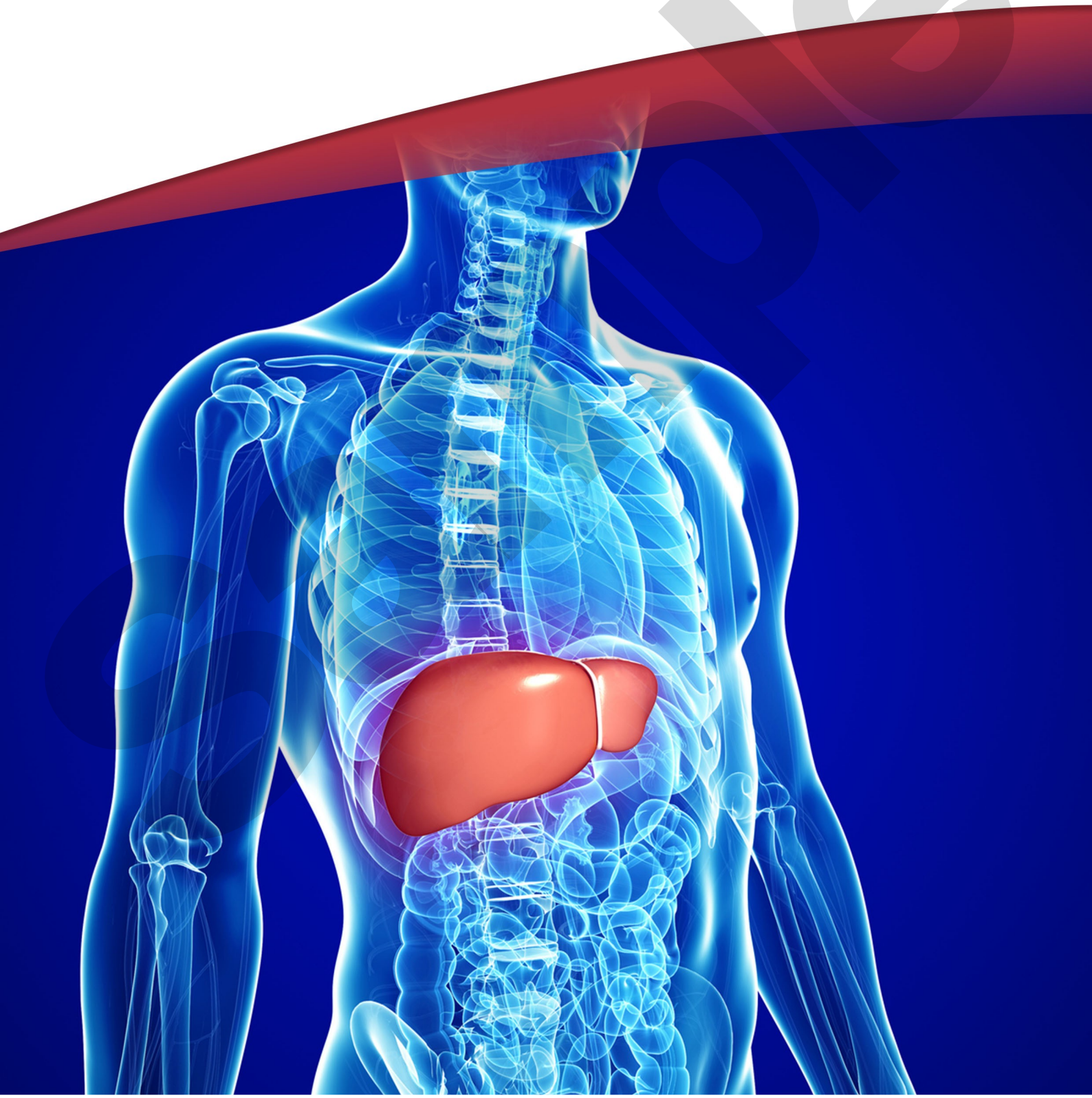
Lifecode GX ®
— Professional Genotype Analysis —

Detoxification Report



The human body is exposed to thousands of toxins every single day which need to be detoxified. Substances including environmental pollutants, food additives, pesticides, medication, alcohol and hormones are transformed from being fat-soluble to water-soluble, allowing them to be more easily excreted from the body via urine and bile.

Detoxification occurs predominantly in the liver in two major phases: Phase 1 Reactions and Phase 2 Conjugation, and a less well-known third phase: Phase 3 Antiporter Activity.

Poor detoxification can impact many systems, leading to various symptoms including:
• **Gastro-intestinal**: halitosis, bitter taste, bloating, fatty stools, constipation, diarrhoea, intolerance to fatty foods, swollen liver, gallbladder problems
• **Immune**: food allergies, skin issues (rashes, itchiness), asthma, recurrent infections
• **Endocrine**: infertility, PMS, weight gain, depression, anxiety, mood swings
• **Nervous**: headaches, dementia, poor memory and concentration, neuralgia
• **Musculo-skeletal**: muscle aches and weakness, arthritis
• **Other**: sensitivity to chemicals and odours, chronic fatigue, anaemia and premature ageing

Detoxification pathways are influenced significantly by genetic variance, as well as nutrition, age, sex, lifestyle habits such as drinking coffee or smoking.

The Detoxification report describes the genes, nutrients, and lifestyle and environmental factors that can impact detoxification. In addition to a detoxification overview diagram, it provides five personalised summary pathways and detailed results, followed by a detoxification guide. The pathways covered are:
• Alcohol
• Mould
• Non-steroidal anti-inflammatory drugs (NSAIDs)
• Paracetamol
• Polycyclic aromatic hydrocarbons (PAHs)

Detoxification Summary

Phase 1 reactions

Cytochrome P450s

CYP1A1 ●●
CYP1A2 ●▲
CYP1B1 ●●▲
CYP2A6 ●
CYP2C19 ●●▼▼
CYP2C9 ●●
CYP2D6 ●●●▲▲
CYP2E1 ●
CYP3A4 ●

Alcohol

ADH1B ●●
ADH1C ●●▲▲▲▲
ALDH2 ●

Pesticides, Lipids

PON1 ●●▼

ROS detoxification

GPX1 ●
NQO1 ●
SOD2 ●●▼▼

Phase 2 conjugation

Glucuronidation

UGT1A1 ●●▼
UGT1A6 ●

Sulphonation

SULT1A1 ●▼
SULT1E1 ●
SULT2A1 ●▼

Acetylation

NAT1 ●
NAT2 ●●▼

Glutathione conjugation

GSTM1 ●
GSTP1 ●●▼
GSTT1 ●

Methylation

COMT ●●▼▼
TPMT ●●

Phase 3 antiporter

Antiporter

ABCB1 ●

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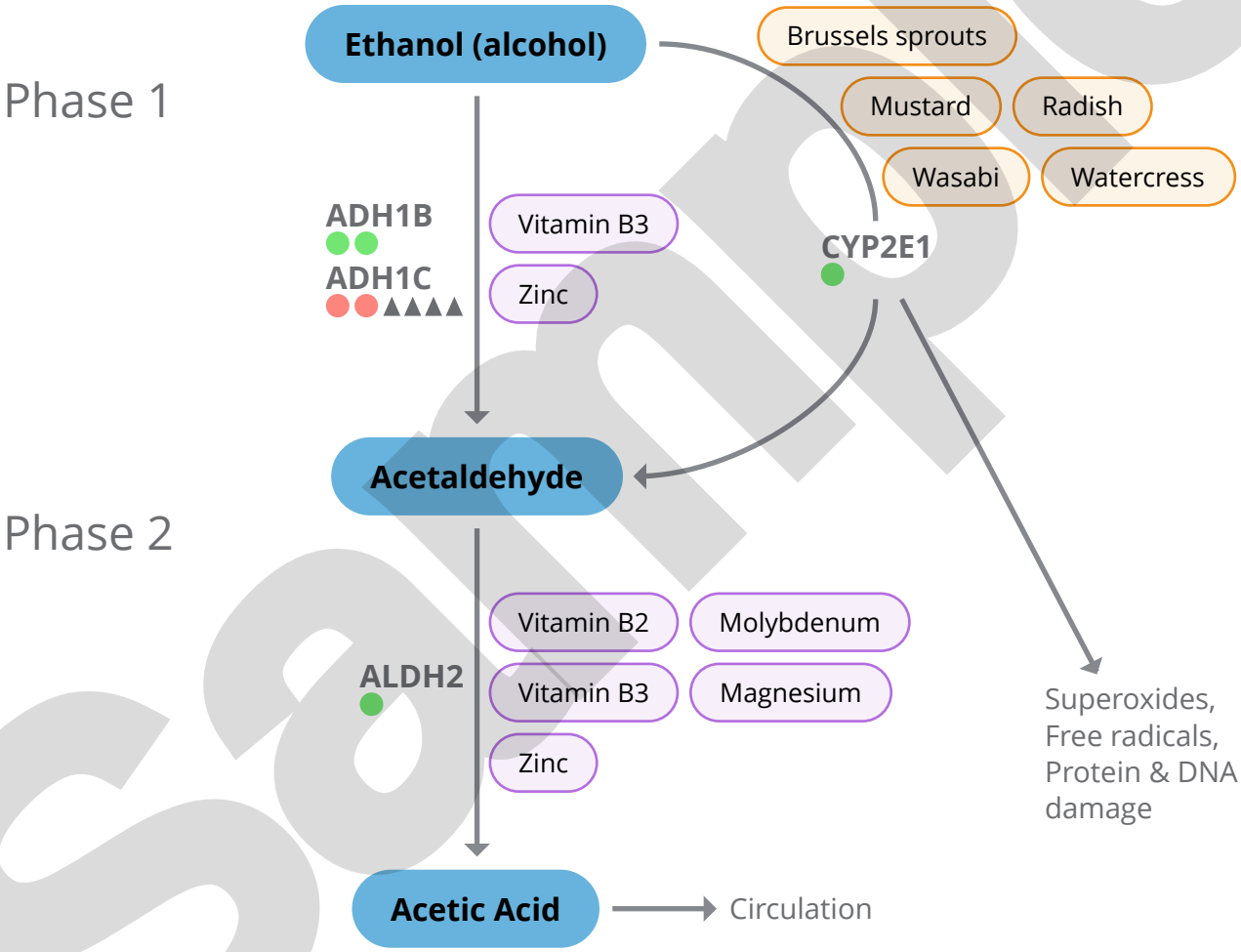
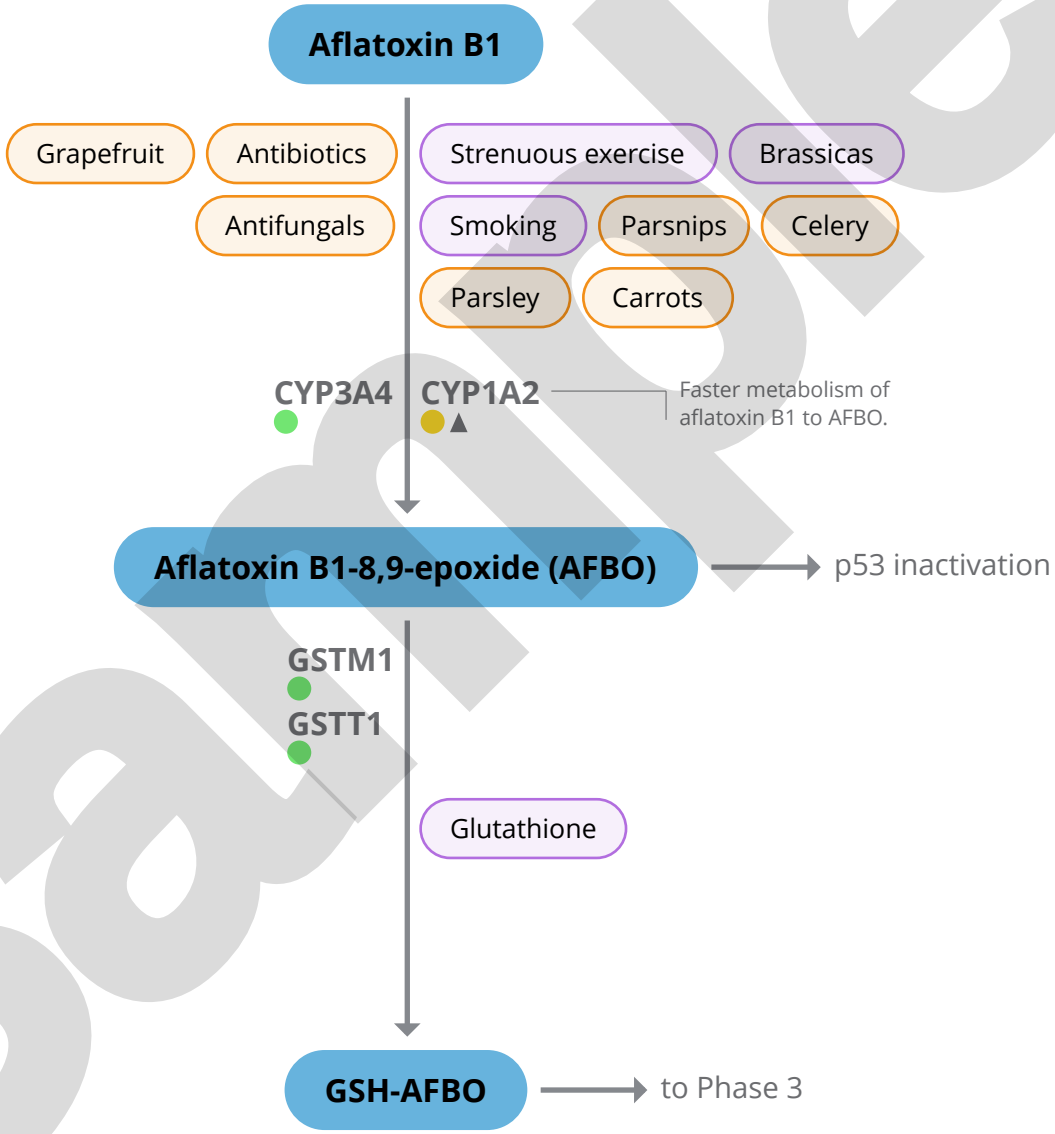
Alcohol Detoxification

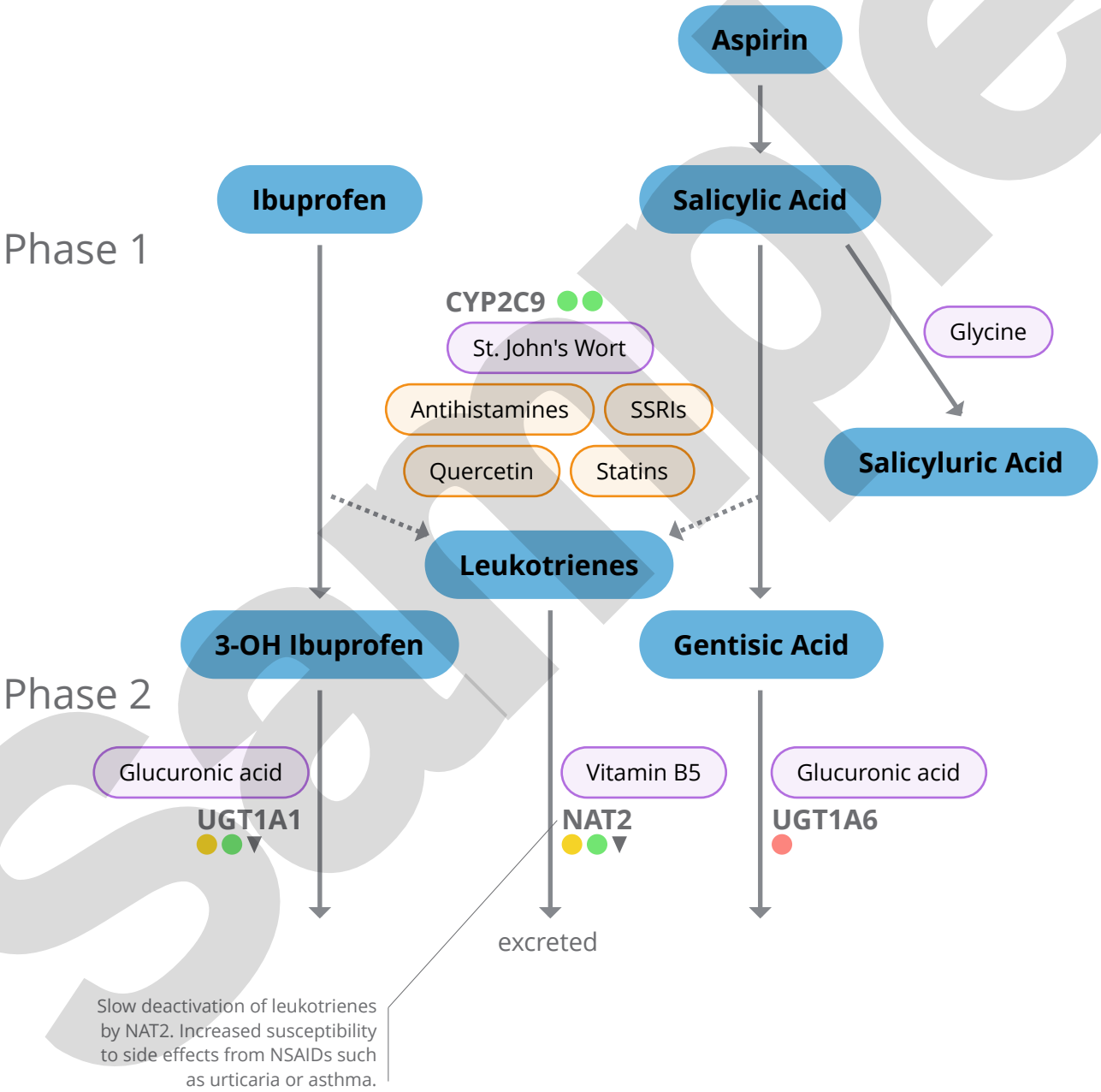


Mould Detoxification

This diagram specifically focuses on aflatoxin B1 but other types of moulds follow a similar detoxification pathway.



Non-steroidal anti-inflammatory drugs (NSAIDs) Detoxification



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Detailed Results for Phase 1

ADH1B
rs1229984

CC

Relatively slow conversion of ethanol to acetaldehyde, compared to the T allele. No exceptional risk of acetaldehyde toxicity or symptoms. Most common genotype in European and African populations, but occurs as low frequency in Asian populations.

Replenish cofactors NAD+ (vitamin B3) and zinc, which may be depleted by alcohol metabolism.

ADH1B
[redacted]

GG

Relatively slower conversion of ethanol to acetaldehyde, compared to the A allele. No exceptional risk of acetaldehyde toxicity or symptoms. Most common genotype in all populations.

Replenish cofactors NAD+ (vitamin B3) and zinc, which may be depleted by alcohol metabolism.

ADH1C
[redacted]

CC ▲▲

Although this is the 'wild' type, it is reported as negative (red) due to higher enzyme activity and rate of conversion of ethanol to acetaldehyde. Increased risk of acetaldehyde toxicity after consuming alcohol which may cause unpleasant symptoms such as facial flushing, urticaria, dermatitis, rhinitis and asthma like reactions, more severe hangovers and protein and DNA damage. Most common genotype in Asians. May be protective against alcoholism.

Replenish cofactors NAD+ (vitamin B3) and zinc, which may be depleted by alcohol metabolism.

ADH1C
[redacted]

TT ▲▲

Although this is the 'wild' type, it is reported as negative (red) due to higher enzyme activity and rate of conversion of ethanol to acetaldehyde. Increased risk of acetaldehyde toxicity after consuming alcohol which may cause unpleasant symptoms such as facial flushing, urticaria, dermatitis, rhinitis and asthma like reactions, more severe hangovers and protein and DNA damage. Most common genotype in Asians. May be protective against alcoholism.

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A Guide to Detoxification

This guide provides detailed explanations of the genes and gene products involved in detoxification.

Toxins

Toxins are exogenous and endogenous substances that are harmful to the body and are capable of causing disease.

Exogenous toxins include alcohol, cigarette smoke, diet (sugar, trans-fats, food additives), environmental pollutants (smoke, pesticides and herbicides), household detergents, cosmetics, radiation, water (chlorine and fluorine), mould, pollen, heavy metals (aluminium, lead, mercury etc.), and pharmaceutical drugs.

The majority of endogenous toxins are products and by-products of digestion, but also result from stress, oxidative stress, dysbiosis, bacterial, fungal or viral infection, hormones and inflammatory chemicals, such as histamine.

The rate at which the liver, and other organs, can eliminate toxins determines individual susceptibility to increased toxic load. High toxic load can cause a wide range of symptoms affecting gastro-intestinal, immune, endocrine, nervous and musculo-skeletal systems.

The detoxification pathways are influenced by nutrition, age, sex, lifestyle habits such as drinking coffee or smoking, as well as genetic variance. In this report we will focus on five detoxification pathways: alcohol, mould, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol and polycyclic aromatic hydrocarbons (PAHs).

Phase 1 Reactions

During Phase 1, substrates are primed for conjugation by the addition or exposure of a binding site via oxidation, reduction or hydrolysis reactions. A significant side effect of Phase 1 detoxification is the production of free radicals as the toxins are transformed, making them more reactive and potentially damaging.

Increased Phase 1 enzyme activity may be helpful and/or unhelpful since it increases the metabolism of environmental toxins but can also alter the efficacy or toxicity of certain prescription medications, and can lead to higher circulating free radicals. For this reason, we report increased Phase 1 enzyme activity due to genetic variance as negative.

The CYP450 enzymes

The cytochrome P450 (CYP450) enzymes are a large superfamily of enzymes, requiring heme and NADPH as cofactors, responsible for metabolising thousands of endogenous and exogenous substances. They are expressed in the membranes of mitochondria and the endoplasmic reticulum of cells - primarily the liver, but also in other organs and systems. CYP enzymes function as monooxygenases and effect oxidation by transfer of one oxygen atom through a number of steps.

Some CYPs metabolise only one or very few substrates while others are responsible for metabolising multiple substrates. Many genetic polymorphisms have been discovered for the CYP450s which can explain the differences in metabolism of steroids, fatty acids, and xenobiotics between individuals.

Inducers increase the activity of CYPs and accelerate the metabolism of the substrates handled by the respective enzymes. Some substrates are also inducers. In general, cigarette smoke, charred food, caffeine, alcohol, cruciferous vegetables and St. John's Wort are all potent inducers of Phase 1 enzymes. On the contrary, inhibitors of CYPs reduce the metabolism of the substrates and may lead to altered efficacy (of prescription medications, for example) or toxicity of any substrate or metabolite.

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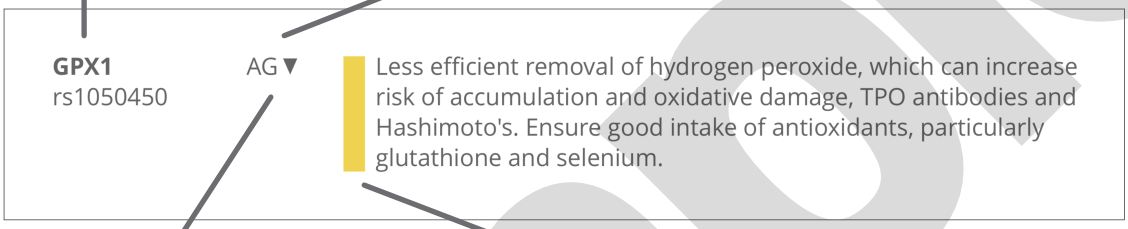
How to Read the Report

Genes

Results are listed in order of the gene short name. The 'rs' number is the reference sequence number that identifies a specific location on the genome. It is also known as a SNP (Single Nucleotide Polymorphism) pronounced 'snip', polymorphism or mutation.

Personalised Result

Your genotype result is shown as two letters (A,G,T or C) which represent the DNA bases present at that location.



Arrow Direction

The direction of the arrow indicates the potential effect of the SNP on gene expression, where applicable - it can increase or decrease activity, or neither.

▲ up-regulates or increases the activity and effect on the gene

▼ down-regulates or decreases the activity and effect on the gene

No arrow - no effect on the activity of the gene

Highlight Colour

The genotype result highlight indicates the potential effect of the SNP on gene function in a particular context.

RED the effect of the variant is negative

AMBER the effect of the variant is somewhat negative

GREEN no variation, or the effect of the variant is positive

Pathway Diagram Key

Cofactor Inhibitor

References

ABCB1 ATP-Binding Cassette, Subfamily B, Member 1

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Delou JMA, Vignal GM, Índio-do-Brasil V, et al. Loss of constitutive ABCB1 expression in breast cancer associated with worse prognosis. Breast Cancer (Dove Med Press). 2017;9:415–428. Published 2017 Jun 10. doi:10.2147/BCTT.S131284. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5479298/)

Schaeffeler, E., Eichelbaum, M., Brinkmann, U., Penger, A., Asante-Poku, S., Zanger, U. M., Schwab, M. Frequency of C3435T polymorphism of MDR1 gene in African people. (Letter) Lancet 358: 383-384, 2001. (https://ncbi.nlm.nih.gov/pubmed/11502320)

ADH1B Alcohol Dehydrogenase 1B (class I), Beta Polypeptide

Macgregor S, Lind PA, Bucholz KK, et al. Associations of ADH and ALDH2 gene variation with self report alcohol reactions, consumption and dependence: an integrated analysis. Human Molecular Genetics. 2009;18(3):580-593. doi:10.1093/hmg/ddn372. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2722191/)

Quertemont E, (2004), Genetic polymorphism in ethanol metabolism: acetaldehyde contribution to alcohol abuse and alcoholism, Molecular Psychiatry; 9, pp. 570–581. (http://www.nature.com/mp/journal/v9/n6/full/4001497a.html#tbl1)

ADH1C Alcohol Dehydrogenase 1C (class I), Gamma Polypeptide

Xue Y, Wang M, Zhong D, Tong N, Chu H, Sheng X, Zhang Z, (2012), ADH1C Ile350Val Polymorphism and Cancer Risk: Evidence from 35 Case–Control Studies, PLOS, Online Research Article. (http://journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0037227)

ALDH2 Aldehyde Dehydrogenase 2 Family (mitochondrial)

Cai Q , Wu J , Cai Q , Chen EZ , Jiang ZY, (2015), Association between Glu504Lys polymorphism of ALDH2 gene and cancer risk: a meta-analysis, PloS one; 10(2): e0117173. (http://europepmc.org/abstract/MED/25680115)

Li D, Zhao H, Gelernter J, (2012), Strong protective effect of the aldehyde dehydrogenase gene (ALDH2) 504lys (*2) allele against alcoholism and alcohol-induced medical diseases in Asians, Human Genetics; 131 (5), pp. 725–737. (http://link.springer.com/article/10.1007/s00439-011-1116-4)

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CYP1A1 Cytochrome P450, Family 1, Subfamily A, Polypeptide 1

Bhagavatula Moorthy, Chun Chu, Danielle J. Carlin, Polycyclic Aromatic Hydrocarbons: From Metabolism to Lung Cancer, Toxicological Sciences, Volume 145, Issue 1, May 2015, Pages 5–15, https://doi.org/10.1093/toxsci/kfv040. (https://academic.oup.com/toxsci/article/145/1/5/1627571)

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CYP1A2 Cytochrome P450, Family 1, Subfamily A, Polypeptide 2

Cornelis MC, BSc; El-Sohemy A, PhD; Kabagambe EK, PhD; Campos H, PhD, (2006), Coffee, CYP1A2 Genotype, and Risk of Myocardial Infarction, JAMA. 2006; 295(10):1135-1141. (http://jama.jamanetwork.com/article.aspx?articleid=202502)

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