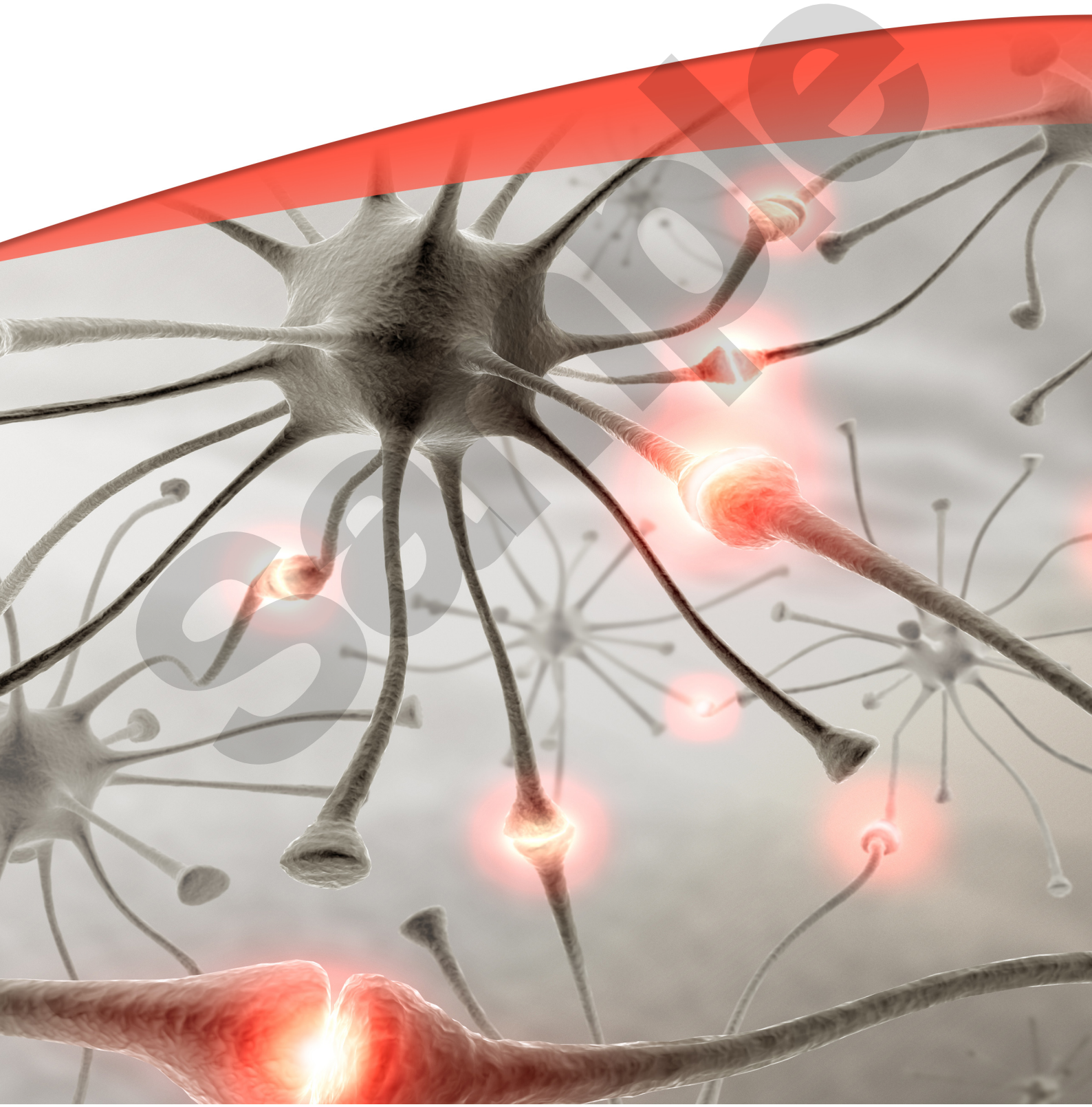
Lifecode GX ®
— Professional Genotype Analysis —

Nervous System Report



Report for Maxim (CP12345678)

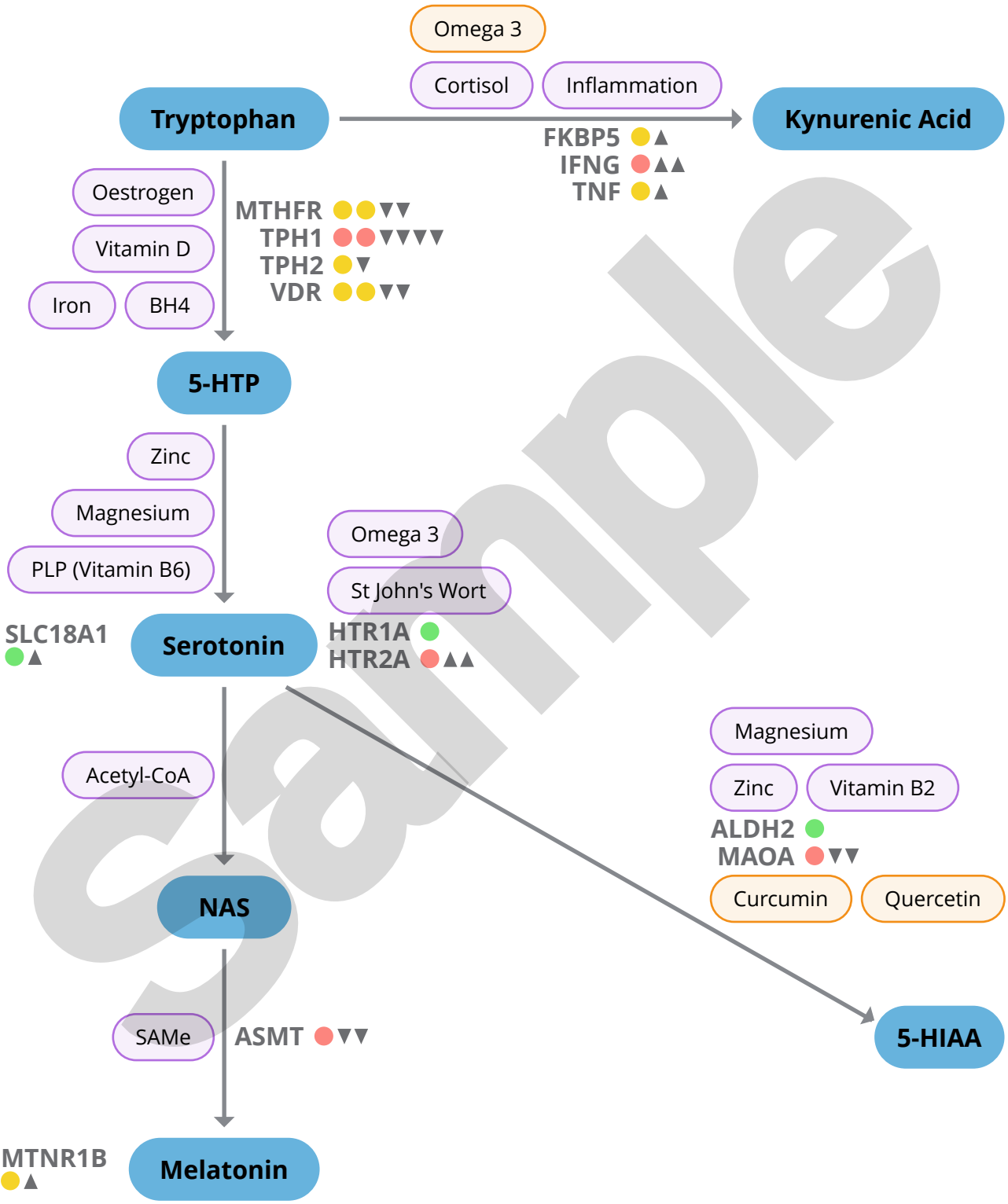
The nervous system is a complex system which enables the transmission of messages around the mind and body, enabling an individual to respond to their environment. The messages are communicated via neurons which are supported and nourished by glial cells. A neurotransmitter is a molecule that carries signals between neurons and across nerve junctions (synapses). In order for us to interact effectively with our environment, the excitatory and inhibitory neurotransmitters must remain in balance.

The main excitatory (stimulating) neurotransmitters are acetylcholine, adrenaline, dopamine, glutamate, histamine, noradrenaline, and phenethylamine (PEA), while the key inhibitory (calming) neurotransmitters are gamma amino butyric acid (GABA), serotonin and melatonin. Their lifecycle involves the synthesis, signalling, transport and metabolism.

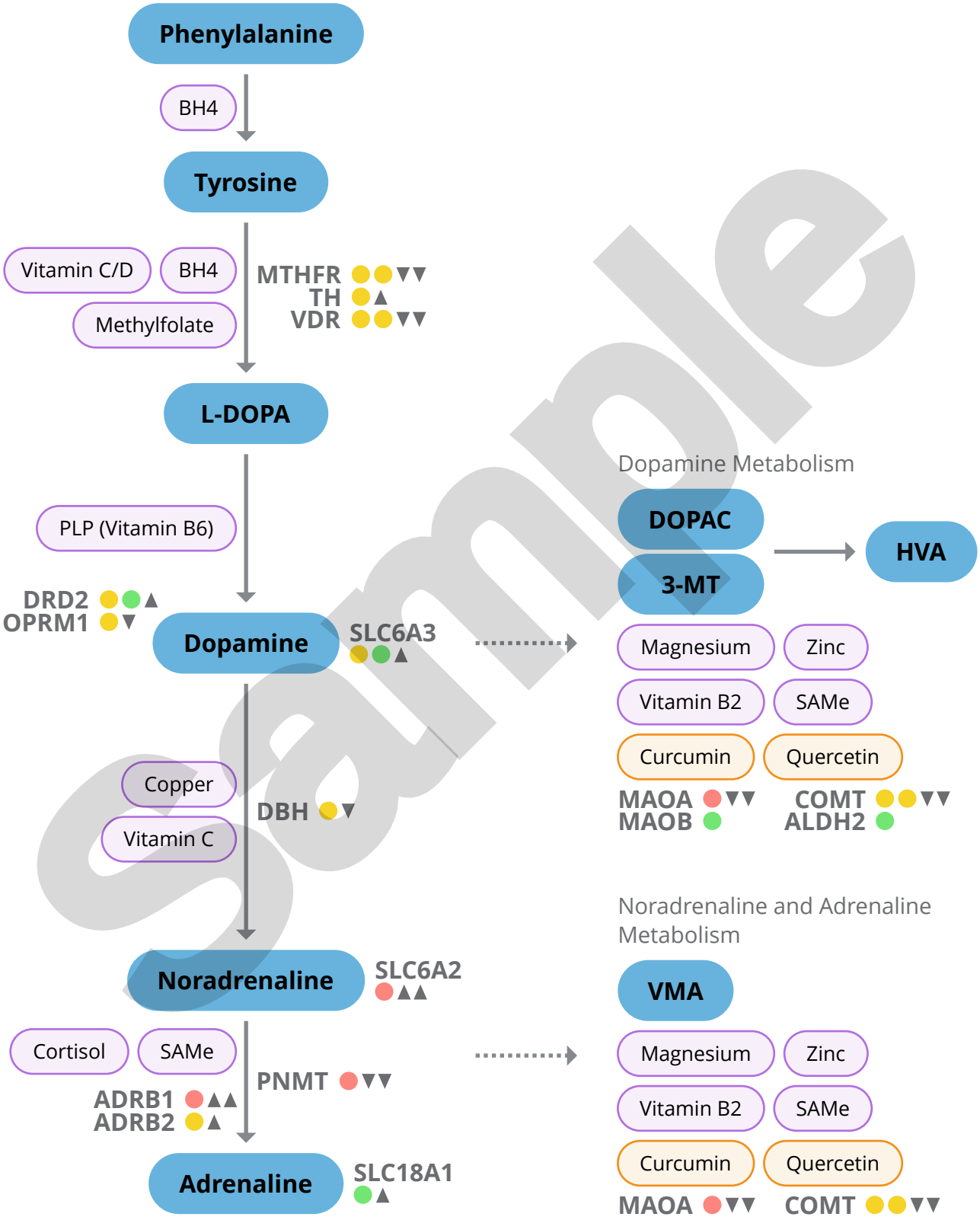
Neurotransmitter imbalances can have serious physical and mental health effects. Symptoms of neurotransmitter imbalance include: mood disorders and depression, attention deficit and obsessive compulsive disorders, addictive behaviours, motor control disruption, anger, aggression and restlessness.

This report examines the genes, nutrients, and lifestyle and environmental factors that can impact the nervous system. It provides personalised summary diagrams and detailed results followed by a generic nervous system guide.

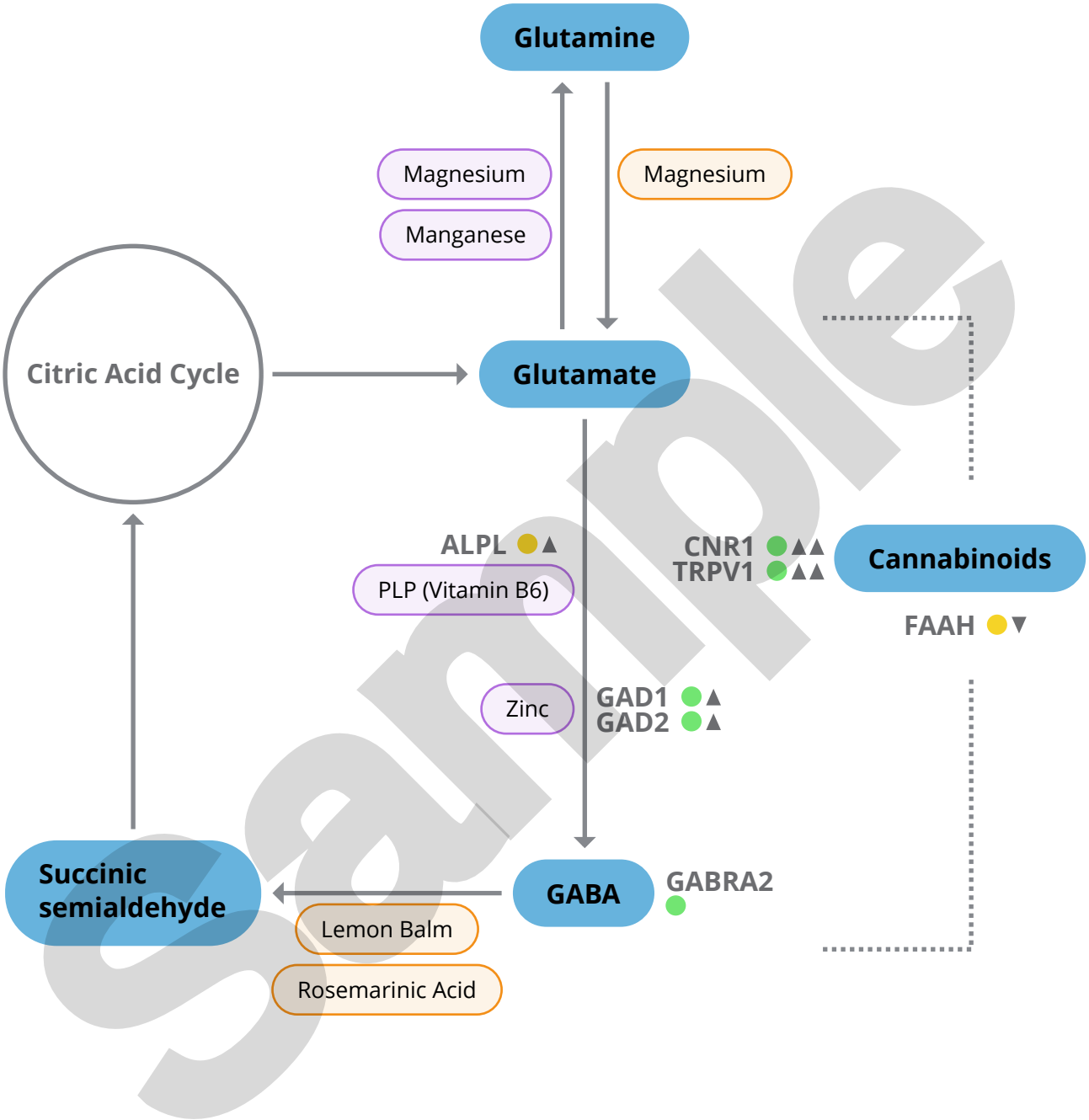
Serotonin and Melatonin Diagram



Dopamine and Adrenergic Diagram



GABA and Cannabinoids Diagram



Detailed Results for Kynurenic Acid

FKBP5
rs1360780
CT ▲

Increased FKBP5 expression and cortisol can stimulate the kynurenine pathway via interferon gamma (INFG) and tumour necrosis factor (TNF), and depletion of tryptophan for serotonin synthesis.
Limit lifestyle behaviours that raise cortisol. Stress reduction techniques such as meditation, yoga and massage may be helpful.

IFN-gamma
rs2430561
TT ▲▲

The T allele is associated with increased IFNG expression which helps the host's defence against viral infection. However, over-expression of IFNG and stimulation of the kynurenine pathway can 'steal' the tryptophan needed for serotonin synthesis and result in lower serotonin levels.
Follow an anti-inflammatory diet including omega 3 (found in oily fish) and brassica foods to inhibit the kynurenic pathway.

TNF
rs1800629
GA▲

Increased TNF activity, which can up-regulate the kynurenine pathway and deplete the tryptophan needed for serotonin synthesis.
If symptoms of inflammation such as redness, heat and pain are present, follow an anti-inflammatory diet - including omega 3 (found in oily fish) and antioxidant rich vegetables and fruits.
Limit alcohol and sugar intake, and adopt a regular exercise routine.

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A Guide to the Nervous System

This guide contains detailed explanations of the neurotransmitters and genes involved in the Nervous System.

Serotonin and Melatonin

Serotonin, or 5-HT, is associated with wellbeing and is popularly referred to as the 'happiness neurotransmitter'. The majority of serotonin is made in the gut where it regulates gastrointestinal movements. The remainder is synthesised in the central nervous system (CNS) where, with melatonin, it affects mood, appetite and sleep. Serotonin also affects cognitive functions including memory and learning.

Melatonin is a sleep hormone naturally produced in the pineal gland of the brain. It regulates sleep and plays a role in maintaining the circadian rhythm, the body's natural time clock. It is also an antioxidant. It suppresses insulin which is not needed during sleep.

Lifecycle

Serotonin synthesis is a two step process starting with the essential amino acid tryptophan. However, reduced availability of tryptophan to make serotonin can be a major factor in depression. Conversely, too much tryptophan can have an inhibitory effect on serotonin production as it inhibits TPH activity. Raised cortisol levels due to stress (exacerbated by an FKBP5 SNP), or inflammation resulting from infection or injury, may cause tryptophan to be redirected to the kynurenic pathway. This 'tryptophan steal' can slow the rate of serotonin synthesis. The extent of inflammation can be modulated by genetics, in particular variants that up-regulate pro-inflammatory molecules. These include IFN-gamma, TNF, and the TDO and IDO enzymes that catalyse kynurenine synthesis.

When tryptophan is not redirected to the kynurenic acid pathway it is converted to 5-HTP by the enzyme tryptophan-5-hydroxylase which exists in two different forms - TPH2 in the brain and TPH1 in the digestive system.

This step can be slowed due to insufficiency of the methyl-folate dependent cofactor BH4, which can be impacted by SNPs on the MTHFR gene. Vitamin D is also a cofactor of this step, which is why we test for VDR SNPs. The subsequent conversion of 5-HTP to serotonin is dependent on vitamin B6 (PLP form).

The serotonin receptors HTR1A and HTR2A are activated by serotonin and control the release of a number of excitatory and inhibitory neurotransmitters, including acetylcholine, adrenaline, dopamine, glutamate, noradrenaline and as well as the hormones corticotropin, cortisol, prolactin and vasopressin. They are the target of many drugs including antidepressants, antipsychotics and anti-migraine agents.

The vesicular monoamine transporter VMAT1 (coded by the SLC18A1 gene), moves serotonin and other neurotransmitters into the vesicles, ready to be released into the synapse. Thus, an increase in VMAT1 (SLC18A1) activity can result in higher levels of neurotransmitters.

Serotonin is broken down to 5-hydroxyindoleacetic acid (5-HIAA) by monoamine oxidase A (MAOA) and aldehyde dehydrogenase 2 (ALDH2).

In the evening, stimulated by darkness, N-acetyl-serotonin (NAS) is created and then converted to melatonin by the acetylserotonin O-methyltransferase (ASMT) enzyme with SAMe as cofactor. Reduced melatonin synthesis can cause circadian dysrhythmia and insomnia. The MTNR1B gene is found mainly in the eyes and brain and is involved in the neurobiological effects of melatonin in response to darkness and light. Variants in MTNR1B are associated with disturbed sleeping patterns (particularly early waking) and increased risk of impaired blood glucose metabolism linked to type 2 diabetes.

Serotonin and melatonin levels can be impacted by nutrition and lifestyle factors such as protein intake and exercise. There are many different triggers and mediators of imbalance, the most common being stress, inflammation, light exposure and genetics.

Imbalance

An imbalance in serotonin levels can lead to an array of problems. Whilst most people are aware of the connection between low serotonin and depression, high levels of serotonin can also be problematic.

Low Serotonin:
- Anxiety or worry
- Depression or low mood
- Appetite, hunger or cravings
- Increased pain sensitivity
- Migraines
- Obsessive compulsive disorder (OCD)
- Insomnia
- Constipation

High Serotonin:
- Anxiety, irritability or restlessness
- Bone loss
- High blood pressure
- Gut sensitivity or diarrhoea
- Carcinoid syndrome
- Headache
- Fatigue
- Weight gain

An imbalance in melatonin levels can also lead to various problems.

Low Melatonin:
- Mood disorders (seasonal affective disorder, bipolar disorder and major depressive disorder)
- Sleep disturbances

High Melatonin:
- Nausea
- Dizziness
- Headaches
- Irritability or anxiety
- Diarrhea
- Joint pain

Follow-up testing

Speak to a health professional about clinical testing such as:

Organic acids
- 5-hydroxyindoleacetate (5-HIAA) (serotonin)

Inflammatory markers
- Kynurenate (KYN)
- Quinolinate (QUIN)
- Picolinate

Methylation markers
- Methylmalonate (B12)
- Formiminoglutamate (FIGLU)
- Xanthurenate (B6)
- SAH: SAMe
- Homocysteine

Genetics
- Methylation
- Oestrogen

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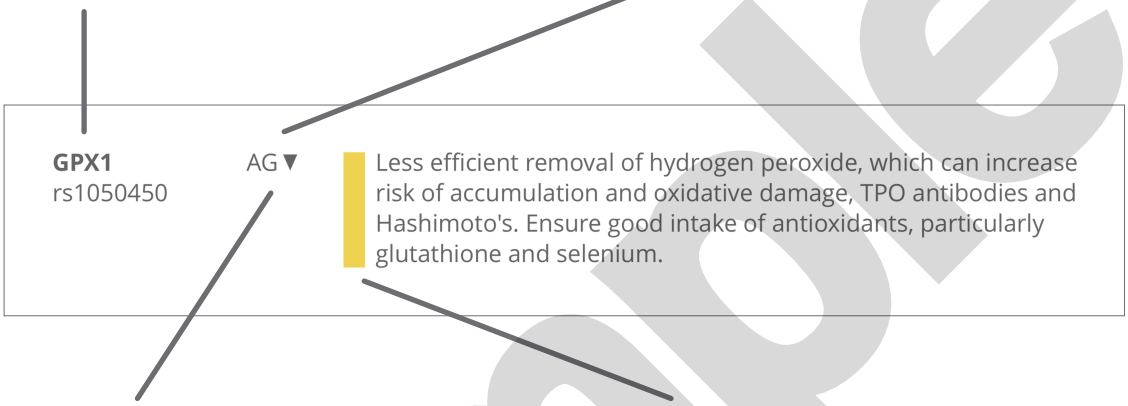
How to Read the Report

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

References

ADRB1 Adrenoceptor Beta 1

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ADRB2 Beta-2-Adrenergic Receptor

Adrenergic-beta(2) receptor polymorphism and athletic performance. Vishnu Sarpeshkar and David J Bentley. J Hum Genet. 2010 Aug;55(8):479-85. doi: 10.1038/jhg.2010.42. Epub 2010 Apr 30. (https://pdfs.semanticscholar.org/735d/bd52384920347e78f9e188593b957887e2f6.pdf)

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ALDH2 Aldehyde Dehydrogenase 2 Family (mitochondrial)

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ALPL Alkaline Phosphatase

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CNR1 cannabinoid receptor 1

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