Lifecode GX ®
— Professional Genotype Analysis —

Metabolics Report

Metabolism refers to all the chemical reactions that take place within each cell and are essential for life. It involves many interconnected pathways that can be divided into anabolism and catabolism. Anabolism uses energy to synthesise sugars, fats, proteins and nucleic acids, whereas catabolism releases energy in the form of ATP (adenosine triphosphate), alongside carbon dioxide, water and ammonia.

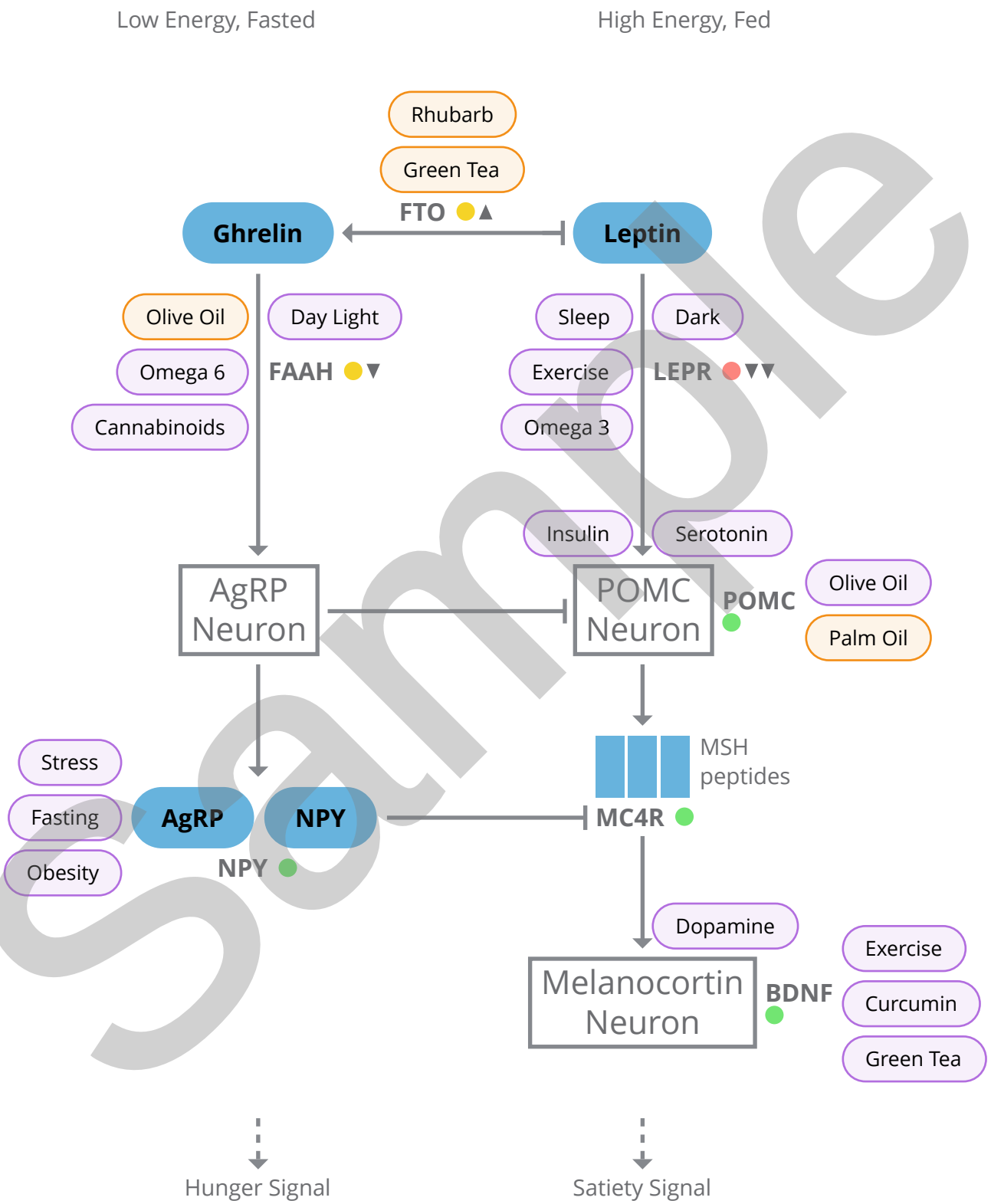
All living organisms, including humans, use their environment to survive by taking in nutrients to support movement, growth, development and reproduction. Most are metabolically flexible, enabling them to adapt to environmental changes and challenges such as scarcity of nutrients (famine), cold and hot climates, and oxygen availability (high altitude).

In recent decades, many populations have experienced increased availability of high calorie-low fibre, processed foods, which alongside decreased physical activity have contributed to metabolic dysfunction, and ultimately metabolic syndrome (MetS). However, these conditions are also affected by genetic make up, quality and composition of food, psychosocial stressors, environmental pollutants and gut microbes. Indeed, over a billion people, about a quarter of the world's population, is now affected by MetS – characterised by abdominal obesity, insulin resistance, hypertension and hyperlipidemia; which can lead to type 2 diabetes, cardiovascular and neurodegenerative diseases and cancer.

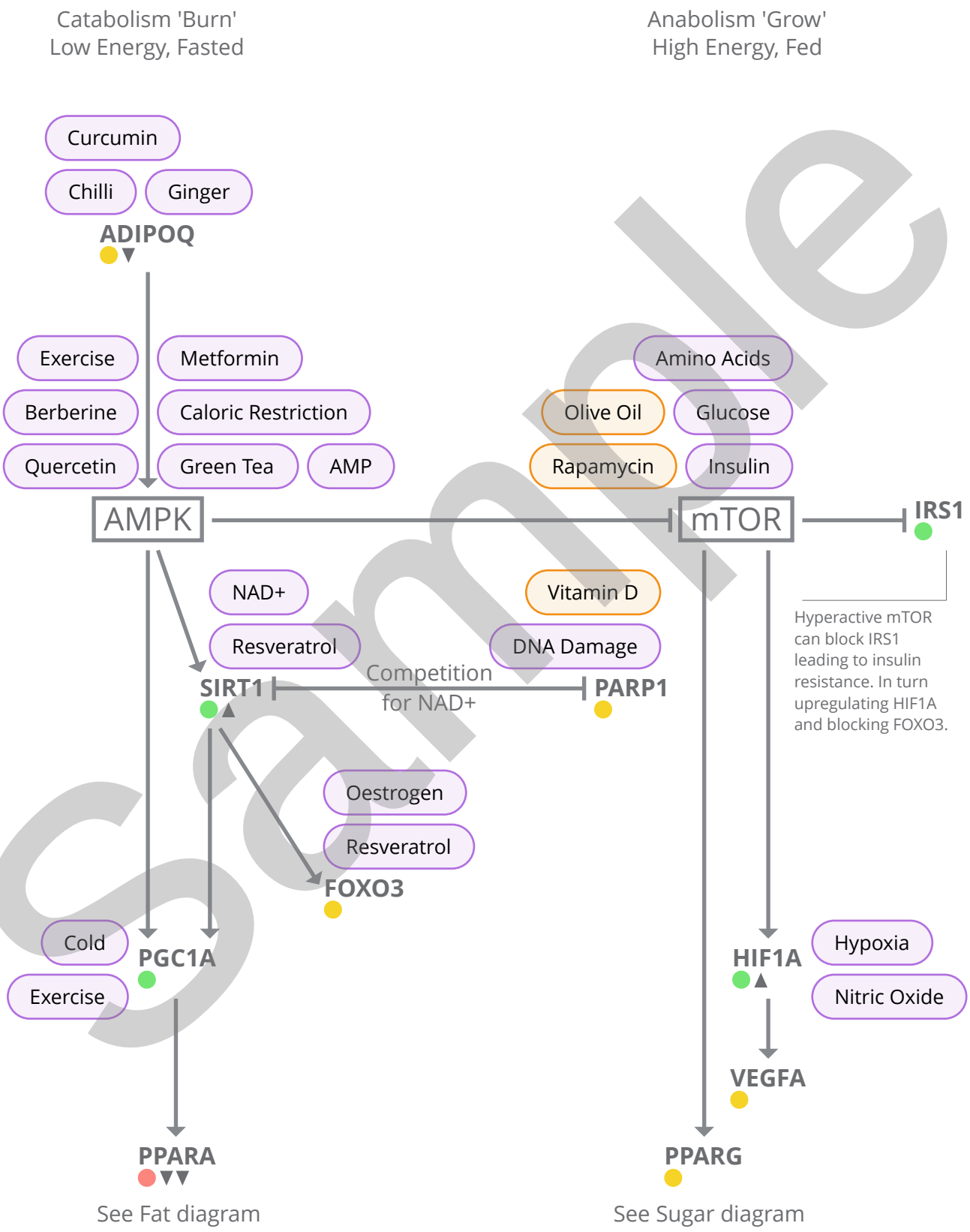
This Metabolics report describes how nutrients are absorbed and metabolised, and the genetic, nutrient and environmental factors that support metabolic flexibility or can lead to dysfunction. It provides six interconnected personalised pathways and detailed results, followed by a generic metabolics guide. The pathways covered are:

- Appetite regulation
- Nutrient sensing
- Sugar metabolism
- Fat metabolism
- Cholesterol and bile
- Mitochondria and inflammation

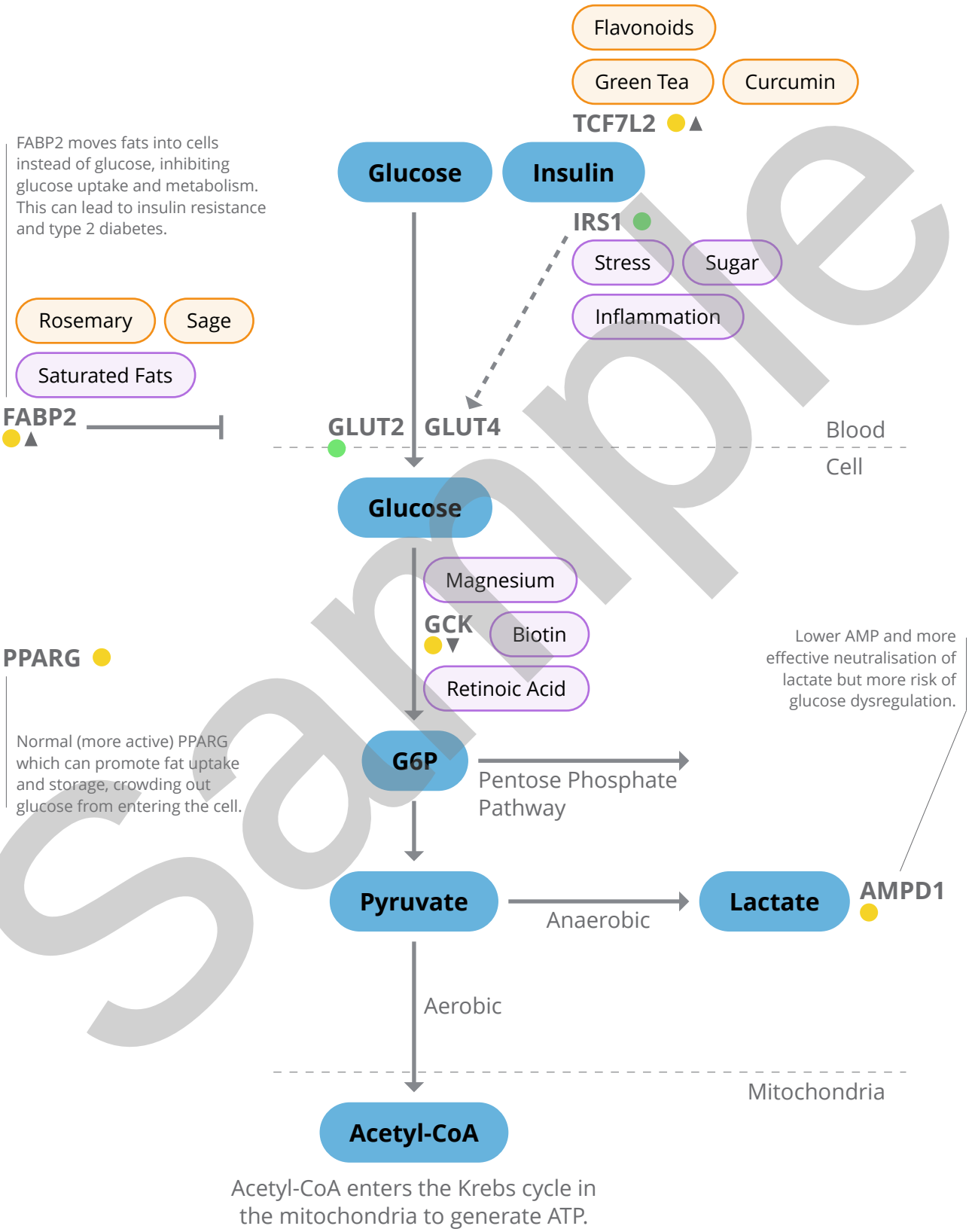
Appetite Regulation



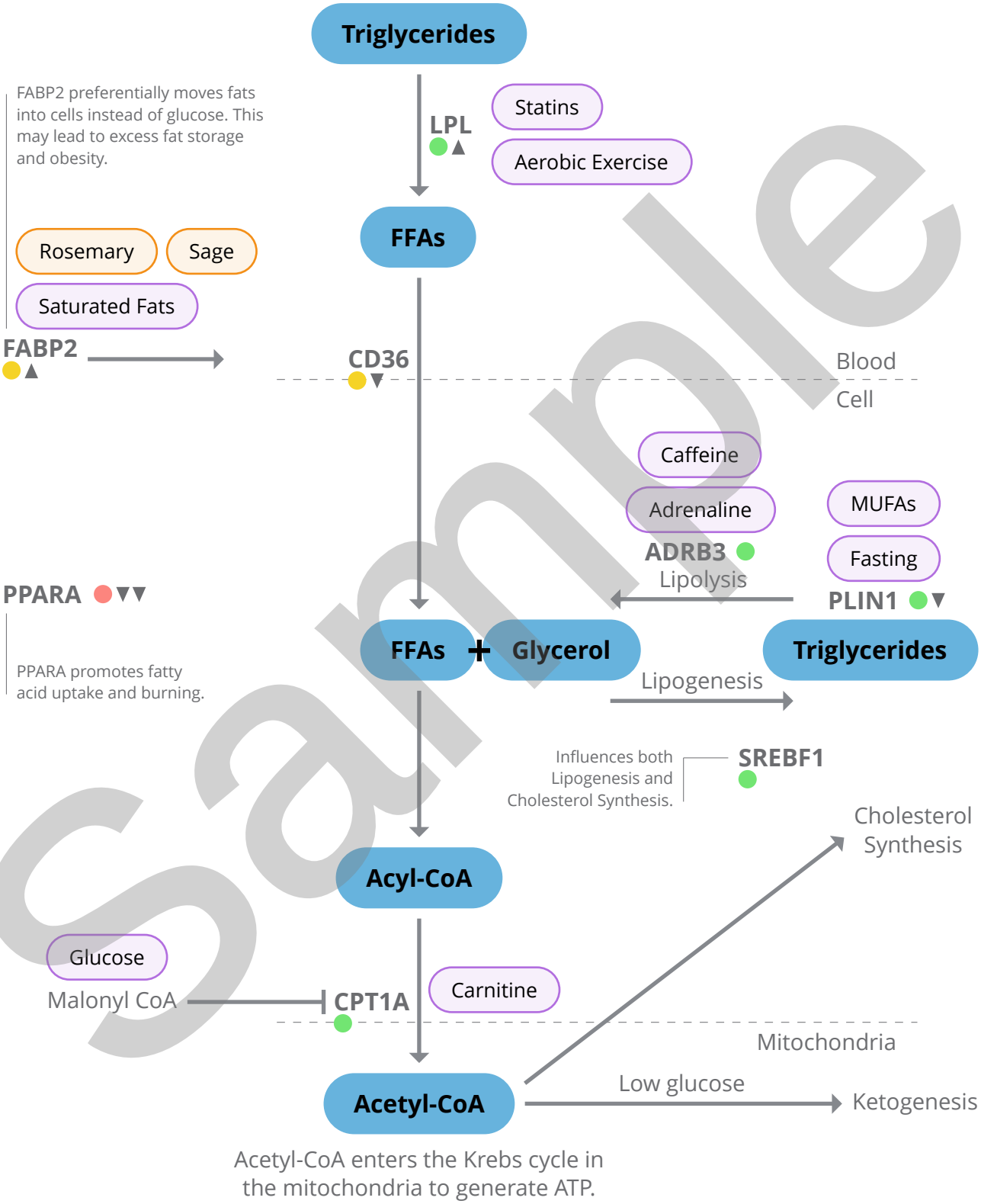
Nutrient Sensing



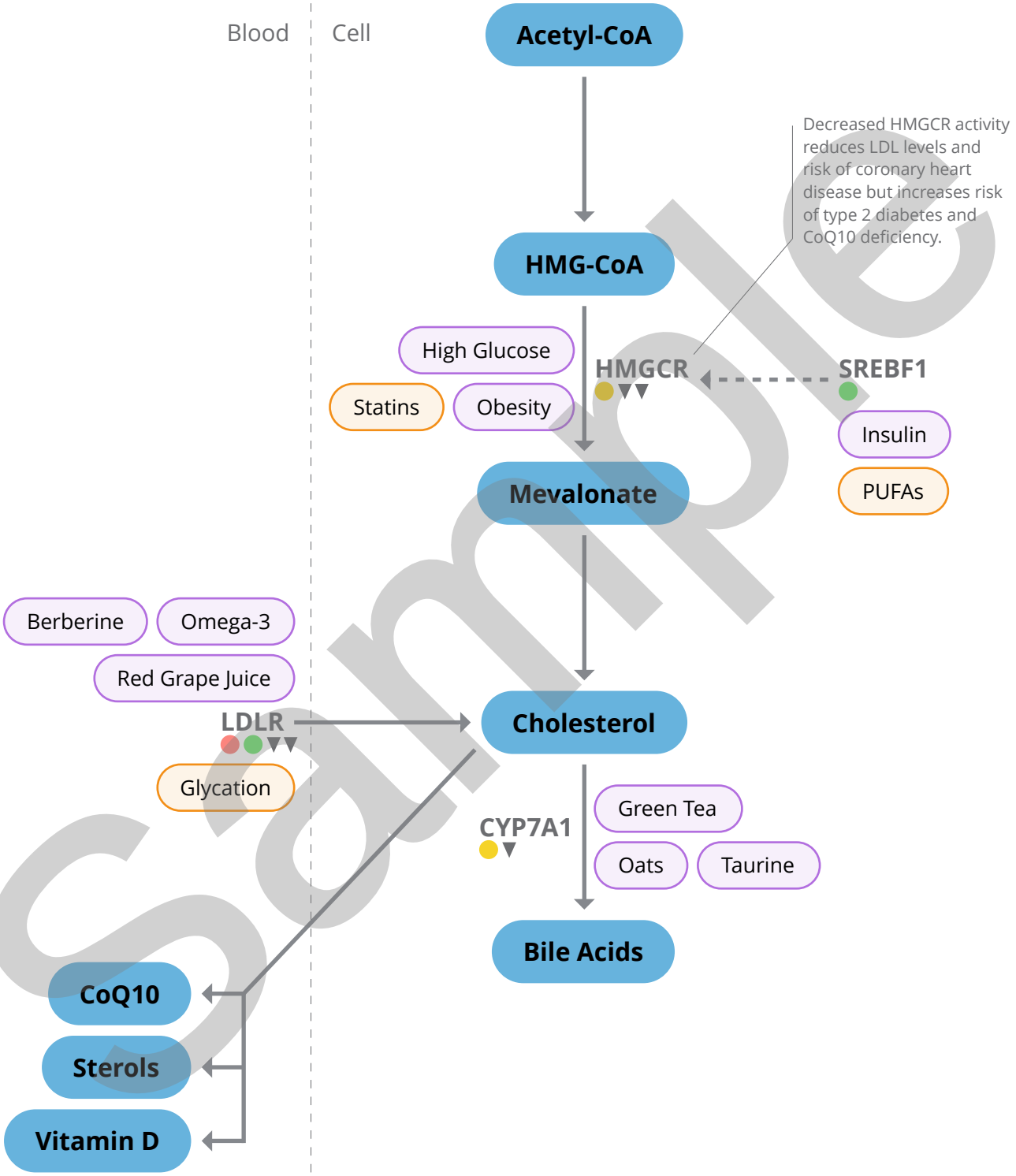
Sugar Metabolism



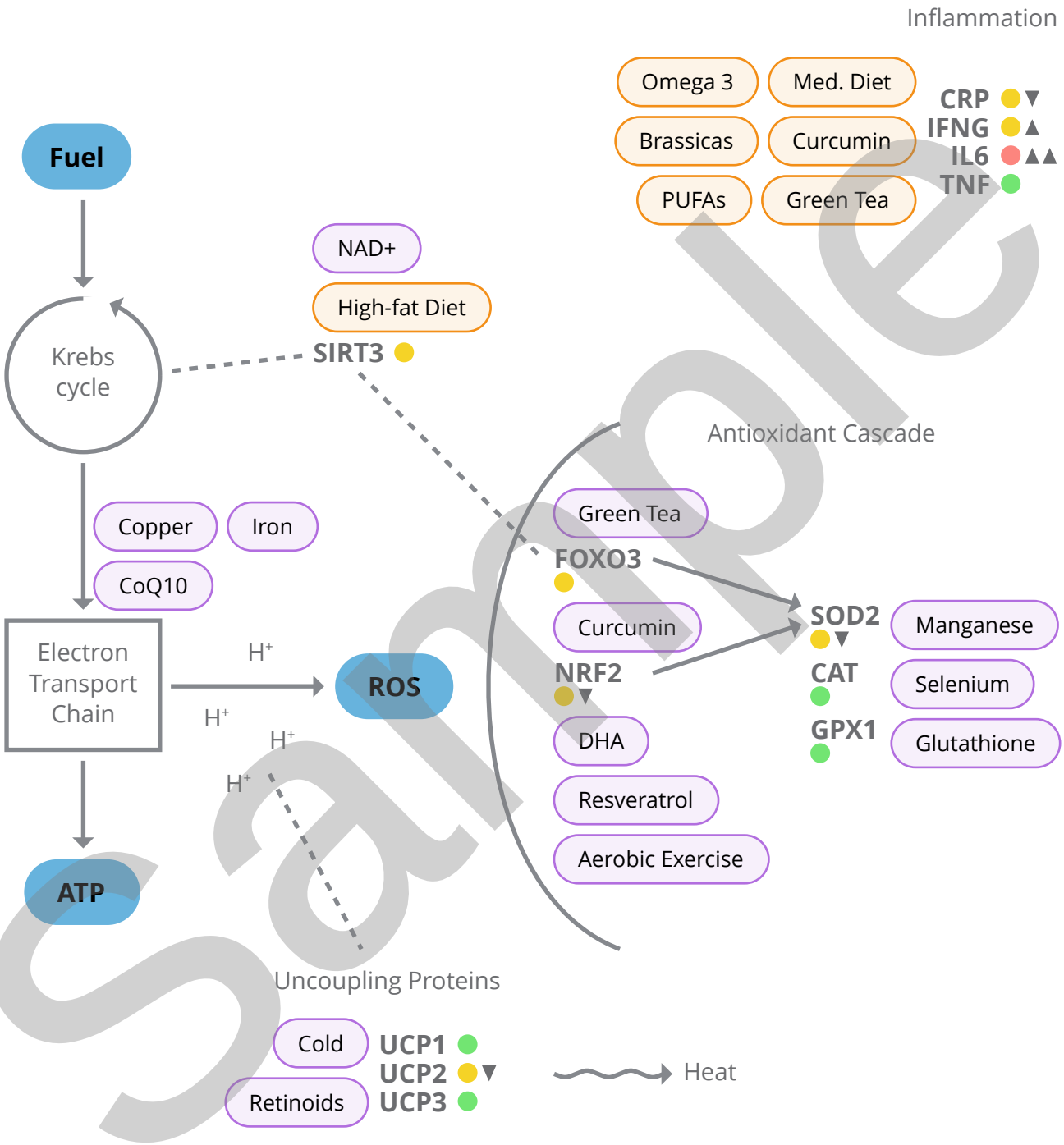
Fat Metabolism



Cholesterol and Bile



Mitochondria and Inflammation



Appetite Regulation

BDNF rs6265	CC	Normal brain-derived neurotrophic factor activity. No impact on appetite. BDNF can be increased by intense exercise, vitamin D, vitamin B3 (niacin), curcumin, green tea, DHA (a component of omega-3 fatty acid) and resveratrol.
FAAH	AC ▼	The A allele confers significantly lower FAAH activity (up to 50%) and slower deactivation of cannabinoids, which may contribute to higher levels. This can lead to higher ghrelin, increased appetite and weight gain. Limit intake of omega-6 fats which can increase cannabinoid levels, snacking, and risk of over-eating. Oleic acid, in olive oil, can help to regulate cannabinoids and ghrelin.
FTO	AT ▲	The A allele confers over-expression of FTO, subsequent increase in ghrelin (hunger), and reduced satiety after meals. Preference for calorie-dense (sweet and high fat) foods and increased risk of obesity. This SNP confers on average 3kg more than the wild genotype. Proteins and complex carbohydrates are preferable to a high-fat diet. Rhubarb and green tea are both FTO inhibitors.
LEPR	GG▼▼	Lower sensitivity to leptin (the 'satiety hormone'), resulting in increased appetite, lower metabolism, and increased risk of obesity. Omega-3 fatty acids (in oily fish), exercise and sleep improve leptin sensitivity.
MC4R	TT	Normal (good) melanocortin receptor sensitivity. Good appetite regulation and fat metabolism. Also consider other SNPs on the pathway.
NPY	TT	NPY and AgRP are stimulated by ghrelin and inhibit the melanocortin pathway (via MC4R) to induce appetite. Normal (not increased) NPY signalling and appetite.

Some pages have been
omitted in the sample

A Guide to Metabolics

This guide contains detailed explanations of the pathways, genes and dietary/environmental factors involved in metabolism. It looks at appetite regulation, nutrient sensing, sugar and fat metabolism, cholesterol and bile synthesis, and mitochondrial function and inflammation.

Appetite Regulation

The brain plays an important role in food intake, energy expenditure and body weight regulation. The gut controls the brain's feeding behaviour via hunger and satiety signals. These signals are mediated by two opposing hormones – ghrelin and leptin – which interact with the central melanocortin system.

Ghrelin is commonly called the 'hunger hormone' as it stimulates appetite, increases food intake and promotes fat storage, via receptors in the brain. As ghrelin is under circadian control, it is higher in the morning (daylight), prompting food seeking (foraging) behaviour.

Leptin is the 'satiety hormone' which inhibits hunger after eating and stimulates metabolism. Levels are higher in the evening (darkness) and when they drop the brain interprets this as a loss of energy and hunger increases.

In summary, ghrelin is associated with a low energy, fasted state and leptin with a high energy, fed state.

Low Energy, Fasted

FTO (fat mass and obesity-associated protein) is commonly called the 'fat gene' due to its connection with increased appetite. It is highly expressed in the brain as well as the heart, kidneys and fat cells. Over-expression of FTO, due to genetic variance, is associated with lower leptin levels, higher ghrelin levels, and an increased preference for calorie-dense (sweet and high fat) foods. A SNP on FTO has been consistently associated with higher body fat, BMI, waist circumference and obesity (on average 3kg heavier). Rhubarb and green tea are both FTO inhibitors.

Cannabinoids promote ghrelin, food intake and energy accumulation. FAAH (fatty acid amide hydrolase) metabolises endogenous cannabinoids including AEA (N-arachidonoylethanolamine, known as anandamide) and 2-AG (2-arachidonoylglycerol) which are involved in the perception of pain, regulation of appetite and immune system function. A SNP on FAAH has lower activity and thus increased levels of cannabinoids. This can confer increased appetite (higher ghrelin), food intake and weight gain. Limit intake of omega-6 fats which can increase cannabinoid levels, ghrelin driven foraging behaviour (snacking), and risk of over-eating. Oleic acid, in olive oil, can help to regulate cannabinoids and ghrelin.

NPY (neuropeptide Y) and AgRP (agouti-related peptide) promote food consumption and energy accumulation. They are stimulated by ghrelin and inhibit the melanocortin pathway (via MC4R), which together increase appetite. Conversely, when energy is higher after eating, neurons that express POMC (proopiomelanocortin) are recruited to antagonise the actions of NPY and AgRP to reduce food intake and stimulate metabolism. AgRP and POMC neurons compose a unique neural circuit known as the melanocortin system.

The NPY gene is expressed in the central nervous system and influences many processes, including stress response, food intake, circadian rhythms, and cardiovascular function. A SNP confers significantly higher NPY and AgRP activity, increased appetite and decreased energy expenditure. This is associated with more 'foraging' behaviour towards food and alcohol, and greater risk of obesity and metabolic dysfunction. NPY is increased in obesity, which can result in a vicious cycle. It is also associated with maladaptive responses to stress (over or under-eating).

The conclusion of this pathway is hunger.

High Energy, Fed

Leptin interacts via its receptor LEPR in the brain, tells it there is enough energy, and sends the message of satiety and suppression of hunger. As adipocytes (fat cells) produce leptin, greater adiposity (fatness) results in higher leptin levels. This can lead to 'leptin resistance' (loss of sensitivity of the receptor) so one never feels full. Variances on the LEPR gene can have the same effect – lower sensitivity to leptin and reduced satiety. Leptin sensitivity can be increased with omega-3 fatty acids, exercise and sleep.

After activation by leptin, the POMC protein is cut into smaller pieces including MSH (melanocortin) peptides. A SNP on POMC can result in a shorter version of the protein and fewer MSH peptides and less binding to MC4R (melanocortin-4 receptor), resulting in greater interest in food and impaired satiety. A high protein diet including tryptophan (in chicken and almonds) and olive oil can increase POMC and help reduce appetite. Serotonin activates POMC, resulting in similar satiety effects as leptin. In addition to negative impacts on mood and mental health, low serotonin has been linked to weight gain, obesity and diabetes. Insulin is also an inducer of POMC, while palm oil inhibits it.

MC4R is an important regulator of energy homeostasis, food intake and body weight via its binding to BDNF (brain-derived neurotrophic factor). A SNP on MC4R indicates a less sensitive receptor, and weaker satiety signalling and metabolism. It is the single most impactful genetic polymorphism predisposing to obesity. Carriers should limit portion size of meals, choose smaller plates and avoid the buffet (and seconds).

BDNF promotes growth, differentiation and survival of neurons and synapses in the central and peripheral nervous systems. In the melanocortin system, BDNF plays an essential role in regulating appetite and energy balance. A SNP can reduce its activity and increase the risk of obesity. BDNF can be increased by intense exercise, vitamin D, curcumin, green tea, omega-3-fatty acids and resveratrol.
The neurotransmitter dopamine also plays a role in controlling eating behaviours, by activating the melanocortin neuron.

The conclusion of this pathway is satiety.

Some pages have been
omitted in the sample

How to Read the Report

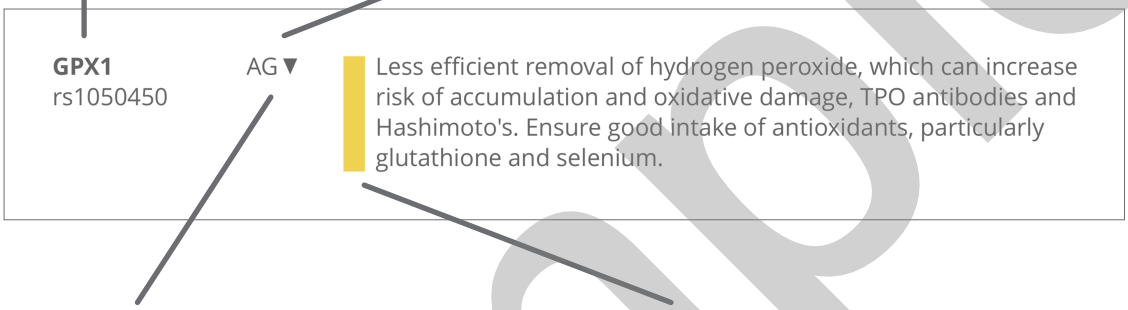
Genes

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.

Multiple attempts are made to achieve the required level of statistical confidence, but if that cannot be met it is reported as **'No result'**.



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

ADIPOQ Adiponectin, C1Q and collagen domain containing

Alimi M, Goodarzi MT, Nekoei M. Adiponectin gene polymorphisms and risk of type 2 diabetes: an updated evidence for meta-analysis. Diabetol Metab Syndr. 2021 Nov 17;13(1):133. doi: 10.1186/s13098-021-00749-x. PMID: 34789338; PMCID: PMC8596906. (https://pubmed.ncbi.nlm.nih.gov/34789338/)

ADRB3 adrenoceptor beta 3

Chenyao Xie, Wenxi Hua, Yuening Zhao, Jingwen Rui, Jiarong Feng, Yanjie Chen, Yu Liu, Jingjing Liu, Xiaoqin Yang & Xiaojing Xu (2020) The ADRB3 rs4994 polymorphism increases risk of childhood and adolescent overweight/obesity for East Asia's population: an evidence-based meta-analysis, Adipocyte, 9:1, 77-86, DOI: 10.1080/21623945.2020.1722549. (https://www.tandfonline.com/doi/full/10.1080/21623945.2020.1722549)

AMPD1 Adenosine Monophosphate Deaminase 1

Cheng J, Morisaki H, Toyama K, Sugimoto N, Shintani T, Tandelilin A, Hirase T, Holmes EW, Morisaki T. AMPD1: a novel therapeutic target for reversing insulin resistance. BMC Endocr Disord. 2014 Dec 15;14:96. doi: 10.1186/1472-6823-14-96. PMID: 25511531; PMCID: PMC4274759. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4274759/)

Ginevičienė V, Jakaitienė A, Pranculis A, Milašius K, Tubelis L, Utkus A. AMPD1 rs17602729 is associated with physical performance of sprint and power in elite Lithuanian athletes. BMC Genetics. 2014;15:58. doi:10.1186/1471-2156-15-58. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4032451/)

Jinnah HA, Sabina RL, Van Den Berghe G. Metabolic disorders of purine metabolism affecting the nervous system. Handb Clin Neurol. 2013;113:1827-36. doi: 10.1016/B978-0-444-59565-2.00052-6. PMID: 23622405; PMCID: PMC4215161. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4215161/)

BDNF Brain Derived Neurotrophic Factor

Singh, R., Takahashi, T., Tokunaga, M., Wilczynska, A., Kim, C., Meester, F., Handjieva-Darlenska, T., Cheema, S., Wilson, D., Milovanovic, B., Fedacko, J., Hristova, K. and Chaves, H., 2014. Effect of Brain Derived Neurotrophic Factor, In Relation to Diet and Lifestyle Factors, for Prevention of Neuropsychiatric and Vascular Diseases and Diabetes. The Open Nutraceuticals Journal, 7(1), pp.5-14. (https://benthamopen.com/contents/pdf/TONUTRAJ/TONUTRAJ-7-5.pdf)

CAT Catalase

Goulas A, Agapakis D, Apostolidis A, Gouda D, Anastassiadis S, Trakatelli C, Savopoulos C, Hatzitolios AI. Association of the Common Catalase Gene Polymorphism rs1001179 With Glycated Hemoglobin and Plasma Lipids in Hyperlipidemic Patients. Biochem Genet. 2017 Feb;55(1):77-86. doi: 10.1007/s10528-016-9777-2. Epub 2016 Oct 4. PMID: 27704307. (https://pubmed.ncbi.nlm.nih.gov/27704307/)

CD36 fatty acid transporter

Karthi M, Deepankumar S, Vinithra P, Gowtham S, Vasanth K, Praveen Raj P, Senthilkumar R, Selvakumar S. Single nucleotide polymorphism in CD36: Correlation to peptide YY levels in obese and non-obese adults. Clin Nutr. 2021 May;40(5):2707-2715. doi: 10.1016/j.clnu.2021.02.044. Epub 2021 Mar 6. PMID: 33933736. (https://pubmed.ncbi.nlm.nih.gov/33933736/)

Zhao, L., Li, Y., Ding, Q., Li, Y., Chen, Y. and Ruan, X., 2021. CD36 Senses Dietary Lipids and Regulates Lipids Homeostasis in the Intestine. Frontiers in Physiology, 12, https://doi.org/10.3389/fphys.2021.669279. (https://www.frontiersin.org/articles/10.3389/fphys.2021.669279/full)

CPT1A carnitine palmitoyltransferase 1A

Gobin S, Thuillier L, Jogl G, Faye A, Tong L, Chi M, Bonnefont JP, Girard J, Prip-Buus C. Functional and structural basis of carnitine palmitoyltransferase 1A deficiency. J Biol Chem. 2003 Dec 12;278(50):50428-34. doi: 10.1074/jbc.M310130200. Epub 2003 Sep 29. PMID: 14517221. (https://pubmed.ncbi.nlm.nih.gov/14517221/)

Robitaille J, Houde A, Lemieux S, Pérusse L, Gaudet D, Vohl MC. Variants within the muscle and liver isoforms of the carnitine palmitoyltransferase I (CPT1) gene interact with fat intake to modulate indices of obesity in French-Canadians. J Mol Med (Berl). 2007 Feb;85(2):129-37. doi: 10.1007/s00109-006-0116-7. Epub 2006 Nov 7. PMID: 17089095. (https://pubmed.ncbi.nlm.nih.gov/17089095/)

CRP C-Reactive Protein

Arouca AB, Meirhaeghe A, Dallongeville J, Moreno LA, Lourenço GJ, Marcos A, Huybrechts I, Manios Y, Lambrinou CP, Gottrand F, Kafatos A, Kersting M, Sjöström M, Widhalm K, Ferrari M, Molnár D, González-Gross M, Forsner M, De Henauw S, Michels N; HELENA Study Group. Interplay between the Mediterranean diet and C-reactive protein genetic polymorphisms towards inflammation in adolescents. Clin Nutr. 2020 Jun;39(6):1919-1926. doi: 10.1016/j.clnu.2019.08.016. Epub 2019 Aug 23. PMID: 31500937. (https://pubmed.ncbi.nlm.nih.gov/31500937/)

Bordoni L, Petracci I, Zhao F, Min W, Pierella E, Assmann TS, Martinez JA, Gabbianelli R. Nutrigenomics of Dietary Lipids. Antioxidants (Basel). 2021 Jun 22;10(7):994. doi: 10.3390/antiox10070994. PMID: 34206632; PMCID: PMC8300813. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8300813/)

Some pages have been
omitted in the sample

Lifecode GX ®
— Professional Genotype Analysis —

Disclaimer

The information provided should not be used for diagnostic or treatment purposes and is not a substitute for personal medical advice. Use the information provided by Lifecode Gx® solely at your own risk.

Lifecode Gx® makes no warranties or representations as to the accuracy of information provided herein. If you have any concerns about your health, please consult a qualified health professional.