

Technical Resource for Clinicians



Genomics and Lifestyle Medicine in Practice

How to easily extract the clinical
information you need

Genomics: The shift to personalised medicine is already underway

Since the completion of the human genome project our understanding of the complexity of the interactions between environmental factors such as diet and genes has progressed significantly. This gave rise to the concept of personalised nutrition, where tailored dietary advice is delivered to individuals based primarily on genetic factors but also including other personal information, such as current diet, lifestyle and phenotype, which are important for personalising dietary advice. This contrasts with most public health advice about diet, which is generic, non-specific healthy eating advice, for example, 'eat at least five portions of fruit and vegetables daily'. It is also a move away from population-based "one-size-fits-all" diets towards nutrigenomic-based personalised nutrition.



This new approach to dietary interventions is a move away from "one-size-fits-all" diets towards nutrigenomic-based personalised nutrition.

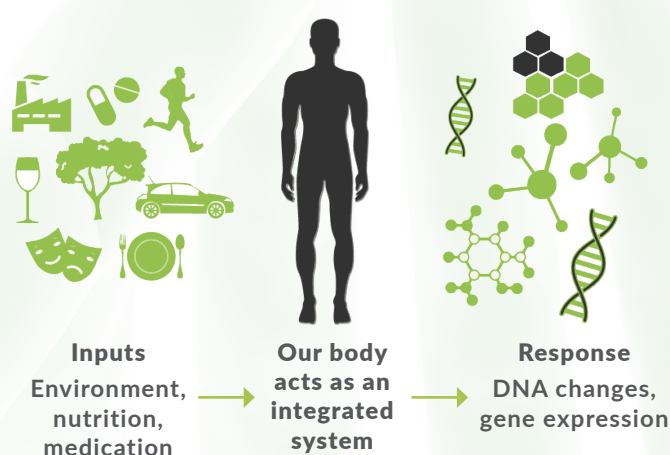
Tackling the rising tide of non-communicable disease

According to Public Health England the prevalence of most non-communicable diseases (NCDs) is on the rise, partly because of better detection but also because of "genuine" rises – driven in part by an ageing population but also by lifestyle choices including smoking, poor diet, physical inactivity, alcohol use and being overweight.

Attitudes toward genetic testing and personalised nutrition

Although most existing research into the public view of genetic testing has been qualitative, health benefits have been reported as key motivators in the uptake of genetic testing. Individuals reporting personal experience of disease seem to be more willing to get a genetic test done.

For those not yet presenting symptoms of NCDs, myDNAhealth believes there is still a need for more public education as genetic testing alone cannot tell people their likelihood of developing a disease. Most diseases occur as a result of interaction between genes and lifestyle and environmental factors.



Most diseases occur as a result of interaction between genes, lifestyle and environmental factors. In the majority of cases, genetic testing, even when carried out to high standards, is only one of the pieces of information about susceptibility to disease.

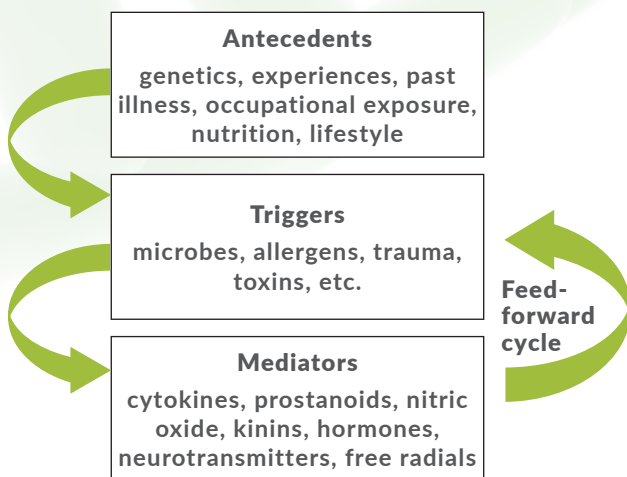
Fundamental principles

- Individualised, patient-centred, scientific-based approach that empowers patients and clinicians to work together to address the underlying causes of disease and promote wellness.
- Requires a detailed understanding of each patient's genetic, biochemical, and lifestyle factors and leverages that data to direct personalised treatment plans that lead to improved patient outcomes.



Our genes are not our destiny as... dietary and lifestyle choices have strong influences on our genetics and health conditions.

Understanding genetic predispositions is informative when assessing antecedents, triggers and mediators. It can be very helpful for nutrition assessment and lifestyle intervention with patients.



What can myDNAhealth provide?

myDNAhealth can help patients adjust to their dietary and lifestyle behaviour to enhance their long-term health and well-being. Personalised nutrition offers a new approach by providing advice about healthy food choices and eating patterns to fit an individual's needs and personal preferences.

myDNAhealth interprets a patient's genetic and lifestyle data based on the knowledge of how current

diet, nutrition and the environment may be interacting with their genes (increasing or decreasing enzyme activity) and provides risk scores covering 26 health and wellness areas.

This unique approach to personalisation analyses and reports; genotype; phenotype, habits and lifestyle; and nutrient sensitivities such as gluten, lactose and caffeine and potential key nutrient deficiencies.

myDNAhealth's algorithm assesses thousands of data points and makes recommendations for a personalised diet and lifestyle plan based on risk scores in each area assessed. The patient receives an easy-to-understand report and they will also gain access to their personalised Meal Plans with weekly menus and recipes.



Lifestyle Medicine: Evidence-based approach to health and well-being

myDNAhealth adopts a rigorous scientific three-step process called RRA, with each step being a requisite in order to process to the next step.

1. Relevancy: Comprehensive scientific literature review which covers functional mechanism (transcription cell signaling, gene expression), biological pathways, single nucleotide

polymorphisms (SNPs) to understand if coding, non-coding or a regulatory region of the gene and epidemiology.

2. **Reliability:** The scientific findings are further scrutinised by the **myDNAhealth** scientific and genetics team and scored according to biological significance, functional mechanism, number of independent studies or papers and demographic profile of groups included in each study.
3. **Actionable:** **myDNAhealth's** scientific and genetics team repeat the process to further scrutinise and score the epigenetic and nutrigenomic evidence i.e. lifestyle and nutrition intervention for gene expression and health.

The **myDNAhealth** combined approach analyses risk factors which may impact gene expression in several key health and wellbeing areas

Stress

Life stressors are among the risk factors for depression and increasingly research is evidencing links to upregulation of the key areas of the immune system involved in inflammation. The problem is that when we're exposed to daily stress, inappropriate inflammation may persist at the cellular level and can trigger a domino effect leading to development of chronic inflammatory conditions. This highlights just how much our psychology can affect our biology.

Responding to stress in a healthy way is vital to our long-term health and well-being. **myDNAhealth's** lifestyle questionnaire is designed to highlight personalised recommendations into how making small changes to daily choices can improve well-being.

Exercise

The health benefits of regular physical exercise are unquestionable from increasing blood flow and the delivery of oxygen to upregulating anti-inflammatory pathways. Research continues to support exercise as a powerful heritable epigenetic mechanism to support health in areas such as cognitive function, ageing, metabolic dysfunction and heart disease.

Sleep

Insomnia is a serious worldwide health threat, affecting nearly one third of the general population. Sleep is when cell maintenance and repair occurs, and when, for example, beta-amyloid plaque, one of the proteins responsible for blocking cell communications is cleared from the brain. Sleep is also important for gene expression, detoxification and methylation, and emerging evidence has assigned an important role to

sleep as a modulator of metabolic homeostasis.

For instance, insufficient sleep (short sleep duration and/or poor sleep quality) has been linked in scientific literature as part of the multifactorial landscape of obesity and appetite control which is impacted by sleep disruption, resulting in overeating. Genome wide analysis studies of obesity have identified hundreds of potential genetic variants which may be involved.

One of these, the **Circadian Locomotor Output Cycles Kaput (CLOCK)** gene which functions as a transcription regulator factor in the regulation of circadian rhythms has generated scientific interest in genetic variation which may be linked to the development of obesity through appetite. Although some promising research is emerging regarding these genetic variations there is currently not quite enough evidence to single out a specific SNP to meet **myDNAhealth's** rigorous RRA principle and merit inclusion within the DNA test. **myDNAhealth** will continue to monitor this exciting new area of research and evaluate for inclusion in the future.

However, as part of the lifestyle questionnaires, **myDNAhealth** does assess sleep quality and links this to the overall epigenetic impact, indicating lifestyle changes which may be useful.

Sensitivity to carbohydrates/sugar metabolism and risk of type 2 diabetes

Since 1996 the number of Britons diagnosed with type 2 diabetes (T2DM) has more than doubled, from 1.4 million to nearly 3.5 million, costing the NHS £10 billion annually. There is also an estimated further 1.1 million currently living with undiagnosed T2D.

We know that the more often blood sugar rises, the more insulin is produced and as more is produced, more sugar is turned into fat. Over time, the body's cells become less responsive (or resistant) to insulin, causing even more insulin to be produced which can contribute to the development of T2D. In addition to excessive sugar consumption, there are other factors that contribute to the development of insulin resistance and T2D including too much highly processed food, physical inactivity and low muscle mass, sleep deprivation, persistently high stress levels, disturbed gut bug ecosystem and low levels of vitamin D.

So what can genetics reveal about a patient's risk potential? Below is a brief outline of some of the common genetic variants which have been shown to have some impact.

Peroxisome Proliferator-Activated Receptor – 2 (PPARG2) has multiple roles in adipose tissue including adipogenesis, lipid metabolism, glucose homeostasis

and insulin sensitisation. Also known as the “thrifty gene” it helps store fat into fat cells. A member of a super family of nuclear receptors, PPARG has a transcription factor role initiating gene expression. As a result, in times of plenty, a PPARG risk variant can contribute to the causes of obesity when an individual consumes too much fat and sugar.

Transcription factor 7-Like 2 (TCF7L2) gene encodes another transcription factor involved with blood glucose homeostasis by switching on several other genes within the cell to initiate receiving insulin to the receptor and glucose to the cell. Individuals with a risk variant of this gene may be more susceptible to insulin resistance and often find it harder to lose weight.

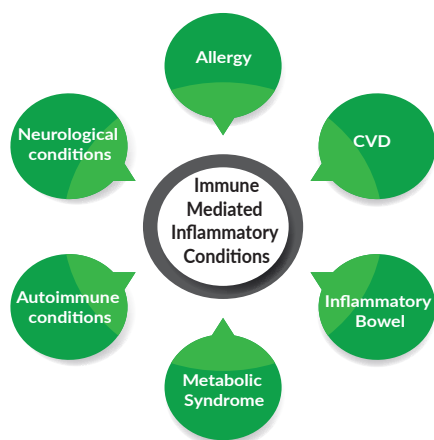
Obesity

Fat Mass and Obesity (FTO) is known as our “hunger” or “snacking” gene and plays a role in appetite regulation and weight gain. A genetic variant is associated with increased BMI, body fat percentage and waist measurement. Evidence shows that by walking daily for 30 minutes a carrier of this variant can lower that risk by up to 30 percent. By watching diet, eating loads of leafy greens, along with exercise the risk could be lowered by up to 50 percent.

Melanocortin-4 Receptor (MC4R) gene is involved in the regulation of our appetite. Patients with the MC4R variant can be deficient in the MC4R protein and may show increased food-intake, obesity and hyperinsulinemia. Recent research shows those carrying a genetic risk variant have an increased preference for high fat foods and decreased preference for sugar foods.

Inflammation: Genetic variants, nutrition and lifestyle

Common inflammatory mediators such as C-reactive



protein, eicosanoids, nitric oxide, cytokines, collagenase/MMP, TNF-alpha and oxidative stress contribute to many wide ranging health problems including cardiovascular, inflammatory bowel, autoimmune and neurological (particularly conditions

such as depression and Alzheimer's) diseases.

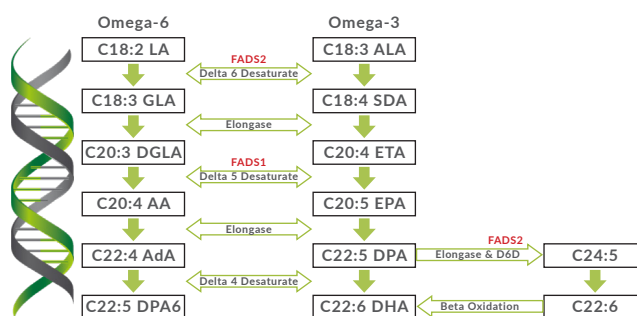
The field of Nutritional Genomics is ever expanding and genetic variants are increasingly being linked to the mechanisms of some of these mediators in inflammation.

Interleukin 6 receptor (IL6R) encodes a subunit of the interleukin 6 (IL6) receptor complex and has a role in inflammatory conditions. IL6 is a cytokine and has both pro- and anti-inflammatory actions through two main signaling pathways. IL6R affects clearance of IL6 through the liver which in turn affects systemic inflammation. Low grade chronic inflammation is associated with obesity and visceral fat deposition, insulin resistance, dyslipidaemia and elevated risk for CVD.

A genetic variant of the IL6R has been associated with reduced C-reactive protein (CRP) and fibrinogen leading to reduced inflammation and therefore, lifestyle modification may be beneficial in those who do not carry this variant.

Tumour Necrosis Factor (TNF-alpha) is a macrophage derived pro-inflammatory mediator which has been associated with inflammatory conditions. A genetic variant of the TNF-alpha gene promoter region is associated with increased production of this cytokine. Those who carry this variant have the capability to produce more TNF-alpha amplifying the inflammatory message and has been outlined in related conditions such as obesity, T2DM and metabolic syndrome. Interestingly, research has established potentially beneficial down-regulatory actions of nutritional factors such as omega 3 polyunsaturated fatty acids (PUFA) and green tea extracts involved with this risk variant.

FADS1 and FADS2 (eicosanoid balance): The essential polyunsaturated fatty acid families of omega 3 and omega 6 influence inflammation through a variety of mechanisms and their balance within cells influences pro- vs anti-inflammatory balance. Levels of key PUFAs including arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are influenced by both diet and gene expression.

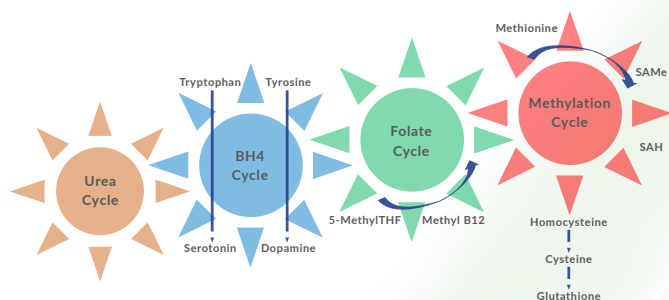


Metabolism of these important fatty acids is through side by side lipid metabolic pathways which share the

same competitive enzymes. The desaturase (D5D and D6D) enzymes are recognised as important determinants of PUFA levels and are encoded by the FADS1 and FADS2 genes respectively. Investigations of FADS1 and FADS2 genetic variants in these two genes have shown changes in PUFA profiles which are known to influence inflammatory balance.

DNA methylation is the intersection of four important biochemical pathways in the body driven by the need for methyl groups essential for important functions such as DNA synthesis, immunity and detoxification.

Studies have also shown that effective methylation capacity is important for the regulation of inflammatory genes and changes are linked to the expression of inflammatory genes. A central enzyme involved in the methylation cycle is produced by a gene you may have heard of, **methylenetetrahydrofolate reductase (MTHFR)** and the efficiency of this influences production of SAMe, a methyl donor, and homocysteine levels.



Genetic variants are strongly associated with reduced SAMe and mild increases in homocysteine, related to inflammatory conditions.

Susceptibility to Alzheimer's disease

Dementia and Alzheimer's disease (AD) was reported as one of the leading causes of death in England and Wales in 2015. (source: Office of National Statistics)

AD is caused by imbalances in the network of synaptic signals that affect memory, the main root cause being excess inflammation. It is also diet, lifestyle and environment which contribute to risk. However, there are genetic factors which may increase a patient's risk and the inflammation can be particularly useful if they also have a family history of AD.

The **APOE** gene provides instructions for making a protein called **apolipoprotein E**. This protein combines with lipids in the body to form lipoproteins which are responsible for packaging cholesterol and other fats and carrying them through the bloodstream. ApoE has recently been found also to be involved in processes other than fat metabolism, such as regulation of the immune system, and cognitive (thought) processes within the brain. There are three main genetic

isoforms of ApoE namely, ApoE2, ApoE3 and ApoE4, determined by two main SNPs making up one allele. The three major isoforms differ from one another only by single amino acid substitutions, yet these changes have profound functional consequences at both the cellular and molecular levels.

Research shows that those who inherit the ApoE4 allele have increased risk of CVD, partly due to dysfunction of LDL in lipid metabolism and this allele is also now linked to Alzheimer's disease, obesity and T2DM.

APOE4 carriers should be coached for the need to follow a healthy diet, rich in phytonutrients, and focus on quality fats high in DHA. In addition, it is known ApoE4 carriers are susceptible to toxins found in cigarettes and alcohol. To lower any further risk of degenerative conditions created by high blood sugar, a low sugar diet is also often recommended.

Coeliac disease

HLA is a risk factor in coeliac disease (CD) and up to 95 percent of CD patients carry either the HLA-DQ2.5 variant whilst the rest carry HLA-DQ8 or HLA-DQ2.2. The role of these HLA molecules in CD is now understood, whereby they preferentially bind to gluten peptides presenting them to T cells in the gut which initiates a cascade of inflammatory events eventually leading to CD lesions.

Up to 40 percent of the European population are positive for HLA-DQ2 or 8 but only three percent go on to be diagnosed which indicates that these SNPs are necessary but not sufficient for disease diagnosis. Because the HLA genotypes do not determine definitive CD, GWAS studies have been performed and have identified another 42 loci which contribute to CD, many of which are associated with other autoimmune conditions. This is the same position **myDNAhealth** takes regarding autoimmunity, in that the genomics is not yet in place for us to identify a group of SNPs which will definitively define or diagnose CD.

However, the risk for developing CD based on HLA genotype analysis can be reported as high, medium or low allowing health professionals to intervene with at-risk patients to make dietary changes that may help to reduce this risk factor and prevent CD.

Clinical Case Study

Results analysis and interpretation with intervention protocols

Below is a case study to illustrate how genetic testing – alongside a lifestyle assessment and case history – can fit into clinical practice for a “worried well” patient.

Patient: Male, 55, BMI 25, does not smoke and drinks alcohol only occasionally. He feels he has a very healthy lifestyle, apart from work stress, and exercises daily. Family history includes Alzheimer’s and cancer. Self-diagnosed as non-coeliac gluten sensitive (NCGS) and has long since removed all gluten, added sugars, refined carbs and unhealthy fats from the diet. On eating wheat or other gluten/gliadin-containing foods, he experiences acute irritable bowel-type symptoms. He describes his gut as his “contact breaker” – any health “blips” seem to show up there. Based on experience trying various eating patterns, he reports that he “does not handle fats well”.

Functional tests: IgG4 lab tests showed intolerance to eggs, almonds and sesame, with moderate reactions to coffee, pineapple and spinach. Functional screen flagged up “a tendency towards metabolic syndrome and a need for blood sugar support”; “a tendency towards a difficulty converting thyroxine (T4) into triiodothyronine (T3); which can cause symptoms of hypothyroidism; and a need for thyroid gland support” and hyperlipidaemia. Hs CRP (high-sensitivity C-Reactive Protein) at 21.52, where optimal is 0.00-5.24. Previous blood work did show higher-than-optimal values for fasting insulin and glucose, and high Haemoglobin A1C. Blood test also showed high homocysteine at 15.60µmol/L, with optimal seen as below 6.00. He also tested well below optimal on folate and low-normal on B12.

Presenting case: Patient is concerned about his poor sleeping pattern (wakes up and can’t get back to sleep) and ongoing inflammation. He has been experiencing a niggling, mild, but ongoing “muscle” soreness. He has opted to get a DNA test to explore his genetic susceptibilities in more detail to see if there is anything that can be tweaked in the interests of super-health and healthy ageing to prolong an active lifestyle.

So, what does the patient's lifestyle and genetics reveal?

Sleep and stress

The patient mentioned he is concerned about his poor sleeping pattern which is further confirmed in the questionnaire result. A further discussion with the patient established he is able to fall asleep but is waking up in the middle of the night which could give “clues” to an overactive mind not being able to “switch off”.

Looking further at the patient’s stress questionnaire result confirms higher levels of stress and anxiety in his life which can be impacting his sleep. Prolonged stress can result in excessive circulating cortisol, potential resultant neurotransmitter imbalance, adrenal fatigue, weight gain and can also affect the gut, impacting digestion. Those with digestive conditions are also likely to suffer from mood disorders.

To help the patient, discuss what’s causing the stress. Consider supporting nutrients that have a calming effect and/or support serotonin and melatonin production to help the patient while he makes some lifestyle changes to destress and get into healthier sleeping patterns. A digestive enzyme can also be beneficial. Further, support the methylation systems and ensure adequate intake of tryptophan rich foods for serotonin and melatonin conversion which help with mood and sleep. Good stomach acid is also required to stimulate absorption of B vitamins. Stress switches off stomach acid due to the fight or flight reaction.

Brain health – APOE4

The patient has APOE3:4 genotype which puts him within the 25 percent of the general population group. This increases his lifetime risk of developing AD by a little more than two times, on average, and given that this patient has a family history, his risk is elevated. However, having the genetics alone does not mean that he will get AD; other factors including environment and diet also play a role.

Excess inflammation is at the heart of many chronic disease processes, and AD is no exception. Therefore, to help reduce the risk factor, it’s very important to communicate the importance of a healthy lifestyle that helps reduce inflammation, lowers stress, improves sleep and removes toxins.

Another important contributor of Alzheimer’s is the sugaring of the brain, known as glycation. Fructose has been implicated as the chief sugar that causes glycation. It is hypothesised that glycation damages the LDL which makes it difficult for the APOE protein to take LDL up into the brain, resulting in poor cholesterol deposition in the brain. This is supported by the fact that people with type 2 diabetes are 2-5 times more at risk of Alzheimer’s than the average population.

From a diet perspective, the patient self-reports he has already removed pro-inflammatory foods such as added sugars and trans fats, found in most refined and processed and take-away foods, and gluten, which is also confirmed by the sugar sensitivity, inflammation and gluten sensitivity questionnaire results and food diary.

The patient can focus on eating low glycaemic load

carbs, healthy fats (MUFAs and PUFAs) and lots of colourful antioxidant rich vegetables and fruit per day. Alongside a balanced diet, supportive nutrients including high DHA omega 3, curcumin, N-Acetyl Cysteine or Glutathione can provide further brain protection.

To further support this potential risk, sleep needs to be improved as well as reducing stress and investigate any hormonal imbalances including thyroid (see function test result), sex hormones, adrenal and cortisol. Also investigate if there are any essential 'brain health' nutrient deficiencies and metal toxicity.

Sugar metabolism and carbohydrate sensitivity

The patient does not have a personal or family history of insulin resistance/T2D – his BMI and waist are well within the healthy range, and he does not eat sugar or refined, highly processed carbs, so at first glance the genetic variants revealed in his report show the importance of treating the patient, not the SNPs. However, his previous blood work did show higher-than optimal values for fasting insulin and glucose, and high Haemoglobin A1C.

The patient has the genetic predisposition for poor sugar metabolism, increased sensitivity to carbs, and should try to maintain an even blood sugar level through dietary changes. However, according to the patient's sugar sensitivity questionnaire result and food diary, he has already eliminated "bad" sugars and "bad" carbs in the diet.

QUESTIONNAIRE RESULT	
Mild Sugar Sensitivity	
ALGORITHM	RESULTS
Insulin	Moderate
Glucose	Moderate
Arterial	Moderate

GENES	RESULTS
ADRB2 Glu27	CG
ADRB2 Gly16	GG
FTO	TT
IL6R	CC
MC4R	CT
PPARGgamma	CG
TCF7L2	CT
TNF-alpha	GG

It is still important to communicate the importance of maintaining a healthy eating lifestyle to reduce the risk of developing health conditions such as insulin resistance and eventual hyperinsulinemia and T2D.

For this patient, we're reinforcing the idea that his refueling strategy after exercising should not depend

on high sugar sports drinks. He is aware of this but admits it is tempting to "put the carbs back" as quickly as possible. He was "delighted" to see TCF7L2 being highlighted, as to his mind it helped explain his Haemoglobin A1C being high, despite his avoidance of refined carbs and sugars except after exercising. A typical post-exercise tub of ice cream is his standard reward for a good workout as part of a refuelling strategy; that should be fine for a "treat", but probably not for a long-term game-plan. It may also indicate the patient is relying more on his immediate glucose stores and is perhaps not efficient in releasing fat for energy, however this needs further investigation as there are some interesting SNPs in this regard.

Methylation

The methylation cycle is a specific biochemical pathway that is responsible for influencing a variety of critical biological processes including the immune system, DNA maintenance, production of energy and detoxification. Genetic mutations may lead to abnormalities in the methylation process.

QUESTIONNAIRE RESULT	
Healthy Toxicity	
Moderately Interrupted Sleep	
GENES	RESULTS
CBS	AA
COMT	AA
MTHFR 677	TT
MTHFR 1298	AC
MTR	AG
MTRR	AA
VDR taq	CT

The patient's results indicate a susceptibility to hypomethylation (too little methyl) and potential raised homocysteine and histamine levels, low serotonin in the brain and a number of nutrient deficiencies. This was confirmed by his blood test, which showed raised homocysteine at 15.60µmol/L. He also tested well below optimal on folate and low-normal on B12.

The SNPs reported here are certainly not the whole methylation picture. Knowing a patient's SNP profile, combined with diet and lifestyle questionnaires, can give 'clues' as to methylation function and help to develop personalised nutritional and lifestyle protocols designed to optimise a patient's health. Here again, it is essential to assess lifestyle, dietary and environmental factors such as folate, alcohol, smoking, exercise, BMI, toxins, medications and infections, which can all affect DNA methylation.

Typical symptoms of hypomethylation can be perfectionism, high accomplishment, high achievement, low pain tolerance, allergy symptoms and low mood.

The patient self-reports “yes” to most of those, and is taking the SNP information as a wake-up call to ensure consistency with the right nutrition and lifestyle changes.

Homocysteine, an intermediate amino acid, is created through the methionine pathway, part of our in-house production of antioxidants and detoxifying compounds. Higher levels of homocysteine may indicate poor functioning of these pathways, and has been linked to vascular inflammation via oxidative stress in conditions such as coronary heart disease, hypertension and obesity.

Health implications of inflammation

The patient is also genetically more prone to inflammation, and may benefit from anti-inflammatory protocols to support gene expression. It is important to note that genetics alone do not affect response or susceptibility to inflammatory conditions; environmental factors also regulate gene transcription. These can include diet, infection, pollution, sleep and stress.

QUESTIONNAIRE RESULT	
Moderate Inflammation	
GENES	RESULTS
IL6R	CC
MTHFR 677	TT
TNF-alpha	GG

The patient described this information as “hugely valuable” for healthier ageing and his goal to remain physically active. The functional test red-flagged his Hs CRP level and the questionnaire result indicates he is symptomatic.

Analysis of the Essential Fatty Acids (EFA) Pathways can provide helpful insights into PUFA imbalances that may further contribute to inflammatory status.

Results suggest the patient has a healthy functioning D5D enzyme, but increased D6D activity – which may impact downstream production of certain omega-6s, leading to heightened inflammation. Although the patient’s essential fatty acid questionnaire result suggest that he is getting an appropriate amount via diet, it is still important to communicate their importance.

QUESTIONNAIRE RESULT	
Healthy Essential Fatty Acids	
GENES	RESULTS
FADS1	CC
FADS2	CT

Oxidative stress and antioxidant needs

The patient is genetically more prone to oxidative stress and therefore may have an increased need

for antioxidants. Recommend starting by increasing natural foods in the daily diet and supplement if necessary. Another piece of SNP information regarded as “huge” by the patient. More motivation for him to get on top of this significantly, which will help with the inflammation “challenge”.

GENES	RESULTS
GSTM1	Deletion
GSTT1	Deletion
MnSOD	CT
NQ01	CT

Glutathione S-transferase gene deletions

The Glutathione-S-Transferases (GST) are a family of enzymes which contribute to the cellular biotransformation of electrophilic compounds. This group of phase II enzymes catalyse the conjugation of glutathione with a variety of endogenous toxins, resulting in corresponding GSH-conjugates which can then be cleared from the body. Various isoforms of GST exist and are present in virtually all tissues, with the highest activity level found in the liver.

The patient’s GSTM1 and GSTT1 genes are absent due to a polymorphic gene deletion. This leads to a complete lack of activity of the corresponding enzymes and is linked to reduced capacity to remove environmental toxins and reactive oxygen species. The patient may therefore have a reduced capacity to metabolise numerous xenobiotics and endogenous compounds. When detoxifying conjugation reactions between these toxins and glutathione are impaired, unstable compounds tend to accumulate. This can contribute to symptoms of fatigue, depression, allergy, asthma, infertility, obesity – and hormonal upsets due to reduced detoxification capacity.

Advice would be to focus on inducing remaining endogenous GST expression and providing antioxidant support. GST enzyme activities are induced in part by phytochemicals such as glucosinolates of cruciferous vegetables, curcumin from turmeric and allylic sulphides from allium vegetables.



Increasing endogenous GST enzyme activity may lead to increased excretion of endogenous toxins at the expense of the patient’s natural glutathione

pool. In this case it may be advantageous to support glutathione levels for the period of a detox programme.

Supplementation protocols, if extra support is required, could include vitamin C, curcumin and brassica extracts, plus additional glutathione support (if needed) such as N-acetyl-L-carnitine or liposomal glutathione.

While the dietary protocol requires cruciferous vegetables and alliums, the patient has a cystathionine-beta-synthase (CBS) genetic variant which may cause sensitivity to sulphur-containing compounds and ammonia. If symptomatic, then consider an organic acids test, for example, to either confirm or find out if there are other reasons for high levels of ammonia (such as overgrowth of ammonia-producing microorganisms in the gut) before starting any treatment protocols. A blood test confirmed the accuracy of the genetic data which red-flagged the patient's urea levels as too high.

If introducing any supplements containing sulphur compounds, start with a low dose and gradually build up. Only continue supplementation if the patient is not experiencing symptoms similar to those of a histamine reaction, such as skin outbreaks, headaches, nausea, fatigue, flushing or brain fog. Alternatively, support detoxification with vitamin C and bioflavonoids, and herbs such as turmeric, ginger, oregano, basil, cinnamon, etc.

Haemochromatosis

The patient is a carrier for hereditary haemochromatosis, a genetic condition that can lead to abnormally increased absorption of iron in the body. However, having the HFE genetic variants does not mean that the patient will have a problem with their iron level; other factors such as environment, diet, and other genes may come into play.

GENES	RESULTS
HFE H63D	CG
HFE C282Y	AG

If you are concerned about a patient's iron levels then consider an Iron Panel Test to check serum ferritin, total iron binding capacity, and serum iron. This patient regularly checks haematocrit and serum ferritin and is normally at high-end of optimal ranges. No further action is required.

However, if necessary, to help manage iron levels, milk thistle has been shown to be useful, due to the ability of silymarin to inhibit the absorption of iron, and alpha lipoic acid may also be helpful due to its ability to counteract iron-induced free radicals damage.

Coeliac disease

According to the algorithm which assesses six HLA SNPs, the patient has DQ2.2 and DQ2.5, which puts him at medium risk for developing CD. He knows he is gluten sensitive and has removed gluten from the diet, so no further action is required.

Fasting

You can also recommend fasting three hours between the evening meal and bedtime, and to fast 12 hours between that meal and breakfast.

NOTES:

Summary: Preventative lifestyle and nutrition guidelines for clinicians

01 A Low Sugar Plan is recommended – can be a low glycaemic load or paleo-style.

02 Ensure adequate intake of protein to further manage blood sugar levels.

03 Gluten-free is recommended.

04 A diet rich in plant sterols, antioxidants and high in omega may be beneficial. Include anti-inflammatory nutrients - omega 3, curcumin and EGCG

05 Support methylation with key nutrients including a folate-rich diet, supplement (if necessary) with L-methylfolate, the other B vitamins, vitamin C, zinc and magnesium.

06 Supplementation protocols to increase endogenous GST enzyme activity (if extra support is required) could include vitamin C, curcumin and brassica extracts plus additional glutathione support (if needed) such as N-acetyl-L-carnitine or liposomal glutathione.

07 Increase daily intake of dark green leafy vegetables (chard, kale, spinach, watercress, rocket), cruciferous vegetables (cauliflower, broccoli, sprouts, cabbage) and alliums (garlic, onions, leeks). These are important to support detoxification and glutathione.

08 Include natural magnesium sources such as dark leafy greens, nuts, fish, avocados etc. Supplement if required.

09 Genetically the patient is a slow metaboliser of caffeine and should consider reducing coffee consumption or switching to caffeine-free alternatives.

10 Patient does not have the genetic variant for lactose intolerance and reports that he tolerates dairy. However, if gastrointestinal or digestive problems were to flare up, this would be worth investigating further, such as by testing IgE levels.

11 Increase intake of organic (pesticide-free) daily portions of colourful fruit and vegetables to support antioxidant needs. Supplement protocols (if needed) can include glutathione, zinc, catalase, vitamin C.

12 Reduce animal omega-6 dietary sources and increase omega-3. Alongside, include cofactors B3, B6, C, E and A, biotin, magnesium and zinc.

13 Further investigation (if deemed necessary) can be: homocysteine, iron levels, vitamin D levels, metal toxicity, sensitivity to sulphur-containing compounds and ammonia and any potential nutrient deficiencies.

14 Methylation: a methylation protocol requires a strong foundation, such as healthy sleep, good gut health and regular bowel movements, adequate adrenal and thyroid function to avoid any side-effects. If the patient is on any pharmaceutical drug, then investigate further to see if any may be antagonising folate. First focus on obtaining daily vitamin and mineral requirements from natural foods, then use supplements as a back-up if necessary. It is important to introduce supplements slowly to gradually build up tolerance and prevent any side-effects.

References online

<https://mydnahealth.co.uk/references/>

myDNAhealth continually update the scientific evidence, so please visit the site page.



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