THE SCIENCE BEHIND DNAFit

DNAFit®
ACHIEVE YOUR GENETIC POTENTIAL

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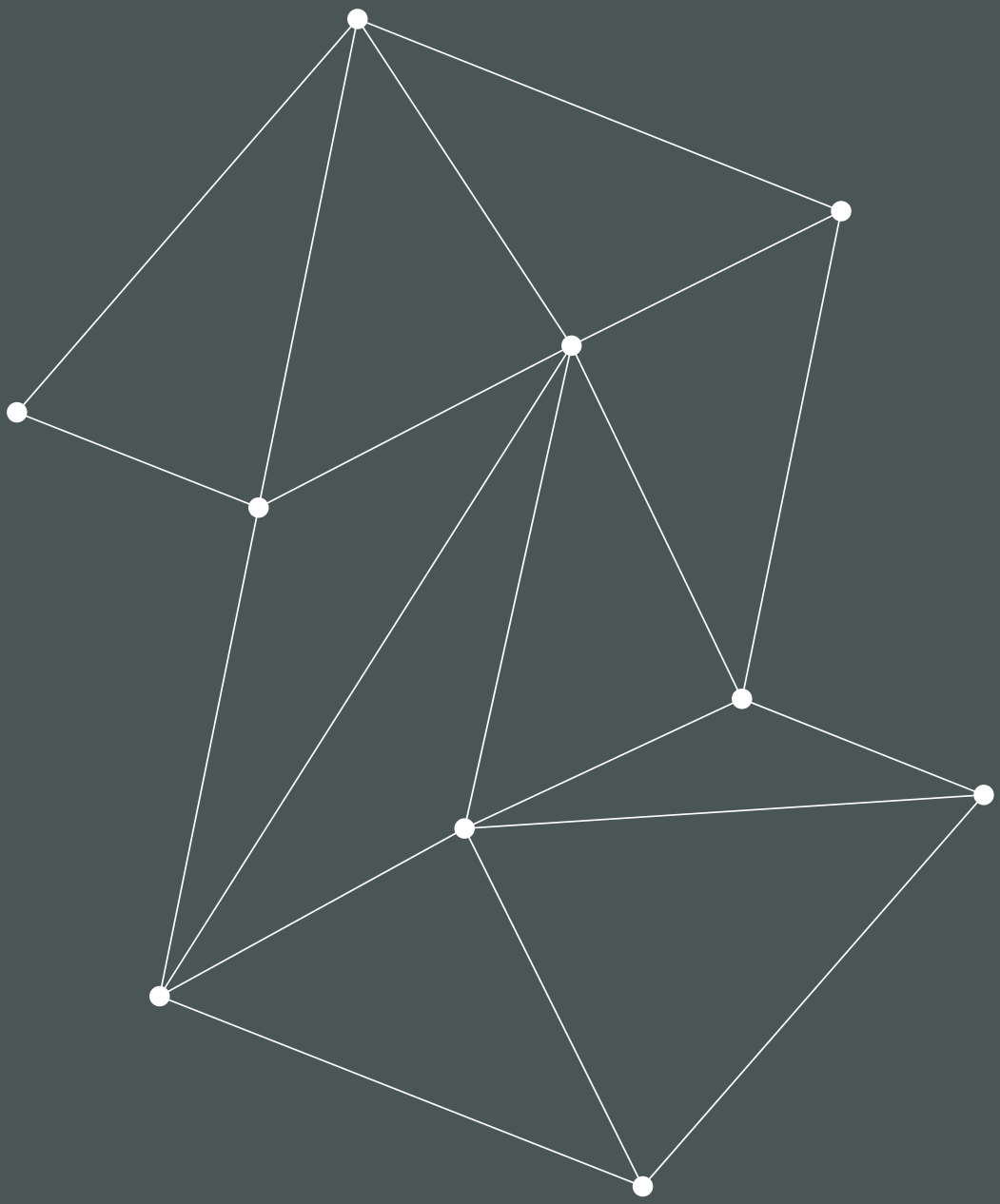

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Introduction

According to the World Health Organization (WHO), health is a "state of complete physical, mental and social wellbeing and not merely the absence of disease". This definition appears in the preamble to the WHO Constitution in 1946 and entered into effect in 1948. The definition has not been amended since. Translating this concept to athlete health, it is therefore unlikely to have a true welfare if we do not consider training, nutrition, rest and psychological wellbeing. The optimal performance of an athlete is based on all these interconnected pillars together.

But taking care of all these factors is not easy. They are complex traits, and are determined jointly by biological (genetic) and environmental factors. Scientific studies in twins have shown that about 50% of the differences in athletic performance (30% - 70% depending on sport) can be explained by the existence of genetic differences between athletes. And not only our genes determine our maximum performance: through the knowledge of the differences in our genes, we can adapt our diet and our training to make the most of them.

The Human Genome

Genetic information is stored in form of a chemical molecule, DNA (deoxyribonucleic acid), built by the union of a number of units called nucleotides. DNA nucleotides are basically composed of a sugar (deoxyribose, hence the name "deoxyribonucleic acid") and a nitrogenous base molecule that can be of four types: adenine, cytosine, guanine and thymine (known by their initials A, C, G and T). The sequence of these letters determines the genetic information, which is read by the cellular machinery, to build the tools that will be used for the proper functioning of the body.

This information is packed in units called "genes". A gene is a segment of the DNA molecule that contains the instructions for how, when and where the body makes each of the many thousands of proteins required for life. Each gene is comprised of multiple combinations of the four letters that make up your genetic code. But most interestingly, all of us have small differences in the information that our DNA contains, and it's these differences that make each of us unique. These genetic variations (also called "polymorphisms", or "Single Nucleotide Polymorphisms-SNPs") are slight changes in the genetic code that are responsible for the observable and not observable differences between individuals and contribute approximately to the 50% of the variation in athletic performance, affecting as many functional characteristics such as the processing of energy, muscle performance, blood flow and oxygenation. In addition, our particular genome also determines the way we respond to environmental factors such as training or nutrition. This is what is called genome-environment interaction.

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Gene-environment interaction

Not everybody responds to the environment in the same way, and this individual response is largely determined by the genetic variations present in our cells. This is what is called geneenvironment interaction, and implies that the effect of environment on a person's health and performance is conditional on the genetic variation in this person's DNA. Therefore, knowing what variants are present in an individual's genome can help to make appropriate exercise, dietary and lifestyle recommendations. It is important to remember that genetics is only one of the many factors that contribute to human health and wellbeing, and therefore a genetic profile should be used as part of the whole picture, not just in isolation.

The DNA markers (variations in the DNA) used by DNAFit has been selected from a large set of scientific studies, after assessing them according to multiple criteria, including:

- Quality and types of study.
- Type of interaction observed.
- Magnitude of effect.
- Biological plausibility.
- Type of intervention.
- Probability of benefit compared with standard guidelines.

The information provided by each of the selected DNA markers is analyzed together using a DNAFit proprietary algorithm, to provide the final report that takes into account all relevant markers for each section of the report, described overleaf (page 3).

Nutrigenetic report (Gene-Diet Interaction)

DNAFit takes a look into specific genetic variants that has been shown to modify our individual responses to environment (and specifically to diet and fitness). There is a large set of evidence that such gene-diet and gene-exercise interactions do happen (For example see Lee at al 2001, with published details on a database containing more than 550 examples of gene–diet interactions), and that nutritional and exercise guidelines based on that genetic information has been proved to provide better outcomes (Nielsen and El-Sohemy, 2014).

The DNAFit Nutrigenetic report uses DNA information to provide information regarding:

- Individual response to Carbohydrate
- Individual response to Fats (Weight management and general health)
- Detoxification (phase 1 and phase 2) ability
- Anti-oxidant need
- Omega-3 need
- Vitamin B requirements
- Vitamin D requirements
- Salt, alcohol & caffeine sensitivity
- Lactose intolerance
- Coeliac predisposition

The following table (page 3) shows some of the examples of gene-diet interactions included in the DNAFit test that can be considered to have potential benefit. Based on published scientific evidence, DNAFit establishes a personalized nutritional recommendation. For instance, individuals with GSTM1 null genotype require an increased cruciferous intake to reduce DNA damage. For them, a personalized nutritional recommendation would be "5-a-day fruit & veg including cruciferous 3-4 times per week", which certainly is quite different to the "standard" guidelines of "5-a-day fruit & veg", without cruciferous vegetable specified at all.

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Gene	Diet component	Effect on	Nutrigenetic advice	References
MTHFR	Folic acid	Homocysteine	Reduced homocysteine	Wald et al 2006, Ashfield-Watt et al 2002, Foht et al 2002
MTHFR	Riboflavin	Hypertension	Blood pressure reduction	Wilson et al 2013, Horigan et al 2010, Ward et al 2011
SOD2	Antioxidants	DNA damage	Increase dietary antioxidants	Ambrosone et al 1999, Cai et al 2004, Li et al 2005, Mikhak et al 2008, Coper et al 2008
APOA2	Saturated fats	BMI	Increased BMI with high saturated fats	Corella et al 2011, Smith et al 2013, Corella et al 2009
APOE	Dietary lipids, alcohol	LDL cholesterol	Reduce saturated fat and alcohol	Ordovas et al 2002, Talmud et al 2005, Ordovas et al 2008
CYP1A2	Caffeine	Cardiovascular disease	Reduce caffeine in slow metabolizers to reduce CVD risk	Cornelis et al 2009, 2007, 2006, Palatini et al 2009
GSTM1 GSTT1	Cruciferous vegetables	DNA damage, cancer	Increase cruciferous	Palli et al 2004, Brennan et al 2005, Lam et al 2009
GSTM1 GSTT1	Vitamin C intake	Serum ascorbic acid	Increase required levels of ascorbic acid	Cahill et al 2009

As an example to understand the table, a genetic variation in the MTHFR gene can produce two different versions of the enzyme. The most common “C” version, and the “T” version, with lower enzymatic activity compared to the C version. People with at least one copy of the T version in their genome are highly likely to have increased homocysteine levels when dietary intake of folic acid is too low. Therefore, increasing the daily intake of dietary folic acid in individuals with that genetic configuration can compensate for the reduced activity of the enzyme.

The genetic evidence is crucial of course, but translating the information from gene-diet studies into personalized advice is not as straight forward as it may seem at first sight. DNA-based dietary advice is very strongly supported by the weight of research available on the topic, and this will increase significantly as research progresses.

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Gene-exercise interaction

In the case of a gene-exercise interaction, the genetic profile modifies our body's response to physical activity, which means that not everybody's health responds the same way to different training methods, and this response depends, to a great percentage, on the individual genetic profile.

The **DNAFit Fitness report** uses DNA information to provide information regarding:

- Power/endurance profile
- Aerobic Response (VO2 Max)
- Recovery
- Injury risk

The following table shows some of the examples of gene-exercise interactions included in the DNAFit test that can be considered to have potential benefit. Based on published scientific evidences, DNAFit then establishes some personalized training recommendations for the individual.

Gene	Environmental factor	Effect on	Excercise genetics advice	References
PPARGC1	Physical activity level	BMI	Increase leisure-time physical activity level	Ridderstrale et al 2006
ADRB2	VO2 Max	Athletic performance	Determine optimal VO2 levels	Moore et al 2001
PPARG	Physical activity level	Fasting insulin level	Polyunsaturated to saturated fatty acid ratio	Franks et al 2004

The genetic variants analyzed by the DNAFit test and their interaction with exercise-lifestyle can help elucidate the ways in which exercise could be tailored to the individual genotype. This improves the effectiveness of the training by providing exercise and dietary recommendations to optimize the individual performance. Recommendations such as the establishment of the ratio between power and endurance activities, the VO2 max tendency, the need for free radical clearance and antioxidants, as well as the type of recovery to minimize the probability of soft tissue injury.

It is important to note that this result should not change the sporting or fitness goal. Rather, it should help understand what is the best way to reach that goal, whatever it may be, by taking advantage of the genetic predisposition.

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What the DNAFit test does and does not

DNAFit looks at the individual genetic profile to establish personalized nutritional and exercise recommendations that will benefit his/her health and wellness with a higher probability than standard "one-size-fits-all" recommendations.

DNAFit does not try to estimate the risk of serious disease, but rather to look at SNPs for which there is a good quantity of evidence to show interaction with specific nutrients, and then provide nutrition (and lifestyle) recommendations to decrease that risk. We only provide recommendations for which we have good scientific evidence. For instance, in one of the previous examples, we have shown that in individuals with the null genotype of the GSTM1 gene, an increase in the intake of cruciferous vegetables is linked to a reduction in DNA damage and cancer risk (in respect to non null-allele carriers). Then DNAFit makes the very simple and logical nutritional recommendation, based on this scientific evidence; increase cruciferous intake for individuals with the presence of the null allele in their genome.

Conclusion

Nutrigenetics represents important extra parameter in the hands of either the health and fitness professional, or individual wishing to make the best informed decisions for their health and fitness, who may now incorporate evidence-based gene/diet/exercise information when devising nutrition and training programs. Health professionals routinely evaluate a range of biological data (biomarkers, height, weight, gender, ethnicity, health issues, and so on) when formulating personalized advice, and it is entirely logical that genotype should also be included where the evidence is sufficient. This is the case for several gene-diet interactions and there is evidence that nutrigenetic advice is better understood and more likely to be followed compared with general dietary advice (Nielsen and El-Sohemy 2012, 2014). It can also be beneficial in longterm weight control [Arkadianos et al, 2007]. This extra benefit of genetically influenced dietary guidance is particularly poignant in the face of a global obesity and inactivity epidemic. As a society, even with greater scientific understanding of what leads to a healthy lifestyle; we have so far failed to reduce obesity or increase activity levels on global scale. As such, any factor that can be proven to increase adherence and understanding can be only a good thing.

The information provided by DNAFit can help to understand more about the potential limitations and strengths of the analyzed individuals, which per se is very useful information for coaches, personal trainers and informed individuals.

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