Learn about the science of genetics

THE GENETICS OF ATHLETIC PERFORMANCE AND FITNESS

GENETICONCEPT

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About **Us**

GenetiConcept is a latin american based company , founded to make this difference through the commercialisation of niche medical technologies and developing a consumer understanding by removing the scientific jargon.The founders of the company have been involved in the DNA and Biochemical testing industries for over 15 years decade and have capitalised on this experience, to bring GenetiConcept to everyone – from absolute beginners to professional athletes. The human genome holds an extraordinary treasure trove of information about human development, physiology, and evolution, and has vastly increased knowledge of how the human body works and its biological responses. With the GenetiConcept range of tests, GenetiConcept places the mysteries revealed by scientific advances in Human Genomics research in your hands by providing access to these developments in an affordable, consumer-friendly way. By analysing the relationship between genes, nutrition and lifestyle our gene tests provide a valuable tool for you to manage your health and wellness.

Using cutting-edge molecular technologies, our dedicated team comprising of experts in both the field of human genetics and nutrigenomics as well as sports science, will provide you with reliable, high-quality services, performed according to the highest international standards.

IMPORTANT NOTE : GenetiConcept.com and AnabolicGenes.com are part of the same company.

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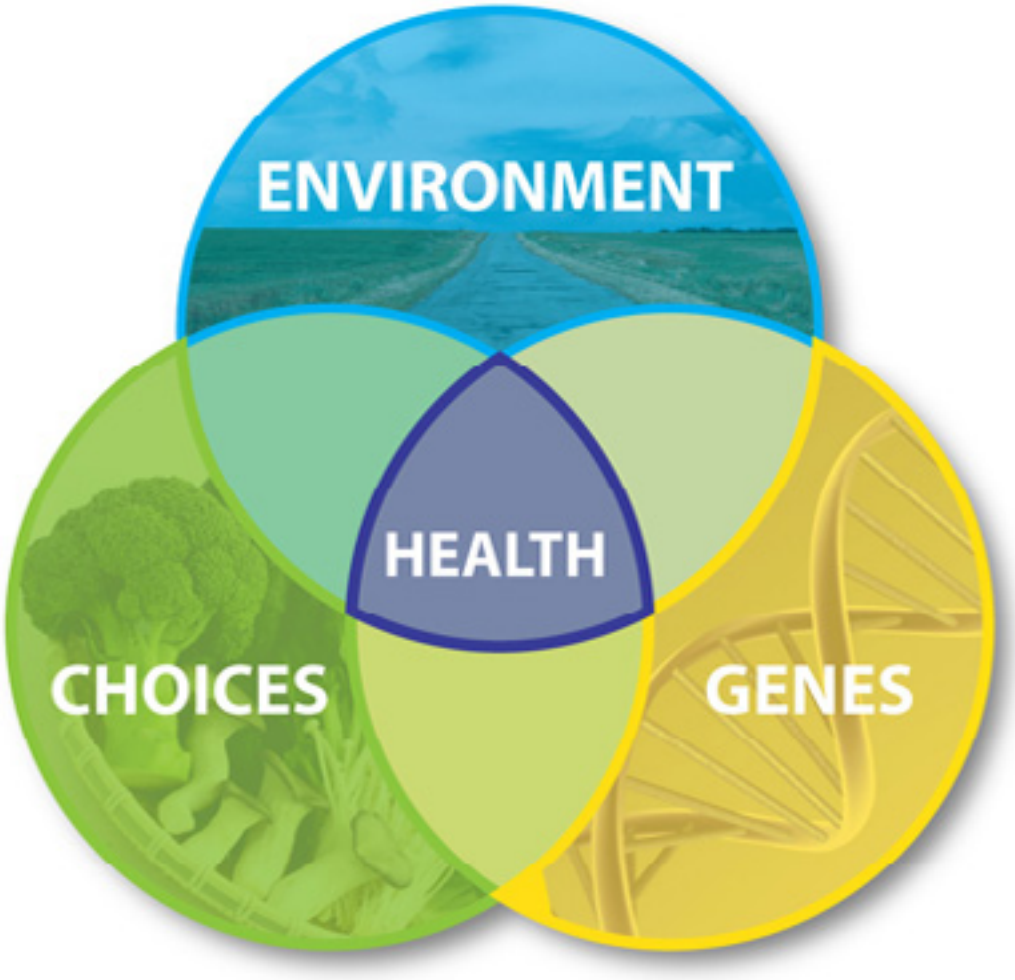
Introduction

HOW OUR ENVIRONMENT SHAPES US ?

There is no doubt that physical fitness is influenced by a wide range of environmental factors. These factors include the development of bespoke training programs, top of the range equipment, personalised nutritional advice as well as, of course, all those hours spent in the gym. All make important contributions to our physical fitness leading to an overall increase in our performance. However there is a critical factor underlying all of this, which may ultimately prove to be the most important of all: your GENETICS.



Every athlete seeks a competitive edge. In sports, it is recognised that good coaching practices are comprised of a mixture of art and science. Scientifically, training theories include progressive overload, super compensation and training-recovery ratios: they have been well studied and are clearly understood. Up until now however, what scientific research within sport has generally lacked, is the individuality required by each athlete to attain optimal fitness and performance. Within the coaching realm, this individuality is generally considered within the art of coaching and includes the ability to recognise training practices that may work well for one athlete, but don't necessarily work well for another.

We know that genetics plays a role in our differing abilities in the gym and out on the track and field. If you take a random sample of people and train them all in the same way, you will not end up with a group of people all performing at the same level1. We accept that some of us naturally inherit the ability to respond better to training. Researchers estimate that a massive 50% of the variation we see in physical fitness performance between individuals is actually due to genetics. This means when you compare your physical performance to that of another, your genetic makeup is as important as all the other factors combined! However, equally, you shouldn't get too excited if you find you have the genetic makeup to rival an elite athlete. Research also shows that much of the difference seen is in response to training; in other words, you won't get the maximum benefit from your genetic potential without putting the effort in!

What is **genetics ?**

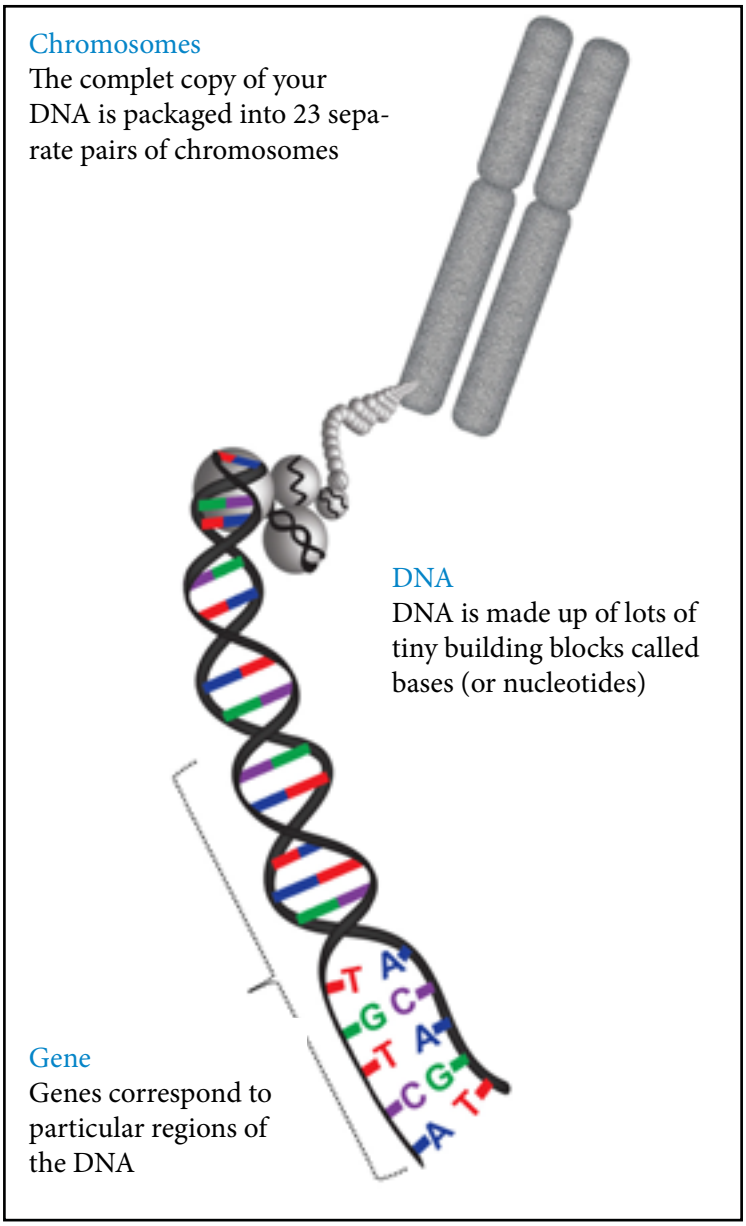
WHAT IS GENETICS ?

Genetics is the study of heredity - the passing of certain traits from parent to child through our genetic material. Much of the current genetic research is concentrated on identifying the specific regions in our genetic material that are responsible for the inheritance of certain traits, such as how our bodies respond to training and nutrition.

WHAT IS DNA ?

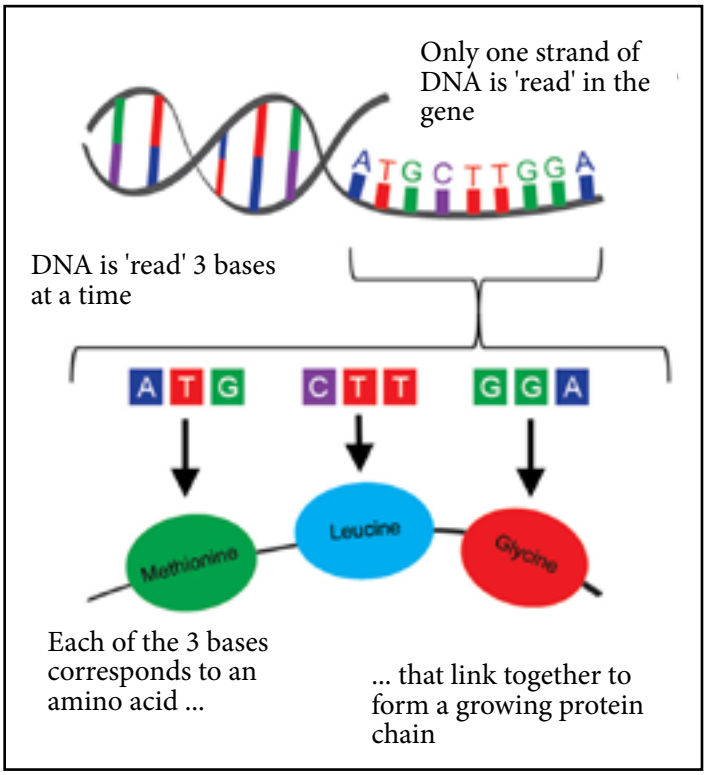
Deoxyribonucleic acid, more commonly known as DNA, is the molecule that is responsible for carrying all our genetic information. Your DNA code operates almost like a recipe book; it contains all the instructions your body needs for your development and function. It is handily packaged into 23 separate pairs of chromosomes. DNA is made up of lots of tiny building blocks called nucleotides, or bases, strung together in a row. There are actually only four types of bases, commonly denoted by the letters A, C, G and T. Every DNA molecule is made up of two of these strands of bases, which wrap around one another to form the double helix structure that we are so familiar with. We all have a completely unique DNA code made up of just these 4 bases.

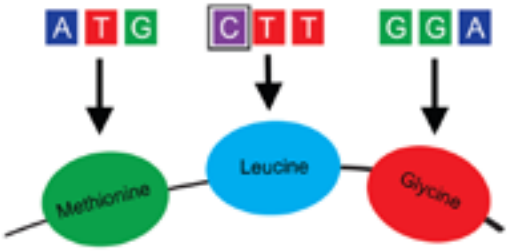
If our DNA is the recipe book, then our genes are the actual recipes – a recipe for making a protein. A gene is a specific stretch of DNA that instructs our body how to make a particular protein. It is these proteins that perform the important biological tasks in our cells. The DNA code or sequence of the gene determines what the protein product will be.



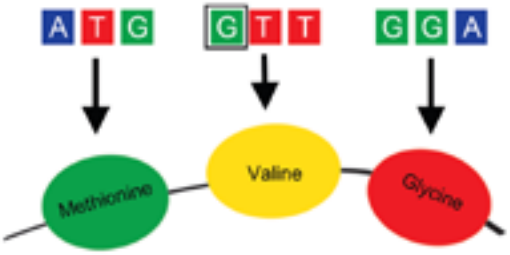
INTERPRETING YOUR DNA CODE

A gene is 'read' as a series of three adjacent bases. Each three-base set represents a different amino acid. Amino acids are simply the building blocks of proteins; by combining lots of amino acids together a protein can be built from the DNA sequence.





If you have the 'C base' then the amino acid leucine will be incorporated into the growing protein chain ...



... whereas if you have the 'G base' you will have the amino acid valine instead, which changes the way the protein functions.

MUTATIONS ARE WHAT MAKE US ALL DIFFERENT

A simple change of just one base in the DNA sequence of a gene (e.g. in our example, a 'C' base for a 'G' base) can lead to a change in the corresponding amino acid, and this can ultimately result in a change to the protein product. A single base change in your DNA code is known as a Single Nucleotide Polymorphism or 'SNP' (pronounced "snip"). Sometimes multiple bases, or even whole regions of DNA can be lost or gained, and these types of mutations are termed indels (short for INsertion-DELetion).

BUT MUTATIONS ARE BAD RIGHT?

This is a common misconception! Yes, mutations CAN be bad if, for example, they prevent an important gene from working properly, but they can also occasionally be beneficial (and in fact the vast majority of mutations are completely neutral and result in no observable effects at all!).

FOR EXAMPLE

Take for example something many of us take for granted: **lactose tolerance**. Most babies can digest milk without getting an upset stomach thanks to an enzyme called lactase. However, up until several thousand years ago, that enzyme was turned off once a person grew into adulthood. Yet today, 35% of the global population — mostly people with European ancestry — can digest lactose into adulthood without any problems. Why is this?

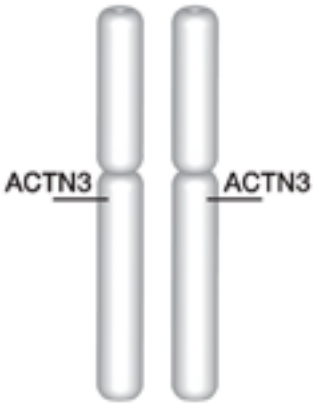
Because a **MUTATION** that first arose in ancient European farmers meant that, for some, that genetic 'off switch' was lost and they carried on producing milk-digesting lactase into adulthood. This happened completely by chance, but of course those people that could digest milk were at an advantage, particularly during times of famine or drought when the additional nutrients milk provides could be the difference between life or death. So the trait spread. It is the small changes that mutations cause that make each of us unique and mean that each of us will respond to fitness training and diet in different ways.

SO YOU CAN TELL ME IF I HAVE A PARTICULAR GENE OR NOT?

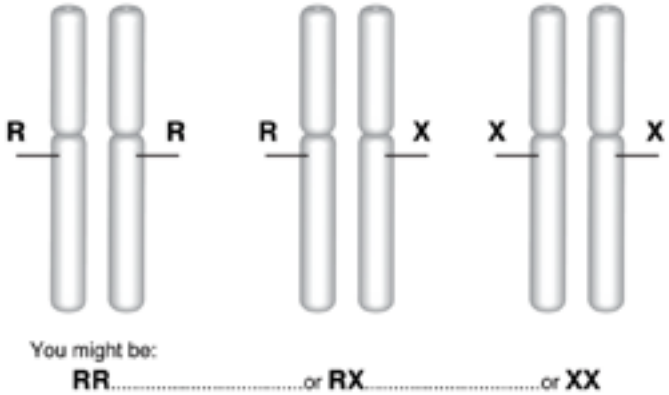
This is another common misconception. Barring a serious genetic defect, we all have a copy of each and every one of the genes analysed by GenetiConcept. In fact, we have two copies – one came from your mother and the other from your father. It is which version of the gene, or genotype, we carry that differs from person to person. Let's take an example: ACTN3 – the gene for 'speed and power', one version of which is found in virtually all elite sprinters and Olympic weightlifters.

The ACTN3 gene is found on chromosome 11

Known as the 'speed and power' gene, one version of this gene - the 'R' version or allele - has been found in almost every Olympic power athlete ever tested



As we all have two copies of every gene, there are 3 possible variations or 'genotypes' of ACTN3



Carriers of an '**R**' allele produce the protein alpha-actinin-3, which is associated with a boost in muscle strength and performance, possibly due to an increase in the overall size and number of fast twitch muscle fibres

Carriers of the XX genotype do not produce any functional alpha-actinin-3 at all.

As you can see, the different versions of a gene are known as alleles. In the case of the ACTN3 gene you can either have an 'R' allele or an 'X' allele. The letter we use to denote each version can either refer to the single base that has been changed (ACGT) or to the amino acid (R, in this case, stands for arginine).

Thus when we say that you have the genotype 'RX' for ACTN3, what we are telling you is you have one 'R' allele of the ACTN3 gene and one 'X' allele of the ACTN3 gene- simple!

Trainability of **genes**

Exercise training affects the way that our genes are expressed; i.e. switched on and off. For example, acute and chronic training can influence the body's insulin resistance, glucose metabolism and use of fats for energy. A training programme can also attenuate the inflammatory response that occurs after an exercise bout, thereby improving speed of recovery and also increase an individual's antioxidant profile and provide more physiological support to the stresses of training.

Additionally, the fact that exercise training can augment aerobic and anaerobic capacity, muscular strength and endurance, power, cardiovascular health and numerous other physiological variables (McCardle et al 1991; Powers & Howley 1990) is well accepted. The degree of physiological adaptation that results from training is now of more interest to us. As will be noted in the following reviews of exercise-oriented genes, training responses can vary widely based on an individual's genetic make-up, with athletes who have one genotype responding more similarly to training compared to those with different genotypes (Bouchard et al 1997). If coaches and athletic practitioners have more understanding of what type of training (plus nutritional and lifestyle patterns) their athletes are most likely to respond to, it will help them to design an optimal training programme.

"With population turnover, World and Olympic records should improve even without further enhancement of environmental factors, as more advantageous polygenic profiles occasionally, though rarely, emerge." Williams and Folland (2008)

Few **genes** we test for

WE TEST FOR 100+ GENES. WE WILL ONLY TALK ABOUT 7 OF THEM.

Also note that this chapter take into account each gene separately without their cumulative effect on each other.

In fact, some traits are **MONOGENIC**, meaning that there is a single gene which determines this trait (example : lactose intolerance, cystic fibrosis, etc...)

Others are **POLYGENIC** meaning that these traits depends on multiple genes (example: 15+ genes determine someone's power profile ; there are at least three genes controlling human eye colour, etc...)

1

ACTN3 Gene

Function: Alpha-actinins are a family of actin-binding proteins that maintain the cytoskeleton. The ACTN3 gene encodes alpha-actinin 3, which is only present in type II (fast) muscle fibres and also has a low expression in brain tissue. Alpha-actinins are found at the Z-line of the muscle where they anchor actin filaments and help to maintain the structure of the sarcomere. Alpha-actinins also interact with a signalling factor that plays a role in the specialisation of muscle fibre type, diameter and metabolism.

Polymorphism: The ACTN3 gene contains a polymorphism which results in two versions of ACTN3: a functional R allele and a null X allele. The genotype that is homozygous for the X allele (XX) is completely deficient in alpha-actinin 3. The percentage of people with two X alleles range from about 1% in African populations to about 18% in Europeans and 25% in East Asians.

Research: It has been demonstrated that male and female elite Sprint athletes have significantly higher frequencies of the R alleles than endurance athletes and sedentary controls (Eynon et al 2010a; Yang et al 2003). Additionally, when Roth et al (2008) studied elite and local black and white bodybuilders, they showed a significantly lower XX frequency in the bodybuilders compared to controls. None of the black bodybuilders were homozygous for the X allele. In a cycling study, it was found that subjects who were not ACTN3 deficient had greater peak power outputs and ventilatory thresholds than cyclists with the XX genotype (Gomez-Gallego et al 2009b).

When studying the ACTN3 gene for endurance performance, mixed results have been found. Shang et al (2010) showed that the XX genotype was significantly over-represented in the female endurance athletes compared to controls. However, no relationship between genotype and endurance-status was found in the male athletes. Doring et al (2010) found that the XX genotype was similar in prevalence between 316 endurance athletes and 304 controls. Additionally, Saunders et al (2007) found when studying 457 male Ironman triathletes compared with 243 controls, that the XX polymorphism was not associated with ultra-endurance performance.

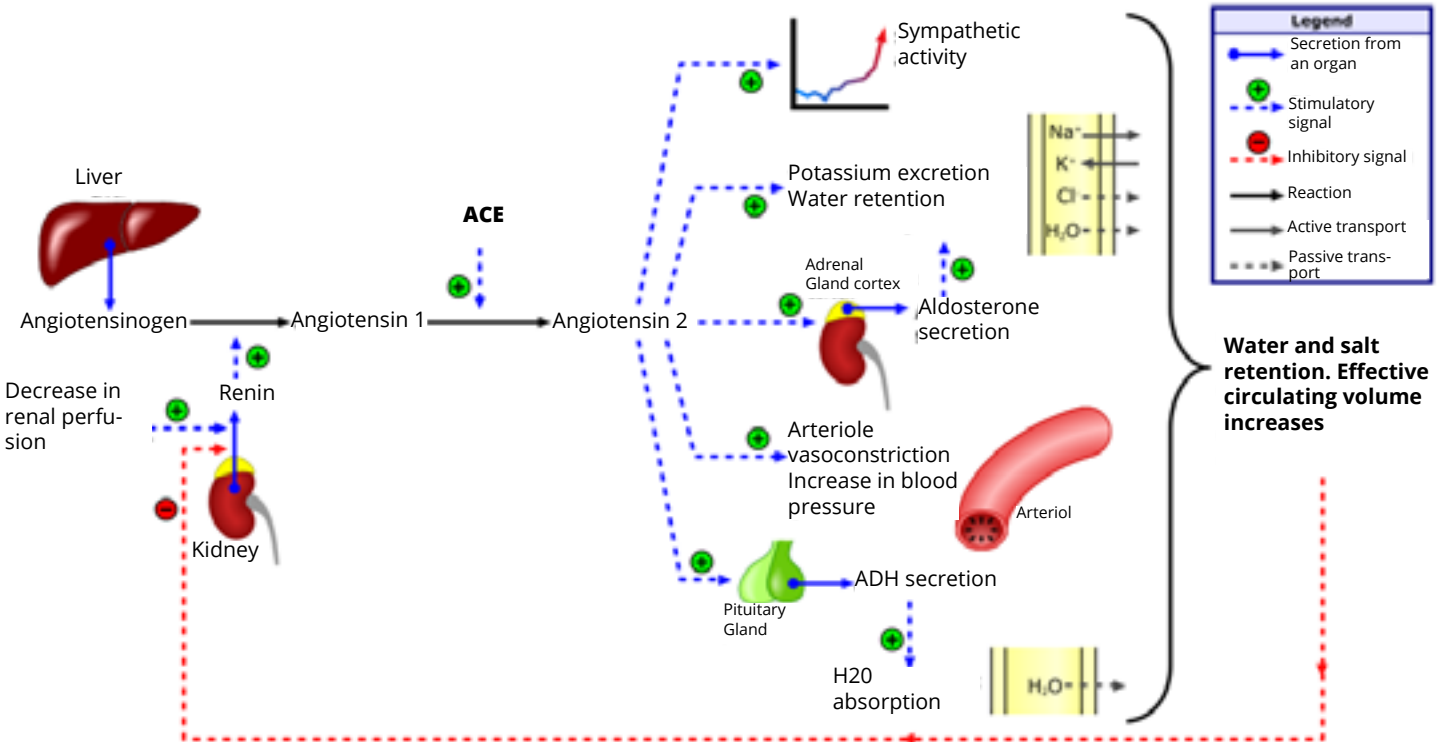
These observations have also been replicated in professional cyclists and Olympic endurance runners (Lucia et al 2006). Collectively these studies suggest that the XX genotype has not yet been shown to be a good marker for endurance performance.

ACTN3

2

Function: ACE is the most studied of all the genes involved in sporting performance. As shown in the diagram below, it is an enzyme that hydrolyses angiotensin I into angiotensin II, an important vasoconstrictor of the renin-angiotensin system and an aldosterone-stimulating peptide. Through its vasoconstricting role, along with the fact that it can deactivate bradykinin (a potent vasodilator) ACE plays an important role in blood pressure regulation. In normal individuals, plasma ACE levels can have as much as a 5-fold inter-individual variation and approximately half of this variation is thought to be due to a polymorphism on the ACE gene.

ACE Gene



Polymorphism: There exists an insertion/deletion (I/D) polymorphism on Intron 16 of the ACE gene: the I allele is associated with lower ACE activity. The frequency of the ACE alleles in a UK study was shown to be II (24%), ID (50%) and DD (26%), although the D allele is higher in Nigerian and Afro-Caribbean populations, whereas the I allele is more common in Pima Indians and South Asians. The II genotype is an endurance profile, associated with increased muscle Delta Efficiency with aerobic type exercise or higher repetition weight training and there is less expectancy for muscle growth. When the ACE I allele and BDRKB2 -9 allele are both present, there seems to be an additive effect on endurance capacity. The ACE I genotype has been associated with an increased percentage of slow twitch type I fibres, higher VO2max, greater aerobic work efficiency, improved fatigue resistance, higher peripheral tissue oxygenation during exercise, greater aerobic power response to training, greater cardiac output and maximal power output in athletes (Ahmetov & Rogozkin 2009). The DD genotype is a power profile, associated with greater muscle growth with weight training and being better at strength sports. Higher circulating ACE levels have been significantly correlated with isometric and kinetic quadriceps muscle strength. Individuals with this genotype should be aware of left ventricular hypertrophy as a result of exercise training and would be advised to monitor exercise intensity. Their diet should also be adjusted for their predisposition to hypertension and glucose dysregulation because they are more prone to fat deposition in the absence of exercise.

Research : Aerobic physical training tests over an 11-week period revealed a 9% improvement in muscular mechanical efficiency in those individuals with two copies of the 'I' allele, whereas DD carriers showed no increase at all. Mechanical efficiency is equivalent to energy expenditure over time: so it is therefore a measure of endurance ability. A second study assessed the maximum duration for which people of different ACE genotypes could perform repetitive elbow flexion with a 15kg barbell. Those carrying the II genotype demonstrated an even greater 11-fold improvement in this endurance activity compared to the DD types over a 10-week training period. Those individuals carrying an 'I' allele tend to display an increased percentage of Type 1 slow twitch 'oxidative' muscle fibres over DD types, providing one possible mechanism for this difference. Slow twitch muscle fibres don't contract as forcefully as fast twitch muscle fibres, but they can contract repeatedly for longer durations without becoming fatigued.

In contrast, the 'D' allele has been associated with greater training related increases in muscle strength and growth as well as a higher propensity for anaerobic endurance. Strength measures taken at different joint angles and speeds of contraction have shown that carriers of the 'D' allele show greater gains in response to isometric training than 'I' allele carriers. Indeed, an excess of the 'D' allele has been found among elite sprinters and swimmers. It has been speculated that skeletal muscle growth (hypertrophy), associated with strength training, is probably the major contributor to the increase in strength seen with medium to long term training, and therefore the 'D' allele may promote hypertrophy and greater strength gains in response to functional overload.

AGT

AGT Gene

3

Function: Angiotensinogen is a protein that is produced mainly by the liver. Plasma angiotensinogen levels are increased by corticosteroids, oestrogen, thyroid hormone, and angiotensin II. It is a precursor of angiotensin, which causes vasoconstriction, increased blood pressure, and release of aldosterone from the adrenal cortex. Like the ACE gene, AGT plays an important role in the renin-angiotensin system.

Polymorphism: Allele C encodes for a threonine instead of methionine in codon 235 of the gene. This variant is associated with higher plasma angiotensin levels and ultimately elevated blood pressure, leading to increased risk for hypertension-associated disorders. The C allele has been associated with elite power sports performance.

Research: When genotyping top athletes, Gomez-Gallego et al (2009a) showed that the CC genotype was significantly more represented in power athletes (34.9%) than the control group (16%) and top endurance athletes (16%). Like the ACE DD genotypes however, AGT CC homozygotes should be aware that they are genetically more susceptible to left ventricular cardiac development with training (Pelliccia & Thompson 2006; Karjalainen et al 1999).

It has been estimated that genetic determinants may explain up to a quarter of the variability in left ventricular dimensions (Pelliccia & Thompson 2006). When studying the ACE and AGT genes together, it appears that the ACE DD and AGT CC combination increases left ventricular mass in athletes more than all other genotype combinations (Diet et al 2001): a synergistic effect between the ACE and AGT genes therefore seems to exist.

Rankinen and colleagues (2000) found that when 476 sedentary people were put through 20-weeks of exercise training, those individuals with the TT genotypes showed an overall decrease in diastolic blood pressure during the training programme, which greatly exceeded the blood pressure changes in CC genotypes. Additionally, in a longitudinal study of TT homozygotes, it was demonstrated that regular moderate-intensity exercise attenuates age-related increases in systolic blood pressure (Rauramaa et al 2002).

ADBR2

ADBR2 Gene

4

Function: The ADRB2 gene encodes for Beta 2 Adrenergic receptors, which play a part in the regulation of cardiac, pulmonary, vascular, endocrine functions and the central nervous system. Adrenaline, predominantly via the Beta 2 adrenergic receptors, plays a major role in maintaining blood glucose levels by promoting glycogenolysis during prolonged exercise.

Polymorphism: Arg16Gly - a polymorphism between arginine and glycine in position 16 of the gene has been associated with altered vasodilator responses to catecholamines during stress, and so modulates the pressor response (increasing cardiac output), as driven by the sympathetic nervous system.

Polymorphism: Gln27Glu - a polymorphism between glutamine and glutamate at position 27 of the gene has been associated with endurance performance and also the ability to lose weight as a result of an exercise programme.

Research: Arg16Gly - When researching airway tone, Snyder et al (2006) found that the genotype didn't influence lung function during exercise, but the Arg16 carriers had a rapid pulmonary recovery to baseline afterwards, whereas the Gly16 homozygotes had persistent bronchodilation during recovery. Tsianos et al (2010) found that ArgArg genotypes had faster marathon running times compared to Gly carriers and also that the Arg polymorphism was associated with lower blood pressure at rest, during and after exercise. In line with this observation, it has also been shown that an excess of Gly carriers have been found in sedentary populations compared with elite endurance athletes (Wolfarth et al 2007). With regards to ADRB2 gene effect on sympatho-excitation, the heart rate at fatigue after a handgrip exercise was greater for Gly16 than for Arg16 genotypes (Eisenach et al 2004). The authors suggested that the Gly16 carriers may be better at a pressor response in the face of increased peripheral vasodilation.

Gln27Glu - Moore et al (2001) showed that the Glu27Glu genotype was almost absent in postmenopausal athletes. Additionally, weight and BMI tended to be higher in the Glu27Glu women and VO2max was lower than other genotypes. This research was supported by McCole et al (2004), who found that in 62 postmenopausal women undergoing habitual physical activity, the highest observed sub-maximal exercise arterio-venous O2 difference (a-vDO2) was observed in women homozygous for the Gln allele compared to the Glu genotype. This polymorphism has also been linked to fat deposition in women: 10 obese women with the Gln27Gln genotype were compared to 9 matched women with the Glu27Glu genotype. Lipolysis and fat oxidation during an exercise test appeared to be blunted in the Glu27Glu group (Macho-Azcarate et al 2003).

PGC1A Gene

5

Function: PPARGC1A (otherwise known as PGC-1alpha) is a co-activator of PPAR-gamma and other nuclear hormone receptors and plays an essential role in energy homoeostasis. It is involved in mitochondrial biogenesis, fatty acid oxidation, adipocyte differentiation, glucose utilisation, thermogenesis, angiogenesis and muscle fibre type conversion towards type I fibres. It is expressed in tissues with high energy demands and is therefore abundant in mitochondria and is consequently associated with endurance performance.

Three subtypes of PPARs are known: PPAR-alpha, PPAR-delta, and PPAR-gamma. It appears that the activation of PPARGC1A may mediate the initial phase of the exercise-induced adaptive increase in muscle mitochondria. Additionally, the subsequent increase in PPARGC1A protein sustains and enhances the increase in mitochondrial biogenesis that is associated with exercise training.

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Polymorphism: The serine allele (SerSer or GlySer genotype) is associated with lower levels of PPARGC1A and consequently reduced aerobic improvements with exercise training when compared to the glycine (Gly) allele. The serine allele may also increase the possibility of raised blood pressure.

Research: Eynon et al found that PPARGC1A GlyGly genotypes were more frequently found in elite endurance athletes compared to sprinters and control subjects (2009b, 2010b). Additionally, Lucia et al (2005) demonstrated that the frequency of the serine allele was significantly lower in world class Spanish endurance athletes than in controls.

In 2007, Stefan et al looked at the relationship between the PPARGC1A gene and insulin sensitivity with exercise training: after nine months of training, individuals with the serine-encoding allele in their PPARGC1A gene experienced lower increases in anaerobic threshold compared to individuals who were homozygous for the glycine alleles.

Additionally, those serine-carrying individuals who also carried the minor G allele of the related PPARD gene had less increases in insulin sensitivity after the training programme. In relation to gene expression, the PPARGC1A gene has also been shown to be stimulated by insulin and decreased by ageing (Ling et al 2004). Presence of the serine allele has also been associated with increased blood pressure, but this has only been noted in younger adults (Vimaleswara et al 08).

The 'G' allele also seems to be linked to increased production of a newly discovered hormone called irisin. Irisin activates the conversion of white fat to brown fat in our bodies. Brown fat is a unique type of fat tissue that burns calories for heat to keep us warm, thus ensuring fewer calories are available to the body to be stored as fat. In other words, elevated levels of irisin can reduce our chances of obesity through increasing our energy expenditure. It also improves insulin function51 and is correlated with larger biceps musculature and resistance to muscle breakdown. There is another (perhaps unsurprising) way to increase irisin production in the body: exercise! PGC1A protein, and hence irisin, is induced by physical exercise in humans, and conversely inactivity and age can reduce it, highlighting the importance of maintaining a healthy level of physical activity as we grow older.

VDR Gene

6

Function: The VDR gene encodes the nuclear hormone receptor for vitamin D3 and is expressed by cells in most organs. VDR activation in the intestines, bones, kidneys and parathyroid glands leads to the maintenance of calcium and phosphorus levels in the blood and bone homeostasis. VDR is also involved in cell proliferation and affects the immune system, organ maintenance and even lipolysis and insulin secretion. Stress hormones such as cortisol are known to decrease the expression of VDR.

Polymorphism: Taq1 - The nomenclature of the VDR Taq1 gene is TT/Tt/tt (or TT/TC/CC in some papers), where t (C) is the minor allele. The 'T' is named after the Taq1 enzyme. The Taq1 is more-or-less 100% linked with the VDR Bsm1 SNP, so often information from the literature for one will infer information for the other – the 'T' allele on Taq1 is equivalent to the 'b' allele on Bsm1 and vice versa. Only Taq1 is tested by the DNA Fit analysis, but Bsm1 is commonly referred to in the literature. The Taq1 tt homozygotes have shown better baseline strength and muscle torque in various muscles tested. The tt genotypes have also have been shown to have higher fasting glucose and insulin levels when physical activity was low, but this was responsive to training adaptations.

Fok1 - The nomenclature of the VDR Fok1 gene is FF/Ff/ff (or CC/CT/TT), where f (T) is the minor allele. The 'F' is named after the Fok1 enzyme. The FF genotype has been associated with greater strength and gains in bone mineral density with exercise, but the literature can be quite confusing in this regard.

Research: Taq1 - Roth (2011) noted that vitamin D deficiency has been consistently associated with lower muscle strength. One study of 501 elderly women (Geusens et al 1997) found that the bb (TT in Taq1) genotypes had a 23% higher quadriceps strength and 7% higher grip strength than the BB genotypes. In contrast, another study looking at 175 young women (Grundberg et al 2005) found greater hamstring isokinetic strength in the BB (tt in Taq1) genotype group. Additionally, in 109 young Chinese women (Wang et al 2006), the bb carriers demonstrated lower knee flexion concentric torque than the B allele carriers. In 253 men and 240 women (Windelinckx et al 2007), the BB homozygotes had higher isometric and concentric quadriceps strength than the b allele carriers.

Fok1 - In a study of 206 healthy men and women (Rabon-Smith et al 2005) who undertook 5-6 months of either aerobic or strength training, it was found that the Ff heterozygotes from the strength training group obtained a significantly greater increase in femoral neck bone mineral density compared to f homozygotes. The evident importance of the F allele in adaptation to strength training was supported by a Japanese study (Nakamura et al 2002), within which athletes with the FF genotype, but not those with the Ff genotype, had increased spinal volume, lumbar spine and femoral neck bone mineral density when compared to controls. The authors suggested that individuals with the FF genotype adapt to impact loading by producing stronger bone structure than those with the Ff genotype.

IL6

7

IL6 Gene

Function: IL-6 is a cytokine secreted by T cells and macrophages, which stimulates an immune response to trauma such as strenuous exercise, leading to inflammation in the muscle and fatty tissue. IL-6 stimulates energy mobilisation, causing an increase in body temperature. IL-6 is also a myokine (muscle cytokine) and regulates the gene for CRP. The immune system of athletes is affected by the intensity and duration of exercise training - the inevitable muscle damage results in an inflammatory repair process, which is mediated by inflammatory cytokines such as IL-6. Overtraining syndrome (OTS) has been hypothesised to be caused by excess cytokine release during exercise, resulting in a chronic inflammatory state.

Polymorphism: The C allele has been linked to an increased IL-6 and CRP response to exercise, which may induce more pronounced fatigue and prolong recovery times. Perhaps because IL-6 levels are hard to measure in the plasma, there is some discrepancy in the literature about whether the C or G allele is associated with higher IL-6 levels, although the best evidence appears to be for the C allele.

Research: In a study of 54 military recruits during their 8-week basic training, it was noted that acute exercise increased plasma IL-6 levels more in subjects with the CG genotype compared to GG homozygotes (Huuskonen et al 2009). Interestingly, subjects with the CG genotype also made the greatest gains in VO2max. In support of this, Yamin et al (2008) found that subjects with the C allele experienced greater creatine kinase (CK) levels than GG homozygotes (3-times the risk of a massive CK response) after eccentric training, showing that the C allele may be a risk factor for exercise-induced muscle injury. The IL-6 gene has been shown to be amongst a number of genes that were predictive of sports performance (Buxens et al 2011) plus the G allele seems to be most common in power athletes compared to control and endurance athletes (Ruiz et al 2010), which may be due to improved muscle repair after eccentric exercise (Yamin et al 2008).

Under-performance syndrome (UPS), another name for overtraining syndrome, is thought to be influenced by cytokine sickness, an over-production and/or an intolerance to IL-6 and other cytokines (Robson et al 2003). This suggestion was supported by Robson-Ansley et al (2007), who noted that an acute period of intensified training can suppress the innate immune system and chronically increase IL-6 levels. These elevated cytokines can in-turn increase fatigue and malaise, which are related to the cytokine theories of UPS. The IL-6 genotype can also influence glucose levels: McKenzie et al (2004) found that baseline fasting glucose levels were higher in the CC genotype compared to carriers of the G allele: 6 months of aerobic training successfully decreased the glucose area under the curve during an oral glucose tolerance test, but a significant decrease only occurred in the GG genotype.

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