MyFitnessGenes®

HEARTGENETICS
GENETICS & BIOTECHNOLOGY

Genetic Evaluation of Athletic Potential

INDEX CASE	
Name:	**N.A.**
Gender:	**N.A.**
Date of birth:	**N.A.**
Age:	**N.A.**
Ethnicity:	**N.A.**
Consultancy referral number:	**N.A.**
Reason:	**Training plan adequacy**
Purpose:	**Genetics of athletic performance**
Specimen type:	**N.A.**

CUSTOMER INSTITUTION	
Referring physician:	**N.A.**
Reference:	**N.A.**
Institution:	**N.A.**
Requisition date:	**N.A.**
Fulfillment date:	**N.A.**

1. WHAT IS ANALYZED IN THIS GENETIC TEST?

This genetic test performed by HeartGenetics analyses DNA in order to evaluate 43 genetic variants from 33 genes. This test is 99% accurate and only needs to be performed once in a lifetime.

This test identifies the athletic genetic profile aiming to inform about athletic potential as well as preventive measures and needs.

The recommendations provided in this report can be used to guide you and your personal trainer to optimize your training plan.

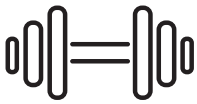
2. Important Disclaimer

Athletic performance is a concept used by athletes and sports amateurs that determines the ability to reach maximum athletic potential. The information on genetic predisposition should be integrated with information on physical characteristics (e.g. age, gender, muscle mass index, VO_2 max) and behaviour (e.g. eating habits, physical activity) in order to establish the best personalised training plan.

There is no evidence that genetic data can be used to determine sport talents. Existent research studies inform about what type of training works best to enable the established goals. HeartGenetics uses up-to-date information, and takes the latest research into consideration for genetic data interpretation. However, there is still much to be known about genetic profiles and sport talents.

The results of this genetic test do not depend on the physical or clinical condition or on the therapeutic management of the individual tested. The information supplied does not confirm or replace any medical condition diagnosis or status, and cannot be used for disease prevention or clinical condition identification. In case of any questions regarding this report's information, or any concerns about the personal health or medical conditions, it is advised to contact a qualified healthcare professional.

3. Areas Under Analysis



Power | power ability

Discover your genetic potential to exert substantial force in a short period of time and improve your power training performance.

Strength and sprint, fibre type, energy generation, metabolic efficiency, blood pressure regulation, cardiac output, muscle hypertrophy

Endurance | endurance capacity

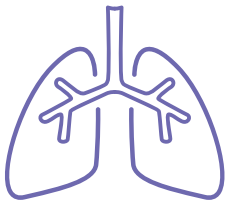
Discover if you are naturally suited to repeat an activity for an extended period of time without experiencing fatigue.

Cardiopulmonary capacity, blood pressure regulation, metabolic efficiency, fibre type, oxygen supply to muscles, fatigue tolerance, angiogenesis, muscular performance, running economy

Power-Endurance | muscular performance and power exercise ability

Discover if you are tailored for the practice of power, sprint, and mixed aerobic-anaerobic sports.

Energy generation, oxygen supply to muscles, glucose homeostasis, lipid metabolism, blood pressure regulation, angiogenesis



VO_2 max | aerobic capacity

Understand your ability to perform dynamic and moderate- to high-intensity exercise that has an impact in your cardiorespiratory fitness.

VO_2 max, oxygen supply to muscles, fatigue tolerance

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Injury | injury proneness

Be aware if you have a predisposition to an increased rate of tendon and ligament injuries.

Exercise-induced muscle damage, inflammation, oxidative stress, soreness, tendinopathies and ligaments rupture, strength, insulin signalling

Recovery Needs | muscle regeneration capacity

Know about the time it takes for your muscles to repair after exercising.

Muscle repair, collagen formation, inflammation, insulin signalling

Energy Refuel Needs | nutritional needs

Know about your nutritional needs and about the balance between training and the adequate intake of antioxidants or omega-3 fatty acids.

Antioxidant needs, PUFA needs, BMI response to exercise

Muscle Building | muscle growth capacity

Discover how easy it is for you to gain muscle strength following power training.

Muscle damage and regeneration, muscle hypertrophy, strength and power, muscle mass

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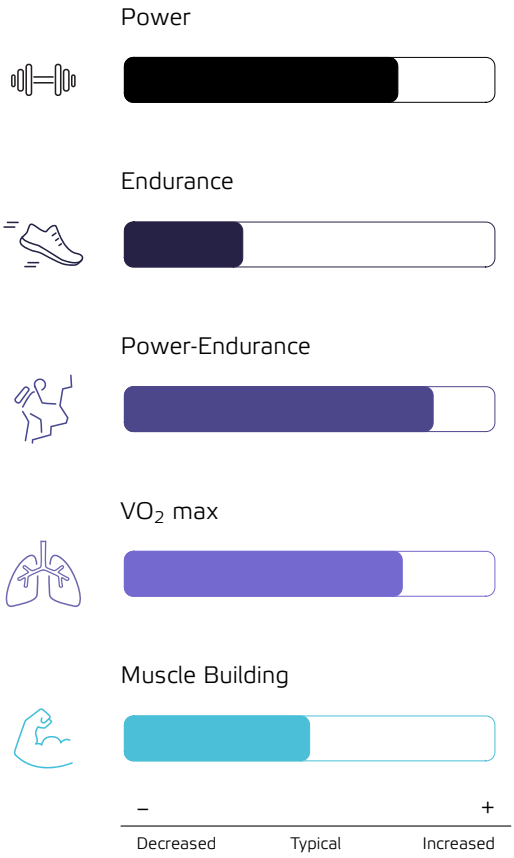
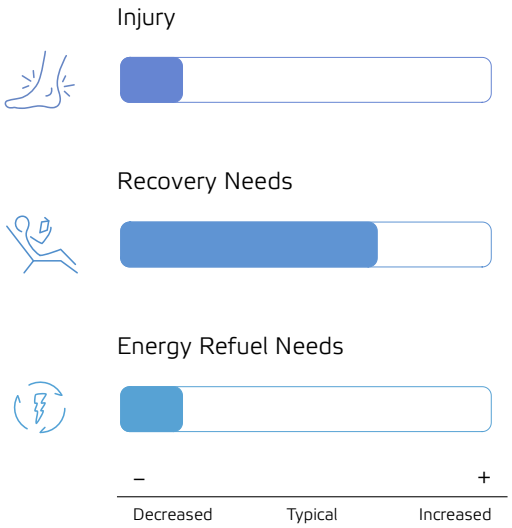
4. Your Genetic Athlete Profile

This section presents your genetic predisposition associated with your athletic performance potential with two different views: 1) your "Athletic Potential"; 2) your "Preventive Measures and Needs". This genetic test identified 31 genetic variants (out of 43 analysed) with a significant impact in the definition of your athlete profile. Your genetic athlete profile leads to a clear set of actions that should be undertaken for personalised training recommendations, depending on your current level of physical activity, desired exercise intensity, and fitness goals. Consult your Fitness/Personal Trainer on how to leverage this capacity to improve your fitness routines.

Athletic Potential



Preventive Measures and Needs

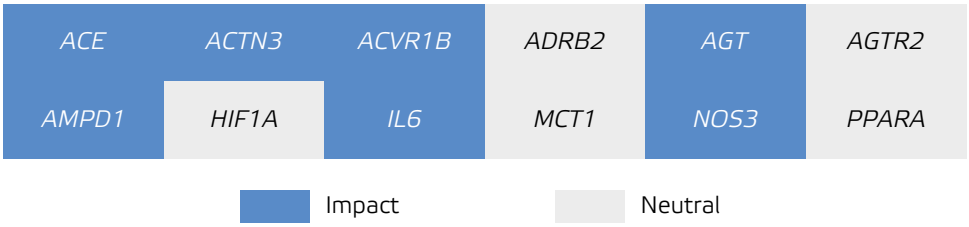


Your Exceptional Potential

5. Power

Your genetics related to power trait:

Your genetic results indicate that you have an increased potential towards power. Your profile shares genetic variants with professional power athletes. You may excel at power, sprint and strength exercises.



Recommendation to training plan according to guidelines:

Advanced level - If you are involved in a power sport, be aware that your strengths most likely lie in the power/sprint/strength exercises. You may work further on this advantage by doing ballistic training, high impact training, weight training or combat sports. Within your current training programme, ensure to work out this capacity 4-6 days per week (depending on your training background and fitness goals), but remember to include adequate rest. To excel in your training, it is important to include aerobic conditioning, core stability, flexibility and mobility training.

Intermediate level - If you are involved in a power sport activity, be aware that your strengths most likely lie in the power/sprint/strength exercises. Within your current training programme, ensure to work out this capacity 3-5 days per week (depending on your training background and fitness goals), but remember to include adequate rest. To excel in your training, it is important to include aerobic conditioning, core stability, flexibility and mobility training.

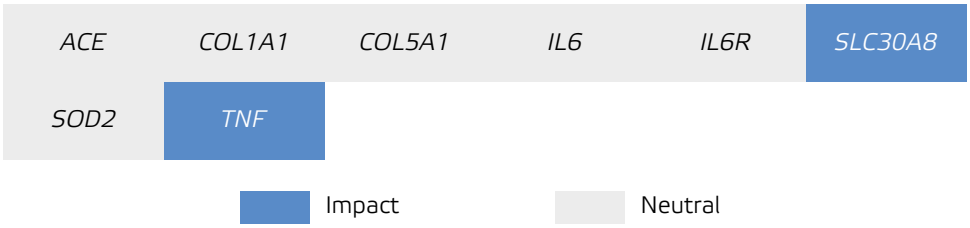
Beginner level - If you are new to physical exercise and although you have an increased genetic potential towards power, make sure you start a training programme that gradually and safely allows you to build on your muscle capacity. Make sure to avoid excessive demands and routines with too much volume/intensity. Consider choosing body-weight exercises first and then add extra weight. In your future training programme, ensure to stimulate muscle strength 2-4 days per week turning it into the foundation of your training (depending on your training background and fitness goals). Remember that each muscle group should rest for at least 48 hours, so do not over-exercise even if you feel you can. For a well-designed training, make sure you include aerobic conditioning, core stability, balance and flexibility.

Recommendations according to the American College of Sports Medicine [1].

10. Injury

Your genetics related to injury trait:

Your genetic results indicate that you have a predisposition for a decreased risk for soft tissue injury, in particular, tendonitis. This means that you don't need to be extra careful with your training volumes and intensities. You could include flexibility workout in order to prevent joint or tendon injuries and improve your maximal Range of Motion (ROM).



Recommendation to training plan according to guidelines:

Advanced level - If you are an elite athlete and although you have a genetic predisposition for low injury risk, consider practicing a sport-specific conditioning exercise routine 1-2 times/week to prevent possible injuries.

Intermediate level - If you practice sports or exercise regularly, consider practicing sport-specific conditioning exercises, besides your sport-specific training, at least once per week to prevent common or accidental injuries. Ensure to take regular measures to protect your tendons and ligaments although you may still benefit from exercises that require balance, power and agility. This helps to improve neuromuscular conditioning and muscular reactions, while decreasing the ligament injury risk.

Beginner level - If you are new to physical exercise and although you have a low genetic susceptibility to injury risk, make sure you have a well-designed exercise routine that includes strength, mobility and joint flexibility training to prevent injuries.

It has also been suggested that optimal hydration before and after exercise may prevent ligament injuries. Always warm up, stretch, strengthen your muscles, and work on agility, change of direction and speed.

Recommendations according to the American College of Sports Medicine [1].

13. TECHNICAL INFORMATION

13.1. METHODOLOGY

1. The DNA extraction was done in the automatic extraction equipment MagNA Pure Compact (ROCHE) through the use of the MagNA Pure Compact Nucleic Acid Isolation Kit I kit (ROCHE). The concentration and quality evaluation was done through the use of the Spectrophotometer MultiskanGo (Thermo Scientific).
2. Genotyping was made via the study of 43 genetic variants in 33 genes, described as associated with athletic potential.
3. Genotyping was achieved using a high-throughput DNA Microchip platform, the iPLEX® MassARRAY® system (Agena Bioscience, Inc.). This array platform allows an optimal genetic analysis by combining the benefits of accurate primer extension chemistry with MALDI-TOF mass spectrometry. The different masses of each generated PCR product are then converted into genotype information.
4. In accordance with Agena Bioscience's iPLEX® chemistry flyer, the MassARRAY® system performs SNP genotyping with a high level of accuracy and reproducibility (>99% accuracy on validated assays).

13.2. GENETIC PANEL

ACE	**angiotensin I converting enzyme** | NM_000789
ACSL1	**acyl-CoA synthetase long-chain family member 1** | NC_000004
ACTN3	**actinin alpha 3 (gene pseudogene)** | NM_001104
ACVR1B	**activin A receptor type 1B** | NM_004302
ADRB2	**Adrenoceptor Beta 2** | ENSG00000169252
AGT	**angiotensinogen** | NM_000029
AGTR2	**angiotensin II receptor type 2** | NM_000686
AKT1	**AKT serine threonine kinase 1** | NM_005163
AMPD1	**adenosine monophosphate deaminase 1** | NM_000036
BDKRB2	**bradykinin receptor B2** | NM_000623
CCL2	**C-C motif chemokine ligand 2** | NC_000017
CCR2	**C-C motif chemokine receptor 2** | NC_000003
COL1A1	**collagen type I alpha 1 chain** | NM_000088
COL5A1	**collagen type V alpha 1 chain** | NM_000093
EDN1	**endothelin 1** | NM_001955
FADS1	**Fatty Acid Desaturase 1** | NM_013402.4
FTO	**Fat Mass And Obesity Associated** | NM_001080432.2
HIF1A	**hypoxia inducible factor 1 alpha subunit** | NM_001530
IGF1	**insulin like growth factor 1** | NM_000618
IL15RA	**interleukin 15 receptor subunit alpha** | NC_000010
IL6	**Interleukin 6** | NM_000600.3
IL6R	**interleukin 6 receptor** | NM_000565
MCT1	**solute carrier family 16 member 1 (SLC16A1)** | NM_001166496
NOS3	**nitric oxide synthase 3** | NM_000603
NRF1	**nuclear respiratory factor 1** | NC_000007
PPARA	**peroxisome proliferator activated receptor alpha** | NM_001001928
PPARGC1A	**peroxisome proliferator-activated receptor gamma, coactivator 1 alpha** | NM_001330751
SLC30A8	**solute carrier family 30 member 8** | NM_173851
SOD2	**Superoxide Dismutase 2, Mitochondrial** | NM_000636.2
TNF	**tumor necrosis factor** | NM_000594
UCP2	**uncoupling protein 2** | NM_003355
UCP3	**uncoupling protein 3** | NM_003356
VEGFA	**vascular endothelial growth factor A** | NM_001025366

13.3. RISKS AND LIMITATIONS

HeartGenetics applies a rigorous quality control which may not exclude the possibility of error that might influence the test results. The reliability of the results is always guaranteed as HeartGenetics, Genetics and Biotechnology SA standard quality recommendations have been followed for the execution of this genetic test. The results presented in this report are limited to the available scientific knowledge at the time this test was developed. The company guarantees the accuracy of the scientific knowledge presented in the report. It has been assumed as truthful all the above declarations about the individual and healthcare professional identity, the purpose of the study, index case and nature of analysed biological products.

13.4. QUALITY ASSURANCE

HeartGenetics, Genetics and Biotechnology SA is an ISO 9001 and ISO 13485 certified company for Quality Management System and applies an External Quality Assessment program from UK NEQAS. The laboratory that performs this genetic test undertakes to, at all times, comply with the all applicable certifications and Law in its territory.

13.5. TERMS AND CONDITIONS

HeartGenetics, Genetics and Biotechnology SA will not be liable whether in contract, tort, warranty, or under any statute, or any other basis of special, incidental, indirect punitive, multiple, or consequential damages in connection with in arising from this document, or improper use of the product described herein or any use of such product outside the scope of the express written licenses or permissions granted by HeartGenetics, Genetics and Biotechnology SA, to the extent allowed by law.
The results presented in Section 14, Genetic Information, are the responsability of the laboratory that performed the genetic test.

In the development of its work, HeartGenetics, Genetics and Biotechnology SA rigorously conforms to all the requirements set out in the legislation of the European Union institutions. It is the responsibility of partners of HeartGenetics, Genetics and Biotechnology SA to meet with the internal standards of the respective legal jurisdiction. HeartGenetics, Genetics and Biotechnology SA does not take responsibility for any eventual violations of existing regulations applicable in its partners' home countries.

14. GENETIC INFORMATION

The table below presents the genetic variants that have been identified as relevant for the design of a personalized training plan. The results are described according to the HGVS nomenclature (`http://www.hgvs.org`), accessed on July 2017.

No other molecular markers from the genetic panel were identified with impact on athletic potential, than those shown in the table.

Gene	Ensembl	Nucleotidic change [1]	Aminoacidic change	Result
ACE	rs4646994	c.2306-109_2306-108ins(289BP ALU)	–	DEL
ACSL1	rs6552828	g.184804262A>G	–	G
ACTN3	rs1815739	c.1729C>T	–	TC
ACVR1B	rs2854464	c.*997A>G	–	GA
ADRB2	rs1042714	c.79C>G	p.Gln27Glu	C
ADRB2	rs1042713	c.46A>G	p.Arg16Gly	A
AGT	rs699	c.803T>C	p.Met268Thr	C
AKT1	rs1130214	c.-350G>T	–	GT
AMPD1	rs17602729	c.133C>T	p.Gln45Ter	C
BDKRB2	rs1799722	c.-192C>T	–	TC
CCL2	rs13900	c.*65C>T	–	CT
CCL2	rs1860189	–	–	CT
CCR2	rs3918358	g.46394419C>A	–	CA
CCR2	rs768539	–	–	TC
COL5A1	rs12722	c.*267C>T	–	C
EDN1	rs5370	c.594G>T	–	GT
FADS1	rs174546	g.61802358C>T	–	CT
HIF1A	rs11549465	c.1744C>T	p.Pro582Ser	C
IL15RA	rs2296135	g.5994694A>C	–	C
IL6	rs1800795	c.-237C>G	–	G
MCT1	rs1049434	c.1470T>A	p.Asp490Glu	A
NOS3	rs1799983	c.894T>G	p.Asp298Glu	G
NOS3	rs2070744	c.-51-762C>T	–	T
NRF1	rs2402970	c.1348+12596C>T	–	C
PPARA	rs4253778	c.1160-396G>C	–	GC
PPARGC1A	rs6821591	c.*445G>A	–	A
SLC30A8	rs13266634	c.973C>T	–	TC
TNF	rs1800630	c.-1043C>A	–	CA
TNF	rs1799964	c.-1211T>C	–	CT
UCP2	rs660339	c.164C>T	p.Ala55Val	T
VEGFA	rs2010963	c.-94C>G	–	CG

[1] The numeric identification associated with each variant is indexed to a reference sequence obtained from Ensembl database (`http://www.ensembl.org/index.html`).

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15. APPENDIX

15.1. EVIDENCES FOR MOLECULAR MARKERS

This appendix includes a detailed interpretation of the genetic study. All evidences are supported through scientific articles indexed in PubMed (http://www.ncbi.nlm.nih.gov/pubmed) accessed in October 2017.

ACE / rs4646994

POWER: Increased Power Performance, Strength, Sprint, Blood Pressure Regulation
INJURY: Exercise-Induced Muscle Damage - Benefit
The *ACE* gene codes for the angiotensin-I converting enzyme, a key enzyme of the renin-angiotensin system responsible for controlling blood pressure [11]. The ACE enzyme converts inactive angiotensin I into active angiotensin II in the liver and degrades bradykinin and other vasodilator peptides. It modulates vasoconstriction, salt and water balance, red blood cell production (erythropoiesis), inflammation, tissue oxygenation, and muscle efficiency [12]. The rs4646994 polymorphism refers to the absence (deletion, D allele) or the presence (insertion, I allele) of a 287-base-pair fragment in the *ACE* gene [13, 14]. The D-allele (genotypes DD or ID) is associated with higher ACE serum levels and higher ACE activity in tissues [13, 15]. The DD genotype has been consistently associated with strength- and power-oriented performance or exercise tasks, being found in significant excess in sprinters and short distance swimmers [16, 17, 18, 19, 20, 21]. In skeletal muscle, the D allele is associated with greater strength gains in response to training, in both healthy individuals and chronic disease states [16]. It must be noted that, in overall performance, other genetic polymorphisms related to the *ACE* genotype, such as polymorphisms in the B2 bradykinin receptor gene (*BDKRB2*), also influence skeletal muscle strength [16]. Moreover, DD genotype carriers have a decreased bradykinin half-life due to their higher ACE serum levels and activity, which might result in an underexpression of nerve growth factor following exertional muscle damage and consequently a decreased sensitivity to pain [22]. For this reason, they are more likely to sustain high-intensity training for longer, reach their maximal power and strength capacity, and practise more often [22].

ACSL1 / rs6552828

VO_2 MAX: Maximal Oxygen Uptake
The *ACSL1* gene encodes for an enzyme involved in lipid biosynthesis and fatty acid degradation, which catalyses the conversion of free long-chain fatty acids into fatty acyl-CoA esters. This gene has a potential role in aerobic metabolism at the adipocyte, cardiomyocyte, liver and skeletal muscle fibre level [23]. A genome-wide association study found the *ACSL1* rs655282 polymorphism to have the strongest association with response of maximum oxygen consumption (VO_2max) to regular exercise, accounting by itself for approximately 6% of the training response of VO_2max [24]. Carriers of the GG genotype present a higher improvement of VO_2max with training compared with those with AA or GA genotypes [24].

ACTN3 / rs1815739

POWER: Increased Power Performance, Strength
ACTN3 encodes for a key protein of the sarcomeric Z-line in skeletal muscle. It is considered the world's most famous "gene for speed". Expression of α-actinin-3 is limited to type II muscle fibres (i.e. fast-twitch, mostly glycolytic) which can generate more force at high velocity [25, 26]. The rs1815739 polymorphism is a C to T substitution that results in the conversion of the codon for arginine (R) at position 577 to a premature stop codon (X) (R577X) [27]. The R-allele codes for a functional α-actinin-3 protein whereas the X allele results in α-actinin-3 deficiency [27]. Studies have demonstrated that the frequency of the RR genotype is higher in power and sprint athletes than in controls and endurance athletes [26]. The R-allele (genotypes RR or RX) has been consistently associated with greater muscle strength, explosive power, and elite power and sprint performance [15, 26, 28, 29, 30, 31, 32, 33]. α-actinin-3 was also suggested to play a role in the determination of muscle fibre type, with the R-allele being associated with an increased proportion of fast-twitch fibres [26, 34] that probably justifies the more dynamic muscle power (power output) demonstrated by athletes with the RR genotype and their advantage in power performance [33].

ACVR1B / rs2854464

POWER: Increased Power Performance, Strength, Sprint
MUSCLE BUILDING: Muscle Strength
The activin receptor type-1B, encoded by the *ACVR1B* gene, has a key a role in regulating the signaling of myostatin, which is in turn a potent regulator of skeletal muscle mass [35, 36]. It is therefore considered a muscle strength gene and a potential regulator of the adaptation to resistance exercise. Genetic studies demonstrated that genetic variations in *ACVR1B* gene influence human muscle strength [37, 38]. The A-allele (genotype AA or GA) was found to be differently associated with sprint and power performance in a large cohort of Caucasian and Brazilian athletes. The A allele is overrepresented in Caucasian (Italian, Polish, and Russian) sprint and power athletes, and this association is even more pronounced when only elite-level athletes are considered [38]. This association was, however, found likely to be ethnicity-dependent due to an observed trend towards an underrepresentation of the A allele in sprint and power Brazilian athletes [38]. In addition, carriers of AA genotype, from the Leuven Genes for Muscular Strength study (LGfMS) cohort, demonstrated higher knee strength compared with G-allele carriers [37]. Enhanced strength with regard to dynamic knee extensor strength was also observed for the AA genotype in follow-up replication analyses in an independent but size-limited study [37].

ADRB2 / rs1042713

ENDURANCE: Increased Endurance Performance, Cardiopulmonary Capacity
Beta-adrenergic receptor (ADRB2) is a member of the G protein-coupled receptor superfamily and plays a functional role in the regulation of the