"The human body is centuries in advance of the physiologist, and can perform an integration of heart, lungs and muscles which is too complex for the scientist to analyse."

Roger Bannister (1955)

"There is likely a minimal set of physical traits or genetic makeup which facilitates achievement to a particular level of success, but I do not believe that genetics are necessarily an absolute limiter of exceptional performances."

Peter Vint (2011)
What is Athletic Performance?

**Strength**

- muscle mass
- force generation
- speed
- agility
- power
- oxidative phosphorylation (ATP)
- creatine phosphate usage
- glycogen usage
- metabolic rate
- resting heart rate
- max heart rate
- lactate threshold
- cardiac output
- ventilatory rate

**Endurance**

- Dean Karnazes

Arnold Schwarzenegger

it all depends on what you want your body to accomplish
Environmental Factors Affecting Performance

- training/conditioning
- skill level
- age
- PED's
- climate/temperature
- altitude

- nutrition: food + water
- sleep
- recovery
- weight

- mental strength
- work ethic
- confidence
- focus on goals
- mental adaptation
- psychology
Genetic Factors Affecting Performance

- gender
- ancestry & ethnicity
- anatomy

- biomechanical factors
- muscle fiber types
- muscle contraction velocity
- muscle elasticity
- soft-tissue strength

- fatigue resistance
- training adaptation
- recovery
- injury resistance
How Scientists Test "Performance"

**Strength/Power**
1) max weight lifted [kg]
2) max power [W/kg]
3) 100m sprint
4) vertical + horizontal jump distance

**Endurance**
1) peak oxygen consumption ($\text{VO}_2$ max) [ml/min/kg]
2) running economy (RE) [ml/kg/km]
3) lactate threshold + clearance

---

**genetics + environment**

**elite athletes vs controls**

**candidate based approach**

**genetic testing for SNP**

**data analysis**
The Human Gene Map for Performance and Health-Related Fitness Phenotypes

239 gene entries: 214 autosomal; 7 on X; 18 mitochondrial
ACE

- **ACE**: angiotensin converting enzyme
  1) converts inactive angiotensin I to active angiotensin II in liver
  2) degrades bradykinin & other vasodilator peptides
- functions= vasoconstriction, salt/water balance, inflammation, RBC synthesis, tissue oxygenation, muscle efficiency.

- I allele: 287bp insertion; lower ACE activity
  I/I genotype -> increased endurance performance \([p=0.009]\)
  increased metabolic response from training, metabolic efficiency

- D allele: deletion variant; higher ACE activity
  D/D genotype -> increased power performance \([p=0.004]\)
  increased strength gain from training, L ventricle mass, \(VO_2\) max

- many studies w/ conflicting results on ACE & athletic performance
  8 show positive association & 5 show no association
  different sports, different criteria for cases/ct's, different methods

ACE

Table 1. By ACE I/D Genotype and Mean Maximum Altitude Achieved

<table>
<thead>
<tr>
<th>ACE genotype</th>
<th>Maximum altitude achieved (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>8559 ± 565</td>
</tr>
<tr>
<td>ID</td>
<td>8107 ± 653</td>
</tr>
<tr>
<td>DD</td>
<td>8079 ± 947</td>
</tr>
</tbody>
</table>

Table 2. ACE I/D Genotype and Success in Ascent to 8000 m

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(climbed &gt;8000 m)</td>
<td>(never climbed &gt;8000 m)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>30 (32.6%)</td>
<td>33 (23.7%)</td>
</tr>
<tr>
<td>ID</td>
<td>41 (44.6%)</td>
<td>69 (49.6%)</td>
</tr>
<tr>
<td>DD</td>
<td>21 (22.8%)</td>
<td>37 (26.6%)</td>
</tr>
<tr>
<td>I-allele frequency</td>
<td>0.55</td>
<td>0.49</td>
</tr>
<tr>
<td>D-allele frequency</td>
<td>0.45</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Table 3. Logistic Regression Analysis of the Categorical Variables Influencing Success in Ascent to 8000 m

<table>
<thead>
<tr>
<th>Significance</th>
<th>0.620</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.184</td>
</tr>
<tr>
<td>Sex</td>
<td>0.118</td>
</tr>
<tr>
<td>Race</td>
<td>0.187</td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
</tr>
<tr>
<td>ACE I-allele</td>
<td>0.002</td>
</tr>
</tbody>
</table>

- alpha-actinin-3: crosslinks actin thin filaments in skeletal muscle type 2 (fast) fibers; thought to play a role in maintaining ordered fiber arrays and coordinating contraction

- R577X: rs1815739; C->T; 25% Asian, 18% European, 1% African

- CC [RR] genotype associated with increased strength (OR=2.31; p=0.0001)
- TT [XX] genotype associated with increased endurance (OR=1.38; p=0.148)

Controversial
- 10 studies showing association between RR and strength/power
- 2 studies showing no association between RR and strength/power
- 1 study showing association between XX and endurance
- 7 studies showing no association between XX and endurance
### ACTN3

<table>
<thead>
<tr>
<th>Study</th>
<th>Region</th>
<th>OR (95% CI)</th>
<th>% Weight (I-V)</th>
<th>Sprint/Power RR/Total</th>
<th>Control: RR/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>European</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al. 2003</td>
<td>Australian</td>
<td>2.31 (1.50, 3.55)</td>
<td>12.74</td>
<td>53/107</td>
<td>130/436</td>
</tr>
<tr>
<td>Niemi &amp; Majamaa 2005</td>
<td>Finnish</td>
<td>1.30 (0.71, 2.35)</td>
<td>6.66</td>
<td>35/68</td>
<td>54/120</td>
</tr>
<tr>
<td>Santiago et al. 2008</td>
<td>Spanish</td>
<td>2.35 (1.24, 4.46)</td>
<td>5.77</td>
<td>29/60</td>
<td>35/123</td>
</tr>
<tr>
<td>Druzhinskaya et al. 2008</td>
<td>Russian</td>
<td>1.13 (0.91, 1.40)</td>
<td>50.56</td>
<td>193/486</td>
<td>441/1197</td>
</tr>
<tr>
<td>Papadimitriou et al. 2008</td>
<td>Greek</td>
<td>2.63 (1.49, 4.63)</td>
<td>7.37</td>
<td>35/73</td>
<td>47/181</td>
</tr>
<tr>
<td>Roth et al. 2008</td>
<td>N American</td>
<td>0.69 (0.36, 1.32)</td>
<td>5.63</td>
<td>13/52</td>
<td>218/668</td>
</tr>
<tr>
<td>Eynon et al. 2009</td>
<td>Israeli</td>
<td>4.00 (2.34, 6.83)</td>
<td>8.21</td>
<td>41/81</td>
<td>49/240</td>
</tr>
<tr>
<td>Massidda et al. 2009</td>
<td>Italian</td>
<td>2.00 (0.83, 4.82)</td>
<td>3.06</td>
<td>17/35</td>
<td>17/53</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 80.0%, p = 0.000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td>1.52 (1.30, 1.77)</td>
<td>100.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>W African</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al. 2007</td>
<td>Nigerian</td>
<td>1.35 (0.49, 3.69)</td>
<td>9.57</td>
<td>54/62</td>
<td>50/60</td>
</tr>
<tr>
<td>Roth et al. 2008</td>
<td>African-American</td>
<td>0.61 (0.26, 1.45)</td>
<td>12.83</td>
<td>10/23</td>
<td>116/208</td>
</tr>
<tr>
<td>Scott et al. 2010</td>
<td>African-American</td>
<td>1.18 (0.71, 1.95)</td>
<td>38.41</td>
<td>79/113</td>
<td>126/190</td>
</tr>
<tr>
<td>Scott et al. 2010</td>
<td>Jamaican</td>
<td>1.05 (0.64, 1.72)</td>
<td>39.19</td>
<td>86/114</td>
<td>232/311</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 0.0%, p = 0.583)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td>1.05 (0.77, 1.43)</td>
<td>100.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity between groups: p = 0.035</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-V Overall (I-squared = 73.5%, p = 0.000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+L Overall</td>
<td></td>
<td>1.41 (1.23, 1.62)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR Higher in Control Group</td>
<td></td>
<td>1.51 (1.12, 2.05)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ACTN3

<table>
<thead>
<tr>
<th>Study</th>
<th>Ethnicity</th>
<th>OR (95% CI)</th>
<th>Weight (I-V)</th>
<th>Endurance: XX/Total</th>
<th>Control: XX/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al. 2003</td>
<td>Australian</td>
<td>1.38 (0.92, 2.08)</td>
<td>23.17</td>
<td>46/194</td>
<td>80/436</td>
</tr>
<tr>
<td>Niemi &amp; Majamaa 2005</td>
<td>Finnish</td>
<td>1.10 (0.33, 3.67)</td>
<td>2.69</td>
<td>4/40</td>
<td>11/120</td>
</tr>
<tr>
<td>Santiago et al. 2008</td>
<td>Spanish</td>
<td>1.34 (0.69, 2.57)</td>
<td>9.10</td>
<td>23/102</td>
<td>22/123</td>
</tr>
<tr>
<td>Paparini et al. 2007</td>
<td>Italian</td>
<td>0.86 (0.35, 2.11)</td>
<td>4.78</td>
<td>8/42</td>
<td>22/102</td>
</tr>
<tr>
<td>Ahmetov et al. 2008</td>
<td>Russian</td>
<td>0.36 (0.23, 0.55)</td>
<td>21.39</td>
<td>26/456</td>
<td>175/1211</td>
</tr>
<tr>
<td>Papadimitriou et al. 2008</td>
<td>Greek</td>
<td>1.49 (0.59, 3.81)</td>
<td>4.46</td>
<td>7/28</td>
<td>33/181</td>
</tr>
<tr>
<td>Eynon et al. 2009</td>
<td>Israeli</td>
<td>2.26 (1.25, 4.08)</td>
<td>11.21</td>
<td>24/74</td>
<td>42/240</td>
</tr>
<tr>
<td>Doring et al. 2010</td>
<td>N American, Finnish, German</td>
<td>1.23 (0.62, 1.85)</td>
<td>23.20</td>
<td>63/305</td>
<td>51/292</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 79.7%, p = 0.000)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td>1.04 (0.65, 1.26)</td>
<td>100.00</td>
<td>51/292</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.11 (0.69, 1.79)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E African</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yang et al. 2007</td>
<td>Kenyan</td>
<td>0.83 (0.14, 5.04)</td>
<td>21.58</td>
<td>3/284</td>
<td>2/158</td>
</tr>
<tr>
<td>Yang et al. 2007</td>
<td>Ethiopian</td>
<td>0.69 (0.27, 1.76)</td>
<td>78.42</td>
<td>6/76</td>
<td>22/198</td>
</tr>
<tr>
<td>I-V Subtotal (I-squared = 0.0%, p = 0.651)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+L Subtotal</td>
<td></td>
<td>0.72 (0.31, 1.65)</td>
<td>100.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.72 (0.31, 1.65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity between groups: p = 0.399</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-V Overall (I-squared = 74.4%, p = 0.000)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>D+L Overall</td>
<td></td>
<td>1.02 (0.84, 1.23)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.05 (0.69, 1.61)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ADRB1, ADRB2, ADRB3

- beta-adrenergic receptors 1/2/3: G-protein coupled receptors in cardiac and adipose tissue that regulate cardiac function and metabolism
- cardiac tissue: activated receptor -> increased cardiac output
- adipose tissue: activated receptor -> increased lipid mobilization for energy production

**ADRB1**: rs1801253; Arg389Gly; C->G
- C allele associates with increased VO$_2$ max and exercise time/endurance (p=0.002)
- G allele associates with decreased VO$_2$ max (p=0.006)

**ADRB2**: rs1042713; Arg16Gly; G->A
- G allele associates with elite endurance performance in males (p=0.03)
- A allele associates with increased BMI and decreased VO$_2$ max (p<.001)

**ADRB2**: rs1042714; Gln27Glu; C->G
- C allele associates with elite distance running in middle age women (p=0.05)
- G allele associates with increased BMI and decreased VO$_2$ max (p=0.0001)

ADRB1, ADRB2, ADRB3

**ADRB3**: rs4994; Trp64Arg; T->C
- C allele associates with elite endurance performance \((p=0.0008)\)

- study: elite Spanish athletes for endurance or strength sports
- TT genotype: no association in endurance or strength vs controls
- TC genotype: association in endurance vs controls but not strength vs controls
- CC genotype: very rare; association in strength vs controls
COL5A1 and COL6A1

- alpha1 chain of type V and type VI collagen
- extracellular matrix (ECM) structural component of musculoskeletal soft tissue
- known mutations involved in various clinical muscle diseases (cause hyperelasticity in the muscles -> decreased function)
- biomechanics: stiffer connective tissue (inflexibility) -> enhanced storage/return of energy -> increased running economy -> increased endurance performance

**COL5A1**
- BstUI RFLP: T/C
- TT genotype (vs CT + CC) associated with increased endurance performance (faster Ironman Triathlon run time) \[p=0.020\]

**COL6A1**
- rs35796750: intron 32, T/C, T= ancestral allele
- CC genotype (vs CT + TT) associated with multiple muscle diseases
- TT genotype (vs CT + CC) associated with increased endurance performance (faster Ironman Triathlon finish time) \[p=0.030\]
EDN1

- endothelin 1: expressed in vascular endothelium; acts as a vasoconstrictor to regulate blood pressure

rs5370: Lys198Asn; G->T
- G allele associates with increased cardiorespiratory fitness (OR=1.95; p=0.00025)
- T allele associates with increased hypertension (p=.0003)
  - for Caucasians only and not African Americans
- T allele decreases the VO$_2$ max and pulse pressure response to training

MSTN

- **MSTN**: myostatin (TGF-B family member)  
negative regulator of skeletal muscle growth

- homozygous mutation in MSTN -> inactivation  
human patient 1-4.5yrs old w/ increased muscle mass

- protein truncation deletion removing C-term domain MSTN -> catalytically dead  
increased muscle mass in livestock (cattle, pigs)

- *Mstn* k/o mouse model -> increased muscle mass & # muscle fibers  
overall more fast glycolytic type II muscle fibers than ct

NRF1, NRF2

- **NRF1**: nuclear respiratory factor 1
  role in exercise adaptation: mitochondrial biogenesis, heme biosynthesis

- rs240790
  CC genotype associated w/ increased VO$_2$ max + RE w/ training [p=0.004]

- rs6949152
  AA genotype associated w/ increased VO$_2$ max w/ training [p=0.047]

- **NRF2/NFE2L2**: nuclear regulatory factor 2
  tranxs factor activating oxidative stress response & antioxidants

- rs12594986, rs8031031, rs7181866
  A/T/G haplotype associated w/ 57% higher training response [p=0.006]

PPARGC1A

- **PPARGC1A**: peroxisome proliferators-activated receptor g coactivator 1a
  activator of ox phos genes that control glucose & lipid metabolism
  skeletal muscle fiber-type formation
  mitochondrial biogenesis

- rs8192678: G -> A; Gly482Ser
  AA genotype associated w/ higher VO\textsubscript{2} max in European men [p<0.0001]
  not associated w/ better VO\textsubscript{2} max or RE in Chinese men

- rs6821591: A -> G; 3' UTR
  GG genotype associated w/ higher VO\textsubscript{2} max & RE in Chinese men
Other Reported Performance Enhancing Polymorphisms (PEPs)

- 2 validated markers w/ multiple positive associations: ACE, ACTN3
- 4 other markers w/ positive associations: ADRB2, AMPD1, APOE, BDKRB2

- physiological categories influenced by human PEPs
  - cardiac function
  - circulatory system
  - respiratory system
  - muscle structure
  - adrenergic receptors
  - mitochondrial function (oxidative phosphorylation)
  - mitochondrial DNA

- 239 total reported PEPs but very few validated
- potential limitations of studies
  - studied only specific populations
  - only specific gender
  - too few subjects
  - different criteria for cases vs controls
  - significant p-values (?)

Athletic performance is determined by a combination of factors

- measure: Ironman Triathlon finish times
  no significant difference in training time/volume between "fast" and "slow" groups
age + weight explain 14% of variance
COL6A1 genotype (TT vs TC/CC) explains 8% of variance
  BDKRB2 +9/+9 & NOS3 GG genotypes associate w/ significantly slower times [p=0.001]

- measure: endurance (VO$_2$ max + LT) + efficient muscle contraction
ACE-I/BDKRB2-9 haplotype significantly associated in Olympic athletes vs ct's [p=0.003]

- heritability of beneficial endurance traits is ~50% (VO$_2$ max, RE, LT)
- heritability of athletic status in women is ~66% (recreational vs elite competition)
  positive associations for SLC9A9, FABP2, UCP1

- can we identify other factors?

Can There be a Perfect Endurance Athlete? - Population Distribution of Genetic Potential

Results = "Using probability calculations, we found only a 0.0005% chance of a single individual in the world having the ‘preferable’ form of all 23 polymorphisms."


the human body works as a "system": if one factor is sub-par, then the whole system loses the capacity to function at optimal performance
What Will the Future Hold for Genetics and Athletics?

- all athletes competing at recreational to elite levels have complicated genetic profiles & environmental histories
  many factors influence potential athletic ability
  actual performance & success is hard to predict

- genetic engineering ("gene doping") to enhance athletic performance
  many new PEP targets will be validated in the near future
  delivery methods are available to allow beneficial "gene therapy"
  will detection ever be able to keep up with "cheating"?

- **scientist** viewpoint= global perspective to understand how certain alleles beneficial to performance arose & how they have spread geographically

- **athlete** viewpoint= develop training program to maximize individual genetic endowment for optimal performance

Direct-to-consumer testing for athletic performance

Atlas Sports Genetics
2008
"Atlas First SportGene Test"

AIBioTech
June 2011
"Sports X Factor"

What is Included?

The following tests are included in the Sports X Factor basic panel, for the total cost of $200:

### Performance Indicators

**ACTN3**
Highly significant associations between ACTN3 genotype and muscle fiber type, with one genotype indicating fast twitch muscle fibers and another slow twitch muscle fibers. Fast twitch fiber type has been associated with elite power/sprinter performance and slow twitch fibers have been related to endurance athletes.

**ACE**
Related to cardiovascular and skeletal muscle function, training responses of muscle efficiency and skeletal muscle hypertrophy. The ACE genotype has been associated with elite endurance performance in runners, whereas a second genotype has been shown to be represented in elite sportsmen with a power/sprint phenotypic.

**PPARGC**
Gene function is associated with cellular energy metabolism. Two genotypes associated with this gene have been positively associated with endurance.

**DI01**
Associated with isometric grip strength and leg-extensor strength.

**VEGFR**
Associated with elite athlete status, endurance performance of female rowers and muscle fiber type composition.

**NOS3**
Associated with elite power sports performance.

**IL6**
Associated with sprint/power sports performance.

### Risk Factors

**Concussion**
Looks at the genes involved in the inflammatory response of the brain after a concussion.

**Heart**
Panel looks at genes involved with Hypertrophic cardiomyopathy (HCM), a condition in which structural abnormalities can be present in the heart. HCM is the number one cause of sudden unexpected cardiac death in young athletes.

http://www.sportsxfactor.com/Home.aspx
### PERFORMANCE INDICATORS

<table>
<thead>
<tr>
<th>Gene</th>
<th>Genotype</th>
<th>Reynolds Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIO1</td>
<td>The Type I iodothyronine dioxygenase (DIO1) protein encoded by this gene is involved in thyroid hormone activation. Higher isoformic grip strength and leg-exursion strength has been associated with the 1a-1 allele of this gene.</td>
<td>Power Score (0-3)</td>
</tr>
<tr>
<td>NOS3</td>
<td>The NOS3 gene encodes nitric oxide synthase 3, and is also known as eNOS. A small change in NOS3 -786T&gt;C polymorphism in this gene has been studied and found to be associated with elite power sports performance.</td>
<td>Power Score (0-4)</td>
</tr>
<tr>
<td>IL6</td>
<td>Interleukin-6 (IL-6) gene encodes a multifunctional cytokine expressed in many tissues involved in inflammatory processes and may additionally modify the regulation of energy balance. One small change in this gene (the IL6 -174G/C polymorphism) is associated with sprint/power sports performance, with the GG genotype exerting a favorable effect. CC genotypes have been associated with obesity in some studies.</td>
<td>Power Score (0-3)</td>
</tr>
<tr>
<td>ACE</td>
<td>Sequence variants in the angiotensin I converting enzyme gene (ACE) have been shown in studies to have positive effects on athletic performance. This test detects the I and D variants of ACE with the D variant favoring improved endurance ability, the I allele promotes more power-oriented events.</td>
<td>Power Score (0-3)</td>
</tr>
<tr>
<td>ACTN3</td>
<td>The actinin-3 (ACTN3) gene encodes for the synthesis of α-actinin-3, a protein necessary for producing fast contractions. The In Type II skeletal muscle fibres. This polymorphism is associated with elite powers/sprint performance. Conversely homozygous XX indicates only slow twitch muscle fibres present. Studies have shown highly significant associations between ACTN3 genotype and athletic performance.</td>
<td>Power Score (0-6)</td>
</tr>
<tr>
<td>PPARGC1</td>
<td>The peroxisome proliferator-activated receptor gamma coactivator-1a (PPARGC1) gene function is associated with cellular energy metabolism. Two genotypes associated with this gene have been positively associated with endurance. The Gly482Ser genotype is associated with endurance. The PPARC1 gene has only been shown so far to have a favorable impact on males.</td>
<td>Endurance Score (0-5)</td>
</tr>
<tr>
<td>VEGFR</td>
<td>Vascular endothelial growth factor receptor 2 (VEGFR2) is essential to induce the full spectrum of VEGF angiogenic responses to aerobic training. One allele associated with this gene (H647D/C polymorphism) has been associated with elite athlete status, endurance performance and muscle fiber type composition in females.</td>
<td>Females Only</td>
</tr>
</tbody>
</table>

### RISK FACTOR ASSESSMENT

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Present - Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussion Marker*</td>
<td>Athletes with the concussion risk factor variant gene who were studied were tested for recovery time after a concussion and found they are more likely to recover slower than non-variant carriers. It is not entirely clear how the marker affects brain recovery, but the gene is involved in the inflammatory response of the brain after injury, and people with the variant appear to take longer to clear their brains of a particular protein called amyloid, which floods in following head trauma.</td>
<td>Absent</td>
</tr>
<tr>
<td>Heart Screen*</td>
<td>Hypertrophic cardiomyopathy (HCM) - A disease of the muscle of the heart in which a portion of the heart is thickened without any obvious cause. We screen for risk factors in 3 genes which represent 80% of known risk factors for HCM.</td>
<td>Absent</td>
</tr>
<tr>
<td>Acquired Arrhythmia*</td>
<td>This test detects the risk of acquired arrhythmia by detecting a variant of the cardiac sodium channel gene SCN5A which is associated with arrhythmia in African Americans.</td>
<td>Absent</td>
</tr>
</tbody>
</table>

### SUMMARY

<table>
<thead>
<tr>
<th>Gene</th>
<th>Description</th>
<th>Reynolds’s Score (Percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance</td>
<td>Total performance score is calculated for both endurance and strength. The score is based on the summary of the results from the genetic markers tested by AIB on the sample received. This score is weighted and calculated based on several factors including the genotype reported and frequency in the general population. VEGFR marker is for females only while one of the two PPARGC genotypes tested is for males only. The score is a guide to help the individual to maximize fitness focusing on strength, endurance and muscle growth (Please refer to individual workout page for instructions on how to obtain a tailor made workout based on performance results). Your results will be provided as a numerical value for each genetic marker and in the summary as the total score calculated for both endurance and power. Included with your total score for each area will be the percentile your score achieved in relation to the database of individuals who have been previously tested with Sport X Factor. An average score will be one that is in the 50th percentile.</td>
<td>Power 10.0 90th Percentile</td>
</tr>
</tbody>
</table>
Direct-to-consumer testing for athletic performance

*It should be emphasized that genes are only one part of the picture. Athletic performance is likely to result from a combination of many factors including genetics, but also skill level, work ethic, environmental factors, and history of training and conditioning. Moreover, many sport activities rely on both power and endurance to be successful.