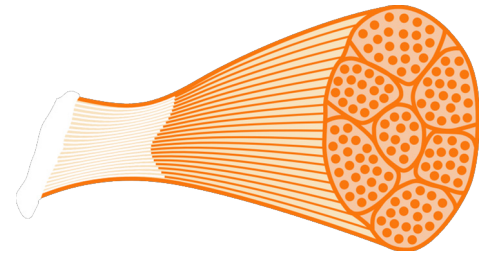


ALPHA ACTININ3 (ACTN3)

The Gene for Speed

Biology Background

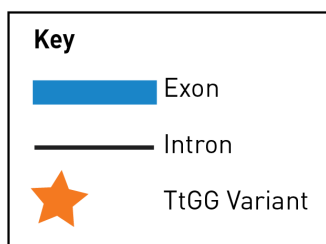
- The alpha actinin 3 (ACTN3) gene produces the ACTN3 protein, which is a structural protein that interacts with actin, a key protein that produces muscle.
- This gene is primarily expressed in skeletal muscle tissue, specifically in type 2 or “fast-twitch” muscle fibers.
- At the molecular level, muscles are essentially repeating units of sarcomeres, or bundles of fibrous proteins (myosin and actin).
- These bundles overlap each other, and their ability to slide past each other forms the basis of the theory of muscle contraction and relaxation.



Muscle

Genomic Locus

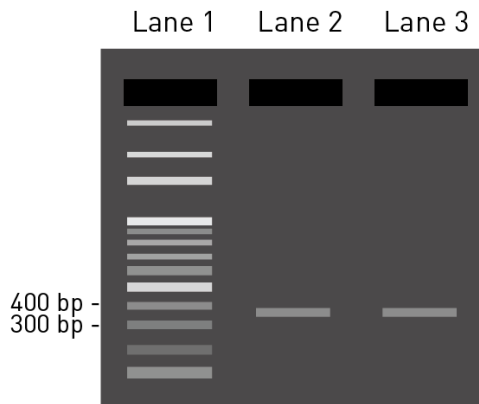
The alpha actinin 3 (ACTN3) gene is located on chromosome 11. The alpha actinin 3 (ACTN3) gene is 16,489 base pairs and consists of 22 exons and 21 introns.



The TtGG Variant

- ACTN3 has a single nucleotide polymorphism (SNP) that confers a nonsense mutation (C >T transition at nucleotide 1747, R557X) in exon 16 (see star) resulting in a truncated protein.
- This destabilized protein is rapidly degraded.

ACTN3 Gel



Lane 1: DNA ladder
Lane 2: 577R CC genotype, 350 bp
Lane 3: R577X TT genotype, 350 bp

*Please note that this variation
can not be detected by size.*

Population Genetics

- Frequencies of the R577X allele are high in the human populations, and approximately 16% of the world's population has ACTN3 deficiencies due to this polymorphism.
- This polymorphic gene has been associated with athletic performance.
- The full-length allele (577R; C at nucleotide position 1747) seems to be present in higher frequencies in sprint and strength athletes.
- The truncated allele (R577X; T at nucleotide position 1747) seems to be present at a higher frequency in endurance athletes.

Influence on Human Health

- Variants that are associated with complex, multifactorial traits such as athletic performance likely contribute only a small amount of effect, with other genetic and environmental factors playing a significant role.
- While having either of these alleles does not mean you will be an athlete, if you are an athlete, your genotype at this locus may affect what type of athlete you are.

Sources

- Online Mendelian Inheritance in Man (OMIM) <http://omim.org/entry/102574>
- Review on ACTN3 and its link to athletic performance: MacArthur and North. A gene for speed?
- The evolution and function of actinin-3. *BioEssays* (2004)
- UCSC Genome Browser
- Human Protein Atlas