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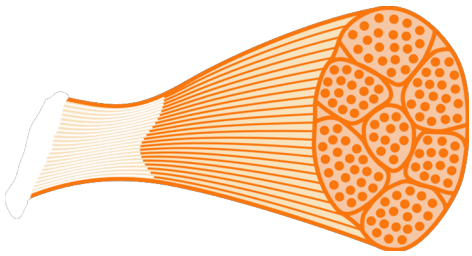
ALPHA ACTININ 3 (ACTN3)

The Gene for Speed

Biology Background

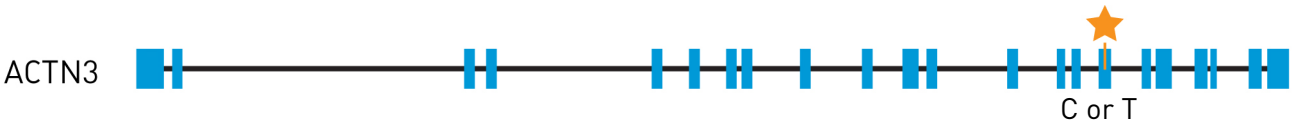
- The alpha actinin 3 (ACTN3) gene produces the ACTN3 protein. The ACTN3 protein is a structural protein that interacts with actin, a key protein that produces muscle.
- The ACTN3 gene is primarily expressed in skeletal muscle tissue, specifically in type 2 or "fast-twitch" muscle fibers.
- At the molecular 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

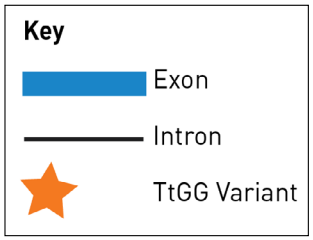
Genomic Locus

The ACTN3 gene is located on chromosome 11. The ACTN3 gene is 16,940 base pairs in length and consists of 22 exons and 21 introns.

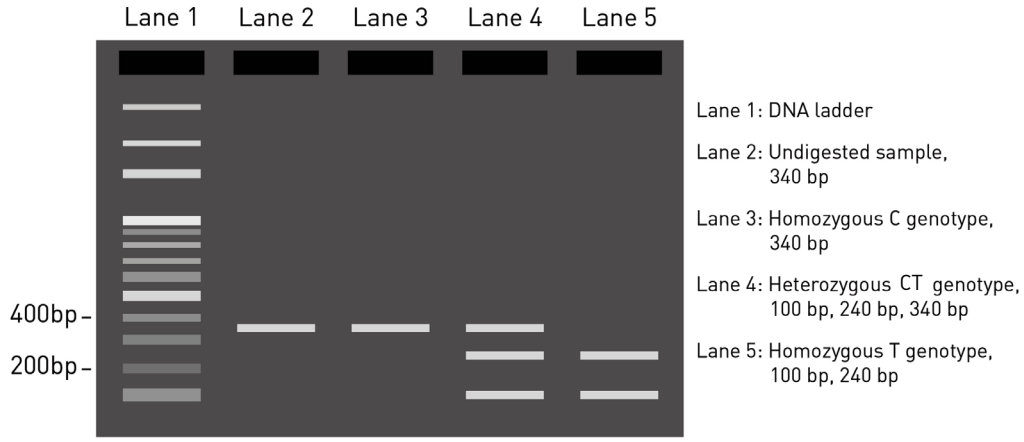


The TtGG Variant

- In this assay, you are studying a single nucleotide polymorphism (SNP) in exon 16 of the ACTN3 gene (see star). This SNP location corresponds to the 577th amino acid in the protein sequence. The nucleotide at this position is typically either a C or a T.
- The C variant results in an arginine (R) for amino acid 577, so this allele is called 577R. The T variant results in a stop codon (X) instead of an amino acid, so this allele is called R577X. The R577X allele produces a shortened protein.
- The shortened protein associated with the R577X allele is unstable and is rapidly degraded.
- The T variant of the R577X allele creates a site for the restriction enzyme DdeI to cut the DNA. Cut versus uncut DNA segments can be detected on a gel.



ACTN3 Gel



Population Genetics

- Frequencies of the R577X allele (the T variant) are high across human populations, and approximately 16% of the world's population has lower levels of ACTN3 protein due to this variant.
- These ACTN3 alleles have been associated with athletic performance.
- The 577R allele (the C variant) seems to be present at higher frequencies in sprint and strength athletes.
- The R577X allele (the T variant), which produces the shortened protein, 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 many other genetic and environmental factors playing a significant role.
- Having either of these alleles does not mean you will be an athlete. However, if you are an athlete, your ACTN3 genotype may affect what type of athlete you are.

Sources

» Online Mendelian Inheritance in Man (OMIM) *http://omim.org/entry/102574*
» National Center for Biotechnology Information (NCBI) Gene *https://www.ncbi.nlm.nih.gov/gene/89*
» NCBI Reference SNP (rs) report *https://www.ncbi.nlm.nih.gov/snp/rs1815739*
» 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)
» Human Protein Atlas
» UCSC Genome Browser