



Personal Genetics Education Project

Ethical, Legal and Social Issues in Personal Genetics

Scientific Supplement: Athletics and Genetics

This lesson explores the intersection of genetic testing and athletics, a relatable lens for many teenagers that gives students an opportunity to think critically about fundamental scientific concepts, the benefits and implications of genetic testing, as well as controversies about genetic testing in the marketplace. This supplement provides additional scientific context for the lesson and more in-depth information on the ACTN3 and APOE genes.

Major Theme: *Your DNA is not your destiny*

Nature and nurture

This is an opportunity to talk with students about the intricate relationship between our DNA (“nature”) and our environment (“nurture”). While ACTN3 is sometimes referred to as the “speed gene,” it is only one of over 200 genes that have been linked to athletic ability, not to mention the influence of numerous environmental factors, such as nutrition, practice, coaching and motivation.

The concept of risk

This is also an opportunity to talk with students about the predictive value of genetic testing and the concept of *likelihood* or *risk*. For example, the E4 version of the APOE gene has been linked to an increased chance of developing Alzheimer’s disease. While APOE is one risk factor, other genetic and environmental factors are also involved. Therefore, a genetic test for APOE is only *partially predictive*. Knowing one’s genetic information and understanding risk could be beneficial for informing lifestyle and healthcare choices as well as future planning.

Genotype does not equal phenotype

The links between ACTN3 and APOE and athletics illustrate the complex relationship between your genetic make-up (*genotype*) and your traits (*phenotype*).

Genetic variation

Any two people share over 99% of their DNA sequence. It is the small differences in our DNA that contribute to the wonderful diversity of people on our planet. A *mutation* is simply a change in DNA sequence and is not necessarily good or bad. Other terms to describe genetic variation include, *variants*, *alleles* and *polymorphisms*.

Introduction to the ACTN3 gene (*alpha-actinin-3*)

The ACTN3 gene plays a role in fast twitch muscle fibers, responsible for generating powerful muscle contractions. There are two versions of the ACTN3 gene that are commonly found in people, R and X. The R variant can produce the actinin-3 protein, while the X variant does not. The R variant of ACTN3 has been linked to sprinting ability in studies showing that elite sprinters rarely carry the X variant. ACTN3 cannot predict which individuals will become elite sprinters; it is unusual for an elite sprinter not to have the R version, but there are exceptions.

ACTN3* :	Elite sprinters	General population
R/R	>97%	~82%
R/X		
X/X	<3%	~18%

*Note: In general, people have two copies of each gene, one that they inherit from their mother and the other from their father.

Mutations are not always bad

People carrying two copies of the X variant (X/X) do not make actinin-3 protein. It is estimated that over a billion people worldwide lack the actinin-3 protein, and most probably don't even know it. While X/X individuals are less likely to be elite sprinters, the X variant has been weakly associated with endurance in some studies of elite athletes.

More in-depth...

Gene regulation

The ACTN3 gene encodes a protein that is expressed specifically in fast twitch muscle fibers. The actinin-3 protein binds to a component of the cytoskeleton, known as actin, that is involved in muscle contractions.

Nature of ACTN3 variants

The R and X variants of actinin-3 differ at a single nucleotide (known as a *single nucleotide polymorphism* or SNP). The R variant encodes the amino acid, arginine (R), at position 577 in the protein. The X variant encodes a stop codon that prematurely signals the ribosome to stop translation (also referred to as a *nonsense SNP*). As a result, individuals *homozygous* for the X variant (X/X) do not produce a functional actinin-3 protein.

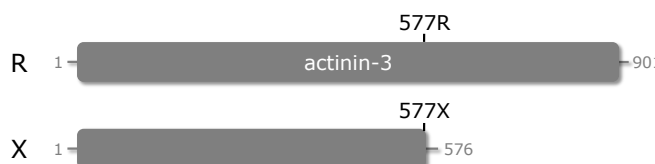


Diagram of the actinin-3 protein encoded by the R and X variants. The X variant produces a short, non-functional protein.

Introduction to the APOE gene (Apolipoprotein E)

The ApoE gene has a well-established link to Alzheimer's disease. There are three common forms of the APOE gene (E2, E3, and E4). People with one copy of the E4 version of the gene are at increased risk for developing Alzheimer's disease, and the risk is even greater for people with two copies of E4*. However, as discussed above, APOE is only one piece of the puzzle:

- While people with two copies of E4 have a significantly increased chance of developing Alzheimer's disease, some never do.
- Some people who do not carry the E4 variant still develop Alzheimer's disease.
- Genetic testing cannot guarantee who will develop the disease, at what age symptoms will start or how rapidly the disease will progress.

*Note: In general, people have two copies of each gene, one that they inherit from their mother and the other from their father.

APOE and concussions

Preliminary evidence also links E4 to increased risk of severe effects from a concussion as well as a debilitating degenerative condition known as CTE, chronic traumatic encephalopathy, which a number of professional athletes (in sports such as football, boxing, and hockey) have developed later in life. Research on the link between CTE and E4 is in its infancy, and larger studies will be needed to validate this connection.

More in-depth...

Nature of APOE variants

The E3 variant is the most common. The E2 and E4 variants each differ from E3 by a single amino acid substitution.

Some variants are protective

Genetic variants do not always increase our risk for disease; some are protective. It is thought that the E2 variant actually decreases one's risk for developing Alzheimer's disease. E3 is considered to be neutral (not associated with increased or decreased risk).

APOE influences multiple traits

The APOE gene is *pleiotropic*, meaning that it influences multiple traits: Alzheimer's disease and possibly recovery from concussions as well as cardiovascular disease.

Resources

Sports and genetics

David Epstein's "[The Sports Gene: Inside the Science of Extraordinary Athletic Performance.](#)"

NPR interview with David Epstein, "[Talent or Skill? Homing in on the elusive "sports gene."](#)"

ACTN3

MacArthur, D. 2008. The ACTN3 sports gene test: what can it really tell you? *Wired*.

<http://www.wired.com/wiredscience/2008/11/the-actn3-sports-gene-test-what-can-it-really-tell-you/>

Macur, J. 2008. Born to Run? Little Ones Get Test for Sports Gene. *The New York Times*.

<http://www.nytimes.com/2008/11/30/sports/30genetics.html?pagewanted=all&r=0>

Yang, N., MacArthur, D.G., Gulbin, J.P., Hahn, A.G., Beggs, A.H., Easteal, S., and North, K. 2003. ACTN3 Genotype Is Associated with Human Elite Athletic Performance. *The American Journal of Human Genetics*, 73(3): 627–631.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180686/?tool=pubmed>

APOE

Alzheimer's Association. "Alzheimer's Disease: Risk Factors."

http://www.alz.org/alzheimers_disease_causes_risk_factors.asp#genetics

Mayo Clinic. "Alzheimer's genes: Are you at risk?"

<http://www.mayoclinic.com/health/alzheimers-genes/AZ00047>

National Institutes of Health. "Alzheimer's Disease Genetics Fact Sheet."

<http://www.nia.nih.gov/alzheimers/publication/alzheimers-disease-genetics-fact-sheet>

U.S. National Library of Medicine. "APOE."

<http://ghr.nlm.nih.gov/gene/APOE>