

September 19, 2018
Juntendo University Corporate Communications

Juntendo University research: The genetics of muscle injuries

(Tokyo, 19 September) To test whether sex-related genetic polymorphisms are associated with muscle injury and stiffness, Noriyuki Fuku from Juntendo University and colleagues report in the journal *Medicine & Science in Sports & Exercise* that ESR1 rs2234693 polymorphism is associated with both muscle injury and muscle stiffness. These findings suggest a role of estrogen in lowering muscle stiffness by suppressing collagen synthesis, as well as having anti-inflammatory and anti-oxidant effects.

Preventing injuries in sport is important, and the determination of risk factors, both genetic and environmental, is instrumental to this end. Muscle injury, and in particular hamstring strain, is the most common sports injury, and muscle stiffness is one of the risk factors associated with it.

Because muscle stiffness is more common in men than in women, it is likely that it is determined not only by environmental factors, but also by a sex-related genetic polymorphism, that is, by a variation in a specific gene. The difference in the likeliness of muscle injury in men and women might be related to the presence of sex-related hormones and their receptors, the molecules that bind to them. In particular, there is evidence that estrogen, a female sex hormone, influence muscle stiffness. Therefore, the gene that encodes estrogen target receptors, the estrogen receptor- α gene (ESR1) has two functional polymorphisms (called rs2234693 and rs9340799), which might influence muscle injury due to muscle stiffness.



To test whether these polymorphisms are associated with muscle injury and stiffness, Noriyuki Fuku from Juntendo University and colleagues run two studies, one on top-level athletes and the other on physically active young people, identifying one polymorphism that has a role in determining the likeliness of injury. The findings are published in the journal *Medicine & Science in Sports & Exercise*. The researchers evaluated, using questionnaires, the muscle injury history of over 1,300 Japanese top-level athletes (many more than in previous studies). They then measured the stiffness of the hamstring muscles of 261 physically active young adults using ultrasounds. For all participants, the polymorphisms under study were analyzed using DNA from samples of saliva.

For the top-level athletes, age, weight and height were roughly the same for athletes who did and did not sustain a muscle injury. In terms of genotype, the polymorphism of rs2234693 was found to be significantly associated with the likeliness of injuries, unlike the polymorphism of rs9340799, which did not show any specific association. For the part of the study involving normally active young people, significant sex-related differences in the stiffness of the hamstring muscle were observed, and also in this case this was associated with the polymorphism of rs2234693. People with the C allele had lower stiffness of the hamstring muscle than people with the T allele. For rs9340799 polymorphism, A/G genotypes showed no influence.

The general conclusion is that ESR1 rs2234693 polymorphism is associated with both muscle injury and muscle stiffness. In particular, the C allele is associated with protection against muscle injury and lower muscle stiffness, whereas the T allele is not. The C allele is associated with higher estrogen action, thus these findings seem to point towards a role of estrogen in lowering muscle stiffness by suppressing collagen synthesis, on top of having anti-inflammatory and anti-oxidant effects. The next step will be to investigate muscle stiffness while muscles are contracting rather than resting, the condition under which injury normally happens.

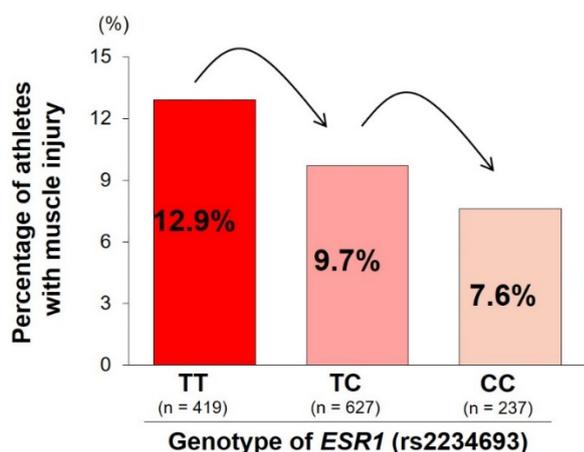


Figure 1. Relationship between genetic polymorphism in the ESR1 T/C (rs2234693) and history of muscle injury

Risk for muscle injury is reduced with one C allele by approximately 30%.
C-allele additive model: OR = 0.70, 95%CI = 0.53-0.92, P = 0.008.

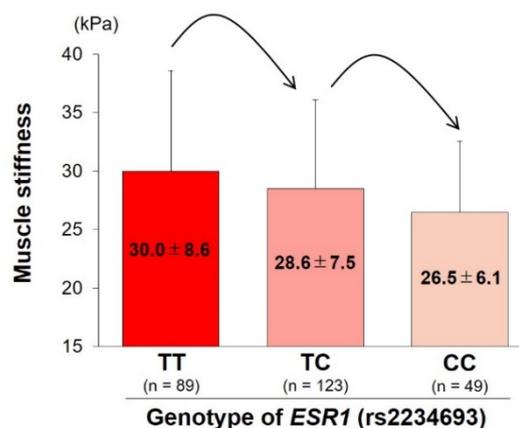


Figure 2. Relationship between genetic polymorphism in the ESR1 T/C (rs2234693) and muscle stiffness

Muscle stiffness is reduced with one C allele.
Correlation: $r = -0.135$, $P = 0.029$.

Background

Genetic polymorphism and genotype

Genetic polymorphism occurs when different people have different forms of the same gene, which are called alleles. Humans have two alleles at each genetic position, one inherited from each parent. Most polymorphisms do not affect the function of the gene, but some do. The polymorphisms under study in this paper are single nucleotide polymorphism, that is, a single nucleotide is changed (the nucleotides in DNA are adenine (A), cytosine (C), guanine (G) and thymine (T)).

The genotype is the combination of alleles carried by an individual that determines the expression of a particular trait (which is called the phenotype); genotypes are indicated with a series of letters that indicate the different alleles.

Reference

Hiroshi Kumagai, Eri Miyamoto-Mikami, Kosuke Hirata, Naoki Kikuchi, Nobuhiro Kamiya, Seigo Hoshikawa, Hirofumi Zempo, Hisashi Naito, Naokazu Miyamoto, Noriyuki Fuku, ESR1 rs2234693 polymorphism is associated with muscle injury and muscle stiffness. *Medicine & Science in Sports & Exercise*
doi: 10.1249/MSS.0000000000001750 (2018)

Further information

Juntendo University : Ayano Nagashima

Juntendo University Corporate Communications

2-1-1, Hongo, Bunkyo-ku, Tokyo 113-8421 JAPAN

E-mail: release@juntendo.ac.jp

Website: <https://www.juntendo.ac.jp/english/>

Research: <https://www.juntendo.ac.jp/english/research.html>

Further information about Juntendo University

Mission Statement

The mission of Juntendo University is to strive for advances in society through education, research, and healthcare, guided by the motto "Jin – I exist as you exist" and the principle of "Fudan Zenshin - Continuously Moving Forward". The spirit of "Jin", which is the ideal of all those who gather at Juntendo University, entails being kind and considerate of others. The principle of "Fudan Zenshin" conveys the belief of the founders that education and research activities will only flourish in an environment of free competition. Our academic environment enables us to educate outstanding students to become healthcare professionals patients can believe in, scientists capable of innovative discoveries and inventions, and global citizens ready to serve society.

About Juntendo

Juntendo was originally founded in 1838 as a Dutch School of Medicine at a time when Western medical education was not yet embedded as a normal part of Japanese society. With the creation of Juntendo, the founders hoped to create a place where people could come together with the shared goal of helping society through the powers of medical education and practices. Their aspirations led to the establishment of Juntendo Hospital, the first private hospital in Japan. Through the years the institution's experience and perspective as an institution of higher education and a place of clinical practice has enabled Juntendo University to play an integral role in the shaping of Japanese medical education and practices. Along the way the focus of the institution has also expanded, now consisting of four undergraduate programs and three graduate programs, the university specializes in the fields of health and sports science and nursing health care and sciences, as well as medicine. Today, Juntendo University continues to pursue innovative approaches to international level education and research with the goal of applying the results to society.