## how do muscles grow?

Charge, S.B.P., & Rudnicki, M.A. 2004. Cellular and molecular regulation of muscle regeneration. Physiological Reviews, 84, 209–38.

Fitness professionals spend countless hours reading articles and research on new training programs and exercise ideas for developing muscular fitness. However, largely because of the topic's physiological complexity, few personal trainers or instructors are thoroughly informed about how muscles actually adapt to, and grow to meet, the progressively increasing overload demands of exercise. In fact, skeletal muscle is the most adaptable tissue in the human body. Already a widely studied topic, muscle hypertrophy is still considered a fertile research area. This column will provide a brief update on some of the intriguing cellular changes that lead to muscle growth, also known as the satellite cell theory of hypertrophy.

#### Muscle Trauma: Activating Satellite Cells

When muscles undergo intense exercise, as from a resistance training bout, the muscle fibers undergo trauma that is referred to scientifically as "muscle injury" or "muscle damage." This disruption of the fibers also causes damage to the muscle cell proteins within the muscle fibers, thus activating satellite cells. These cells, located on the outside of the muscle fibers between the *basal lamina* (basement membrane) and the *plasma membrane* (sarcolemma) of muscle fibers, proliferate to the injury site (Charge & Rudnicki 2004). In essence, a biological effort to repair or replace dam-

aged muscle fibers begins with the satellite cells fusing together and to the muscle fibers, often leading to increases in muscle fiber cross-sectional area or hypertrophy. The satellite cells have only one nucleus and can replicate by dividing. As the satellite cells multiply, some remain as organelles on the muscle fiber, whereas the majority differentiate (the process that cells undergo as they mature into normal cells) and fuse to muscle fibers to form new muscle protein strands (or myofibrils) and/or to repair damaged fibers. Thus, the muscle cells' myofibrils increase in thickness and number. See Figure 1.

After fusing with muscle fibers, some satellite cells serve as a source of new nuclei to supplement the growing fibers. With these additional nuclei, muscle fibers can synthesize more proteins and create more contractile **myofilaments**, known as **actin** and **myosin**, in skeletal muscle cells. Higher numbers of satellite cells are found in slow-twitch muscle fibers than in fasttwitch muscle fibers within the same muscle, because the slow-twitch fibers are regularly going through cell maintenance repair from daily activities.

#### **Growth Factors**

Growth factors are hormones or hormone-like compounds that stimulate satellite cells to produce gains in muscle fiber size. These growth factors have been shown to affect muscle growth by regulating satellite cell activity.

**Hepatocyte growth factor** (HGF) is a key regulator of satellite cell activity. It has been shown to be the active factor in repairing muscle damage and may also be responsible for directing satellite cells to migrate to the damaged muscle area (Charge & Rudnicki 2004).

**Fibroblast growth factor** (FGF) is another important growth factor in repairing muscle following exercise. The role of FGF may be in the revascularization process (formation of new blood capillaries) during muscle regeneration (Charge & Rudnicki 2004).

A great deal of research has been focused on the role of **insulin-like growth factors-I and -II** (IGFs) in muscle growth. The IGFs play a primary role in regulating the amount of muscle mass growth, promoting changes occurring in the DNA for protein synthesis and promoting muscle cell repair. Insulin also stimulates muscle growth by enhancing protein synthesis and facilitating the entry of glucose into cells. The satellite cells use glucose as a fuel substrate, thus enabling their cell growth activities. Glucose is used for intramuscular energy needs as well.

Growth hormone is also highly recognized for its role in muscle growth. Resistance exercise stimulates the release of growth hormone from the anterior pituitary gland, with released levels being very dependent on exercise intensity. Growth hormone helps trigger fat metabolism for energy use in the muscle growth process. In addition, growth hormone stimulates the uptake and incorporation of amino acids into protein in skeletal muscle.

**Testosterone** also affects muscle hypertrophy. This hormone can stimulate growth hormone responses in the pituitary, thereby enhancing cellular amino acid uptake and protein synthesis in skeletal muscle. Testosterone can increase the presence of neurotransmitters at the fiber site, which can help activate tissue growth. As a steroid hormone, testosterone can interact with nuclear receptors on the DNA, resulting in protein synthesis. Testosterone may also have some type of regulatory effect on satellite cells.

#### Muscle Growth: The "Bigger" Picture

This discussion clearly shows that muscle growth is a complex molecular biology cell process involving the interplay of numerous cellular organelles and growth factors, occurring as a result of resistance exercise. However, for client education some important applications need to be summarized:

# figure 1: structure of skeletal muscle and satellite cell activation



Figure 1 shows the structural layers of muscle to muscle fibers. Satellite cells on the outside of the muscle fibers proliferate to the "trauma" site from an overload training stimulus, leading to repair and replacement of damaged muscle fibers.

- Muscle growth occurs whenever the rate ٠ of muscle protein synthesis is greater than the rate of muscle protein breakdown.
- Both the synthesis and the breakdown of proteins are controlled by complementary cellular mechanisms.
- Resistance exercise can profoundly stimulate muscle cell hypertrophy and the resultant gain in strength. However, the development for this hypertrophy is relatively slow, generally taking several weeks or months to be apparent (Rasmussen & Phillips 2003). Interestingly, a single bout of exercise stimulates protein synthesis within 2-4 hours after the workout, and the rate of synthesis may remain elevated for up to 24 hours (Rasmussen & Phillips 2003).

Highlighting some specific factors that influence these adaptations will be helpful to your clients:

All studies show that men and women respond to a resistance training stimulus very similarly. However, owing to gender differences in body size, body composition and hormone levels, gender will have a varying effect on the extent of hypertrophy one may possibly attain. Although the upper limit of muscle growth is truly unknown, most resistance training studies report increases in cross-sectional muscle area of 30%-70% (Gardiner 2001).

Aging also mediates cellular changes in muscle, decreasing the actual muscle mass. This loss of muscle mass is referred to as sarcopenia. Happily, the detrimental effects of aging on muscle have been shown to be restrained or even reversed with regular resistance exercise. What's more, resistance exercise also improves the connective tissue harness surrounding muscle, thus being most beneficial for injury prevention and in physical rehabilitation therapy.

Heredity differentiates the percentage and amount of the two markedly different fiber types. In humans the cardiovascular-type fibers have at different times been called red, tonic, type I, slow-twitch or slow-oxidative fibers. By contrast, the anaerobic-type fibers have been called white, phasic, type II, fast-twitch or fastglycolytic fibers. Further subdivisions of type II fibers are the IIa (fast-oxidativeglycolytic) and IIb (fast-glycolytic) fibers. It is noteworthy that the soleus, a muscle involved in standing posture and gait, generally contains 25%-40% more type I fibers, while the triceps has 10%–30% more type II fibers than the other arm muscles (Foss & Ketevian 1998).

The proportions and types of muscle fibers vary greatly between adults. It is suggested that the new, popular periodization models of exercise training, which include light, moderate and high-intensity training phases, satisfactorily overload the different muscle fiber types of the body while also providing sufficient rest for protein synthesis to occur.

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cise and Sport Sciences Reviews, 31 (3), 127-31.

### muscle hypertrophy summary

- Resistance training leads to trauma or injury of the cellular proteins in muscle. This prompts cell-signaling messages to activate satellite cells to begin a cascade of events leading to muscle repair and growth.
- Several growth factors are involved that regulate the mechanisms of change in protein number and size within the muscle.
- The adaptation of muscle to the overload stress of resistance exercise begins immediately after each exercise bout, but the effect often takes weeks or months to physically manifest itself.
- The most adaptable tissue in the human body is skeletal muscle, and it is remarkably remodeled after continuous and carefully designed resistance exercise training programs.