MECHANISMS OF MUSCLE HYPERTROPHY IN RESPONSE TO OVERLOAD

Harridge Stephen
(King's College London, United Kingdom)

Muscle is a highly plastic tissue being able to alter its size, composition and metabolic profile in response to the different challenges it may face. Overloading a muscle through high resistance strength training is known to increase muscle size. Two basic requirements are necessary for a muscle to hypertrophy. Firstly, there must be a net gain in protein. This is achieved by exercise and nutritionally mediated increases in protein synthesis. The second is that there must be an increase in the number of muscle nuclei in order to maintain the myonuclear domain. This is achieved through the donation of nuclei from activated satellite cells, the muscle's stem cells. Evidence suggests that the myonuclear domain is approximately 2000 µm². In other words, this is the maximum area that an individual nuclei can manage. For a fibre to enlarge new nuclei (managers) must be added to oversee the enlarged fibre, maintaining the protein to DNA ratio.

How does a muscle increase its rate of protein synthesis and add these new nuclei? The cues for these processes are provided by the action of systemic (such as testosterone) and local factors (such as IGF-I) which respond to the overload stimuli provided by resistance training. IGF-I is primarily produce in the liver under the control of growth hormone, but studies on hypophysectomised rats have shown that muscle hypertrophy can still occurs in response to overload even in the absence of circulating GH and IGF-I. This is because IGF-I is produced locally in muscle in response to overload and to damage for both autocrine and paracrine actions. IGF-I is a unique growth / repair factor, in that it stimulates both the proliferation and differentiation of satellite cells. Studies of muscle cells in culture have shown that IGF-I is a potent stimulator of protein synthesis. IGF-I works through activation of the mTOR / AKT (PKB) signalling pathway. IGF-I is also interesting in that alternative splicing of the IGF-I gene results in different E-peptides which may have different physiological roles in the repair / adaptation process. The MGF splice variant has been suggested to kick-start satellite cells activation by promoting satellite cell proliferation, whilst IGF-IeA, which is more highly expressed, and contributes more to maintaining higher rates of muscle protein synthesis.

Like many physiological processes, the regulation of muscle hypertrophy is not the product of a single factor, but a numerous factors working in concert with one another. For example, whilst testosterone and IGF-I are positive regulators of muscle mass and are upregulated by high-resistance exercise, growth differentiation factor 8 (myostatin) is a negative regulator. Its mutation in the Belgian Blue breed of cattle results in a highly hypertrophied phenotype and this factor is down regulated with strength training exercise.

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