Mechano Growth Factor (MGF): The Most Powerful Anabolic Growth Factor Ever?

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The transformation serum is a real-life occurrence that takes place for all bodybuilders who want to make it to the top. They use their bodies as their laboratories, trying the newest substances medical science has to offer to create the perfect monster…bigger and stronger. This is the quest for every bodybuilder on the planet— to find the magic ingredient that transforms them into a heavily muscled monster! Well, a new substance called Mechano Growth Factor (MGF) may be just the thing in the near future to make testosterone the next-best choice in anabolics.

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IGF-1 Increases Muscle Hypertrophy Through Satellite Cell Activation

Insulin-like growth factor (IGF-1) is produced by the liver and induced by growth hormone. IGF-1 is a main regulator of muscle tissue mass and is known to play an important role in the muscle hypertrophy adaptations to muscle overload. Over the years, researchers have discovered that IGF-1 isn’t only produced in the liver, but is produced directly within muscle.

Previous research indicates that IGF-1 is involved in the maintenance of skeletal muscle tissue and also in the prevention of cell death and is an important regulator of protein synthesis.1,2 IGF-1 has a critical role in the activation of satellite cells or muscle stem cells that are required for local tissue repair after exercise. Satellite cells normally just lay around

muscle fibers quietly until they become activated and fuse with muscle fibers. Muscle-fiber damage induced by heavy resistance exercise seems to have potent effects on activating satellite cells, in that satellite cells become activated and fuse with the damaged muscle fibers, causing muscle hypertrophy.4

It's also interesting to note that with aging, there’s a loss of skeletal muscle mass and regenerative capacity. The reduced capacity to regenerate older muscle seems to be due to the decreased ability to activate satellite cells.5 Satellite cells are so important for muscle repair and growth that if you destroy satellite cells through gamma irradiation, you can overload muscle and no growth occurs.3 Muscle gene expression of IGF-1 increases dramatically after muscle overload, even if there’s no GH being produced, as patients with GH deficiency can still increase IGF-1 levels in muscle after muscle overload.18

Two Forms of IGF-1: Muscle-liver & Mechano Growth Factor

Two forms of IGF-1 have been discovered that have different mechanisms of action. The first form, IGF-1Ea, has a similar structure to the major form produced in the liver. It’s been termed the muscle-liver type IGF-1 as it’s produced not only in the liver, but in muscle as well. The other form of IGF-1 has been termed IGF-1Ec, also known as Mechano Growth Factor (MGF), as it’s only markedly upregulated in response to exercise and/or muscle damage. Both MGF and muscle-liver type IGF-1 are increased in muscle in response to muscle loading, but have different biological effects. In vitro (test tube) studies have shown that when MGF is added to muscle satellite cells, the cells rapidly increase in number, but they don’t become mature muscle stem cells until muscle-liver IGF-1 is added to the test tube. When muscle-liver IGF-1 is added, it causes an increase in cell density and satellite cells fuse with muscle fibers.17 MGF’s main role is to initiate satellite cell activation to kick-start the muscle growth process, while muscle-liver type IGF-1 promotes differentiation of immature satellite cells into mature muscle fibers.7 MGF is expressed before muscle-liver type IGF-1 in muscle, which suggests that they work independently of each other.

Recent research has shown that MGF is expressed in muscle soon after damage, which occurs at the same time satellite cells become activated. MGF is considered the “growth pulse” that activates the initial spark to activate satellite cells, but it lasts just a few days. Later, several days after the initial muscle damage, MGF levels begin to decline while muscle-liver type IGF-1 levels start to rise in muscle (research suggests 7-11 days later). It’s thought that the MGF gene is expressed first, then is spliced toward the muscle-liver type IGF-1, which is more abundant in muscle and therefore, the major supplier of mature IGF-1, which upregulates protein synthesis.8

GH has been shown to produce large increases in serum IGF-1 from the liver, yet muscle hypertrophy from GH alone is controversial and modest at best, but the serum levels of IGF-1 in the blood are a fraction of the muscle-produced IGF-1 levels.10 When GH was administered to elderly men, there were large increases in liver-muscle specific IGF-1, with only small increases in MGF.10 This could be the reason GH has such a poor effect on increasing muscle hypertrophy, as a more specific drug that increases MGF is needed.

Testosterone is a potent stimulator of muscle hypertrophy, as there’s a dose-dependent increase in muscle fiber hypertrophy and satellite cell number. Testosterone-induced skeletal muscle hypertrophy is associated with increased satellite cell replication and activation.19 The big question that needs to be researched is, “Does testosterone increase MGF”? So, what happens when you compare MGF and muscle-liver type IGF-1 head-to-head? Although both have anabolic effects in muscle, muscle-liver type IGF-1 takes months to develop muscle hypertrophy, while MGF makes the same increase in muscle mass in a few weeks.

A 35 Percent Increase in Muscle Mass in Three Weeks!!

The study that should turn the heads of all bodybuilders was a head-to-head comparison of the two titans of anabolic growth: MGF versus muscle-liver type IGF-1. LET’S GET READY TO RUMBLE!!!!!!!!!! MGF was inserted into rat leg muscles by intramuscular injection. This resulted in a 35 percent increase in the weight of the injected muscle within three weeks, and the analyses showed that this was due to an increase in the size of the muscle fibers.12 Additionally, there was a increase in muscle strength of 25 percent.

Similar experiments by other groups have also been carried out using a viral construct containing the liver-muscle type of IGF-1, which resulted in a 15 percent increase in muscle mass, but this took over four months to develop.11 Hence, the dual role MGF plays in inducing satellite cell activation as well as protein synthesis suggests it’s much more potent than the muscle-liver type or IGF-IEa for inducing rapid hypertrophy.

Eccentric Contractions Stimulate MGF Greater than Concentric Contractions

MGF is stimulated by muscle damage. When a muscle is placed on stretch or for even greater effect, stretch combined with muscle contraction, it leads to a rapid increase in MGF.6 I know I’m beginning to sound like a broken record, stressing the need for bodybuilders to emphasize eccentric contractions in their training, but a new study suggests that eccentric contractions have far superior growth potential than concentric or isometric contractions. In a recent issue of the Journal of Applied Physiology, researchers reported that not only will performing eccentric contractions reduce myostatin expression (myostatin suppresses muscle growth), but heavy eccentric contractions also increase both muscle-liver type IGF-1 and MGF to a greater extent than concentric contractions.9 The researchers concluded that eccentric training appears to have the greatest potential for inducing muscle hypertrophy than any other training type.

MGF— The Key to Reversing Muscle Loss?

Older men can increase muscle mass, but it takes a whole hell of a lot longer than a teenager! Well, MGF might be the answer why. The resting levels of MGF in muscle are 100-fold lower than muscle-liver mediated IGF-1.7 Interestingly, resting levels of MGF aren’t different between young and older men at rest, but MGF isn’t increased in aging muscle after resistance exercise compared to young men. For example, young and elderly men performed 10 repetitions of leg extensions in which muscle biopsies were taken immediately post-exercise and examined for MGF gene responses. In young subjects, MGF mRNA levels were significantly increased in response to resistance exercise, but there was no significant change in older subjects. Furthermore, the muscle-liver type IGF-1 was unchanged in both groups.7

There was a huge variation in the response among subjects— some young subjects increased MGF levels by as much as 864 percent after resistance exercise. In another study comparing MGF responses in older and younger men, 20 young men (20-35) and 18 older men (60-75) performed 3 sets x 8-12 repetitions to volitional fatigue of squats, leg presses and knee extensions. MGF increased by 49 percent in the young group of men, however, MGF didn’t increase at all in the older men.16 These human studies are in agreement with animal studies showing that older rats have a blunted MGF response to mechanical damage of muscle. For example, Owino, Yang and Goldspink studied the ability of muscle to express MGF as well as muscle-liver type IGF-1 at different ages of rats (young, middle-aged and old) in response to muscle overload. In young rats, when muscle was overloaded, MGF was rapidly increased in muscle. In middle-aged rats, the increase in MGF was moderate and in old rats, the MGF response was very low and attenuated.14 The young rats increased MGF levels by about 1,000 percent after five days of muscle overload, as opposed to older rats who had only an approximate 250 percent increase. These studies suggest that MGF is needed to initiate the hypertrophy response of muscle by activating satellite cells. But as we age, muscle MGF responses are blunted.

GH is responsible for increasing IGF-1 in the liver, but the effects of GH on muscle hypertrophy have been controversial. Peripheral levels of IGF-1 may not be as important for muscle growth as growth factors produced in muscle as MGF. For example, mice that have been genetically engineered to not produce liver-mediated IGF-1 have normal bodyweights and muscle mass, despite low plasma levels of IGF-1.15 The study demonstrates the importance of locally produced IGF-1 in muscle— including MGF— for muscle growth and tissue maintenance.

Most of the studies so far have been investigating the role of MGF as a treatment for muscle loss with aging. A recent study by Hammeed, et. al.,10 reported that GH administration can increase MGF levels. In that study, elderly men were assigned to three groups: 1) GH administration alone; 2) 12 weeks of resistance exercise alone, and 3) resistance exercise plus GH administration. After 12 weeks, GH alone caused MGF mRNA to be increased by 80 percent compared to baseline. Twelve weeks of resistance training alone significantly increased the mRNA expression of MGF by 163 percent and muscle-liver IGF-1 by 68 percent. However, after 12 weeks of training combined with GH treatment, MGF mRNA increased by 456 percent and muscle-liver IGF-I-E by 167 percent. The results of the study concluded that GH administration alone to elderly men increases mainly muscle-liver IGF-1 levels in muscle by 238 percent in elderly men, with small increases in MGF. The muscle-liver IGF-1 levels were found to be two- to three-fold higher than that of MGF after GH administration.

Interestingly, the group that received GH combined with resistance exercise had larger increases in MGF compared to the group receiving GH or resistance exercise alone. The results seem to indicate that GH results in the upregulation of the IGF-1 gene in muscle. When GH is combined with resistance exercise, there’s a greater increase in MGF gene expression. When the researchers examined muscle hypertrophy, there was only a correlation between the changes in muscle MGF and muscle size, while there was no correlation between muscle-liver IGF-1 and muscle size. It could be that greater changes in MGF need to occur for older men to achieve substantial increases in muscle hypertrophy.

What Happens IF MGF is Injected?

It was interesting that when researchers compared resting levels of MGF in young and older men, there was no difference at rest. However, MGF expresses much more MGF after a single bout of resistance exercise, which may be the reason younger men make larger gains in muscle mass than older men after an identical training regimen. The resting levels of MGF are 100-fold lower than muscle-liver mediated IGF-1.7 MGF is only expressed in response to muscle damage, but if a bodybuilder were to inject MGF…well, let’s just say there would probably be some kick-ass muscle growth, as MGF not only activates satellite cells, but also upregulates protein synthesis in muscle.

One study showed that the basal levels of MGF in muscle were directly related to muscle cross-sectional area (how big your muscles are).10 A leading pioneer in MGF research, Dr. Goldspink, noted that although his research has much more to learn about MGF, gene therapy has advantages over injecting the MGF peptide, as the peptide version would have to be administered more often.13 Dr. Goldspink has recommended that MGF, rather than the liver-muscle form of IGF-1, be used as a generic therapeutic agent for muscle wasting. Another big advantage that MGF has is that once injected into a muscle, it has direct anabolic actions that are site specific, without the worry of affecting other organs such as the prostate (as testosterone does). More human research needs to be conducted with MGF injections as only animal studies have been conducted, but the animal studies are impressive so far.

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