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## **Abstract**

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### **“Molecular Regulation of Muscle Hypertrophy and Gene Doping”**

The aim of our present study is to detect the misuse of growth factors for enhancement of muscle function administered in different ways, including gene transfer. The growth hormone/IGF-I axis has been regarded as an important main regulator of tissue growth in general. However, locally produced forms of insulin-like growth factor (IGF-I) are important and it is now appreciated that they occur in different forms with different functions. We cloned two main forms of IGF-Is that are expressed by human skeletal muscle and both are derived from the IGF-I gene by alternative splicing.

One of these is expressed in response to physical activity which has now been called “mechano growth factor” (MGF). The other is similar to the systemic or liver type (IGF-IEa) and is important as the provider of mature IGF-I required for up regulating protein synthesis. MGF differs from systemic IGF-IEa in that it has a different peptide sequence which is responsible for activating muscle satellite (stem) cells. Therefore, it appears these two forms of IGF-I have different actions and that they are important regulators of muscle growth. Growth hormone treatment apparently up regulates the level of IGF-I gene expression and when it is combined with resistance exercise more is spliced towards MGF. As the manipulation of muscle mass is so effective, there are now new challenges in relation to misuse of these procedures in athletics and professional sports.

The misuse of MGF represents a parallel challenge to its development for the treatment of a range of medical conditions in which muscle loss is a problem. As growth hormone and IGF-I are already used for doping it is very likely that MGF, which is much more potent, will be misused when it becomes more generally available. In collaboration with the HFL at Newmarket and the Department of Chemistry at Nottingham Trent University, UK, a mass spectrometer methods are being developed to detect signalling molecule patterns that can be used to rapid screen for the use of exogenous substances. Also the London group are developing confirmatory tests to distinguish between the growth factors using specific antibodies. This involves measuring the expression of specific genes when serum from athletes that screen positive, are added to cells in culture. The detection of gene doping per se involves the use of blood white cells using qRT-PCR with specific primers.

Key Words: Misuse of Muscle Growth Factors