

## Project Review

### **“The use of blood mRNA technology to detect abuse with GH and IGF-I in sport”**

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Growth hormone (GH) is a naturally occurring hormone produced by the pituitary gland. It has strong anabolic properties regulating body composition and is widely accepted as being a major drug of abuse in sport. The majority of GH's anabolic actions are mediated through the generation of insulin-like growth factor-I. There are reports that IGF-I is also being abused by athletes either alone or in combination with GH. The use of both drugs is banned under the World Anti Doping Agency (WADA) list of prohibited substances.

The detection of exogenously administered GH and IGF-I poses a formidable challenge, as they are identical to the hormones that are produced naturally in the body. While androgenic anabolic steroids and related substances can be measured by mass spectrometry, no such methods have been developed for testing for misuse with GH and IGF-I.

The GH-2000 and GH-2004 teams have developed a test for the detection of abuse with GH based on two GH-dependent markers, IGF-I and P-III-P. At present these proteins are measured by immunoassay.

A new technology to measure blood messenger RNA (mRNA) has been developed which could have significant potential in the fight against doping. Preliminary evidence has shown that patients with acromegaly (growth hormone excess) and GH deficiency have altered levels of messenger RNA (mRNA) for GH and GH releasing hormone in the blood and therefore blood mRNA levels are potential markers of GH and IGF-I abuse. Unlike our previous studies, blood mRNA is measured by a different technique known as reverse transcriptase – polymerase chain reaction (RT-PCR).

Although the aim of this pilot study will be to evaluate whether the measurement of mRNA in blood can be used to detect GH, this new technology could also be used in the fight against doping with other protein hormones.

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### **Results and Conclusion**

This study confirmed the presence of GH and GHRH mRNA in the circulation and is the first study to demonstrate the presence of small but quantifiable concentrations of circulating IGF1 and IGFBP3 mRNA. We have assessed the intraindividual variability of mRNA concentrations for GH, IGF1 and IGFBP3 and have shown that this variability is high. There were no significant changes in circulating mRNA for GH, IGF1 or IGFBP3 in response to rhGH administration for 4 days in 10 recreational athletes or in response to rhIGF1/rhIGFBP3 administration for 28 days in 30 recreational athletes. There is a weak correlation between circulating mRNA concentrations for GH, IGF1 and IGFBP3 and IGF1 peptide concentrations.

The high intraindividual variability of these mRNA species limits their utility as a marker of GH and IGF1 misuse. The administration of rhGH and rhIGF1/rhIGFBP3 to recreational athletes does not result in significant changes in these mRNA concentrations and therefore it is unlikely that at present mRNA technology will prove a useful method for detecting GH or IGF1 misuse.