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Abstract

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“Surrogate Markers For Transgene Expression – Global Gene Expression Analysis”

Conventional strategies to test for abuse of drugs have relied on being able to detect the presence of the agent in a blood or urine sample. However, gene therapy drugs have given the would-be abusers the opportunity to administer the genes directly, making it almost impossible to develop assays that can detect the products of such genes. One way to address this problem is to measure the universe of effects that the therapeutic gene has at the proteome or transcriptome level rather than searching for the presence of the gene or gene product. In this way, the abuse of a gene therapy drug could be detected by the tell-tale fingerprint of surrogate markers that it leaves behind.

Research is underway to evaluate different approaches and methodologies to the detection of gene doping. Growth hormone (GH) is a drug that could be abused for performance enhancement in sport. Therefore, initial research is focussed on the Insulin-like Growth Factor (IGF-1) / Growth hormone (GH) axis, selected due to the availability of samples from a rodent model and on-going GH work in the human. In addition, there is a high probability that surrogate markers of IGF-1 / GH will also be effective for detection of the abuse of alternative agents such as anabolic steroids.

The challenge is to distinguish between samples collected from treated and untreated subjects. The first approach is to utilise mass spectrometry with advanced pattern recognition algorithms such as Artificial Neural Networks (ANNs) for the rapid detection of protein marker patterns in serum. The system will be “trained” to identify samples with an unusual profile, possibly indicative of a drug administration or gene doping. The second approach is to use transcriptomic and proteomic methods to detect and compare the expressed mRNA or proteins in the control subjects and those under treatment. Once surrogate markers have been identified and characterised, detection systems, capable of simultaneously monitoring markers indicative of an individual affected by a gene therapy agent, will be developed. The ability to apply these technologies at the point of sample collection, whether at a sporting event or out-of-competition is considered a desirable and potentially achievable aim.