

PROJECT REVIEW

“Application of a minimally-invasive method for mRNA sampling and addition of miRNA to the detection of r-HuEpo use by athletes”

Y. Pitsiladis, P. Herzuk (University of Glasgow, UK)

An ongoing research project funded by the World Anti Doping Agency (WADA) in 2008 entitled “A Gene Microarray Based approach to the Detection of recombinant Human Erythropoietin Doping in Endurance Athletes” was designed to formulate new methods with improved discriminatory power relative to current available detection protocols and in doing so eliminate the possibility of false-positives due to athletes living and/or training at altitude and false-negatives due to inadequate detection. The ongoing funded project, albeit of great scientific and diagnostic potential given recent data, focuses solely on mRNA as mRNA transcribed from DNA is translated into protein.

However, current opinion would suggest that micro RNA (miRNA), a class of recently discovered small RNA molecules, play a major role in post-transcriptional regulation, thought to regulate approximately 30% of all human protein coding genes. Therefore, it would be prudent for the purposes of the ongoing research project funded by WADA to assess the miRNA target interactions that correlate with effects on target mRNA levels in order to provide the necessary insight into the interaction between mRNA and miRNA and consequently the impact of gene expression on protein synthesis. This elaborate study provides a unique opportunity to gather all the data necessary to develop a robust diagnostic test in the shortest timescale possible. The additional funds requested will also allow the piloting of a simple, minimally invasive, safe and cost effective method of sampling, storing and extracting RNA from saliva.

“Application of a minimally-invasive method for mRNA sampling and addition of miRNA to the detection of r-HuEpo use by athletes”

Y. Pitsiladis, P. Herzuk (University of Glasgow, UK)

Result and Conclusions

Recombinant human erythropoietin (rHuEPO) improves performance and is frequently subject to abuse by athletes. The use of rHuEPO is prohibited by the World Anti-Doping Agency. To improve the sensitivity of current detection methods, new “omics”-based methods such as gene expression have generated promising results using whole blood (08C19YP). Current research focused on saliva gene expression and on blood-derived microRNAs (key post-transcriptional regulators of gene expression). 9 genes were commonly expressed in saliva after 2 weeks of rHuEPO administration, at the end of administration and 4 weeks after the end of rHuEPO administration. Furthermore, a handful of blood-derived miRNAs were identified using different techniques, i.e. microarray, qPCR and sequencing. Further thorough validation experiments are required before any solid conclusion can be drawn. Nevertheless, “omics” signatures of rHuEPO administration from saliva gene expression and blood-derived miRNA provide further support for the idea that “omics” biomarkers have the greatest known potential to improve the performance of current anti-doping methods such as the Athlete Biological Passport for rHuEPO detection.