

## **PROJECT REVIEW**

### **“Circulating microRNAs as stable biomarkers for detection of erythropoiesis-stimulating agent abuse”**

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MicroRNAs (miRNAs) are small (19 to 25-nucleotides) noncoding transcripts involved in many cellular mechanisms, including erythropoiesis and response to hypoxia. MiRNAs have been found in tissues and also in serum and plasma as well as other body fluids, in a remarkably stable form that is protected from endogenous RNase activity and harsh conditions. Moreover, plasmatic miRNAs were shown to be very specific and sensitive biomarkers.

Due to all these aspect miRNAs can serve as potential biomarkers for detection for detection of various cancers, diseases and injuries. Erythropoietin-erythropoietin receptor (EPO-EPOR) signaling plays a master role in the erythropoiesis. Several studies have reported a major role of miRNAs in erythropoiesis. Specific miRNAs were shown to accumulate to very high levels in red blood cells and were associated with early development and maturation of erythroids.

In this project, we are going to investigate whether circulating microRNAs can serve as biomarkers for erythropoiesis stimulating agent abuse. To this end we will analyze miRNA levels in serum and plasma by miRNA microarrays and quantitative real-time PCR (qRT-PCR). Plasma and serum samples are derived from clinical studies of healthy subjects injected with erythropoiesis-stimulating agent (C.E.R.A and Dynepo).

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### **Results and Conclusions**

MicroRNAs (miRNAs) are small (19 to 25 nucleotides) non-protein coding transcripts involved in many cellular and physiological mechanisms. The role of miRNAs has been mainly investigated in tissues. Recently, a new class of miRNA was found in cell-free body fluids such as plasma. These new class of miRNAs are called “circulating miRNAs”. Circulating miRNAs have been shown to be very stable, specific and sensitive biomarkers. Therefore, they could be altered in a specific manner by doping interventions.

In this project, we investigated whether circulating microRNAs can serve as biomarkers for erythropoiesis stimulating agent abuse. To this end, we analyzed miRNA levels in plasma by miRNA microarrays and quantitative real-time PCR. Plasma samples are derived from clinical studies of healthy subjects injected with erythropoiesis-stimulating agent (C.E.R.A).

Based on microarray results, we observed a highly significant difference in the levels of microRNAs in plasma after C.E.R.A injection. We demonstrated that a specific microRNA, miR-144, exhibit a high increase and that its change can detected significantly in a long-term manner after CERA stimulation. Interestingly, it has been reported that miR-144 is essential in erythropoiesis in different organisms such as zebrafish, mouse and human.

These findings suggest the potential of using specific circulating microRNAs as sensitive and informative biomarkers in anti-doping field.