

# Circulating microRNAs as emerging cardiac biomarkers responsive to acute exercise

de Gonzalo-Calvo D.

Dávalos A.

Fernández-Sanjurjo M.

Amado-Rodríguez L.

Díaz-Coto S.

Tomás-Zapico C.

Montero A.

García-González Á.

Llorente-Cortés V.

Heras M.E.

Boraita Pérez A.

Díaz-Martínez Á.E.

Úbeda N.

Iglesias-Gutiérrez E.

**Background:** Circulating microRNAs (c-miRNAs) are mediators of intercellular communication with great potential as cardiac biomarkers. The analysis of c-miRNAs in response to physiological stress, such as exercise, would provide valuable information for clinical practice and a deeper understanding of the molecular response to physical activity. Here, we analysed for the first time the acute exercise response of c-miRNAs reported as biomarkers of cardiac disease in a well-characterized cohort of healthy active adults. **Methods:** Blood samples were collected immediately before and after (0 h, 24 h, 72 h) a 10-km race, a half-marathon (HM) and a marathon (M). Serum RNA from 10-km and M samples was extracted and a panel of 74 miRNAs analysed using RT-qPCR. c-miRNA response was compared with a panel of nine cardiac biomarkers. Functional enrichment analysis was performed. Pre- and post-M echocardiographic analyses were

carried out. Results: Serum levels of all cardiac biomarkers were upregulated in a dose-dependent manner in response to exercise, even in the absence of symptoms or signs of cardiac injury. A deregulation in the profiles of 5 and 19 c-miRNAs was observed for 10-km and M, respectively. Each race induced a specific qualitative and quantitative alteration of c-miRNAs implicated in cardiac adaptations. Supporting their discriminative potential, a number of c-miRNAs previously associated with cardiac disease were undetectable or stable in response to exercise. Conversely, 'pseudo-disease' signatures were also observed. Conclusions: c-miRNAs may be useful for the management of cardiac conditions in the context of acute aerobic exercise. Translational aspects of the work: Circulating microRNAs could offer incremental diagnostic value to established and emerging cardiac biomarkers, such as hs-cTnT or NT-proBNP, in those patients with cardiac dysfunction symptoms after an acute bout of endurance exercise. Furthermore, circulating miRNAs could also show 'pseudo-disease' signatures in response to acute exercise. Clinical practitioners should be aware of the impact caused by exercise in the interpretation of miRNA data. © 2018

Elsevier B.V.

Biomarkers

Circulating microRNAs

Exercise

Heart disease

amino terminal pro brain natriuretic peptide

copeptin

creatine kinase

creatine kinase MB

fatty acid binding protein 3

galectin 3

lactate dehydrogenase

microRNA

myoglobin

troponin T

biological marker

circulating microRNA

microRNA

MIRN103A2 microRNA, human

MIRN375 microRNA, human

adult

aerobic exercise

Article

diagnostic value

echocardiography

heart disease

human

marathon runner

normal human

priority journal

reverse transcription polymerase chain reaction

blood

cardiac muscle

classification

endurance

exercise

female

heart disease

male

metabolism

middle aged

physiological stress

physiology

time factor

Adult

Biomarkers

Circulating MicroRNA

Exercise

Female

Healthy Volunteers

Heart Diseases

Humans

Male

MicroRNAs

Middle Aged

Myocardium

Physical Endurance

Stress, Physiological

Time Factors