Universität Basel

Research Project

Exercise, Arterial Cross-Talk Modulation and Inflammation in an Ageing Population: miRNA substudy

Third-party funded project

Project title Exercise, Arterial Cross-Talk Modulation and Inflammation in an Ageing Population: miRNA substudy
Principal Investigator(s) Hanssen, Henner ;
Co-Investigator(s) Streese, Lukas ; Papassotiropoulos, Andreas ; de Quervain, Dominique ;
Organisation / Research unit
Departement Sport, Bewegung und Gesundheit / Präventive Sportmedizin (Hanssen)
Department
Faculty of Medicine
Departement Sport, Bewegung und Gesundheit
Departement Sport, Bewegung und Gesundheit / Präventive Sportmedizin (Hanssen)
Project start 01.04.2015
Probable end 01.03.2018
Status Completed

We have previously validated a multidisciplinary research perspective encompassing epigenetic pathways embedded in vascular and exercise medicine. Exercise can improve microvascular phenotype leading to healthier ageing and better cardiovascular (CV) outcome. Cardiorespiratory fitness has been identified as a sixth vital sign and a valid surrogate marker for cardiovascular and all-cause mortality. Regular intensive exercise has previously been shown to induce reprogramming of DNA methylation of p66^{Shc} gene promoter, thereby inhibiting p66^{Shc} gene expression and reducing systemic oxidative stress. This molecular pathway was associated with improvements of retinal microvascular health and may represent a mechanistic link whereby exercise protects against age-related oxidative stress and microvascular damage. Retinal vessel analysis is a new diagnostic approach to quantify microvascular remodeling and stratify CV risk. The retinal phenotype has been associated with incidence CV disease and mortality. Circulating microRNAs (miRNAs) are small non-coding nucleotides that regulate cell function. Upstream of the vascular phenotype, miRNAs are post-transcriptional regulators of inflammation, oxidative stress and lipid metabolism, which contribute to the progression of atherosclerosis. Analyzing circulating miRNAs has the potential to improve CV risk stratification and better understand the underlying gene expression in cardiovascular disease. Previous studies have highlighted the potential of single target miRNAs as a biomarker-guided CV therapy and novel tool in personalized medicine. The investigation of specific single miRNA expressions after acute or long-term exercise interventions have illustrated new insights in vascular regeneration processes. However, the next step, to identify new pathways from upstream gene regulation to the downstream manifest phenotype, is to use an untargeted circulating miRNA approach in combination with sensitive vascular phenotyping. In our approach, exercise is used as a treatment concept to identify miRNAs that may be targeted in future treatment strategies, such as development of gene-specific inhibitors or mimetics of miRNA expression.

In this study, we will assess untargeted circulating miRNAs by next generation sequencing (NGS) in 38 healthy older active (HOA), 36 healthy older sedentary (HOS) as well as 84 older sedentary CV risk patients (OSR) aged 50 to 80 years. Our first aim is to determine the association of long-term physical activity with retinal endothelial function and circulating miRNA profile in HOA and HOS as well as OSR. Our second aim is to examine the effects of a high-intensity interval training (HIIT) on retinal endothelial function and circulating miRNA profile in OSR. Data acquisition of retinal endothelial function and blood

sampling have been performed between 2016 and 2018. The proposed one-year grant will enable NGS from available blood samples to analyze miRNA expression and associations with retinal microvascular phenotype in active and sedentary older adults. The study will allow for an innovative approach to define new pathways from genotype to phenotype in order to disentangle molecular interactions in the process of microvascular ageing associated with physical activity behavior.

Financed by
Other sources

Add publication

Add documents

Specify cooperation partners