

## Age-related differences of microRNA-21 in leukocytes and its association with physical performance.

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### ABSTRACT

**INTRODUCTION:** Several studies suggest chronic inflammation as an underlying biological mechanism for the decline in physical performance of elderly (Cesari et al., 2004; Tiainen et al., 2010). Moreover, it has been shown that habitual exercise ameliorates the higher proinflammatory gene expression in leukocytes of elderly (Gano et al., 2011). Within the last years several microRNAs (short, non-coding RNAs) have been demonstrated to regulate gene expression also in the context of exercise immunology (Wessner et al., 2010). Interestingly, some of these microRNAs (miRs) such as miR-21 and miR-146 are involved in pathways important for ageing as well as inflammatory processes (Olivieri et al. 2012). Therefore, the main aims of the current study were (1) to investigate whether miR-21 and miR-146 levels in leukocytes are affected by age and (2) to correlate performance levels of elderly to miR gene expression levels.

**METHODS:** Healthy young (n=7, age: 25.28 ± 2.3 years) and old (n=25, age: 83.40 ± 5.63 years) females participated in the study. After an overnight fast, leukocytes were isolated from heparinized blood using BD Vacutainer CPT tubes. miR-21 and miR146 gene expression in leukocytes was determined by quantitative RT-PCR using miScript Primer Assays (Qiagen, Hilden, Germany). Additionally, leukocyte numbers and inflammatory markers (hs-CRP, hs-IL6, IL1-ra) were quantified. In order to relate potential inflammatory markers to the fitness level of the elderly, several functional tests were performed (handgrip, 6min walking test, chair-rise test, isokinetic measurement of knee extension and flexion). Differences between groups were detected by unpaired t-tests. Correlations between markers were characterized using Pearson correlation coefficients.

**RESULTS:** Interestingly, miR-21 expression in leukocytes was significantly enhanced in the elderly (+55.1%,  $p=0.036$ ) while miR-146a levels were not affected by age ( $p=0.492$ ). However, miR-21 correlated significantly with hs-CRP levels ( $r=0.352$ ;  $p=0.033$ ), we did not detect any associations between miR-21 expression and performance parameters of the elderly: Handgrip ( $r=0.533$ ;  $p=0.121$ ), 6-min Walking Test ( $r=0.231$ ;  $p=0.220$ ), Chair Rise ( $r=0.336$ ;  $p=0.070$ ), Peak Torque knee extension ( $r=0.589$ ;  $p=0.105$ ) as well as flexion ( $r=0.203$ ;  $p=0.291$ ).

**CONCLUSION:** In conclusion these preliminary results show that miR-21 seems to be enhanced with age but not influenced by fitness level of the elderly. Gene targets of miR-21 have been identified in the TGF- $\beta$  signaling pathway. Therefore, next steps would be to associate the changes in miR-21 with its potential targets to further elucidate its role in the ageing process.

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