

Inflammatory Activity of Extracellular Vesicles Induced by Different Exercise Regimens

ShT-03.2-1

S. Fondi^I, P. Ceccaroli^{II}, E. Polidori^{II}, R. Agostini^{II}, V. Stocchi^{III}, **M. Guescini^{II}**

^IUniversity of Urbino Carlo Bo, Urbino, Italy, ^{II}Via I Maggetti,26, Urbino, Italy, ^{III}Università San Raffaele Pisana, Rome, Italy

Regular physical exercise promotes systemic adaptations that positively affect the cardiovascular, nervous and immune systems, promotes weight loss and counteracts sarcopenia. Moreover, the level of physical activity is the major modifiable risk factor for metabolic and cancerous diseases (Fiuza-Luces C et al. (2018) *Nat. Rev. Cardiol* 15, 731–743). Exercise-induced benefits have been linked to the secretion of myokines. However, recent evidence suggests extracellular vesicles (EVs) as new players through which muscle communicates with other tissues or organs (Guescini M et al. (2015) *PLoS ONE* 10, e0125094).

Our study focused on the secretion of EVs in response to different physical exercise regimens. We conducted our research on healthy individuals who were subjected to various exercise protocols: acute aerobic exercise (AAE) and training, acute maximal aerobic exercise and altitude aerobic training. The most significant finding was the increase in EV secretion in the sedentary condition compared to trained participants following AAE. This result underscores the role of exercise in modulating EV secretion and its potential implications for health and disease. Specifically, we observed an upregulation of EV-associated miR-206, miR-133b and miR-146a following AAE, and this trend appeared to be intensity-dependent. Furthermore, our findings showed that THP-1 macrophage treatment with exercise-derived EVs led to an increase in the mRNAs encoding for IL-1b, IL-6 and CD163 using baseline and immediately post-exercise EVs (Maggio S et al. (2023) *Int. J. Mol. Sci.* 24, 3039). These findings provide a deeper understanding of the release of circulating EVs and their role as mediators of the inflammatory processes associated with exercise. Importantly, we also highlighted that the release of EV-miRNAs into the bloodstream depends on the subject's fitness condition; the more trained the subjects are, the less circulating EV-miRNAs increase following an exercise bout.