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ABSTRACT N. 069

EXERCISE AS MEDIATORS OF HEALTH BENEFITS INDUCED BY PHYSICAL EXERCISE

## EXERCISE ONCOLOGY AND BIOMARKERS: HOW SKELETAL MUSCLE INTERACTS WITH INFLAMMATION AND IMMUNITY

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Regular physical activity is now recognized as a key component of cancer prevention and survivorship care. Large epidemiological and clinical studies show that higher physical activity and cardiorespiratory fitness are associated with a reduced incidence of several cancers and with lower cancer-specific mortality and recurrence rates. Recent mechanistic work highlights skeletal muscle as an active endocrine and immunomodulatory organ: contracting myofibres release “exerkines” (including myokines and metabolites) that modulate systemic inflammation, insulin and IGF-1 signalling, and anti-tumor immunity, affecting pathways such as NF- $\kappa$ B and PI3K/Akt/mTOR. These exercise-induced factors provide a mechanistic framework to understand how structured exercise can influence tumor biology and treatment response (1). Within this framework, exercise oncology is increasingly moving from symptom management to biomarker-driven, mechanism-based interventions. Our group has contributed to this evidence by investigating home-based lifestyle programs in breast cancer survivors enrolled in the MoviS trial (NC-T04818359) (2). Across several analyses and conference communications, we showed that 12-24 weeks of combined aero-

bic training and nutritional counselling improve free-living glycaemic profiles, insulin resistance, lipid status and inflammatory markers, while enhancing cardiorespiratory fitness and objectively measured physical activity. Parallel work has characterized dietary patterns and their quality, and monitored physical activity using wearable sensors during and after lifestyle interventions, providing a detailed picture of behaviour change and its physiological correlates. Building on these data, ongoing translational studies use patient sera in 3D breast cancer models to link lifestyle-induced systemic changes (e.g. in the IGF-1 axis and metabolic biomarkers) to functional readouts of tumorigenic potential (3). Taken together, current literature and our translational findings support a biomarker framework in which muscle-derived signals, metabolic and inflammatory indices, and tumor- or immune-related markers are integrated with new clinical outcomes of muscle functionality, such as VO<sub>2</sub>max and exercise capacity. This integrated view may help identify responders to exercise-based interventions, refine personalized prescriptions, and position structured physical activity as a genuine adjuvant strategy in oncology rather than a purely supportive measure.

**Keywords:** Exercise oncology, skeletal muscle, exerkines, biomarkers, cardiorespiratory fitness.