

Exercise-induced extracellular vesicles delay tumor development via igniting the inflammation in the immunologically cold breast cancer model

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Introduction: Epidemiological evidence highlights the role of physical activity in breast cancer is crucial due to its potential to reduce cancer risk and improve outcomes. However, there is still a need for a more comprehensive understanding of how lifestyle factors, such as exercise, can modulate the anticancer immune response.

Purpose of the work: Given the relationship between host physical status and immune fitness, this preclinical study aimed to explore the impact of exercise-induced extracellular vesicles (EVs) on the immune tumor microenvironment and breast cancer progression.

Materials and Methods: Mice underwent a treadmill-based exercise regimen, with plasma collected post-exercise for EVs isolation. Two transplantable breast cancer models (4T1 and E0771) were treated with exercise-induced EVs prophylactically and therapeutically, along with monitoring tumor growth and profiling of systemic and local immune microenvironment.

Results: Notably, regular exercise led to a significant increase in plasma EVs levels in active mice. Treatment with exercise-induced extracellular vesicles resulted in a marked delay in tumor growth (approximately 30%, $p < 0.05$) compared to untreated controls. Analysis of lymphoid and myeloid cell subpopulations revealed discernible immunomodulatory effects of EVs on the tumor microenvironment. Further examination of tumor-infiltrating lymphocytes suggested that the observed delay in tumor growth in the treatment group may be attributed to the influx of cytotoxic CD8⁺ T cells.

Conclusions: This study unveils impact of physical activity on EVs production and their potential therapeutic role in breast cancer. Our findings suggest that extracellular vesicles could serve as an immunomodulatory treatment to trigger inflammation in the tumor bed.

The authors declare that they have no conflict of interest in relation to the above work.

This work was presented during a poster session at the School of Immunology 2024.