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Exploring Exercise Oncology Through 3D In Vitro Models: Impact of Exercise-Conditioned Serum on Breast Cancer Cell Tumorigenicity

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Purpose: Cell culture models in exercise oncology enable the assessment of exercise effects on cancer cell tumorigenicity and the identification of physiological predictors. Our research group pioneered the application of 3D translational in vitro approaches to evaluate exercise effects in breast cancer survivors and to explore potential predictors of exercise-conditioned serum activity.

Methods: Thirty breast cancer survivors completed a 12-week lifestyle intervention (LI) including aerobic exercise training and educational counseling. A subset performed two acute exercise sessions at 40% heart rate reserve (HRR; Moderate EX) and 70% HRR (Vigorous EX). Sera collected before and after LI, and post-exercise, were used to stimulate triple-negative breast cancer (TNBC) cells and patient-derived organoids (PDOs) to assess 3D spheroid formation in semi-solid matrices.

Results: Compared to pre-intervention sera, LI-conditioned sera significantly reduced TNBC spheroid formation, indicating decreased tumorigenic potential. IGF-1 emerged as a significant predictor of these effects. Exercise-conditioned sera also showed less capacity to form TNBC cell spheroids, compared to those collected at rest. Particularly, the strongest effects were observed 3h post-Moderate EX ($-14.3 \pm 6.7\%$). Similar trends were partially confirmed in PDOs, supporting the translational relevance of these findings.

Conclusions: These results reinforce the potential of aerobic exercise interventions to control tumor progression and recurrence risk in breast cancer survivors. Translational in vitro models represent a promising tool to predict the role of exercise-induced metabolic and physiological changes, advancing knowledge in exercise oncology and supporting personalized exercise prescriptions.

Keywords

Breast cancer survivors; 3D cell culture models; lifestyle; aerobic exercise

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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