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Aerobic Exercise Training and β 2-Adrenergic Signaling in the Regulation of Immunosuppression in Cancer

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Sympathetic nervous system (SNS) hyperactivation contributes to tumor progression and cancer-associated immunosuppression. Aerobic exercise training (AET) is known to reduce sympathetic overactivity; however, its role in modulating tumor-induced immunosuppression via β 2-adrenergic receptor (β 2-AR) signaling remains poorly understood.

Objective:

To investigate how β 2-AR signaling regulates tumor-associated immunosuppression and whether AET modulates immune function in preclinical tumor models.

Methods:

In vitro experiments were performed using the murine colon carcinoma CT26 cell line and primary splenocytes treated with propranolol (β -adrenergic antagonist, 5–20 μ M) or clenbuterol (β 2-AR agonist, 1–10 μ M). Cell growth and gene expression of immune checkpoint molecules (PD-L1, Galectin-9, and VISTA) were assessed. In vivo, BALB/c mice underwent six weeks of AET on a treadmill prior to CT26 tumor inoculation. Animals were allocated to sedentary or trained groups, with or without propranolol treatment (5 mg/kg/day). Tumor growth, tissue mass, and immune cell populations in the spleen, lymph nodes, and tumors were analyzed by flow cytometry.

Results:

In CT26 cells, β 2-AR activation increased VISTA expression, suggesting enhanced tumor-associated immunosuppression, whereas propranolol had no significant effect on checkpoint expression. In primary splenocytes, β -adrenergic blockade increased cell proliferation, indicating improved immune function. In vivo, AET induced a trend toward reduced tumor mass and significantly increased CD8⁺ T cell proportions in the spleen. However, these effects were not observed when AET was combined with propranolol treatment. Notably, AET prevented the reduction of CD8⁺ T cells in lymph nodes observed in sedentary tumor-bearing mice.

Conclusion:

AET partially counteracts tumor-associated immunosuppression and modulates systemic immune profiles. However, the contribution of SNS signaling requires further investigation, as β -adrenergic blockade appears to improve immune function in vitro but attenuates some AET-induced immune benefits in vivo. These findings support AET as a relevant adjuvant strategy to enhance anti-tumor immunity.

Keywords

Neuroimmunology; β 2-adrenergic signaling; aerobic exercise training

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

Author: DA SILVA VIEIRA, Janaina (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo)

Co-authors: Ms SILVA BORGES, Gabriela (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo); SANTOS, Pedro Henrique (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo); KAFOURI, Gabriel (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo); MEIRIANE DA SILVA CRUZ, Sabrina (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo); ARANHA CAMARGO, Anamaria (Instituto de Ensino e Pesquisa Sírio-Libanês); TAMI AMANO, Mariane (Instituto de Ensino e Pesquisa Sírio-Libanês); CHAKUR BRUM, Patrícia (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo)

Presenter: DA SILVA VIEIRA, Janaina (School of Physical Education and Sport and Dept of Physiology and Biophysics, Institute of Biomedical Sciences University of Sao Paulo)

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