Scientific Foundation SPIROSKI, Skopje, Republic of North Macedonia
South East European Journal of Immunology. 2025 Mar 31; 8(CITIM):051
https://doi.org/10.3889/seejim.2025. 6114
eISSN: 1857-9388
Category: *CITIM - Cancer Immunotherapy & Immunomonitoring (CITIM2025)*
Section: *Invited Lectures*

The exercise of mobilizing the immune system in cancer patients

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Citation: Straten PT. The exercise of mobilizing the immune system in cancer patients. SEE J Immunol. 2025 Mar 27;8(CITIM):051. https://doi.org/10.3889/seejim.2025.6114.
Keywords: Immune cell infiltration; NK cells; exercise and immunotherapy; checkpoint inhibitors; lung cancer
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Received: 01-Mar-2025
Accepted: 25-Mar-2025
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Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

Cells of the immune system, e.g., CD8 T cells and Natural killer (NK) cells are capable of recognizing and killing cancer cells. Naturally elicited anti-cancer immune responses lead to infiltration of immune cells into tumors and the presence of these cells impact on disease progression, i.e., overall survival of the patient and also correlate with response to check point inhibition (CPI) therapy. We recently demonstrated that tumors in exercising mice show increased immune cell infiltration, in turn associated with an over 60% reduction in tumor incidence and growth across several murine tumor models. Mechanistically we could show that efficacy was dependent on NK cells, which were engaged through an epinephrine-dependent mobilization. Together these results link exercise with improved immunological control of tumor progression, suggesting that exercise could be a beneficial partner for immunotherapy. We translated these findings to clinical testing and recently finalized a clinical trial where exercise was combined with immunotherapy (HI AIM NCT04263467). HI AIM was a randomized controlled trial (70 patients, 1:1) for patients with metastatic non-small cell lung cancer. Patients in the treatment arm, receive an exercise-intervention consisting of supervised and group-based exercise training, comprising primarily intermediate to high intensity interval training three times per week over 6 weeks. Primary outcome was mobilization of circulating NK cells (TBNK kit assay). Secondary outcome other circulating immune cells, infiltration of immune cells in tumor, inflammatory markers, aerobic capacity measured by VO_2 max test, physical activity levels and quality of life measured by questionnaires, and clinical outcomes. All patients received standard oncological treatments; checkpoint inhibitors, checkpoint inhibitors combined with chemotherapy or oncological surveillance. Blood samples and biopsies (ultrasound guided), harvested before, during and after the 6-week training program, will form basis for immunological measurements of an array of immune cells and markers. Preliminary analyses, based on examination of blood samples from 15 patients in the treatment group, adrenalin and nor-adrenalin demonstrated rapid increase as did T and NK cell numbers and frequencies. High intensity interval training in lung cancer patients, concurrent with standard treatment is feasible and safe. The applied exercise regiment led to acute increase in (nor-)adranalin as well as T and NK cells. Further analyses will include extensive serum and immune cell analyses, as well as correlations to the clinical data of the patients.