

## Exercise boosts anti-cancer immunity and reduces inflammation in Lynch Syndrome patients: Study

September 19 2023



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Regular and intense aerobic exercise may reduce the risk of colorectal cancer in patients with Lynch Syndrome (LS) by improving the immune



system's ability to detect and remove potentially harmful cells, according to researchers at The University of Texas MD Anderson Cancer Center.

The findings, published in <u>Clinical Cancer Research</u>, revealed that LS carriers participating in a high-intensity training (HIIT) regimen saw a reduction of the inflammatory marker prostaglandin E2 (PGE2) in both the colon and the blood. Researchers also found higher levels of two types of immune cells, natural killer (NK) and CD8<sup>+</sup> T cells, suggesting an increased immune response in the colon.

"It was mind-blowing to me that exercise induced such strong and durable change," said study lead, Eduardo Vilar-Sanchez, M.D., Ph.D., professor of Clinical Cancer Prevention. "We found that high-intensity training not only enhances how the body could fight <u>cancer</u> at its earliest stages, but it also gives many other <u>health benefits</u>."

LS is a hereditary condition affecting more than 1 million Americans that carries a high lifetime risk of colorectal cancer (CRC) and endometrial cancer. Men with LS have a 60%-80% risk of developing CRC, while that risk is 40%-60% for women. Women also face the same amount of chance of developing endometrial cancer.

This non-randomized study followed 21 LS patients between the ages of 18 and 50 over a 12-month period. Eleven patients were assigned to the exercise group and 10 to receive usual care. All 21 patients were given activity trackers. The exercise group enrolled in three 45-minute HIIT cycling sessions a week, while usual care patients were only told about the benefits of working out.

Participants in the <u>exercise group</u> recorded a median of 164 weekly exercise minutes at a heart rate >70%, while the usual care group recorded a median of 14 weekly exercise minutes.



At the start of the study, both groups completed a baseline health questionnaire and underwent a standard-of-care lower gastrointestinal (GI) endoscopy with biopsies and blood collection. Cardiopulmonary exercise testing (CPET) was performed at the second visit, within 30 days of the primary endoscopy. All participants received a 1-year endoscopy followed by a CPET at the fourth checkup, within 30 days of the 1-year endoscopy. There were no significant adverse events.

Expression analysis by next-generation sequencing showed statistically significant changes in <u>gene expression</u> in the normal colorectal mucosa between the exercise and usual care groups. In the group that exercised, 13 genes became more active, while 33 genes became less active when compared to the group that did not exercise. Activated genes were involved in immune signaling pathways, whereas suppressed genes were linked to muscle contraction and metabolism.

Researchers also found that when the body's ability to use oxygen (VO2peak) increases, it stimulates production of myokines and cytokines, which help regulate your immune system. Exercise was also linked to lower levels of PGE2 and an increase in certain immune cells in the colon, including CD8<sup>+</sup> T cells and CD57+ NK cells, which play important roles in cancer defense.

"It can be difficult for patients to commit to taking a pill," Vilar-Sanchez said. "If we are able to validate the preventive benefits of this approach in future studies, we hope to offer a 'lifestyle prescription' and give LS patients a new way to possibly lower their cancer risk over time."

Future randomized <u>clinical trials</u> will be needed to confirm the preventive efficacy of aerobic <u>exercise</u> training in LS carriers and to further elucidate the possible immune-related pathways underlying any reductions in cancer risk.



Limitations to the study included the <u>small sample size</u> without race heterogeneity and the non-randomized nature of the design. Participants knew their allocation before signing informed consent, which might have impacted their willingness to participate in the trial. In addition, differences in timing of collection of the specimens and storage in the freezer could have driven differences in metabolite levels.

**More information:** Nan Deng et al, Exercise Training Reduces the Inflammatory Response and Promotes Intestinal Mucosa-associated Immunity in Lynch Syndrome, *Clinical Cancer Research* (2023). DOI: 10.1158/1078-0432.CCR-23-0088 , doi.org/10.1158/1078-0432.CCR-23-0088 , aacriournals.org/clincancerres ... ces-the-Inflammatory

Provided by University of Texas M. D. Anderson Cancer Center

Citation: Exercise boosts anti-cancer immunity and reduces inflammation in Lynch Syndrome patients: Study (2023, September 19) retrieved 11 May 2024 from <u>https://medicalxpress.com/news/2023-09-boosts-anti-cancer-immunity-inflammation-lynch.html</u>

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