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Contribution ID: **83** Type: **3 - Talk**

Exercise suppresses prostate tumor aggressiveness by altering intratumoral lipid metabolism

Thursday 23 July 2026 15:30 (15 minutes)

Although prior work suggests that exercise reduces the risk of high-grade prostate cancer, the underlying biological mechanisms remain unclear. We aimed to uncover potential mechanisms using transcriptomic approaches following a 12-week aerobic exercise intervention utilizing the transgenic adenocarcinoma of the mouse prostate (TRAMP) model.

Methods: Twelve TRAMP mice, 8-10 weeks of age, were randomized to exercise or control group (n=6/group). Mice in the exercise group were singularly housed in cages with voluntary running wheels. Mice in the control group maintained normal group housing and activity. At euthanasia, prostate tumors were excised, weighed and processed for immunohistochemistry and transcriptome analysis. Outputs of sequencing data were assessed for quality and accuracy. Differential expression was filtered to identify genes that had a ≥ 1.5 log fold change with an adjusted $p<0.05$. Gene ontology and pathway analyses were performed to reveal pathways activated.

Results: No significant difference was observed in body or genitourinary weight between groups. Pathology revealed a 50% reduction in moderately and poorly differentiated tumors in the exercise group. In representative tumor samples 32 genes were significantly modified. Among the top 20 transcripts that decreased in the exercise group were genes involved in lipolysis such as Lipe, Plin1, Slc7A10. Among the top transcripts with higher expression in the exercise group was Dgat2L6 that is involved in the synthesis of diglycerols and triglycerols. Biological processes most impacted centered on triglyceride catabolic process, lipid homeostasis, lipid metabolic process, and triglyceride metabolic process.

Conclusion: Our results suggest that exercise differentially affect pathways that overcome high oxidative stress thresholds and protect against high-grade tumors.

Keywords

Aerobic Exercise
Prostate Cancer
Transcriptomics
Lipid Metabolism

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

Author: PATEL, Darpan (University of Texas Medical Branch at Galveston)

Co-authors: Dr KUMAR, A. Pratap; RIVAS, Paul; GHOSH, Rita; CHEN, Yidong; IKENO, Yuji; LI, Zhao

Presenter: PATEL, Darpan (University of Texas Medical Branch at Galveston)

Session Classification: Oral Session