MedicalXpress

What mediates the beneficial effects of exercise on breast cancer outcomes?

September 8 2017

The ability of serum obtained from women with breast cancer immediately after finishing two hours of moderate to intense exercise to prevent the growth and survival of breast cancer cells lines in vitro and in mice was attributable, at least in part, to epinephrine activation of the Hippo signaling pathway.

The study is published in *Cancer Research*, a journal of the American Association for Cancer Research, by Pernille Hojman, PhD, group leader in the Centre for Physical Activity Research at Copenhagen University Hospital in Denmark.

Hojman explained that accumulating epidemiological evidence indicates that exercise can lower a woman's risk of breast cancer recurrence but that relatively little is known about the molecular mechanisms underlying this protection. It is important that we fully understand this if we are to design training interventions that molecularly target tumor progression and metastasis, she said.

Hojman colleagues have previously reported that two hours of moderate to intense exercise by women who have survived breast cancer increases the level of a number of factors in the serum and that this serum reduced the survival of breast cancer cell lines in vitro. In this study, the researchers set out to determine which factor was responsible for the effect on cell viability and the mechanisms behind it.

Hojman and colleagues obtained blood samples, which they processed to

attain serum, from seven healthy women and 20 women who were being treated with adjuvant chemotherapy after surgery for early-stage breast cancer, before and after two hours of moderate to intense exercise. The exercise in which the women with breast cancer participated was part of a six-week standard exercise rehabilitation program at the Copenhagen University Hospital.

Serum obtained after exercise from both healthy women and those with breast cancer reduced the survival of two breast cancer cell lines, MCF-7 and MDA-MB-231, in vitro compared with serum obtained before exercise. It also significantly reduced the ability of MCF-7 cells to form tumors if injected into mice. Forty-five percent of mice receiving the cells exposed to serum obtained after exercise developed tumors compared with 90 percent of mice receiving cells exposed to serum obtained at rest.

The effects of the serum obtained after exercise on MCF-7 cell survival and ability to form tumors in mice were significantly reduced if epinephrine was blocked from attaching to its receptor on the surface of the MCF-7 cells. Blocking epinephrine did not significantly alter the effects of serum obtained after exercise on MDA-MB-231 cells.

Further analysis showed that epinephrine in serum obtained after exercise activated a known tumor suppressor signaling pathway, the Hippo signaling pathway, in MCF-7 cells but not in MDA-MB-231 cells.

"The results of this study show that moderate to high intensity exercise leads to an acute increase in levels of epinephrine, which can reduce breast cancer cell viability and tumor growth via activation of the Hippo signaling pathway," said Hojman. "Although these data suggest that it might be optimal for women with breast cancer to exercise at a moderate to high intensity, further studies are needed to confirm this. Women who have been diagnosed with breast cancer should consult a doctor before

embarking on an exercise program.

"MCF-7 cells are hormone receptor-positive and MDA-MB-231 cells are triple-negative," added Hojman. "There are epidemiological data that suggest that exercise might be better at reducing the risk of recurrence of hormone receptor-positive breast cancer compared with triple-negative breast cancer, which might explain why the effects of serum obtained after exercise were more pronounced on MCF-7 cells. In addition, these cell lines differ in which mutations they carry, and the difference in the exercise effect might be a result of this."

According to Hojman, the main limitation of the study is that this is a model of breast cancer recurrence and metastasis and not the natural processes.

Provided by American Association for Cancer Research