Calorie restriction and exercise show breast cancer prevention differences in postmenopausal women

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Scientists at the University of Texas at Austin have identified pathways by which a reduced-calorie diet and exercise can modify a postmenopausal woman's risk of breast cancer.

The results, presented at the American Association for Cancer Research's Seventh Annual International Conference on Frontiers in Cancer Prevention Research, suggest that both caloric restriction and exercise affect pathways leading to mTOR, a molecule involved in integrating energy balance with cell growth. Dysregulation of the mTOR pathway is a contributing factor to various human diseases, including cancers. Diet and exercise reach mTOR through different means, with calorie restriction affecting more upstream pathways, which could explain why caloric restriction is more efficient in delaying tumor growth than exercise in animal models.

"One of the few breast cancer modifiable risk factors is obesity," said lead author Leticia M. Nogueira, Ph.D., a research graduate assistant at the University of Texas. "Our study may provide a good scientific basis for medical recommendations. If you're obese, and at high risk for breast cancer, diet and exercise could help prevent tumor growth."

Epidemiological data has suggested that inducing a so-called "negative energy balance" (where less energy is taken in than expended) through eating a low-calorie diet or increasing exercise levels, decreases the postmenopausal breast cancer risk associated with obesity. Although the mechanism responsible for these anti-obesity strategies was unknown, scientists have suspected hormone alteration plays a critical role. Increased fat tissue is known to be associated with alterations in adipokines, proteins secreted by fat tissue that help modify appetite and insulin resistance. For example, increased levels of leptin and decreased levels of adiponectin have been associated with breast cancer risk.

For the study, Nogueira and colleagues sought to compare the changes in adipokines, and their downstream signaling pathways proven to be altered in human breast cancers, following either caloric restriction or exercise in a mouse model of post-menopausal obesity.

For eight weeks, they administered a high-fat diet to 45 mice that had their ovaries surgically removed to model the post-menopausal state. During week nine of the study, the diet-induced obese mice were randomly assigned to one of three groups: a control group, permitted to eat at will; a group fed a diet reduced in calories by 30 percent; and a group that was permitted to eat at will but exercised on a treadmill for 45 minutes a day, five days a week. At week 16, researchers collected tissue from the mice for analysis.

At the study's end, the mice fed a calorie-restricted diet weighed an average of 19.9 grams – significantly less than the control mice (average weight 28.8 grams) and the exercised mice (average weight 26 grams). The calorie-restricted mice and the exercised mice showed no significant difference in percentage of body fat, but both groups had significantly less body fat than the sedentary mice that were fed at will.

In addition, blood levels of leptin, a hormone that plays a role in fat metabolism, were significantly reduced in the calorie-restricted and exercised mice compared to the controls. The calorie-restricted mice also displayed increased blood levels of adiponectin, a hormone produced in fat tissue that regulates some metabolic processes, compared to the exercised mice.

Some of the cell signaling pathways regulated by these hormones converge at mTOR, Nogueira explains. She and her colleagues found that the key proteins found downstream of mTOR activation were less active in both the calorie-restricted and exercised mice compared to the controls.

"These data suggest that although exercise can act on similar pathways as caloric restriction, caloric restriction possesses a more global effect on cell signaling and, therefore, may produce a more potent anti-cancer effect," Nogueira said.

Source: American Association for Cancer Research