

Cells' 'neighborhood' can help prevent breast cancer

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Exercise has given Lu-Ann Doria more energy, confidence and strength. It may also help her stay cancer-free, doctors say.

Doria, 57, began working out for the first time three years ago, after recovering from breast <u>cancer</u> therapy. At first, she was so fatigued she had to nap before dance class.

Now, Doria is exercising five days a week. She has tried step aerobics, a dance class called Zumba, even weightlifting.

"I feel like I can do things; before, I was talking myself out of things," says Doria, of Rye, N.Y., who works with a personal trainer at the YMCA through a joint program with Livestrong for <u>cancer survivors</u>.

And, even with <u>rheumatoid arthritis</u>, Doria says, "I sleep better. I don't feel stressed. Two weeks ago, I went to my rheumatologist, and she lowered my medication. She said, 'I don't feel any inflammation in your body. Keep doing what you're doing.' "

Researchers have known for years that people who are active and trim are less likely to develop cancer. And survivors who exercise and keep a healthy weight are less likely to relapse.

Only recently, however, have scientists begun to untangle how staying active helps keep cancer at bay.



While exercise may not change the inner workings of a tumor cell, physical activity may change the cell's neighborhood - the surrounding tissue, blood vessels and <u>immune cells</u> - known as the "microenvironment," says Patricia Ganz, a <u>breast cancer</u> specialist at UCLA's Jonsson Comprehensive Cancer Center.

"It's a new frontier for cancer research," says Pamela Goodwin, professor of medicine at Mount Sinai Hospital, University of Toronto.

Healthy neighborhoods are as important to cells as they are to children, says William Li, president of the Boston-based Angiogenesis Foundation, which funds research in cancer and other diseases.

He compares a lone tumor cell to a "bad kid" living in a good neighborhood. Even an aspiring juvenile delinquent won't be able to cause much trouble if he's surrounded by watchful parents, neighbors and local police. Exercise helps improve the neighborhood, keeping cancers in check, Li says. Failing to exercise - and putting on a lot of weight - damages the neighborhood, making it easier for cancers to wreak havoc.

In particular, exercise helps to prevent chronic inflammation, a process that can fuel cancers by changing the neighborhood around a tumor cell. Exercise helps lower levels of both insulin and sex hormones, such as estrogen, which release growth factors that let tumor cells survive and spread, Li says. And, as Doria has learned, exercise also helps relieve psychological stress, which may further reduce inflammation, Ganz says.

But smoking, heavy drinking, being obese and eating processed foods all increase inflammation.

Doctors still have lots to learn, of course, and they're quick to note that many unknown factors may cause cancer.



"We don't want women with breast cancer to feel like they caused their breast cancer or that they caused it to come back," Goodwin says.

Still, doctors are discovering a growing number of ways the tumor environment can stop cancers before they start, or help them spread, Ganz says. Doctors already target the tumor neighborhood with drugs such as Avastin, which cut off a cancer's blood supply. Learning more about the microenvironment may provide new tools, such as drugs that curb inflammation to prevent cancer or treat it more effectively, Ganz says.

"The microenvironment, in some cases, may make the difference between a tiny little cancer that doesn't hurt you, and one that becomes a major danger to your life," says Lynn Matrisian, a cancer biologist at the Vanderbilt University School of Medicine in Nashville.

"It's an entirely new way of thinking about cancer," Li says. "The microenvironment actually protects us from cancer in ways we don't fully understand."

Scientists believe the body may be battling hidden cancers all the time.

With 10 trillion cells in the human body, "we are all developing microscopic cancer cells continuously," Li says.

Most of the time, these cancers never grow beyond the size of a pinprick, or grow too slowly to cause trouble; people who have them live long lives and die of other causes, Li says.

Autopsy studies, for example, show that most old men have cancer cells in their prostates, and most women have malignant cells in their breasts, even if they've never been diagnosed with cancer. And by age 70, virtually everyone has cancer cells in their thyroid glands, Li says.



Interestingly, while Japanese men also develop microscopic malignancies in the prostate, they are much less likely to be diagnosed with a noticeable prostate cancer, Ganz says. That suggests something about their lifestyle, such as their diet or physical activity, may keep their tumors under wraps.

There are many ways the <u>microenvironment</u> could drive cancer, says researcher Robert Weinberg, of the Whitehead Institute for Biomedical Research, and a biology professor at Massachusetts Institute of Technology.

For example, insulin and a related protein, called insulin-like growth factor, can interfere with a cancer cell's efforts to commit suicide, Weinberg says. A cell's internal security system often goes on alert when cancer genes become active, ordering the cell to self-destruct.

Insulin, however, can bind to the cancer cell and silence those suicide instructions. In this way, high circulating insulin levels can rescue tumor cells that were "otherwise perched precariously on the brink of death."

Malignant cells also may release chemicals that trick their neighbors into helping them.

"The tumor doesn't grow in a vacuum," Weinberg says. "It will recruit and co-opt normal cells that will then provide support to the cancer cell."

For example, cancer cells hijack the wound-healing process, Li says.

Normally, the body heals wounds through inflammation, which sends growth signals to the skin and blood vessels, to help them rebuild damaged tissue. All of these steps are critical to healing acute wounds, such as a gash on the leg, and the human species wouldn't have survived without them, Matrisian says.



The body also activates inflammation to battle cancer cells detected by the immune system.

Tumor cells manage to both evade and manipulate this response, however, Li says.

First, <u>cancer cells</u> mask themselves, to avoid being destroyed by the immune system's killer cells.

Second, tumors use the growth signals created during inflammation to feed themselves. Then, tumor cells emit more inflammatory signals, helping them grow even larger, attracting their own blood supply, which acts like a highway to bring tumors the supplies they require to live, Li says. "It's a vicious cycle of growth," Li says. "It's like wild fire out of control."

Chronic inflammation and infections contribute to a number of cancers, such as those of the colon, cervix, stomach, liver and esophagus.

People have lots of opportunities to halt that cycle, however.

Exercising, for example, sends out anti-inflammatory signals that make it harder for tumors to grow, Li says.

Breast cancer survivor Laurens Flanagan, 36, of Greenville, S.C., has made a number of lifestyle changes since having a mastectomy at age 29.

Today, Flanagan follows a "flexitarian" diet, eating lots of vegetables but little meat. She practices "hot" yoga, which helps her break a sweat. And she cycles long distances.

She knows her healthy lifestyle can't eliminate the risk of cancer. Two years ago, her breast cancer returned in the tissue under her arm, despite



her mastectomy and her workouts.

"If I can eat better and exercise and keep my weight down, I feel better," Flanagan says. "I've spent a lot of time thinking, 'What if my cancer comes back?' Now, I think, 'If my cancer comes back, I'll just beat it again.' "

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