Stress Hormones May Play New Role In Speeding Up Cancer Growth

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New research suggests that hormones produced during periods of stress may increase the growth rate of a particularly nasty kind of cancer.

The study showed that an increase in norepinephrine, a stress hormone, can stimulate tumor cells to produce two compounds. These compounds can break down the tissue around the tumor cells and allow the cells to more easily move into the bloodstream. From there, they can travel to another location in the body to form additional tumors, a process called metastasis.

The research also suggests the same hormone can also stimulate the tumor cells to release another compound that can aid in the growth of new blood vessels that feed cancer cells, hastening the growth and spread of the disease. The work was reported in the latest issue of the journal *Cancer Research*.

“This opens up an entirely new way of looking at stress and cancer that's different from current interpretations,” explained Ronald Glaser, a professor of molecular virology, immunology and medical genetics, and director of the Institute for Behavioral Medicine Research at Ohio State University .

Glaser and Eric Yang, a research scientist in the same institute, focused on the role of these three compounds. Two of them, both matrix metalloproteinases -- MMP-2 and MMP-9 -- play a role in breaking down the scaffolding that cells attach to in order to maintain their shape.

The third compound, vascular endothelial growth factor (VEGF), is important in the growth of new blood vessels into tumor cells.

Earlier work by researcher Anil Sood at the University of Texas had shown that the same stress hormones can stimulate ovarian tumor cells to produce these three compounds. The key to that discovery was that the two stress hormones – epinephrine and norepinephrine – would bind to places on the surface of ovarian cancer cells, called adrenergic receptors, and stimulate the release of MMP-2, MMP-9 and VEGF which might then foster cancer growth.

The Ohio State team wanted to see if the same occurred with other cancer cells.

They turned to cell lines Glaser had developed decades ago to study nasopharyngeal carcinoma (NPC), a serious, incurable head and neck cancer that occurs most frequently among people of Chinese descent.

They treated Glaser's cell line with norepinephrine and, as predicted, the cells all produced MMP-2, MMP-9 and VEGF. This showed that the receptors for this hormone were present on cells in Glaser's cell line, but that might have been just a laboratory aberration in the tissue cultures.

“We needed to see how relevant this finding was to what happened with actual tumors,” he said. Glaser asked colleagues for samples of actual NPC tumors to look for the presence of similar receptors. They studied tumor samples which included different types of NPC tumors. All had the sought-after receptors.

“From this we can say that there is likelihood that all NPC tumors will have these receptors as well,” he said.

“MMP-2 and MMP-9 contribute to the aggressiveness of these tumors,”

Yang said. “It isn't clear exactly how they are operating but they may work with VEGF to facilitate blood vessel growth in new tumors so that they can grow.”

The target adrenergic receptors for these hormones are well-known to clinicians dealing with high-blood-pressure patients. Typically, such patients are given a class of drugs known as beta-blockers which lead to a lowering of blood pressure levels.

Glaser and Yang wanted to see how these same drugs affected these tumor cells. They added propanol, a beta-blocker, to the tumor cells and then exposed them to both norepinepherine and epinephrine. With the drug present, the levels of MMP-2, MMP-9 and VEGF didn't increase.

“This suggests a new approach to possibly fight some cancers – the prescribing of beta-blocker-type drugs that would block these receptors and perhaps slow the progression of the disease,” Glaser said.

“Using this approach may not cure this cancer but perhaps we could slow down its growth, making the tumor more sensitive to anti-cancer therapy, and therefore extending the patient's lifespan and improve their quality of life.”

Working along with Yang and Glaser were Min Chen, Tim Eubank, Clay Marsh, Scott Jewell, Nicholas Flavahan, Carl Morrison, Peir-En Yeh and Stanley Lemeshow, all of Ohio State, and Anil Sood and Yang Li, both of the M.D. Anderson Cancer Center at the University of Texas.

Source: Ohio State University