Prostate cancer cells thrive on stress

January 25 2013

Not surprisingly, a cancer diagnosis creates stress. And patients with prostate cancer show higher levels of anxiety compared to other cancer patients.

A new study by researchers at Wake Forest Baptist Medical Center indicates that stress is not just an emotional side effect of the diagnosis; it also can reduce the effectiveness of prostate cancer drugs and accelerate the development of prostate cancer.

The findings are published in the February issue of the *Journal of Clinical Investigation*.

The Wake Forest Baptist team, headed by George Kulik, D.V.M., Ph.D., associate professor of cancer biology, tested the effects of behavioral stress in two different mouse models of prostate cancer.

One model used mice that were implanted with human prostate cancer cells and treated with a drug that is currently in clinical trial for prostate cancer treatment. When the mice were kept calm and free of stress, the drug destroyed prostate cancer cells and inhibited tumor growth. However, when the mice were stressed, the cancer cells didn't die and the drug did not inhibit tumor growth.

In the second model, mice genetically modified to develop prostate cancer were used. When these mice were repeatedly stressed, the size of prostate tumors increased. When the mice were treated with bicalutamide, a drug currently used to treat prostate cancer, their prostate

tumors decreased in size. However, if mice were subjected to repeated stress, the prostate tumors didn't respond as well to the drug.

After analyzing the data, the Wake Forest Baptist researchers identified the cell signaling pathway by which epinephrine, a hormone also known as adrenaline, sets off the cellular chain reaction that controls cell death. Considering that prostate cancer diagnosis increases stress and anxiety levels, stress-induced activation of the signaling pathway that turns off the cell death process may lead to a vicious cycle of stress and cancer progression, Kulik said.

Yet in both models in which the mice were given beta-blocker, stress did not promote prostate tumor growth. Beta-blocker is a drug that inhibits the activation of anti-death signaling by epinephrine.

"Providing beta-blockers to prostate cancer patients who had increased epinephrine levels could improve the effectiveness of anti-cancer therapies," Kulik said. "Our findings could be used to indentify prostate cancer patients who will benefit from stress reduction or from pharmacological inhibition of stress-inducing signaling."

The researchers now plan to test the same signaling mechanism that was identified in mice to determine if it also works in the same way in human prostates, Kulik said.

"We are at the very beginning of understanding complex stress-cancer interactions with multifaceted responses to stress that affect cancer cells, tumor microenvironment, and the organism overall," he said. "We hope that components of this signaling pathway could be used as biomarkers to predict whether and how a given tumor will respond to stress and anti-stress therapies."

More information: Behavioral stress accelerates prostate cancer

development in mice, 2013;123(2):874–886. doi:10.1172/JCI63324

Why stress is BAD for cancer patients, 2013;123(2):558–560. doi:10.1172/JCI67887