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**News Release**

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## **Some Cancer Cells Mimic Stem Cells to Evade Chemotherapy**

*USU Scientist Announces New Findings*

**BETHESDA, Md.** — Anti-cancer treatments often effectively shrink the size of tumors, but some might have an opposite effect, actually expanding the small population of cancer stem cells believed to drive the disease, according to findings presented Sept. 19 by Vasyl Vasko, M.D., Ph.D., a scientist at the Uniformed Services University of the Health Sciences' (USU), Department of Pediatrics, at the American Association for Cancer Research's second International Conference on Molecular Diagnostics in Cancer Therapeutic Development.

"Our experiments suggest that some treatments could be producing more cancer stem cells that then are capable of metastasizing, because these cells are trying to find a way to survive the therapy," said Dr. Vasko.

"This may help explain why the expression of stem cell markers has been associated with resistance to chemotherapy and radiation treatments and poor outcome for patients with cancers including prostate, breast and lung cancers," Dr. Vasko said. "That tells us that understanding how to target these markers and these cells could prove useful in treating these cancers."

The cancer stem cell markers include Nanog and BMI1, both of which contribute to stem cells' defining ability to renew themselves and differentiate into different cell types, Dr. Vasko said. These same molecules are found in embryonic stem cells.

Researchers have recently debated the notion that some therapies are not capable of eradicating cancer because they do not target the cancer stem cells responsible for tumor development. To test this hypothesis, Dr. Vasko, along with scientists from the CRTRC Institute for Drug Development in San Antonio and from the Johns Hopkins University, set out to measure both stem cells markers and tumor volume before and after treatment in a mouse model.

They selected a rare form of cancer, mesenchymal chondrosarcoma (MCS), which has not been well described and for which there is no effective treatment. The researchers first determined that Nanog and BMI1 stem cell markers were more highly expressed in metastatic tumors compared to primary tumors. "This suggests that expression of the marker plays some role in development of metastasis," Dr. Vasko said.

*Learning to Care for Those in Harm's Way*

They then applied various therapies - from VEGF inhibitors such as Avastin to the proteasome inhibitor Velcade - in mice implanted with human MSC, and analyzed the effects on tumors. Some of the treatments seemed to work, because they led to a dramatic decrease in the size of the tumors, Dr. Vasko said. But analysis of stem cell expression before and after treatment revealed that even as some anti-cancer treatments shrank tumors, they increased expression of Nanog and BMI1. "These treatments were not enough to completely inhibit tumor growth, and the cancer stem cell markers were still present," Dr. Vasko said.

Use of the agents Velcade and Docetaxel led to the most significant increase in stem cell markers within the treated tumor, while ifosfamide and Avastin inhibited expression of the markers in this cancer subtype.

"We hypothesize that the tumor escapes from chemotherapy by induction of stem cell marker expression," he said. "The small number of cells that survive the treatment could then generate another tumor that metastasizes."

Dr. Vasko doesn't know how this happens, but theorizes that "dying cells could secrete a lot of factors that induce expression of stem cell markers in other cancer cells. I think they are trying to survive and they use a mechanism from their experience of embryonic life."

If scientists understood the pathways cancer stem cells use to survive treatment or increase their ranks, then therapeutic targets could be developed, Dr. Vasko said. Some novel therapies are already being tested against cancer stem cells, he added.

The Uniformed Services University of the Health Sciences is located on the grounds of the National Naval Medical Center and across from the National Institutes of Health (NIH) in Bethesda, Maryland. USU is the nation's federal school of medicine and graduate school of nursing. USU's nationally ranked military and civilian faculty conduct cutting edge research in the biomedical sciences and in areas specific to the DoD health care mission.

For more information, contact the Office of External Affairs at (301) 295-1219. *Source: American Association for Cancer Research*