Number of cancer stem cells might not predict outcome in HPV-related oral cancers

22 January 2014, by Amanda J. Harper

(Medical Xpress)—New research from The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) suggests that it may be the quality of cancer stem cells rather than their quantity that leads to better survival in certain patients with oral cancer.

The researchers investigated cancer stem cell numbers in oral cancers associated with human papillomavirus (HPV) and in oral cancers not associated with the virus. Typically, patients with HPV-positive oral cancer respond better to therapy and have a more promising prognosis than patients with HPV-negative tumors. The latter are usually associated with tobacco and alcohol use.

The OSUCCC – James team's findings, published in the journal *Cancer*, suggest that relying on the number of cancer stem cells in a tumor might inaccurately estimate the potential for the tumor's recurrence or progression.

"We show that high levels of cancer stem cells are not necessarily associated with a worse prognosis in head and neck cancer, a finding that could have far-reaching implications for patient care," says principal investigator Quintin Pan, PhD, associate professor of otolaryngology and scientist with the OSUCCC – James Experimental Therapeutics Program.

Head and neck cancer is the sixth most common cancer worldwide, with an estimated 600,000 cases diagnosed annually. Although the disease is often linked to alcohol and tobacco use, cancer-causing types of HPV are a major risk factor for the malignancy, and cases of HPV-associated oral cancers have tripled in the past 30 years.

Cancer stem cells make up only a small percent of the malignant cells within a tumor. When these cells divide, they can produce either more cancer stem cells or the nondividing malignant cells that constitute the bulk of a tumor.

Research has shown that cancer stem cells are highly resistant to chemotherapy and radiation and those cancer stem cells that survive treatment cause tumor recurrence. For these reasons, it is thought that tumors with high numbers of cancer stem cells are more likely to recur.

In this study, Pan and his OSUCCC – James collaborators hypothesized that patients with HPV-positive tumors had better outcomes because their tumors had fewer cancer stem cells than tumors with HPV-negative tumors. They discovered just the opposite, however.

Comparing numbers of cancer stem cells in human tumor samples and in oral-cancer cell lines, they found that the HPV-positive samples had 2.4 to 62.6 times more cancer stem cells than did the HPV-negative samples.

"Most cancer biologists would have expected tumors with high cancer stem cell numbers to be very difficult to cure because cancer stem cells are thought to convey resistance to conventional therapy," adds Ted Teknos, MD, study collaborator and director of head and neck cancer surgery at the OSUCCC – James.

"However, it may be that HPV-induced head and neck cancer is highly curable primarily because the stem cells are sensitive to therapy. It's not the presence or absence of stem cells that is important in cancer, but rather how well does your therapy eliminate them."

More information: "Elevated intrinsic cancer stem cell population in human papillomavirus-associated head and neck squamous cell carcinoma." Zhang M, Kumar B, Piao L, Xie X, Schmitt A, Arradaza N, Cippola M, Old M, Agrawal A, Ozer E, Schuller DE, Teknos TN, Pan Q. *Cancer*. 2013 Dec 30. DOI: 10.1002/cncr.28538.

[Epub ahead of print]

Provided by Ohio State University Medical Center