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Enzyme found to be a predictive marker of survival in head and neck cancer

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Most treatment for advanced head and neck cancer requires chemotherapy with a drug called cisplatin, an inorganic platinum agent that inhibits cell growth. A substantial number of patients do not respond well to this therapy, but oncologists are unable to prescribe alternative agents because they don't know which patients will respond to platinum therapy and which won't. However, new research from Fox Chase Cancer Center suggests that levels of ERCC1--an enzyme that helps repair cisplatin-related DNA damage--offer a predictive marker of survival in squamous carcinoma of the head and neck. The findings might eventually help guide treatment selection for patients with recurrent and metastatic disease.

Ranee Mehra, M.D., a medical oncologist at Fox Chase Cancer Center and principal investigator on the study, will present her findings at the 2010 annual meeting of the American Association for Cancer Research.

"This retrospective analysis of tumor tissue looked at levels of ERCC1 in patients who did and did not respond to adjuvant therapy, which includes radiotherapy with or without platinum therapy," says Mehra. "The results open avenues to testing other agents that could be more effective in specific patients and have a better side-effects profile."

Mehra and her colleagues created tissue microarrays from cancer tumors of the head and neck taken from 109 patients treated at Fox Chase. Based on tissue from 76 patients who received adjuvant radiation or platinum-based chemoradiation, researchers found that low ERCC1

levels were associated with increased survival from the adjuvant therapy. In the 33 patients treated with surgery alone, there was no association with ERCC1 status and survival.

"This is definitely a step toward personalized medicine," says Mehra. "When we saw there was a survival difference in patients who received the treatment based on this biomarker, we were very excited. These findings provide support for the concept that personalized medicine could be possible in a practical way in these cancers."

According to Mehra, the retrospective analysis of tissue from 109 patients with squamous carcinoma of the head and neck could not have been conducted without Fox Chase's extensive tissue bio-repository. "To have enough samples with annotated clinical data to do this kind of study is not something every center has," she says.

Funding for the research was provided by Fox Chase's Keystone Program in Head and Neck Cancer, directed by Barbara Burtness, M.D.; Drew Ridge, M.D., Ph.D.; and Erica Golemis, Ph.D. The Fox Chase Keystone Programs for Collaborative Discovery, launched in February 2008, are a suite of innovative team-based cancer research initiatives organized by a group of scientists, clinicians, and other research professionals seeking to integrate and focus their joined expertise on a significant question in cancer.

"As an investigator, I see a great opportunity in these results," says Mehra. "While the data are retrospective and preliminary, our goal now will be to validate this assay, reproduce the results with tumors from a different source, and design a prospective study to test a patient's tumor and treat accordingly based on ERCC1 level."

The research efforts of the members of the Keystone Program in Head and Neck Cancer seek to maximize understanding and override the

sources of resistance to therapy. Many of the physicians and scientists in this program work on specific proteins identified as highly relevant to head and neck cancer. While surgery is an effective means for treating some head and neck cancers, it is fraught with drawbacks and often not an option for late-stage patients, who require radiation coupled with drugs and other systemically-acting agents. Fox Chase's Keystone Program is focused on reducing the overall incidence of head and neck cancers and devising treatment strategies based on specific molecular targets such as ERCC1.

Provided by Fox Chase Cancer Center