Enzyme is Possible New Therapy Target for Head and Neck Cancer

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(PhysOrg.com) -- Researchers at Winship Cancer Institute, Emory University, have demonstrated that the enzyme RSK2 promotes tumor invasion and metastasis in head and neck cancers.

The drug fmk, developed at the University of California, San Francisco, already has been identified as capable of specifically targeting RSK2 in myeloma cells. This suggests the possibility that fmk or a related compound could be used to treat head and neck cancer.

The results of research with RSK2 were published online March 15 in the Journal of Clinical Investigation.

One of the top ten deadliest forms of cancer, head and neck cancers come from the soft tissues of the nose and throat, and the majority are linked to tobacco use. It is estimated that more than 35,000 new cases appeared in the United States in 2009. The five-year survival rate has not improved in more than 30 years.

First author Sumin Kang, PhD, while working with Jing Chen, PhD, associate professor of hematology and medical oncology at Emory University School of Medicine, previously had shown RSK2's importance for proliferation in multiple myeloma cells.

Kang, now an Emory assistant professor of hematology and medical oncology, has established her own laboratory at Winship to investigate RSK2 as an anti-cancer target. Kang and Chen's work also has found that

RSK2 is activated through a family of genes called Src tyrosine kinases, which often are put into overdrive by cancer-causing mutations.

"This finding is important because we have now shown that RSK2's critical role is not limited to hematopoetic cells (blood cells)," Kang says. "In addition, this is the first connection between RSK2 signals and tumor metastasis and invasion."

Examining dozens of biopsies from patients' tumors by staining them with antibodies, Kang and colleagues observed that the RSK2 enzyme was increasingly turned on as tumors became more invasive. For tumors that had metastasized to the lymph nodes, 62 percent had RSK2 turned on, compared to a quarter of head and neck tumors that had not yet metastasized. The authors also found that introducing RSK2 into human head and neck tumors could drive invasion and metastasis in cell culture, and that interfering with RSK2 impaired invasion and metastasis in a model where human tumors are implanted into mice. It appears that RSK2 changes properties of tumor cells' internal skeletons, but it also turns on other genes, whose function Kang is probing now.

"The role of RSK2 depends on the cancer type," Kang says. "With head and neck cancers, inhibiting RSK2 can block invasion and metastasis but it can't shrink the tumor."

This contrasts with myeloma, where RSK2 is required for proliferation, she adds. For head and neck cancer, it may be best to combine a RSK2 inhibitor such as fmk with another anti-proliferative drug, a possibility now under investigation.

"This study has provided clear evidence to support the involvement of RSK2 in human head and neck cancer metastasis," says co-author Georgia Chen, PhD, Emory associate professor of hematology and medical oncology. "Using patients' tissue samples is essential to

determining clinical impact, and we are glad that the Head and Neck SPORE Histology Core has facilitated this and other relevant studies."

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