New study identifies novel role for PEA-15 protein in cancer growth

Surprising discovery finds protein known to slow ovarian cancer can also enhance cancer cell proliferation

HONOLULU – A new study from the University of Hawaii Cancer Center reveals that PEA-15, a protein previously shown to slow ovarian tumor growth and metastasis, can alternatively enhance tumor formation in kidney cells carrying a mutation in a cancer-promoting gene called H-Ras.

The H-Ras oncogene is mutated in many human malignancies, and previous reports have shown the ability of H-Ras to contribute to the development, proliferation and metastasis of these tumors. Conversely, PEA-15 had been reported to inhibit tumor cell proliferation and metastasis by opposing H-Ras signals. In ovarian and breast cancer, PEA-15 is proposed to have promising therapeutic potential and in ovarian cancer PEA-15 has shown promise as a marker of prolonged patient survival.

This new study is the first finding of a pro-cancer effect of PEA-15 on proliferation and as such suggests caution in pursuing the use of PEA-15 as an anti-cancer therapeutic. The study results were published online today in the journal Oncogene.

“Our findings reveal a surprising mechanism by which PEA-15 can enhance H-Ras driven transformation of cells, rather than stop it,” said Joe W. Ramos, Ph.D., associate professor at the University of Hawaii Cancer Center and co-director of its Cancer Biology Program. “We showed that in a common scenario in which a cell contains a Ras mutation, PEA-15 can accelerate the rate of tumor formation both in vitro and in vivo,” he added.

In contrast to reports suggesting a tumor-suppressor function of PEA-15, Ramos said the discovery confirms that PEA 15 expression can also trigger tumor growth. “What we now know is that PEA-15 can either enhance or impair the formation of tumors depending on the signaling pathways active in a specific tumor cell.”

“As with most cancers, an interplay of factors determines the fate of a patient,” noted Florian Sulzmaier, a researcher at the UH Cancer Center and first author of the newly published study. “PEA-15 might still be worth considering for treatment of certain cancers. However, care should be taken in tumor types that carry Ras mutations that could change the outcome of a therapy.”

The article, PEA-15 potentiates H-Ras-mediated epithelial cell transformation through phospholipase, appeared in today’s online edition of Oncogene. Ramos’ colleagues included researchers from the University of Hawaii, the Cancer Institute of New Jersey and the Academic Medical Center, University of Amsterdam, The
Netherlands.

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