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

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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."

More information: The article, PEA-15 potentiates H-Ras-mediated epithelial cell transformation through phospholipase , appeared in today's online edition of *Oncogene*.

Provided by University of Hawaii Cancer Center