Tiny genetic variation can predict ovarian cancer outcome

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Yale Cancer Center researchers have shown that a tiny genetic variation predicts chances of survival and response to treatment for patients with ovarian cancer.

The findings, published in the journal *Oncogene*, provide new insights into the biology of a new class of [cancer marker](#) and suggest a genetic test may help guide the treatment of women with ovarian cancer.

"This gives us a way to identify which women are at highest risk for resistance to platinum chemotherapy, the standard treatment for ovarian cancer, and helps identify ovarian cancer patients with the worst outcomes," said Joanne Weidhaas, associate professor of therapeutic radiology and senior author of the study. "There just aren't many inherited gene variants than can do that."

Women who possess the biomarker identified by the Yale team – a variant of the well-known KRAS oncogene – are three times more resistant to standard platinum chemotherapy than women without the variant. Also, post-menopausal women with the variant are significantly more likely to die from ovarian cancer. About 12-15 percent of Caucasians and 6 percent of African-Americans are born with the variant of the gene, which helps regulate destruction of damaged cells. This variant is found in up to 25% of newly diagnosed ovarian cancer patients.

Although good alternatives to [chemotherapy](#) are not yet available for

women with ovarian cancer and this variant, several drugs in development which target the KRAS gene and associated pathways have shown great promise, Weidhaas said.

Weidhaas is a co-founder of a company that has licensed intellectual property from Yale that has developed a diagnostic test based on the Kras-variant.

The [biomarker](#) intrigues scientists because it is a functional variant in an area of DNA that does not code for proteins. Instead this variant disrupts how a microRNA controls gene expression.

"This is a new paradigm," Weidhaas said.

Yale researchers have also found this microRNA variant of the KRAS gene is associated with an increased risk of developing breast cancer and lung cancer. Other researchers have found associations with poor outcome in colon as well as head and neck cancers.

In laboratory tests, researchers blocked the variant and significantly reduced growth of [ovarian cancer](#) cells. This suggests targeting the variant site may someday help treat cancer in these patients.

Provided by Yale University