

BRCA1 mutations in breast and ovarian cancer can predict treatment resistance

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Mutations in the BRCA1 gene are one of the most common risk factors for breast and ovarian cancers. Although tumors that harbor BRCA1 mutations initially respond well to cancer treatments, many tumors eventually become less responsive.

This month, two studies in the *JCI* investigated the mechanisms underlying the <u>treatment resistance</u> associated with some BRCA1 mutations, and the findings provide information that may help predict which treatments will be effective in women with breast and <u>ovarian cancer</u>.

A team led by Jos Jonkers at the Netherlands Cancer Institute discovered that a mouse harboring an analog of the cancer-associated human BRCA1 mutation, BRCA1184delAG, expresses a BRCA1 protein that is missing a structural component called a RING domain. Loss of the RING domain predicted poor treatment responses in both mouse and human mammary tumors.

Neil Johnson's lab at the Fox Chase Cancer Center examined treatment resistance in <u>breast cancer cells</u> expressing the same BRCA1185delAG mutation and determined that the RING-deficient BRCA1 protein was also responsible for loss of sensitivity to certain types of cancer treatments.

These findings identify specific BRCA1 mutations that are more likely to develop therapy resistance, which may lead to more accurate predictions and personalized treatments for breast and ovarian cancers.

More information: Rinske Drost et al, BRCA1185delAG tumors may acquire therapy resistance through expression of RING-less BRCA1, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI70196

Yifan Wang et al. RING domain-deficient BRCA1

promotes PARP inhibitor and platinum resistance, Journal of Clinical Investigation (2016). DOI: 10.1172/JCI87033

Simon N. Powell. BRCA1 loses the ring but lords over resistance, *Journal of Clinical Investigation* (2016). DOI: 10.1172/JCI89209

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