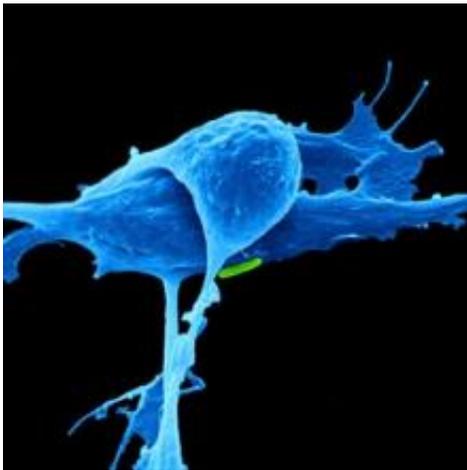


Breast, ovarian cancer risk may have association with sense of smell

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The association between menstrual cycle activity and breast and ovarian cancer risk may have an unexpected intermediary - odors.

Keck Medicine of USC researchers have discovered for the first time that the estrous cycle (the equivalent of human [menstrual cycle](#)) in [mice](#) carrying a mutation known to cause familial predisposition to breast and [ovarian cancer](#) in humans is more readily stimulated by scent than in normal mice. Even more surprising was the finding that the ovary, independently of the nose, mediated the olfactory signals.

"This research indicates that a better sense of smell may contribute to the

elevated [cancer risk](#) of women with BRCA1 mutations," said corresponding author Louis Dubeau, professor of pathology and medical director of molecular pathology, USC Norris Comprehensive Cancer Center. "We found that the presence of the mutation in the ovary mediated a stronger response to scent, implying that the mutation may influence the menstrual cycle, which in turn is an established risk factor for breast and ovarian cancer."

The research will be published Oct. 21, 2015 in the peer-reviewed journal *PLOS ONE*.

Springing off the observation that menstrual cycles often synchronize between female college roommates, indicating some sort of communication with environmental signals, the scientists compared female mice genetically engineered to carry the BRCA1 mutation to normal, or wild-type mice. They isolated the females from males, causing estrous to pause in the females. When the females were exposed to male bedding, those with the BRCA1 mutation restarted estrous faster than the wild-type mice.

To confirm that the results were mediated by the ovary independently of the nose, the scientists transplanted ovaries from mice with the BRCA1 mutation into wild-type mice and also transplanted ovaries from normal mice into the genetically engineered mice carrying the mutation. The wild-type mice with the BRCA1 mutation present in their ovarian transplants responded more quickly when introduced to the male scent than mutant mice with wild-type ovarian transplants carrying the mutation in all tissues except the ovary.

"We've known for a long time that smell receptors are expressed in all kinds of tissues, but we know very little about what these receptors do outside of the nose," Dubeau said. "Only certain tissues in the breast and reproductive organs have an elevated cancer risk in women who carry a

BRCA1 mutation. We found that BRCA1 [mutations](#) do not only influence these tissues directly, but also indirectly by changing how they communicate with other cells. This research is one of several examples shown in my laboratory where BRCA1 controls how different cells communicate from a distance. If we can understand how disruption in such communications leads to elevated cancer risk in BRCA1 mutation carriers, we can develop therapies to control these cancers, including perhaps therapies based on smell."

More information: Liu Y, Pike MC, Wu N, Lin YG, Mucowski S, Punj V, et al. (2015) Brca1 Mutations Enhance Mouse Reproductive Functions by Increasing Responsiveness to Male-Derived Scent. *PLOS ONE* 10(10): e0139013. [DOI: 10.1371/journal.pone.0139013](https://doi.org/10.1371/journal.pone.0139013)

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