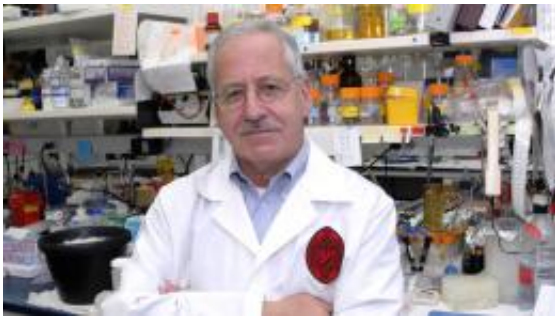


Cancer predisposition from genetic variation shows strong gender bias

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Peter Stambrook, PhD

(PhysOrg.com) -- Cancer predisposition resulting from the presence of a specific gene variant shows a strong gender bias, researchers at the University of Cincinnati (UC) have demonstrated.

In addition, the research indicates that the risk for development of cancer in individuals harboring the [gene variant](#) can be further increased as a result of environmental exposure.

Peter Stambrook, PhD, a professor in the department of [molecular genetics](#), biochemistry and microbiology, and colleagues report their findings this week in [Proceedings of the National Academy of Sciences](#) (PNAS). Co-authors include researchers from Wright State University and the Laboratory for Health Protection Research, National Institute of Public Health and the Environment, the Netherlands.

Stambrook says the gene CHEK2 is part of a [DNA damage](#) response pathway that can have an impact on whether or not cancers develop. A CHEK2 variant, CHEK2*1100delC, is associated with increased risk of cancer.

"Women who carry this particular gene variant are predisposed to developing breast or [ovarian cancer](#)," says Stambrook, "while men have a higher risk of developing prostate cancer."

Stambrook's team has produced a mouse model in which the CHEK2 gene was replaced by the variant and found that the overwhelming majority of mice that developed cancer were female—about 80 percent, as opposed to slightly more than 15 percent for males. This contrasts sharply with the incidence of cancer in wild-type mice (those with the normal CHEK2 gene), in which male and female mice developed cancer to about the same extent but at a much lower frequency.

Stambrook says his team will be exploring possible reasons behind the difference, looking at hormonal involvement and possible interactions between the gene variant and estrogen receptors or estrogen itself.

By using a known carcinogen, dimethyl benzanthrane, the researchers also determined that mice that harbor the variant are more susceptible to an environmental challenge than those that don't. The compound was administered orally to female mice.

"When they delivered the compound, the lifespan of the mice was reduced significantly—they developed breast cancer as well as other types of cancers," Stambrook says. "In addition, the mice that harbored this variant were more susceptible—in other words, they developed tumors more quickly than wild-type mice."

Stambrook says that by learning more about the signaling pathway of the

CHEK2 gene, researchers can explore ways to "rescue" it and identify potential therapeutic targets.

"It's an interesting gene," says Stambrook, "and there are a lot of interesting directions that this finding will take us."

Source: University of Cincinnati ([news](#) : [web](#))

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