DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

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Gene Variant Increases Breast Cancer Risk

An international research consortium under the leadership of scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) has shown that a common gene variant increases the risk of developing breast cancer.

In roughly five to ten percent of breast cancer cases there is a family history of breast cancer– i.e., hereditary and, thus, genetic factors play a role here. Alterations in the genes known as BRCAI and BRCAII are a major cause of familial breast cancer – these are responsible for roughly 25 percent of such cases.

“In Germany, 75 percent of familial breast cancers are not attributable to mutations in BRCAI and BRCAII. We assume that these cancers are caused in part by rare mutations and in part by unfavorable combinations of risk variants in various genes, which, on their own, have only little effect. Only very few of these have been identified so far – we are searching for the other ones,” said Associate Professor Dr. Barbara Burwinkel of the DKFZ.

Members of the AKAP protein family are responsible for transmitting important signals in a cell. Scientists have suspected these proteins to be involved in cancer development. A large international study headed by Barbara Burwinkel has now delivered proof that this is true for breast cancer.

In collaboration with the German Consortium for Familial Breast and Ovarian Cancers, the research team studied six gene variants in the AKAP family. Two of these, both located on the AKAP9 gene, have indeed been found to be associated with an increased breast cancer risk. Since the two gene variants are always inherited together, further investigations will have to determine whether one of these or both variants in combination are responsible for the risk effect. This finding was confirmed by a large international study in collaboration with researchers from Germany, the United Kingdom, the U.S.A. and Australia. The study included 9,523 breast cancer patients including 2,795 familial breast cancer cases and almost 14,000 healthy women.

For women carrying the two variants in both copies of their AKAP9 genes, the risk of developing breast cancer in the course of their lifetimes is elevated by 17 percent. In women from breast cancer families, this effect is even more substantial: their risk is increased by 27 percent. If only one of the AKAP9 copies is affected, the breast cancer risk is only slightly elevated by approximately eight percent or twelve percent for women from breast cancer families, respectively.

“This shows that the AKAP9 variants have much less effect on breast cancer risk than, for example, BRCA mutations. On the other hand, these variants are much more common in the population. We also do not know yet which control cycles of the cell metabolism are affected and how this can lead to cancer,” said Barbara Burwinkel to qualify the finding. “But there is already evidence suggesting that the two variants also increase the risk of developing lung cancer or colon cancer.”

Bernd Frank, Miriam Wiestler, Silke Kropp, Kari Hemminki, Amanda B. Spurdle, Christian Sutter, Barbara Wappenschmidt, Xiaoqing Chen, Jonathan Beesley, John L. Hopper, Australian Breast Cancer Family Study Investigators, Alfons Meindl, Marion Kiechle, Tracy

Slange , Peter Bugert, Rita K. Schmutzler, Claus R. Bartram, Dieter Flesch-Jany , Elke Mutschelknauss, Katie Ashton, Ramona Salazar, Emily Webb, Ute Hamann, Hiltrud Brauch, Christina Justenhove , Yon-Dschun Ko, Thomas Brüning, Isabel dos Santos Silva, Nichola Johnson, Paul P. D. Pharoah, Alison M. Dunning, Karen A. Pooley, Jenny Chang-Claude, Douglas F. Easton, Julian Peto, Richard Houlston, Gene Environment Interaction and Breast Cancer in Germany Group, Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer Investigators, Australian Ovarian Cancer Study Management Group, Georgia, Chenevix-Trench, Olivia Fletcher and Barbara Burwinkel: Association of a Common *AKAP9* Variant With Breast Cancer Risk: A Collaborative Analysis. Journal of the National Cancer Institute, vol. 100, page 1, 2008

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).