

### **“Breast Cancer Genes” BRCA1 and BRCA2: For Which Cancer Cases Are They Responsible?**

Spelling mistakes – mutations – in the genes BRCA1 and BRCA2 were identified as risk factors for breast cancer some years ago. To find out whether and to what extent these mutations play a role in other cancers, epidemiologists at the German Cancer Research Center (DKFZ) have now conducted a study\* related to the whole population of Sweden. They found out that risk families are affected by an increased incidence not only of ovarian cancer, which was already known, but also of pancreatic, stomach and prostate cancers. What came as a real surprise for the scientists was that most cases of ovarian cancer in risk families are not associated with BRCA mutations.

The basis of the large-scale investigation conducted by Dr. Justo Lorenzo Bermejo and Professor Kari Hemminki is the Swedish Family Cancer Register. This is a collection of tumor diagnosis data of all Swedish citizens born after 1931. Among the 10.2 million entries the Heidelberg scientists concentrated on 948,000 families registered at least in the third succeeding generation. To this group they applied the criteria used by the German BRCA Consortium to define high-risk groups who are advised to take a gene test for BRCA1 and BRCA2 mutations (see below for criteria).

The incidence of certain cancers in risk families was compared with the average disease rate among the Swedish population. The investigators found specific increased incidences of cancer in the different risk groups: In families with two cases of breast cancer diagnosed before the age of 50, the incidences of ovarian cancer (6.16 percent in the risk group vs. 1.76 percent in the normal population) and early age pancreatic cancer (0.16 percent vs. 0.03 percent) were found to be significantly increased. When relatives were affected by breast and ovarian cancer, the incidences of ovarian cancer (68.9 vs. 1.76 Prozent) and stomach cancer (1.88 vs. 0.92 percent) among family members were above average. In families with a case of male breast cancer, there was an increased incidence of early age prostate cancer (0,27 vs. 0,02 percent).

Although these correlations already became apparent in earlier investigations, the new population-related study with its large number of cases is the first to facilitate exact risk assessment for members of affected families.

The BRCA Consortium has assessed the probabilities in the different risk groups of actually carrying a mutation in the BRCA1 or BRCA2 gene, respectively. Also known is the risk for mutation carriers of actually developing cancer. Thus, it is possible to calculate the percentage of cases related to BRCA gene alterations for each type of cancer.

However, in their study the Heidelberg epidemiologists have found incidences that were considerably higher than the calculated numbers in many cases. An example is ovarian cancer: Women in one of the risk groups were affected four times more frequently than could be explained merely by the presence of BRCA gene alterations.

“This is a very important result of our study. It proves that in these families there are additional genetic factors involved in cancer development that we have not yet discovered”, Dr. Justo Lorenzo said. “It also shows that negative results of BRCA gene testing for members of risk families does not justify to sound the all clear.”

At the same time, epidemiologist Lorenzo comments the results as follows: “Although members of risk families are affected by some cancers slightly more frequently, the individual risk remains low. Our main concern continues to be the highly increased risk of breast and ovarian cancers.”

\*Justo Lorenzo Bermejo and Kari Hemminki: Risk of cancer at sites other than the breast in Swedish families eligible for BRCA1 and BRCA2 mutation testing.

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Examples of criteria indicating an increased risk of BRCA1 or BRCA2 mutations:

- \* At least two cases of breast cancer diagnosed under the age of 50;
- \* A case of male breast cancer;
- \* A separate case of breast cancer and of ovarian cancer;
- \* Two cases of breast cancer including one diagnosed under the age of 50.

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.).

This press release is available at [www.dkfz.de/pressemitteilungen](http://www.dkfz.de/pressemitteilungen)

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