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# Danish researchers find new breast cancer gene in young people

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Over the past 20 years, our knowledge of hereditary diseases has taken a quantum leap, and several hereditary gene variants have been found that may predispose to the development of cancer. We have known for a long time that mutations in human BRCA1 and BRCA2 genes may lead to the development of cancer, especially in the ovaries and breast. But

researchers around the world also know that there are still a great number of variants in our hereditary systems that may lead to life-threatening diseases such as breast cancer.

A research team from the University of Copenhagen, BRIC and Rigshospitalet has embarked on a new chapter in the research and is now adding important knowledge to our understanding of hereditary genes and the biological mechanisms that underlie the development of breast cancer. They have located the RBBP8 gene and described its functions as a crucial factor in the development of breast cancer in a group of very young women.

"We have studied the biological significance of RBBP8 gene variants in a group of young women with breast cancer. It is a patient group where we assume that genetic factors play a role. We have now shown that RBBP8 normally protects the cells against damage to the genome and that a reduced RBBP8 function may, conversely, lead to cancer," says Research Director Claus Storgaard Sørensen, BRIC, the University of Copenhagen.

The RBBP8 gene which does the coding for the CtIP protein, has not previously been associated with the development of hereditary breast cancer. In the new study, just published in *The Journal of Clinical Investigation*, it is the conclusion that these are rare variants and mutations.

## Specific Patient is the Starting Point

The study is based on a specific patient, but the group has subsequently studied the RBBP8 gene in both Danish patients and in larger international cohorts.

The researchers screened 129 young Danish patients who had been

diagnosed with breast cancer at a young age, under 35, and subsequently, we performed extensive gene sequencing of a larger group of 1,092 patients with breast cancer or other cancers that did not have mutations in the BRCA1 or BRCA2 genes.

The mutations in RBBP8 may explain why some very young women develop breast cancer. The basic scientific studies of the protein show that RBBP8 plays a crucial role in protecting and regulating the human body's DNA because it repairs damage to the chromosomes.

"Our collaboration has created rapid progress because we have the opportunity to combine clinical data and basic scientific methods. This helps to improve our understanding of the complex mechanisms and rare gene variants that present an increased risk of developing breast cancer and other cancers," says Clinical Professor Finn Cilius Nielsen, who on a daily basis is the Head of Genomic Medicine at Rigshospitalet and National Genome Center East in Glostrup.

## Further Studies are Needed

The researchers hope that this study will form the basis for discoveries of more genes that may predispose to the development of cancer and, in the long term, offer studies that may help the early detection, diagnosis and treatment of cancer patients. Further studies, including family studies and international studies, are needed to more accurately map the risk of mutations.

The research is supported by the Lundbeck Foundation, the Danish Cancer Society and the Novo Nordisk Foundation. The project has lasted for five years—with participation by the Center for Genomic Medicine and the Department of Oncology at Rigshospitalet, the University of Copenhagen, BRIC, and with the help of the Danish Cancer Biobank and international collaboration partners.

**More information:** Reihaneh Zarrizi et al, Germline RBBP8 variants associated with early-onset breast cancer compromise replication fork stability, *Journal of Clinical Investigation* (2020). DOI: 10.1172/JCI127521