

## **Search for new genomic changes associated with high risk of cancer**

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Hereditary cancer is estimated to account for up to 10% of the worldwide cancer burden and breast cancer is one of the top cancers with a large proportion (10-15%) of hereditary cases. Many cancer-predisposing genes are involved in the balance between cell growth and cell death or in maintaining genome integrity. There are about 500 known cancer-causing genes with reported mutations in somatic and/or germline DNA. Of those genes about 100 have been shown to be mutated in germline DNA of human and could be inherited from parents to their children and predispose them to hereditary cancers. Among genes which are associated with inherited cancers and BRCA1, BRCA2, CHEK2, PALB2 and NBS1. Identification of predisposing mutations enables specific management including prevention, early detection and treatment. Cancers that arise in mutation carriers usually have specific clinical characteristics, prognosis and sensitivity to treatment.

With the advent of deep sequencing of DNA and whole-exome sequencing, it is now possible to apply a powerful new technology to identify new mutations associated with a high risk of cancer. Now, we studied (grant funded by Narodowe Centrum Nauki, registration project number 2015/17/B/NZ5/02543) a large series of women with breast cancer from families with clustering of breast cancer (families with hereditary breast cancer – HBC) using TaqMan-PCR and multiplex-PCR (715 cases) and using whole exome sequencing (617 cases). This study led to identification of spectrum of breast cancer predisposing mutations in a large group of Polish families with HBC.