

Constitutional methylation of *BRCA1* gene and breast cancer risk

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Methylation of CpG islands in promoter region of genes is an epigenetic modification that causes silencing of genes and might be associated with cancer risk if it is present in peripheral blood. It has been suggested that constitutional methylation of *BRCA1* promoter correlates with breast cancer risk, especially with triple-negative tumors.

In this study we evaluated an association of *BRCA1* methylation in peripheral blood with breast cancer risk and assessed correlation with clinical features of tumors. We examined three groups of women: 504 triple-negative breast cancer cases, 438 non-TNBC cases and 500 healthy controls. All women were negative for 13 common Polish *BRCA1* germline mutations. Moreover, 274 FFPE tumor tissues were tested to estimate association between constitutional and somatic *BRCA1* promoter methylation. Methylation status was assessed using methylation-sensitive high-resolution melting (MS-HRM). Additionally, we genotyped variant c.-107A>T in *BRCA1* gene to assess its potential correlation with *BRCA1* methylation. The results show that *BRCA1* methylation detected in peripheral blood is significantly associated with the risk of TNBC (OR 5.25, p<0.001) and correlates with methylation in paired tumors. The variant c.-107A>T was not detected in tested women from Polish population.

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