We read with great interest the paper by Akbari and colleagues [1] in a recent issue of Breast Cancer Research. The authors reported on the absence of RAD51C mutations in 454 patients with BRCA1/2-negative familial breast cancer/ovarian cancer (BC/OC). In the initial report by Meindl and colleagues [2], RAD51C mutations were identified in 6 out of 480 patients with BRCA1/2-negative familial BC/OC. Interestingly, on the basis of histopathologic features, including intermediate grade (G2), estrogen receptor-positive (ER+), progesterone receptor-positive (PR+), and HER2-negative (HER2−) expression, RAD51C-associated BCs were found to be similar to BRCA2-associated BCs [2]. BRCA2 is known to play a significant role in male BC (MBC); however, no occurrence of MBC was observed in the six RAD51C families described [2].

To investigate the role of RAD51C in MBC, we screened for RAD51C mutations in 97 MBC patients selected from our population-based series of 126 cases because they were previously found negative for BRCA1/2, CHEK2, PALB2, and BRIP1 mutations [3,4]. Notably, 25.8% of cases showed a positive first-degree family history of BC or OC or both. The majority of MBCs were invasive ductal carcinomas (74.5%), G2 (53.5%), ER+ (90.7%), PR+ (82.6%), or HER2− (85.4%). Overall, 66% of the MBCs showed an ER+/PR+/HER2− phenotype. All patients provided informed consent to the study. We carried out mutation screening of the nine exons and intron/exon boundaries of RAD51C by high resolution melting (HRM) analysis, a rapid closed-tube mutation scanning method with high sensitivity and specificity. Cases displaying abnormal profiles were evaluated by direct sequencing. Primers are available upon request.

We found no truncating RAD51C mutations. We identified a novel intronic variant, IVS3 c.738-16G>T, in 1 out of 97 MBCs (1%). By in silico analysis, performed with Splice Site Prediction (Berkeley Drosophila Genome Project, Lawrence Berkeley National Laboratory, Berkeley, CA, USA) and NetGene 2 Server software (Center for Biological Sequence Analysis, Technical University of Denmark, Lyngby, Denmark), the IVS3 c.738-16G>T variant is predicted not to affect splicing. This variant was also identified in 2 out of 173 (1.2%) population controls examined. We also found a neutral polymorphic intronic variant, IVS6 c.904+34T>C (rs28363318), in 16 out of 97 (16.5%) MBCs.

Overall, our results, which are based on a relatively large MBC series, are consistent with the findings by Akbari and colleagues [1] and with data on 92 patients with hereditary gynecological cancer in which no deleterious RAD51C mutations were identified [5] and would suggest that the impact of RAD51C mutations on BC predisposition might be more limited than initially reported. In conclusion, we found no evidence that RAD51C mutations may contribute to MBC susceptibility. Further studies on larger MBC series are needed to confirm our findings.

**Abbreviations**

BC, breast cancer; ER, estrogen receptor; G2, intermediate grade; MBC, male breast cancer; OC, ovarian cancer; PR, progesterone receptor.

**Competing interests**

The authors declare that they have no competing interests.

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