Absence of constitutional \( H2AX \) gene mutations in 101 hereditary breast cancer families

A N A Monteiro, S Zhang, C M Phelan, S A Narod

METHODS AND RESULTS

Each of these patients was from a family with three or more cases of breast cancer. These families were selected because they have previously been tested for the presence of germline mutations in \( BRCA1 \) and \( BRCA2 \) using the protein truncation test (PTT) and no mutations were found. There were, on average, 4.2 cases of breast cancer per family (range 3 to 11) with an average of 3.0 cases of breast cancer in first degree relatives per family (range 2 to 9). Seventeen of the families also contained cases of ovarian cancer. For each family, a single patient affected with breast cancer was studied, with a mean age of diagnosis of 47 years (range 24 to 72 years).

The \( H2AX \) gene contains a single exon with 432 nucleotides. The coding sequence of the \( H2AX \) gene was evaluated by direct sequencing of a 561 bp fragment amplified using the following primers: F5'-CGTCTGTTCTAGTGTTTGAGC-3' and R5'-TGAGGGCGTGGTGCCCTTAAA-3'. No mutations or sequence variants were found in the 101 patients.

DISCUSSION

Our results suggest that germline \( H2AX \) mutations are unlikely to be common in families with familial breast cancer. Furthermore, the absence of polymorphic variation in this gene precludes the possibility that missense variants within the coding region of \( H2AX \) are associated with breast cancer risk in the population as a whole. It is, of course, possible that rare disease causing mutations in \( H2AX \) exist, and these might be uncovered in a larger study.

ACKNOWLEDGEMENTS

This work was supported by the Canadian Genetic Diseases Network, the Canadian Breast Cancer Research Foundation (Ontario chapter),...
and the Canadian Breast Cancer Research Initiative. CMP is funded by US Army grant DAMD17-00-1-0478. ANAM is funded by the Julia Murtha Fund, US Army award DAMD17-99-1-9389 and NIH CA92309.

Authors' affiliations
A N A Monteiro, Strang Cancer Prevention Center and Department of Cell and Developmental Biology, Weill Medical College of Cornell University, 1300 York Avenue, New York, NY 10021, USA;
S Zhang, C M Phelan, S A Narod, Center for Research in Women’s Health, 790 Bay Street, Suite 750A, Toronto MSG1N8, Ontario, Canada;
Correspondence to: Dr A N A Monteiro, Laboratory of Molecular Canada Health, 790 Bay Street, Suite 750A, Toronto M5G1N8, Ontario, S Zhang, C M Phelan, S A Rod, University, 1300 York Avenue, New York, NY 10021, USA;

REFERENCES