

Analysis of *PTEN* in two *BRCA1* and *BRCA2* wild-type familial breast cancer patients

Sir,

Our study was designed to sequence the entire exonic regions and intronic junctions of the *BRCA1*, *BRCA2*, and *PTEN* genes with regard to identifying the influence of *PTEN* mutations in two Iranian families with familial breast cancer and *BRCA1/2* wild-type genes [Figure 1].

Mutations in particular sets of genes are associated with an increased risk of hereditary breast and ovarian cancer (HBOC). These genes are categorized into three groups according to their impact on cancer susceptibility. The first group leading to elevated breast cancer risk (40% up to 85%)^[1] with mutations of high penetrance include *BCRA1*, *BCRA2*, *TP53*, *PTEN*, and *STK11*.^[2] *PTEN*

mutations, as a rare but high penetrance mutation, are considered following the two major known breast cancer susceptibility genes, *BRCA1* and *BRCA2*, in HBOC development.^[3] Human genomic *PTEN* gene locus on chromosome 10q23.3 contains 9 exons encoding a 5.5 kb messenger RNA that has a 403 amino acid open reading frame.^[4]

Whole gene sequencing was done for three genes in these families. The *BRCA1* and *BRCA2* in the proband of the families were normal, and no germline abnormality was found in these two genes that are mainly responsible for familial breast cancer. However, two new germline sequence variants were detected in the *PTEN* gene: One deletion (del T IVS4-29) and one single-nucleotide substitution (IVS2+65 G>A) [Figure 2a and b]. Both new changes found in the *PTEN* gene were analyzed by the two servers NetGene 2 and alternative splice site predictor. Del T IVS4-29 change was imposed in NetGene 2 site, the 3' splice site acceptor changed in the consensus sequences, but did not delete the consensus sequences. The IVS2+65 G>A variation did not cause a new change in splicing site.

Despite new achievements in this area, many factors leading to breast cancer predisposition are still

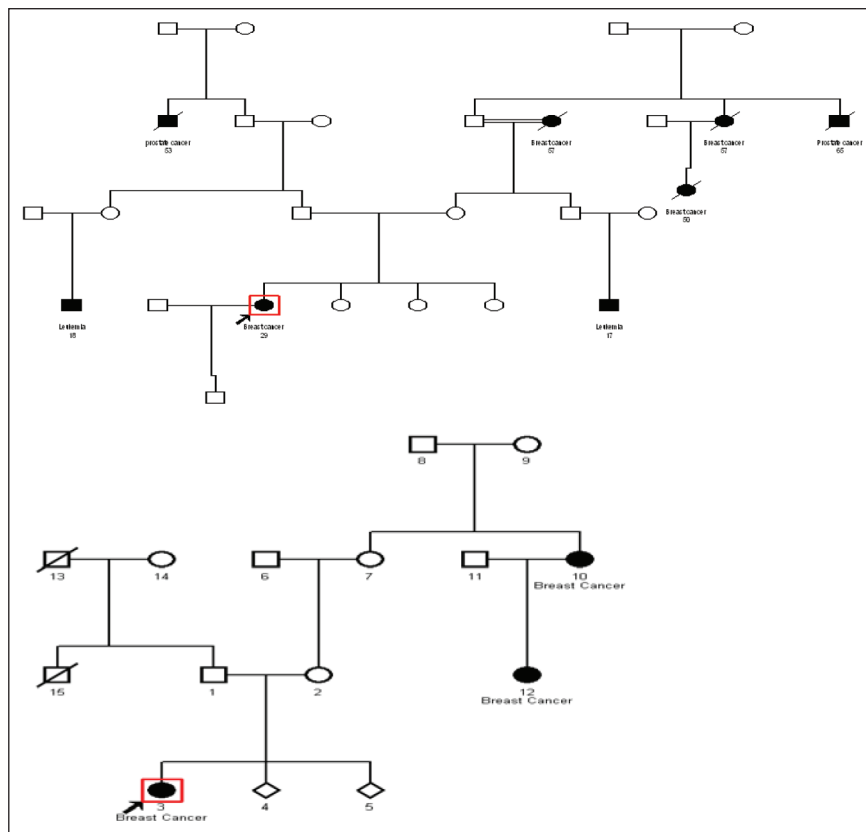


Figure 1: Pedigrees of the two families with familial breast cancer carrying new germline sequence variants in the *PTEN* gene: One deletion (del T IVS4-29) and one single-nucleotide substitution (IVS2+65 G>A)

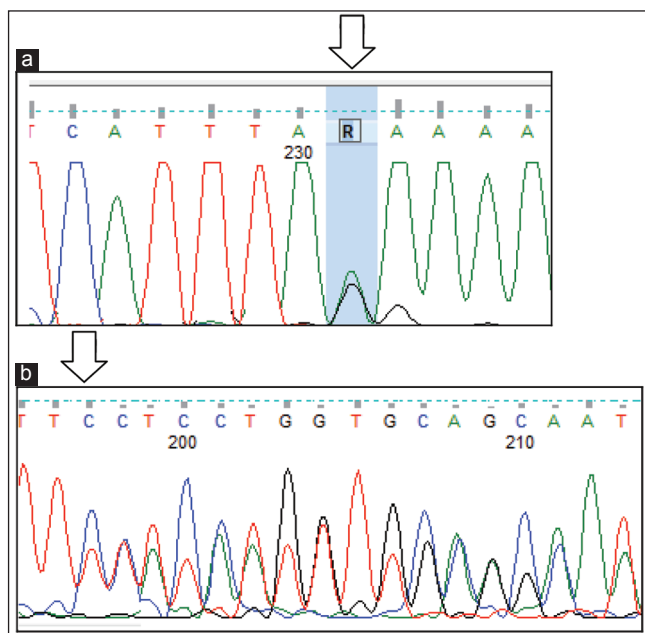


Figure 2: (a) Heterozygous IVS2+65 G>A of the *PTEN* gene. (b) Heterozygous del IVS4-29 of the *PTEN* gene

unknown, and thus need to be identified with further investigations.

All the investigations to promote strategies of early cancer diagnosis, which is critical for the survival of affected individuals, might be advantageous.

As the main mechanism for activating the *PTEN* protein is proteasomal degradation,^[5] any changes in protein structure influence the integral role of it. The specific variations that we detected may make some mute changes in the protein interactions which may prevent it from performing its task. It can be cleared by the study of protein structure in future investigations.

To the best of our knowledge, the study we present here is the first analysis of the *PTEN* gene in *BRCA1* and *BRCA2* wild-type breast and/or ovarian cancer in Iranian families.

Financial support and sponsorship

This work was supported by grants from Iran University of Medical Sciences project number 1021.

Conflicts of interest

There are no conflicts of interest.

**Mansoureh Akouchekian,
Simin Hemati¹,
Zohreh Ataei Kachoei**

Department of Medical Genetics and Molecular Biology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, ¹Department of Oncology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Address for correspondence: Dr. Mansoureh Akouchekian, Department of Medical Genetics and Molecular Biology, Faculty of Medicine, Iran University of Medical Sciences, Crossroads of Hemmat and Chamran Expressways, P.O. Box: 15875-6171, Tehran, Iran.
E-mail: akouchekian.m@iums.ac.ir

REFERENCES

1. Lalloo F, Evans DG. Familial breast cancer. *Clin Genet* 2012;82:105-14.
2. Melchor L, Benítez J. The complex genetic landscape of familial breast cancer. *Hum Genet* 2013;132:845-63.
3. Shiovitz S, Korde LA. Genetics of breast cancer: A topic in evolution. *Ann Oncol* 2015;26:1291-9.
4. Feilletter HE, Coulon V, McVeigh JL, Boag AH, Dorion-Bonnet F, Duboué B, *et al.* Analysis of the 10q23 chromosomal region and the *PTEN* gene in human sporadic breast carcinoma. *Br J Cancer* 1999;79:718-23.
5. Zhang P, Chen JH, Guo XL. New insights into *PTEN* regulation mechanisms and its potential function in targeted therapies. *Biomed Pharmacother* 2012;66:485-90.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Access this article online

Quick Response Code:



Website:

www.jmsjournal.net

DOI:

10.4103/1735-1995.165976

How to cite this article: Akouchekian M, Hemati S, Ataei Kachoei Z. Analysis of *PTEN* in two *BRCA1* and *BRCA2* wild-type familial breast cancer patients. *J Res Med Sci* 2015;20:629-30.