Mutation and Polymorphism Report

Authors: A.S.B. Khoo[1], P. Balraj[1], L. Volpi[1], and S.Nair[2]
Affiliations: [1]Division of Molecular Pathology, Institute for Medical Research, 50588 Kuala Lumpur, Malaysia; [2]Division of Surgery, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia
Corresponding Author Address and E-mail: Alan Khoo, Division of Molecular Pathology, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia; Tel: (603)-4402421/4402423; Fax: (603)-2934114; E-mail: alankhoo@imr.gov.my

Title : A new BRCA1 germline mutation (E879X) in a Malaysian breast cancer patient of Chinese descent
Keywords: BRCA1, breast cancer, Malaysian Chinese
Species: Human
Change is: Mutation

Gene/Locus
Name: breast cancer 1, early onset
Symbol: BRCA1
Genbank accession number: L78833
OMIM accession number: 113705
Locus specific database: Breast Cancer Information Core, BIC http://www.nhgri.nih.gov/Intramural_research/Lab_transfer/ Bic/
Chromosomal location: 17q12-24
Inheritance: autosomal dominant

Mutation / polymorphism name
Nucleotide change-Systematic name: c.2754G>T
Amino acid change-Trivial name: E879X
Mutation / polymorphism type: nonsense
Polymorphism frequency:
Detection method: direct sequencing
Detection conditions: Forward primer: 5'-acagtcgggaaacaagcatagaa-3' Reverse primer: 5'-tttggcattatcaactggcttatc-3' Standard 30 cycle PCR, annealing temperature 60 C
Diagnosis method developed: Mutation disrupts normal MboII restriction site

Evidence for existence and effect of mutation:

	Yes	No	Don't know
1. Base change found on repeat PCR sample	X		
2. Base change segregates or appears with trait	X		
3. Base change affects conserved residue	X		
4. Expression analysis supports hypothesis for causation			X
5. Normals tested (50 required)	X		

Ancillary data

1. **Haplotype association :**
2. **Ethnic background/Population association :** Chinese ethnic group
3. **Geographic association :** Malaysia
4. **Frequency** (of mutation) **in population:**
5. **Clinical phenotype of proband :** Unilateral breast cancer at age of 58 years
6. **Homologous allele** (if recessive trait)**:**
7. **PIC:** (if microsatellite)

8. Other:
9. Present in HGMD listing: Yes: No: X
(http://www.cf.ac.uk/uwcm/mg/hgmd0.html)

Comments

Information on BRCA1 mutations in non-Caucasians is lacking (Szabo and King, 1997). Our patient was a 58 year old postmenopausal nulliparous woman of Malaysian Chinese descent who presented with grade III infiltrating ductal carcinoma (T_3 N_0 M_0) of her left breast. The tumor was negative for estrogen receptor by immunohistochemistry but strongly positive for c-*erb*B-2 and p53. The patient underwent mastectomy with axillary clearance, local radiotherapy, adjuvant chemotherapy and tamoxifen. She had no known family history of breast cancer. Her sister had been diagnosed with cervical cancer about 2 decades previous, while her paternal grandmother died from an abdominal tumor (details not known). Direct sequencing of the entire BRCA1 coding region (Miki et al., 1994) of our patient showed that she was heterozygous for a polymorphism c.2685T>C (Y856H) (Tang et al., 1999) and a novel mutation, c.2754G>T(E879X) both of which were in exon 11. The mutation is predicted to result in the lost of the C-terminal region (Monteiro et al., 1996).

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