BRCA2

BRCA2 and BRCA2 (/ˌbrækəˈtuː/are a human gene and its protein product, respectively. The official symbol (BRCA2, italic for the gene, nonitalic for the protein) and the official name (breast cancer 2, early onset) are maintained by the HGNC. Orthologs, styled Brca2 and Brca2, are common in other mammal species.

BRCA2 is a human tumor suppressor gene (specifically, a caretaker gene), found in all humans; its protein, also called by the synonym breast cancer type 2 susceptibility protein, is responsible for repairing DNA.

BRCA2 and BRCA1 are normally expressed in the cells of breast and other tissue, where they help repair damaged DNA or destroy cells if DNA cannot be repaired. They are involved in the repair of chromosomal damage with an important role in the error-free repair of DNA double strand breaks.

If BRCA1 or BRCA2 itself is damaged by a BRCA mutation, damaged DNA is not repaired properly, and this increases the risk for breast cancer.

Thus, although the terms “breast cancer susceptibility gene” and “breast cancer susceptibility protein” (used frequently both in and outside the medical literature) sound as if they describe a proto-oncogene or oncogene, BRCA1 and BRCA2 are “normal”; it is their mutation that is abnormal.

The BRCA2 gene is located on the long (q) arm of chromosome 13 at position 12.3 (13q12.3).

The human reference BRCA 2 gene contains 28 exons, and the cDNA has 10,254 base pairs coding for a protein of 3418 amino acids.

Disseminated Medulloblastoma with Germline BRCA2 6174delT Mutation

Xu et al. describe an 8-year-old child who had disseminated anaplastic medulloblastoma and a deleterious heterozygous BRCA2 6174delT germline mutation. Molecular profiling was consistent with Group 4 medulloblastoma. The posterior fossa mass was resected and the patient received intensive chemotherapy and craniospinal irradiation. Despite this, the patient succumbed to a second recurrence of his medulloblastoma, which presented 8 months after diagnosis as malignant pleural and peritoneal effusions. Continuous medulloblastoma cell lines were isolated from the original tumor (CHLA-01-MED) and the malignant pleural effusion (CHLA-01R-MED). They provide their analyses, including in vitro and in vivo growth, drug sensitivity, comparative genomic hybridization, and next generation sequencing analysis. In addition to the BRCA2 6174delT, the medulloblastoma cells had amplification of MYC, deletion at Xp11.2, and isochromosome 17, but no structural variations or overexpression of GFI1 or GFI1B. This is the first pair of diagnosis/recurrence medulloblastoma cell lines, the only medulloblastoma cell lines with BRCA2 6174delT described to date, and the first reported case of a child with medulloblastoma associated with a germline BRCA2 6174delT who did not also have Fanconi anemia [1].

1)

Xu J, Margol AS, Shukla A, Ren X, Finlay JL, Krieger MD, Gilles FH, Couch FJ, Aziz M, Fung ET, Asgharzadeh S, Barrett MT, Erdreich-Epstein A. Disseminated Medulloblastoma in a Child with Germline BRCA2 6174delT Mutation and without Fanconi Anemia. Front Oncol. 2015 Aug 27;5:191. eCollection 2015. PubMed PMID: 26380221.