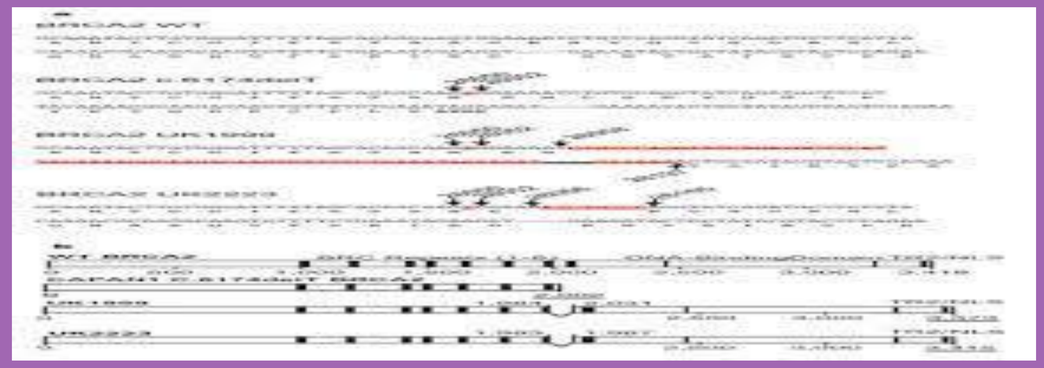
Introduction

According to Mandal, almost from the beginning of life on earth, mankind was affected and suffered by breast cancer. Almost In every era in recorded history, it is mentioned and written about. Breast cancer's symptoms are visible. At late stages the lumps advance toward the tumors. This process has been recorded by physicians in ancient times. She stated that this is because; breast cancer is not like the other internal cancers. Breast lumps tend to show themselves. Galen's theories on breast cancer were accepted until the 17th century. She found that in 1680, Francoisdela Boe Sylvius a French scientist began to reject the funny theory of cancer. He hypothesized that cancer was not caused by the black bile. He said it cause from a chemical which transformed lymphatic fluids from acidic to acrid. In 1730s, a physician from Paris under the name of Daude Deshais Gendron rejected the theory of Galen. Mandal mentioned that he believed when glandular and nerve tissue get mix with lymph vessels, cancer begins to develop. In 1895, a Scottish surgeon George Beatson discovered when he removed ovaries from the breast cancer; the breast tumor began to shrink. From that time on, many surgeons began to remove both ovaries. They performed a radical mastectomy for breast cancer patients. The tumor began to shrink after removing the ovaries because of the estrogen.

Mandal found that Estrogen which is released from the ovaries helped the tumor to grow and to become larger. But removing the ovaries "Estrogen" helped the tumor to shrink meaning to get smaller. With the advent of modern medicine, from 1995, almost ten percent of breast cancer patients went under mastectomy. This period was followed by the new the rapies for breast cancer like: hormone treatments, surgeries and biological the rapies. Scientists isolated the genes that caused breast cancer, like the genes: ATM, BRCA2, and BRCA1. According to Doamekpor, BRCA1 and BRCA2 are human genes. They produce proteins that eliminate and suppress tumors. They repair the damages to our DNA. He stated that if a mutation happens in one of the genes and BRCA1 or BRCA2 do not work properly. DNA damages may not be repaired; this process leads to cancer.



The left image is for BRCA1, and the right image is for BRCA2 from RaptorX. We wanted to identify BRCA1 and 2 domain region



. Identification of BRCA2 ORF restoring mutations in carboplatin resistant tumors in BRCA2c.6174delT mutation carriers (Stacey).

Methodology

To identify genes responsible for Tamoxifen resistance in breast cancer have been applied by random transfection of CDNA libraries. In order to find novel genetics for dominant mechanisms in anti-estrogen resistance in human breast cancer, they have used cancer cell line ZR-75-1. This cell line is dependent on estrogen. Progression of these cells to anti estrogen resistance is low. Random regulation of gene expression in ZR-75-1 cells with 5 azacytidine produced anti- estrogen resistance (Lambert). Over 800 million ZR-75-1 cells have been infected with a murine retrovirus and subjected to culture with 1 Mmol/L of 4hydroxyTamoxifen for 4-5 weeks. 80 cell lines were generated to have resistance to 4 hydroxy Tamoxifen.

Also they used PCR (Lambert, 2012). They used Fluorescence in situ hybridization for showing CAPANI and PIR12 cells had three copies of the BRCA2 gene (in Result section). I used RaptorX website to show BRCA1 and BRCA2 domain site residues

Results

Expression of BCRA1p130Cas protein has been analyzed. The data showed that both in univariate and in multivariate analysis, a high expression level of BRCA1p130 Cas in 8% of the primary tumors was associated with an increased rate of relapse, and accordingly a high expression level of BRCA1p130cas was associated with a poor response to first line Tamoxifen therapy (Lambert). Proteins with tumors with high BCRA1p130cas levels showed reduced response compared with low intermediate levels of BCRA130cas. Lambert states that the response of Breast Cancer to Tamoxifen treatment is determined by the different properties the tumor cells have. Sex steroid hormone receptor negative tumors are unlikely to respond the antiestrogen. High levels of BRCA1p130cas protein were found in malignant tumors. These variable levels were also found in nonmalignant breasts (Lambert). All breast tumors are derived from the estrogen dependent epithelial precursor cell population, one third of the carcinomas are ER Alpha negative, but do not express EGF receptor (Lambert). The majority of breast cancers are ER Alpha positive growing tumors. According to (Stacey), cells with loss of BRCAs function are highly sensitive to (ADP-ribose) polymerase and are defective in homologous recombination. The resistance to PARP inhibition can be acquired by a mutation in BRCA2. PIR clones from the human CAPA/ni pancreatic cancer cell line were derived. They carry c.6174delT frame shift mutation. PIR clones can cause DNA damage induced RAD5 nucleau foci. New BRCA2 isoforms were expressed as a result of intragenic deletion of c.6174delT mutation causing the ORF to be restored. When BRCA2 deficient cells reconstituted with revertant BRCA2 alleles; the PARP inhibitor sensitivity and HR deficiency were rescued (Stacey).

Comparison Between deletion genes in BRCA1and BRCA2 on Tamoxifen

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