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Original Research Article

Gene mutation can be treated in breast cancer by gene therapy

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ABSTRACT

Breast cancer or carcinoma is mostly characterized by a series of genetic mutations or gene mutations and is therefore ideally place for gene therapy intervention. The aim of gene therapy is to deliver a nucleic acid based drug to either correct or destroy the cells harbouring the genetic aberration. More recently cancer gene therapy has evolved to also encompass delivery of RNA interference technologies, as well as cancer DNA vaccines. However the bottleneck in creating such nucleic acid pharmaceuticals lies in the delivery. Deliverability of DNA is limited as it is circulating nucleases, therefore numerous strategies have been employed to aid with biological transport. This review will discuss some of viral and non viral approaches to breast to breast cancer therapy an present the findings of clinical trials of these therapies in breast cancer patients. Also detailed are some of the most recent developments in non viral approaches to targeting in breast cancer gene therapy. This include transcriptional control, and the development of recombinant, multifunctional bio- inspired system.

1. Introduction

Cancer also known as malignant neoplasm, is a broad group of various diseases. In cancer, cells divide and grow uncontrollably, forming malignant tumours, and invade nearby parts of the body. There are over 200 different known cancers that afflict humans. Malignant neoplastic lesions are the sixth leading cause accounting for 4.7% of the total medically certified deaths in India.[1]

Breast cancer is by far the most frequent cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers), and ranks second overall (10.9% of all cancers). It is now the most common cancer both in developed and developing regions with around 690000 new cases estimated in each region (population ratio1:4).[2] Breast cancer is the Most Common cancer in all urban areas the world, and 2nd most common in the rural areas.[3,4] The most recent data Population Based Cancer Registry PBCR 2016 - 2018 tells us that breast cancer accounts for 35% to 40% of all cancers in women. Breast cancer alone accounts for around 18% of total female neoplasm deaths.[5] Breast cancer is a malignant proliferation of epithelial cells lining the ducts or lobules of the breast.[6] Human breast cancer is a clonal disease. A single transformed cell is the product of a series of somatic (acquired) or germ line mutations is eventually able to express full malignant potential.[7] Thus, breast cancer may exist for a long period as either a non invasive disease or an invasive but non metastatic disease. These facts have significant clinical ramifications.[8] There are specific genetic mutations that can predispose individuals to developing breast cancer and other cancers, and mutations in these genes can account for approximately 5% of all breast cancers. These genes include BRCA1, BRCA2, p53 and PTEN. The BRCA1 gene is located on chromosome 17.

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This gene is mutated in families with early-onset breast and ovarian cancer. Breast cancer will develop in approximately 85% of women with BRCA1 gene mutations during their lifetime.[9,10]

2. Materials and Methods

A total number of 100 patients and 50 healthy controls were taken for the study. This study was conducted at The Departments of Gynaecology & Obstetrics, Biochemistry, Physiology and Pahtology Owaisi Hospital & Research Centre. (a teaching hospital to Deccan College of Medical Sciences, Hyderabad, T.S. India) The cases and samples were collected from female breast cancer patients presenting and admitted to the department of Surgical oncology, Medical oncology, Radiation Oncology. Owaisi Hospital & Research Centre. (a teaching hospital to Deccan College of Medical Sciences, Hyderabad, T.S. India) This prospective study was carried out on 100 patients and 50 healthy controls. The invasive duct carcinoma otherwise specified benign breast lesions including fibroadema and fibrocystic disease. Fresh tissues were taken, which were then subjected to RNA extraction.[11] The BCL mRNA level was assessed using real- time reverse transcription Polymerase Chain Reaction (PCR).[12]

3. Results

There was significant higher levels of BCL6 mRNA in malignant cases compared to healthy controls ($p<0.001$). The level of BCL6 mRNA was higher in cases showing advanced tumor stage ($p<0.04$), triple negative subtype and associated in situ component ($p<0.001$) compared to cases with an early stage, luminal or Her 2-neu positive subtypes and those lacking in situ component.[6,13] These genes include BRCA1, BRCA2, p53 and PTEN.[14]

4. Discussion

Risks of breast cancer was determined with inherited mutations in the tumor suppressor genes BRCA1 and BRCA2. We selected 100 index cases, regardless of family history of cancer, and carried out molecular analysis across entire families. The lifetime risk of breast cancer among female mutation carriers was 82%, similar to risks in families with many cases. Risks appear to be increasing with time: Breast cancer risk by age 50 among mutation carriers born before 1940 was 24%, but among those born after 1940 it was 67%. Lifetime risks of breast cancer was 54% for BRCA1 and 23% for BRCA2 mutation carriers.

5. Conclusion

BCL6 is up-regulated in breast cancer and is associated with poor prognostic features such as advanced stage an triple negative molecular subtype. BCL6 inhibitors might be considered as targeted therapy for breast cancer. These genes include BRCA1, BRCA2, p53 and PTEN.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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