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**Title of the Ph.D thesis:** **Molecular Analysis of BORIS gene in Indian Female Breast Cancer Patients**

## ABSTRACT

Breast cancer is the third most common malignancy in the world, with more than 1 million women being diagnosed with breast cancer each year. It 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 also ranks second overall (10.9% of all cancers).

The study was designed to find out mutation(s) of BORIS and CTCF gene and their protein expression through immunohistochemistry in breast carcinoma and its further correlation with various clinico-pathological variables.

**The present study encompasses the following findings:**

It was found that 20% of mutations (21/105) were present in BORIS gene and all were missense mutations and 14.29% of mutations (15/105) were present in CTCF gene where 9.52% were missense and 4.76% were silent mutations in Indian female breast cancer cases.

A significant association of BORIS gene mutations was observed with various clinico-pathological variables like menopausal status, clinical stage, nodal status, ER and PR expression. These observed missense mutations of BORIS in tumors exhibited in postmenopausal, clinical stage (II & III), lymph node negative, ER- positive and PR negative, were seemingly associated with malignancy and poor prognosis. We found significant association of CTCF gene mutations with clinico-pathological variables like menopausal status, clinical stage, nodal status and ER status.

These missense and silent mutations of CTCF, observed in tumors largely exhibited in postmenopausal, clinical stage (II & III), lymph node negative, and ER- positive, were seemingly associated with malignancy.

It was found that out of 105 breast cancer cases, 20 cases (21/105, 20.0%) showed low or no expression (+), 34 cases (34/105, 32.39%) with moderate (++) expression and 50 cases (50/105, 47.61%) had high (+++) expression for BORIS protein. Significant association was observed in BORIS protein expression with clinico-pathological variables like clinical stage, nodal status, ER status and PR status. When BORIS mutations and protein expression were correlated with clinico-pathological variable, a significant association found in high level of BORIS protein (+++) expression.

Hence it seems that progression of breast cancer was found to be related with high BORIS protein expression along with large number of mutation with disease progression.

We found that out of 105 breast cancer cases, 55 cases (55/105, 52.38%) showed low or no expression (+), 40 cases (40/105, 38.09%) with moderate (++) expression and 10 cases (10/105, 9.53%) had high (+++) expression for CTCF protein. Significant association was observed in CTCF protein expression with clinico-pathological variables like histological grade, clinical stage nodal status and ER status. When CTCF mutations and protein expression were correlated with clinico-pathological variables, we found a significant association in low CTCF protein expression (+) category in the cases where large numbers of mutations were seen. Hence it seems that progression of breast cancer was found to be related with lower CTCF protein expression along with large number of mutations with disease progression, showing its antiproliferative nature.

In conclusion, BORIS and CTCF mutations may be used as a prognostic factor for breast cancer risk in our population and these gene mutations in combination may help in assessing breast cancer risks in Indian women.