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Title of the thesis: **Molecular Analysis of Cytokine Genes in Indian Female Breast Cancer Patients**

ABSTRACT

Breast cancer remains the most common malignancy in women- worldwide and is the leading cause of cancer related mortality in female with an estimated 1.38million new cancer cases diagnosed in 2008 (23% of all cancer). It is now one of the most common cancers both in developed and developing regions. Inflammatory cells and cytokines were recently suggested to play a key role in breast carcinoma. Recently, many single nucleotide polymorphisms (SNPs) are detected in cytokine promoter region, which are associated with variable level of gene transcription.

The study was design to investigate the relevance of four most important cytokines including IL-6, TNF- α , TNF- β and IFN- γ polymorphism and their expression during the breast carcinogenesis and well defined clinical pathological parameters.

Findings of the study:

Part I (Cytokine gene polymorphism):

- The IL-6 genotypes: GG genotype significantly higher in lymph node positive patients (p=0.003); grade I & II (p<0.05) and PR receptor positive patients (p<0.001).
- High producer Allele A, and genotype GA (p<0.001) of TNF- α (-308) is significantly higher in patients as compared to healthy controls. The GA genotype higher in post-menopausal patients (p=0.02).

- The TNF- β (+252) genotypes GG higher in grades III ($p < 0.05$) of patients; genotype AA higher in patients with pre-menopausal status ($p < 0.05$).
- The IFN- γ (+874) genotype AT higher in grade III; and AT higher in HER-2/neu receptor negative category ($p = 0.003$).

Parts II (Cytokine gene expression)

- The IL-6 expression is significantly higher in clinical stages including earlier stage (I+IIa), lymph node (-ve), post-menopausal, progesterone receptor negative (-ve), tumor grade III and HER-2/neu receptor negative category of patients.
- The TNF- α expression is more prevalent in breast cancer tissue than adjacent normal tissue. The expression of TNF- α in Her-2/neu (+ve) and post-menopausal was significantly higher.
- The TNF- β expression is significantly higher in patients. The expression is also significantly higher in earlier stage (I+ II a), Lymph node (-ve), Post-menopausal and PR negative.
- The IFN- γ expression is significantly higher in breast cancer tissue. The expression is also significantly higher in post-menopausal patients.

In conclusions, the Cytokine Genotypes may be utilized as predictive biomarker for the development of breast cancer. These DNA based genetic markers can further be utilized for the predicting clinical outcome following breast cancer. Cytokine gene expression may be clinically utilized as new prognostic biomarkers of cancer development and progression. The results may be beneficial for the advancement in breast cancer diagnosis, prevention and treatment.