

## Lactoferrin Expression Profiling is Essential for Cancer Cell Proliferation and Metastasis, Correlates with Clinical Features, as Well as Early Stages of Breast Cancer

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**Abstract :** Introduction: As a complex disease, breast cancer results from several genetic and epigenetic changes. Lactoferrin, a member of the transferrin family, is reported to have a number of biological functions, including DNA synthesis, immune responses, iron transport, etc., any of which could play a role in tumor progression. This study aimed to investigate the bioinformatics data and experimental assay to find the pattern of promoter methylation and gene expression of LTF in breast cancer to study its potential role in cancer management. Material and Methods: To evaluate the LTF promoter's methylation status, we studied the MS-PCR and Real-Time PCR on samples from patients with breast cancer and normal cases. This study includes 67 patient samples, including tumoral, plasma, and normal tissue adjacent samples, as well as 30 plasma samples from standard cases and 10 tissue samples of breast reduction cases. Subsequently, bioinformatics analyses such as cBioPortal databases, string, and geomatics were conducted to disclose the prognostic value of LTF in breast cancer progression. Results: The analysis of LTF expression showed an inverse relationship between the expression level of LTF and the stages of tissues of breast cancer patients ( $p < 0.01$ ). In fact, stages 1 and 2 had a high expression in LTF, while, in stages 3 and 4, a significant reduction was observable ( $p < 0.0001$ ). LTF expression frequently alters with a decrease in the expression in ER+, PR+, and HER2+ patients ( $P < 0.01$ ) and an increase in the expression in the TNBC, LN<sup>-</sup>, ER<sup>-</sup>, and PR- patients ( $P < 0.001$ ). Also, LTF expression is significantly associated with metastasis and lymph node involvement factors ( $P < 0.0001$ ). The sensitivity and specificity of LTF were detected, respectively. A negative correlation was detected between the results of level expression and methylation of the LTF promoter. Conclusions: The altered expression of LTF observed in breast cancer patients could be considered as a promotion in cell proliferation and metastasis even in the early stages of cancer.

**Keywords :** LTF, expression, methylation, breast cancer

**Conference Title :** ICCMB 2024 : International Conference on Cellular and Molecular Biology

**Conference Location :** Toronto, Canada

**Conference Dates :** June 13-14, 2024