INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: **Towards understanding the expression and regulation of GPER1, and its significance thereof in human breast cancer**

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SHORT ABSTRACT

G-Protein Coupled Estrogen Receptor-1 (GPER1) is a novel membrane-associated estrogen receptor and a major player in the short-term non-genomic actions of estrogen. GPER1 signaling is implicated in various estrogen-influenced physiological and pathological conditions including breast cancer. However, the clinical significance of GPER1 and regulation of its expression in breast cancer is not completely understood, particularly, considering the contribution of the nuclear estrogen receptors. The thesis work focuses on these less-addressed areas in the field of GPER1 biology and presents evidence from cell line model-based experiments and *in silico* analyses. Towards this, a polyclonal antibody against N-terminus of GPER1 was generated. Using this antibody, GPER1 protein expression was profiled in the breast cancer tissue sections. The clinical significance of GPER1 in breast cancer was studied. To the best of our knowledge, this is the first retrospective study with respect to GPER1 in an Indian population. Reduced expression of GPER1 was observed in tumors as compared to normal breast tissue. A significant positive association was observed between the expressions of GPER1 and ERα. By unraveling the involvement of ERα in the regulation of GPER1 expression, the functional connect for the association observed in the clinical samples was established. For the first time, the expression of GPER1 transcript variants was profiled in breast cancer cells. Investigations on understanding the basis for the reduced expression of GPER1 in tumors revealed the role of DNA-methylation in the regulation of basal GPER1 expression. Finally, global transcriptome changes associated with the GPER1-activation were profiled by microarray. The contribution of GPER1-mediated signaling in estrogen action was highlighted. It is hypothesized that GPER1 signaling counteracts ERα signaling in breast cancer cells. Collectively, the thesis work highlights the tumor suppressor role and therapeutic potential of GPER1 in breast cancer.