STUDY DESIGN

Looking to the diverse role of TGF-β family members in breast tumorigenesis and their increasing use in the clinical management, it was envisaged that their might be helpful and may serve as biomarker. It is also necessary to look for the comprehensive usefulness of different molecules of the pathway because each has a defined special role in the signaling cascade and has a potential to be helpful in breast cancer management. Emerging technological advancement has allowed a combination of techniques which would assess the molecule’s utility to point towards the diverse biological role of molecules. The current prospective study therefore explored the molecules of TGF-β signaling viz. growth factors, their cognate receptors and their signaling mediators (SMADs).

The current study looked for TGF β family members; (i) growth factors (TGF-β1, TGF-β2, TGF-β3) at protein (circulatory and tumoral; with ELISA) and mRNA [with real time PCR (RT-PCR)] levels, (ii) their receptors (TβR-I, TβR-II, TβR-III; RT-PCR) and (iii) signaling mediators (SMAD-3, SMAD-4, SMAD-7)] at mRNA (RT-PCR) in breast cancer and correlated them to known clinico-pathologic prognosticators of the disease. The incidence of TGF beta axis molecules in the cohort of all patients was compared between early- and advanced-stage breast cancers.

The work embodied in this thesis is divided into four sections according to the objectives:

I. Prognostic utility of circulating levels of TGF-β isoforms (TGF-β1, TGF-β2, TGF-β3)

II. Tumoral protein levels of TGF-β isoforms: Correlations with clinico-pathologic prognosticators

III. Gene expression of TGF-β axis molecules in relation to clinico-pathologic prognosticators
   i. Growth Factors (TGF-β1, TGF-β2, TGF-β3)
   ii. Signaling Receptors (TβR-I, TβR-II, TβR-III)
   iii. Signaling Mediators (SMAD-3, SMAD-4, SMAD-7)
IV. Gene and protein expression correlations

i. Correlations of transcript levels of TGF-β axis molecules with Estrogen receptor

ii. Juxtaposing circulating, tumoral and transcript levels in their ultimate utility in breast cancer

The multi-factorial analysis and inference derived thereof is likely to pave way to a possibility of better prediction of breast cancer prognosis. The inference is also likely to be useful to identify the subset of breast cancer patients likely to benefit from anti TGF-β strategies.