Cancer is a highly complex genetic disorder. The mechanics of the molecular pathways that control cell cycle are often mutated in neoplasia which can encompass multiple genetic alterations. Cell cycle progression of mutated cell leading to uncontrolled cell proliferation is critically dependent on the cumulative mitogenic stimuli received from diverse sources. Breast cancer is the second most common malignancy in Indian women with an increasing incidence due to a rapid change in the 'life style'. The clinical decisions are often tricky due to its biological heterogeneity, availability of a variety of therapeutic options and wide spectrum of responsiveness.

It is very well known that breast carcinogenesis is a multi-step process controlled by many hormones, growth factors and cytokines. Growth and differentiation in a multicellular organism is regulated by a number of physiological networks including hormones and growth factors. Breast physiology thus is a cumulation of responses to such stimulations; both in normal and abnormal conditions. Both these classes of molecules act through specific receptor proteins. Bioavailability of hormones and growth factors to the breast epithelial microenvironment is also one of the most important aspects which need detailing in individual patient.

Breast cancer is thought to arise from an unopposed estrogen action from the time of Beatson (1896) who demonstrated spontaneous regression of breast cancer following oophorectomy. To date, presence of Estrogen and progesterone receptors is the most well-defined predictive marker connected to the responsiveness to endocrine therapy. However, it would be difficult to predict or treat the patients with estrogen and progesterone receptor negative patients.

Researchers then changed their attention to the growth factors in the quest of uncovering antiestrogen failures. Many growth factors and their receptors have been reported to play an important role in the normal mammary gland development, differentiation and are well implicated in the genesis as well as progression of breast cancer. The need of the time was to look for the ‘complete markers’ or the other options which can help diagnosis, can predict therapeutic responsiveness, predict recurrence and likelihood of survival.
It is widely believed that breast cancer is hormone dependent or growth factor dependent. With the increased evidences of loss of hormone dependence, importance of growth factors was also realized. Over-expression of HER-2 [Epidermal growth factor receptor -2] has materialized the option of Herceptin. HER-2 quantitation can now be used as a predictive marker in ER negative tumors. Knowledge of molecular markers of breast neoplasia is an obvious need to identify women at high risk of developing breast cancers and / or breast cancer progression.

Many growth factors like epidermal growth factors, vascular endothelial growth factors, fibroblast growth factors, and insulin like growth factors have increased attention after the successful launch of Herceptin. At present, growth factor research has seen a great escalation with many molecules from growth factor families are under clinical trials. Researchers are now targeting specific cellular processes and try to find out ‘newer’ and ‘complete’ marker for breast cancer.

Transforming Growth Factor Beta (TGF-β) is a large family of polypeptide growth factors capable of regulating an array of cellular processes and hypothesized to have a dual role in breast carcinomas. They act as a tumor suppressor in early stages of carcinogenesis when it inhibits the outgrowth of cells via its antiproliferative functions. At the later stages of the disease, they are believed to promote tumor progression, in part by enhancing tumor cell motility and invasiveness; imparting a capability to metastasize. Tumor promoting effects of TGF-βs correlate with their increased secretion by tumor cells during progression. It is also proposed that TGF-βs undergo a ‘shift’ (TGF-β switch) during tumor progression from being predominantly an anti-promoter during early stages of neoplasia to becoming conductive to cancer invasion and perhaps metastasis, at later stages.

Incidence of breast cancer in India is increasing at an alarming rate. Moreover, majority of them are detected at a fairly advanced stage as with all other tumor types. This is linked to socio-economics and inadequate health care delivery system. At our institute, we often encounter advanced stage tumors that are large sized, axillary lymph node positive, ductal origin, poorly differentiated; hence aggressive. The early stage tumors (smaller sized) are also often node positive (>four positive lymph nodes)