

Molecular Prognostic and Predictive Factors

HER2

The next major advance in the evolving role of prognostic and predictive markers in the diagnosis and therapeutic decision making for breast cancer came with the discovery of the importance of the *HER2* receptor tyrosine kinase in the biology and the clinical course of disease in breast cancer. **Normal cells have one copy of the *HER2* gene on each chromosome 17 (CHR17), and when this gene is expressed in normal breast epithelial cells, it transmits signals regulating cell growth and survival.** In approximately **15% to 25% of breast cancers, the *HER2* gene is found to be amplified 2-fold to greater than 20-fold in each tumor cell nucleus relative to CHR17,** and this amplification drives gene expression, generating up to 100 times the normal number of *HER2* receptor proteins at the cell surface.

HER2- positive breast cancer is significantly correlated with several **unfavorable pathologic tumor characteristics**, including larger tumor size, positive axillary nodes, higher nuclear grade, and higher proliferative index. In addition to the prognostic significance, retrospective studies have suggested that *HER2* over expression may have a predictive role for response to adjuvant chemotherapy and endocrine therapy.

The Herceptin molecule (Herceptin is the drug used against *HER2* positive tumour cells) has been shown to demonstrate a high specificity and affinity for the *HER2* protein and in preclinical studies was shown to be most effective against tumor cells with *HER2* over expression. The therapeutic efficacy and tolerability of Herceptin therapy has been investigated in several clinical trials, and this drug has proved to be a remarkably effective therapeutic agent in both the metastatic and, more recently, the adjuvant setting, particularly in combination with cytotoxic chemotherapy.

Demonstration of *HER2* neu receptors can be done by using the following techniques:

1. Immunohistochemistry antibodies against Her2 receptors are applied to the tissue and if the antigen (Her2) is present a reaction is visualized by means of a dye or a color producing enzyme which is used to label the antibody.