

Breast cancer is a heterogeneous disease, often characterized by variation in type and quantity of protein and gene expression. One source of variation is the presence or absence of Human Epidermal Growth Factor Receptor 2 (HER2), a trans-membrane receptor overexpressed in approximately 20% to 30% of breast cancers. HER2-positive breast cancers are generally more aggressive and metastatic than other breast cancer subtypes. In 1998 the FDA approved a targeted therapy called Herceptin™ (Trastuzumab) that significantly increases survival for most patients with HER2 positive breast cancers when combined with chemotherapy. Trastuzumab is an antibody that binds to and deactivates the cellular signaling of overexpressed HER2, and recruits the body's immune system to destroy cancer cells. Although this drug represents a major advance in targeted therapy for HER2 positive cancers, it has some drawbacks, including high-cost and elevated risk for congestive heart failure. It is therefore paramount that assays used to determine HER2 status be made as precise and accurate as possible in order to avoid the financial and health burdens in instances when there is no clinical benefit. Nevertheless, there has been an overall lack of scientific consensus regarding the best method for the identification of HER2 overexpression. Currently there are 3 different antibody assays used by pathologists to look for HER2 overexpression using a technique called immunohistochemistry (IHC) on surgically removed breast cancer tissue. This study compares the effectiveness of these three antibodies: *CB11*, *4B5* and *HercepTest*. Based on the latest national standards for interpreting HER2 IHC results we found that CB11 did clearly show HER2 expression on the membrane of cancer cells, with significant staining of the cytoplasm and non-cancerous connective tissues. This trend with CB11 has been observed in the literature, yet its true extent and potential to misguide HER2 treatment has not been well discussed.