Serum antibodies specific for tumor antigens in breast cancer may be useful diagnostic biomarkers

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Background: Breast cancer is immunogenic and a number of tumor antigens have been identified using serum from breast cancer patients. We questioned whether humoral immunity to tumor associated antigens (TAA) in breast cancer patients could be used as a biomarker to predict disease. Methods: Serum antibody responses to a panel of TAA were measured in serum from breast cancer patients (n=100-200) and age-matched controls (n=100-200) using ELISA. Results: Breast cancer patients have increased antibody response to p53 (10% vs. 1%, p<0.001), HER2 (13% vs. 5%, p=0.004), MUC1 (20% vs. 3%, p<0.001), topoisomerase II alpha (7% vs. 3%, p=0.001), insulin-like growth factor binding protein 2 (IGFBP2, 14% vs. 1%, p<0.001), cyclin D1 (8% vs. 5%, p=0.04), and cathepsin D (5% vs. 3%, p=0.05). To determine the potential diagnostic value of these serum antibodies, we measured antibody levels to these TAA in an independent sample set which included 184 breast cancer patients and 134 normal donors. Responses were used to construct receiver operating characteristic (ROC) curves. The samples were judged as positive or negative for breast cancer using measurements derived either from a single marker or a combination of the markers. We found that antibody response to p53 alone was not a significant predictor of breast cancer (AUC=0.48, p=0.538), but combining responses to 2 antigens (p53 and HER-2/neu) resulted in an AUC of 0.61 (p=0.006), and combining responses to 4 antigens (p53, HER-2/neu, IGFBP-2 and TOPO2α) increased the area under the curve to 0.63 (p=0.001). Using an algorithm weighted on logistic regression coefficients of independent antibody markers resulted in an AUC of 0.70 (p<0.001). Conclusions: This data suggests that a panel of autoantibodies to breast cancer associated antigens may serve as useful biomarkers for diagnosis.