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Combined measurement of CA 15-3 with novel autoantibodies improves diagnostic accuracy for breast cancer

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Abstract

Cancer Antigen 15-3 (CA 15-3) is clinically used as a diagnostic biomarker only for the advanced breast cancer. Recently, measuring autoantibodies against tumor-associated antigens (TAAs) has been shown promising results for early cancer detection. However, both antigen and antibody biomarkers have never been tested in combination for breast cancer detection. Thus, in this study, we measured serum CA 15-3 protein levels concurrently with novel autoantibodies from patient and control serum samples to evaluate the diagnostic advantage in breast cancer. We first interrogated a T7 breast cancer cDNA phage library for TAAs using sera from normal and breast cancer patients. Identified novel TAA phage proteins were then used to develop enzyme-linked immunosorbent assays (ELISAs) to measure corresponding autoantibodies in 273 breast cancer patients, 154 normal and 40 other cancer patient serum samples. Meanwhile, the same samples were measured for the CA15-3 concentrations. Receiver operating characteristic (ROC) analysis was used to evaluate predictive accuracies with single marker as well as combined markers. Sequencing analysis revealed that two phage-expressed proteins were within open-reading-frame (ORF) and had significant homology to proteins hnRNPF and FTH1. Autoantibodies against hnRNPF and FTH1 alone were found significantly higher in patients than in the control serum samples ($P<0.01$), and the AUC for hnRNPF and FTH1 alone were 0.725 and 0.686 respectively. However, when the two autoantibody biomarkers were analyzed in combination with serum CA 15-3 values, the AUC increased to 0.92, and the optimal sensitivity and specificity became 81% and 93% respectively. Further mRNA analysis has shown that hnRNPF and FTH1 were significantly upregulated in tumor tissues. Our results indicated that combined serologic biomarkers of TAAs and autoantibodies improve the diagnostic accuracy for breast cancer.

Biography

Xuejun Dong is the Director and Professor of Clinical Examination Center of Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University. He has published more than 90 papers in journals.