Prostate specific antigen (PSA) is a serine protease expressed at high levels in prostate epithelium and elevated PSA in serum is a well-established marker of prostate cancer. Recently, the relative proportions of free PSA and PSA complexed to the serine protease inhibitor alpha-1-antichymotrypsin (PSA-ACT) have become important variables in distinguishing between prostate cancer and benign prostatic hyperplasia. The production of PSA in female tissues such as the breast has been clearly demonstrated and low levels of PSA are present in female sera. The objective of this study was to measure and compare the relative proportions of free PSA and PSA-ACT in the serum of women with breast cancer, benign breast disease, or women with no known malignancies. PSA was measured with an established immunoassay for total PSA and a novel immunen assay for free PSA, both with a detection limit of 0.01 ng/mL (1 ng/L). The percentage of breast cancer patients with free PSA as the predominant molecular form (>50% of total PSA) in serum was five times higher than that of healthy women or women with benign breast disease, and free PSA decreased in the serum of breast cancer patients following surgery. The diagnostic use of free PSA for breast cancer is limited at this point due to the low diagnostic sensitivity (<20%), however, free PSA as the predominant molecular form shows high diagnostic specificity (>90%) in comparison to women free of breast cancer or with benign breast disease. These results suggest that the clinical applicability of free PSA for breast cancer diagnosis and the biological mechanism behind its increase should be further investigated.

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