98 QUANTITATIVE ANALYSIS OF PROSTATE SPECIFIC ANTIGEN AND MUTANT P53 PROTEIN IN BREAST TUMOR CYTOSOLS: RELATIONSHIPS WITH OTHER PROGNOSTIC INDICATORS

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It is becoming evident that combinations of prognostic factors allow more accurate prediction of disease behaviour, and hence patient survival, in breast cancer. To examine the utility of this approach using biochemical markers, we have quantitated 965 breast tumor cytosols for estrogen receptors (ER) and progesterone receptors (PR), carcinoembryonic antigen (CEA), p53, and prostate-specific antigen (PSA), the latter only recently demonstrated by our group in breast tissue and associated with a favourable prognosis. Each of the highly sensitive immunofluorometric assays utilized the same time-resolved fluorescence detection system. Contingency tables using multiple cutoff levels indicated ($p<0.001$) and CEA-negative status ($p<0.001$). CEA-positive status was associated with receptor-positivity ($p<0.001$) and PSA-negativity ($p=0.03$). Further evidence suggested progestin-mediated p53 gene repression and estrogen-linked CEA gene derepression in these tissues. A model outlining possible causal relationships between the markers asayed is also proposed, from which different outcomes may be expected. In a subset of specimens (n=276) for which TNM stage was defined, a preliminary test of our model by relating each marker status individually to disease stage revealed the presence of mutant p53 to be associated with stages II or III ($p=0.01$) while PSA presence was associated with stages 0 or I ($p=0.003$). By stratifying for receptor status, it was found that the greatest division of specimens into high or low stages was coincident with their categorization into either p53-positive and PSA-negative, or p53-negative and PSA-positive groups, respectively ($p=0.006$). This is the first report incorporating both p53 and PSA into a panel with prognostic potential in breast cancer.