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Molecular staging of prostate cancer with the use of an enhanced reverse transcriptase-PCR assay

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Abstract

Objective. Because up to 40 percent of surgically treated patients with prostate cancer are subsequently found to be clinically understaged, a more sensitive staging modality to identify extraprostatic disease prior to surgery is required.

Methods. We describe an enhanced reverse transcriptase (RT) polymerase chain reaction (PCR) assay utilizing oligonucleotie primers specific for the human prostate-specific antigen (PSA). This assay identifies PSA-synthesizing cells from reverse transcribed mRNA. This assay was applied to RNAs extracted from the peripheral blood lymphocytes of 65 patients with clinically localized prostate cancer. In addition, blood from 20 women, 20 young men, 25 age-matched control men under treatment for

benign prostatic hyperplasia (BPH), and 18 men with established, untreated metastatic prostate cancer was tested.

Results. An RTPCR assay for PSA can recognize one PSA-expressing cell diluted into one hundred thousand lymphocytes. The sensitivity of this assay can be enhanced by the addition of digoxigenin-modified nucleotides to the PCR reaction and this assay was applied to RNAs extracted from the peripheral lymphocyte fraction of 148 prostate cancer patients and controls at this institution. Although no specimen from women or men without cancer was positive in this assay, 14 of 18 metastatic prostate cancer patients were positive (77.8%). Additionally, 25 of 65 (38.5%) patients with clinically localized disease (T1-2b) were positive from blood specimens obtained prior to surgery. Final pathologic results from this group of patients identified a correlation between positivity on this assay and the presence of capsular tumor penetration (sensitivity, 68%; specificity, 84%) as well as a strong correlation with the finding of carcinoma at the surgical margin (sensitivity, 87%; specificity, 76%). Logarithmic regression analysis of the results of the RT-PCR assay indicates its remarkable superiority to digital rectal examination, computed tomography scan, endorectal coil magnetic resonance imaging, PSA, prostate-specific antigen density, or Gleason score for predicting the true pathologic stage of prostate cancer in these surgically treated patients.

Conclusions. An RT-PCR assay using PSA primers to detect prostate cells in the peripheral circulation of surgical-candidate patients is significantly correlated with capsular penetration and tumor-positive surgical margins. This molecular assay provides a sensitive and specific means to stage correctly apparent localized prostate cancer prior to radical prostatectomy.



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