American Association for Cancer Research
95th AACR Annual Meeting
March 27-31, 2004
Orange County Convention Center
Orlando, Florida

4478 Artifical neural network based on PSA, percent free PSA, and three new prostate cancer biomarkers.

Carsten Stephan, Xu Chianliang, Tadaaki Kishi, Terukazu Nakamura, David A. Brown, Samuel N. Breit, Henning Cammann, Klaus Jung, Eleftherios P. Diamandis. *Urology, Berlin, Germany, Pathology and Laboratory Medicine, Toronto, ON, Canada, Immunology, Sydney, Australia, Pathology, Medical Biometry, Berlin, Germany.*

There is an urgent need for new tumor markers for the differential diagnosis of prostate cancer (PCa) and benign prostatic hyperplasia (BPH) in order to avoid unnecessary prostate biopsies. New algorithms like logistic regression (LR) and artificial neural networks (ANN) have been shown to further improve differentiation between PCa and BPH. We measured 3 newly developed serum assays for human kallikrein 11 (hK11), macrophage inhibitory cytokine (MIC-1), and macrophage migration inhibitory factor (MIF) within an PSA and %fPSA based ANN. Serum samples from 371 patients (135 PCa and 236 BPH) within the PSA range 0.5-20 ng/ml were analyzed with the Immulite PSA and free PSA assay (DPC, CA). All samples were also analyzed for the hK11 (Toronto, Canada), MIC-1 (Sydney, Australia) and MIF (Berlin, Germany). Prostate volume was available in 288 patients. For all groups the ANN- and LR-output values were calculated and compared in Receiver operator characteristic (ROC) curves using the areas under the curve (AUC) and the significance levels at 95% sensitivity and specificity. An extra module from SPSS (neural connection) was used to develop the different ANNs. Results: The values of PCa and BPH patients for hK11 (median: 0.139 vs. 0.166, p=0.001), MIC-1 (805 vs. 949, p=0.002), PSA (8.0 vs. 4.0), %fPSA (8.3% vs. 16.8%) and prostate volume (30.5 vs. 42.4 ml, p<0.0001) differed significantly whereas MIF (1594 vs. 2035, p=0.065) did not reach significance. PSA and %fPSA did not correlate to any of the 3 new markers (r between -0.165 and 0.17) but they did to each other (r=-0.41). MIC-1 correlated to hk11 (r=0.31) but no other correlation was found. The AUCs for the new parameters alone (hK11: 0.60; MIC-1: 0.60; MIF: 0.56) did not increase efficiency compared to PSA (AUC: 0.76) and %fPSA (0.80). But the combination of hK11, MIC-1, MIF, PSA, %fPSA, and age revealed a significantly larger AUC with 0.85 for LR and 0.86 for the best ANN. Including prostate volume for 288 patients further increased the differences between AUC for PSA (0.64), %fPSA (0.69), and LR (0.87) for the best ANN (0.91). For this group the specificities at 90% sensitivity remarkably increased from 29% (PSA) and 30% (%fPSA) to 54% (LR), 56% (ANN), and 80% (best ANN). We conclude that all new developed tumor markers for PCa only partially reach the discriminating power of PSA or %fPSA if used alone. However, the combined use of these new markers in an ANN significantly improves the specificity and sensitivity, especially by including prostate volume.

Copyright © 2004 American Association for Cancer Research. All rights reserved.
Citation information: Proceedings of the AACR, Volume 45, March 2004