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European Association of Urology

## Words of Wisdom

### Auto-Antibody Signatures in Prostate Cancer

Wang X, Yu J, Sreekumar A, Varambally S, Shen R, Giacherio D, Mehra R, Montie JE, Pienta KJ, Sanda MG, Kantoff PW, Rubin MA, Wei JT, Ghosh D, Chinnaiyan AM

N Engl J Med 2005;353(12):1224–35.

### Looking for Other Markers Than PSA for Prostate Cancer Detection

#### Expert's summary:

In an era where PSA is increasingly challenged as an effective prostate cancer marker, a combined effort by the University of Michigan and the Harvard Medical School has used protein marker microarrays to identify auto-antibodies against tumour antigens in patients with prostate cancer. The authors constructed phage-protein microarrays in which peptides derived from the prostate cancer cDNA library were expressed as a prostate cancer phage fusion-protein. Phage-protein microarrays were then screened to identify phage-peptide clones that bind auto-antibodies in serum samples from patients with prostate cancer and controls.

They looked in total for a panel of 22 antigens derived of prostate cancer, found of potential interest at discriminating between patients with and without cancer.

In 60 patients and 68 controls, this 22 bio-marker assay reached a sensitivity of 81.6% and a specificity of 88.2%. The panel of peptides was far better than PSA for detecting prostate cancer.

#### Expert's comments:

This very important contribution opens the way for new avenues in prostate cancer detection.

One of the most promising approaches to cancer early detection, is not to look for cancer itself, but to look for immune responses to cancer. Interestingly, these new tests do not exclude using them in conjunction with PSA in order to increase their sensitivity and specificity. This panel of peptides was found to be far better than PSA for prostate cancer detection with an ROC curve which was close to perfection at 0.97. It is interesting to see that the area under the ROC curve of PSA was very elevated in the entire group of patients, close to 0.80, much better than many previous studies, although in the subgroup of patients with PSA between 2.5 and 10 ng/ml, the area under the ROC curve was within the generally observed value of 0.50.

In an Editorial O. J. Finn [1] makes the link between diagnostic and therapeutic possibilities, in other words using these auto-antibody signatures at the same time to establish the diagnosis, but also if the T cell response is investigated, to allow to know whether the tumour is likely or not to be destroyed by the immune system.

We, however, certainly have to be cautious about these new methodologies, because the results need to be verified in larger, unselected populations. Although there has been an explosion of knowledge in cancer biology and molecular biology, most of the recently detected marker substances have not found a place yet as a tool for diagnosis of cancer and for prostate specifically.

For instance, despite the enthusiasm about the results of proteomics, E.P. Diamandis [2] has recently warned that there are still many concerns. Using the auto-antibody signature for prostate cancer detection, large amounts of proteins do not need to be present, but rather very low levels of specific antigens, which indeed are much easier to detect given our available powerful immunological technology.

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## References

- [1] Finn OJ. Immune Response as a Biomarker for Cancer Detection and a Lot More. *N Engl J Med* 2005;353(12):1224–35.
- [2] Diamandis EP, van der Merwe D-E. Plasma protein profiling by mass spectrometry for cancer diagnosis: opportunities and limitations. *Clin Cancer Res* 2005;11(3):963–5.

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## Incidence and Follow-Up of Patients with Focal Prostate Carcinoma in 2 Screening Rounds After an Interval of 4 Years

Postma R, de Vries SH, Roobol MJ, Wildhagen MF, Schröder FH, van der Kwast TH

*Cancer* 2005;103:708–16

### Expert's summary:

This study evaluated the clinicopathologic features of patients with focal carcinoma ( $\leq 3.0$  mm in only one core of sextant biopsies, lacking Gleason patterns 4 and 5). The patients underwent radical prostatectomy (RP,  $n = 103$ ) or were monitored regularly (the “wait and watch” method [WW],  $n = 108$ ). RP specimens were categorized into minimal tumours (volume  $< 0.5$  ml, no Gleason patterns 4 and 5, organ confined, and negative surgical margins) or moderate-to-advanced tumours (volume  $\geq 0.5$  ml, Gleason pattern 4 or 5 detectable, extracapsular extension, or positive surgical margins). The median tumour volume in RP specimens was 0.13 ml, and in 78.6% of the cases it was  $< 0.5$  ml. In 3 specimens, no tumour was found. A prostate-specific antigen (PSA) density cutoff level of  $\leq 0.1$  ng/ml/cm<sup>3</sup> predicted a tumour volume of  $< 0.5$  ml in 94% of cases. Because it was part of the European Randomized Screening Study for Prostate Cancer, the study also showed that the proportion of patients with focal prostate carcinoma increased significantly, from 16% during the first screening round to 29% during the second round, 4 years later. The median tumour volume in the first round (PSA  $\geq 4$ ) was 0.16 ml, and that in the second round (PSA  $\geq 3$ ) was 0.07 ml, but this difference did not reach statistical significance.

### Expert's opinion:

The authors concluded that the WW policy with delayed curative intent may be recommended in patients 55–75 yr old who have focal carcinoma and a PSA density  $< 0.1$  ng/ml/cm<sup>3</sup>. Natural-history

data from other cohorts have shown the indolent character of low-grade prostate cancer, with 15-year disease-specific survival rates of approximately 80% [1,2]. The follow-up time of the present study is still short, and the mortality in the RP and WW groups cannot be analyzed yet. A Scandinavian randomized study [3] showed better results for patients with RP, but most cancers were clinically detectable. Even then, because of a small absolute reduction in prostate cancer mortality, 19 patients needed to be treated to prevent one death at 10 years. Respective speculations for today's low-risk small tumours increase this number to 100 patients [4]. This is ethically unacceptable. It is impossible to stop prostate cancer screening, but if the PSA threshold is lowered from 4 to 3 or even lower, and 12 biopsies are routinely done, we are going to find a large number of insignificant cancers. Surgeons like to operate, but it is not meaningful to shoot mosquitoes with a cannon. Proper guidelines for screening and the WW policy are urgently needed.

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## References

- [1] Albertsen PC, et al. 20 year outcomes following conservative management of clinically localized prostate cancer. *JAMA* 2005;293:2095–101.
- [2] Johansson JE, et al. Natural history of early, localized prostate cancer. *JAMA* 2004;291:2713–9.
- [3] Bill-Axelsson A, et al. Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med* 2005;352:1977–84.
- [4] Klotz L. Active surveillance for prostate cancer: for whom? *J Clin Oncol* 2005;23:8165–9.

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