PROSTATE CANCER

Fetuin-A—a marker for metastatic disease?

Mintz *et al.* have presented the first report implicating fetuin-A in prostate cancer and have shown that autoantibodies against fetuin-A have prognostic utility as indicators for metastatic disease.

Isolated antibodies from sequentially-acquired serum samples from a patient with advancing prostate cancer taken over a period of 7 years were analysed by phage display fingerprinting. Increased phage recovery was evident in samples from year 7 (when the patient presented with elevated PSA, more bone lesions and a biopsy-confirmed metastasis) relative to previous sampling time points.

Sequence analysis of phage clones revealed enrichment of a single peptide—CTFAGSSC—over the sampling period. Relative recovery frequency of CTFAGSSC increased from 27.5% in year 1 to 91.0% in year 9, and this enrichment was concomitant with the patient developing advanced metastatic prostate cancer.

Isolated serum antibodies showed increased reactivity to CTFAGSSC over

time and were specific for this peptide motif. Sequencing and BLAST analysis of a protein band identified using purified serum antibodies on whole-cell lysates suggested fetuin-A as the putative antigen. Increased expression of fetuin-A in metastatic prostate cancer compared with normal prostate tissue was then confirmed by immunohistochemistry.

Furthermore, fetuin-A antibodies showed stronger serum reactivity in samples from patients with metastatic castration-resistant disease than in men with organ-confined cancer. Receiver-operating characteristic analysis for antibody detection in normal controls and metastatic prostate cancer samples indicated an AUC of 0.91, indicating that fetuin-A reactivity could identify patients with metastatic disease.

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Original article Mintz, P.J. *et al.* Discovery and horizontal follow-up of an autoantibody signature in human prostate cancer. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1500097112