PROSTATE CANCER

Sarcosine: the saga continues...

Two recent studies have provided further evidence that sarcosine is not a reliable biomarker of prostate cancer invasiveness and aggressiveness.

An earlier metabolomics study (Sreekumar, A. *et al. Nature* **457**, 910–914; 2009) indicated that the level of sarcosine—also known as *N*-methylglycine—in urine collected after digital rectal examination (DRE) was associated with prostate cancer progression, as well as being able to differentiate between men with and without the disease. However, the findings of another team contradicted these results. Klaus Jung's group showed that sarcosine in urine supernatant did not improve diagnostic performance compared to level of free PSA (Jentzmik, F. *et al. Eur. Urol.* **58**, 12–18; 2010).

Jung and colleagues have further investigated sarcosine's diagnostic potential, publishing their data recently in *The Journal of Urology*. The group measured sarcosine levels in matched samples of malignant and nonmalignant tissue from 92 patients with prostate cancer, using gas chromatography–mass spectrometry. They correlated the sarcosine levels with tumor grade, stage and biochemical recurrence, and estimated the accuracy of sarcosine as a biomarker of tumor aggressiveness.

Median sarcosine levels were 7% significantly higher in malignant than nonmalignant samples, but the values noticeably overlapped. Sarcosine levels were not markedly different between samples of different tumor grade or stage, and there was no relationship with Gleason score. Using Kaplan–Meier curves, the team sought to determine whether sarcosine levels were related to biochemical recurrence; no association was found.

These findings are in accordance with those of another study, published in *Prostate Cancer and Prostatic Diseases*. This team attempted to resolve the controversies surrounding sarcosine as a biomarker for prostate cancer by creating four algorithms (urine supernatant and sediment sarcosine/creatinine and urine supernatant and sediment log₂[sarcosine/alanine]). 110 men with abnormal DRE—71 of whom had prostate cancer and 39 of whom had no evidence of malignancy—were enrolled in the study, along with 20 healthy volunteers. Urine was collected after DRE, and levels of PSA, PCA3, sarcosine, alanine and creatinine measured, to create the algorithms.

Data from the urine supernatant algorithms did not differ significantly between healthy patients and those with no evidence of malignancy, but values were significantly higher in patients with prostate cancer. The areas under the curve (AUCs) for the sarcosine algorithms were nonsignificantly higher than the AUCs for serum PSA and urine PSA mRNA. The highest AUC for any algorithm was for sediment log₂[sarcosine/alanine], but even this was not significantly better than that of serum PSA. Inclusion of the sarcosine algorithm did, however, improve the diagnostic accuracy of PCA3 and %free PSA, compared to either variable alone.

Negative data has certainly dampened enthusiasm for sarcosine in the scientific community—will future research help it to recover? We await the results of the next sarcosine study with interest.

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Original articles Jentzmik, F. *et al.* Sarcosine in prostate cancer is not a differential metabolite for prostate cancer aggressiveness and biochemical progression. *J. Urol.* **185**, 706–711 (2011) | Cao, D. L. *et al.* Efforts to resolve the contradictions in early diagnosis of prostate cancer: a comparison of different algorithms of sarcosine in urine. *Prostate Cancer Prostatic Dis.* doi:10.1038/pcan.2011.2