TRIAL WATCH

Telomerase testing

Measurements of the level of telomerase activity in urine can be used to detect early stage bladder cancer in men, according to a case–control prospective study published in the *Journal of the American Medical Association*.

Bladder cancer represents the fourth most common malignancy in men and the tenth most common in women, and approximately 20% of patients with this cancer die each year. When the disease is diagnosed and treated in the early stages, the chances of survival are good, indicating the importance of early detection for this cancer type.

Current approaches for detecting bladder cancer are invasive, costly or have limited sensitivity. A reliable, simple and non-invasive test is therefore urgently needed. One potential marker of bladder cancer is telomerase activity, which can be detected in urine samples using the highly sensitive telomeric repeat amplification protocol (TRAP) assay.

Maria Aurora Sanchini and colleagues conducted a study to define the diagnostic accuracy of different telomerase activity cutoff values in terms of sensitivity and specificity. The study, which was performed in Italy, included 218 men — 84 healthy individuals and 134 patients at first diagnosis of histologically confirmed bladder cancer. Urine samples were analysed using both cytological assays and the TRAP assay, and the results were compared. Patients were diagnosed with bladder cancer based on bioptic and cystoscopic examinations (direct visual examination of the urinary tract).

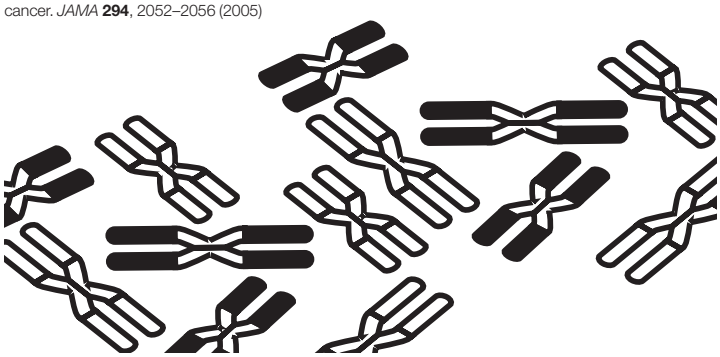
Using a 50 arbitrary enzymatic unit (AEU) cutoff value established in an earlier pilot study, the authors validated their initial results in a new set of patients. In these patients, the TRAP assay could detect bladder tumours with 90% sensitivity and with 88% specificity. Specificity increased to 94% for individuals aged 75 years or younger. The TRAP assay was also able to detect telomerase activity in patients with low-grade tumours or with negative cytology results.

The sensitivity of the TRAP assay in detecting bladder tumours was similar in the subgroups of patients with different tumour grades at all AEU cutoff values. In particular, the sensitivity at 50 AEUs was 93%, 87% and 89% for patients with grades I, II or III tumours, respectively.

The authors suggest that the assays should not be recommended for use in routine screening programmes because of the low incidence of bladder cancer. Rather, the TRAP assay should be aimed at high-risk subgroups, such as smokers, who have an approximately threefold increased risk of developing bladder cancer compared with non-smokers, or patients with symptoms of bladder cancer. It can also be used to monitor recurrence in patients who have been previously treated for bladder cancer.

Further prospective studies on larger patient populations are needed to better determine the ability of this assay to detect low-grade tumours and disease recurrence. This is especially important, as this tumour type is characterized by a high relapse rate.

ORIGINAL PAPER Sanchini, M. A. *et al*. Relevance of urine telomerase in the diagnosis of bladder cancer. *JAMA* **294**, 2052–2056 (2005)



METASTASIS

Easing the pain

Bone is often the only clinically detectable site of metastasis from prostate cancer and usually presents as bone pain. This pain is very difficult to control with the current approaches of radiotherapy, chemotherapy, bisphosphonates and analgesics, so new therapies are needed. Patrick Mantyh and colleagues report in *Cancer Research* that a blocking antibody to nerve growth factor (NGF) attenuates bone pain in a mouse model of prostate bone cancer.

The authors injected canine prostate tumour cells into the intramedullary space of the femur of nude mice. Tumour-induced pain-related behaviours, such as guarding the limb and flinching, were observed at 9 days post-injection and increased until 19 days post-injection, when the mice were euthanized. Similar to humans, significant bone formation and destruction was seen and the newly formed bone in the tumour-bearing compartment had the characteristic scalloped appearance seen in patients with prostate cancer.

Intraperitineal injection of anti-NGF antibodies at day 7, 12 and 17 post-sham or prostate cancer cell injection, significantly reduced time spent guarding the limb and spontaneous flinching. The pain attenuation effect was greater than when morphine sulphate — a common treatment for bone pain — was given to the mice. The authors suggest that the antibody might be particularly effective because nearly all nerve fibres that innervate bone express the neurotrophin receptors TRKA (also known as NTRK1) and p75, and these are the receptors through which NGF sensitizes and/or activates peripheral receptors of pain.

The treatment had no effect on bone formation or destruction, or on tumour growth. Importantly, the antibody did not change the intensity or density of sensory or sympathetic nerve fibres in the skin or bone of the treated mice, and also did not change the tactile or thermal sensitivity of the mice. The antibody would not be expected to cross the blood–brain barrier, so adverse effects in the central nervous system are unlikely.

So, anti-NGF therapy might have fewer side effects than high-dose opiates and, as prostate cancer patients with bone metastases often live for more than 5 years after diagnosis, the possibility of long-term control of bone pain could greatly improve their quality of life.

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References and links

ORIGINAL RESEARCH PAPER Halvorson, K. G. *et al*. A blocking antibody to nerve growth factor attenuates skeletal pain induced by prostate tumor cells growing in bone. *Cancer Res.* **65**, 9426–9435 (2005)