GLOSSARY

METHYLATION-SPECIFIC
POLYMERASE CHAIN
REACTION

A technique used to detect CpG methylation in genomic DNA, using sodium-bisulphate-modified DNA as a template, and primers for specific methylated promoters

DNA METHYLATION
SCORE (M-SCORE)

The sum of the log hazard ratios for each gene, analyzed by multivariate logistic regression analysis for pathology.

Vitamin D analog BXL628 arrests prostate growth in patients with benign prostatic hyperplasia

Proliferation of prostate cells, as in benign prostatic hyperplasia (BPH), is inhibited by binding of agonists such as vitamin D₃ to the vitamin D receptor expressed on the prostate cell surface. Analogs of these agonists are sought that have minimal effects on calcium homeostasis while inhibiting proliferation and inducing apoptosis of prostate cells. One such analog, BXL628, has shown these effects in rats.

Italian researchers have conducted a multicenter, double-blind, randomized, placebo-controlled trial to assess the effect of BXL628 in men with BPH. Patients were ≥ 50 years old and had a prostate volume of at least 40 ml. In all, 119 patients participated; 57 received BXL628 and 62 received placebo. After 12 weeks, mean prostate volume in the BXL628 group had decreased by 2.90%, while that of the control group had increased by 4.32% ($P < 0.0001$).

Vitamin D₃ analogs are known to affect calcium homeostasis, but no significant effect on calciuria was observed. Currently, 5 α reductase inhibitors are the standard treatment for BPH, but these have been associated with sexual dysfunction; no adverse sexual effects were reported in this trial, and no patients withdrew because of adverse effects.

The authors conclude that, with its different mode of action and favorable safety profile, BXL628 offers an alternative to current treatments for BPH, and might also be suitable for combination therapy.

Jim Casey

Original article Colli E *et al.* (2006) BXL628, a novel vitamin D₃ analog arrests prostate growth in patients with benign prostatic hyperplasia: a randomized clinical trial. *Eur Urol* **49**: 82–86

Smoking could influence prostate cancer progression via gene hypermethylation

Enokida and colleagues have demonstrated for the first time that hypermethylation of several key genes is significantly associated with smoking status in prostate cancer.

METHYLATION-SPECIFIC POLYMERASE CHAIN REACTION was used to analyze prostate tissue from 164 men with prostate cancer and 69 with benign

prostatic hyperplasia; these results were confirmed by bisulphate DNA sequencing. The analyzed genes were *APC*, *GSTP1*, and *ABCB1* (formerly known as *MDR1*). The DNA METHYLATION SCORE (M-SCORE) was calculated for each group of patients.

Hypermethylation was found to be a significant predictor of disease status (prostate cancer versus benign prostatic hyperplasia) for each of the three genes ($P < 0.001$). A significant correlation between aberrant methylation and smoking status was seen for *GSTP1* ($P = 0.018$), but not for *APC* or *ABCB1* ($P = 0.109$ and $P = 0.094$, respectively).

However, when the methylation status of all three genes were analyzed together, the M-score was significantly higher in prostate cancer patients who currently smoked, compared to those who had never smoked ($P = 0.008$), and there was a significant association between M-score and pack-years smoked in the prostate cancer group ($P = 0.039$). Additionally, M-score was significantly associated with features of advanced disease, such as high tumor stage, high Gleason sum, and a high preoperative PSA level.

The authors conclude that smoking could influence prostate cancer progression through CpG hypermethylation of related genes in a dose-dependent fashion, but they acknowledge that the median follow-up time of 33.9 months was shorter than that required for a thorough analysis.

Tamsin Osborne

Original article Enokida H *et al.* (2006) Smoking influences aberrant CpG hypermethylation of multiple genes in human prostate carcinoma. *Cancer* **106**: 79–86

Upper urinary tract surveillance in patients with stage Ta bladder cancer

There is a conspicuous lack of information available to help urologists make decisions on surveillance strategies for the upper urinary tract (UUT) in patients with stage Ta transitional-cell carcinoma of the bladder. To address this issue, Canales *et al.* of the University of Minnesota and Veterans Administration Medical Center, Minneapolis, have carried out a retrospective, single-institution study to investigate patterns of bladder tumor recurrence associated with the subsequent development of a UUT