vaccine therapy was 13.9 months, which was greater than for those receiving nilutamide alone; however, those who began treatment with nilutamide, but had vaccine added to the regimen on PSA progression, had a median time to treatment failure of only 5.2 months.

The authors conclude that the potential synergy of combined prostate cancer vaccines with antiandrogens warrants further study.

Alexandra King

Original article Arlen PM *et al.* (2005) Antiandrogen, vaccine and combination therapy in patients with nonmetastatic hormone refractory prostate cancer. *J Urol* **174:** 539–546

A role for the *NF1* gene in the development and progression of colon cancer?

Aberrant activation of Ras is involved in the development of a range of cancers. The *NF1* gene product, neurofibromin, acts as a tumor suppressor by 'switching off' the active form of Ras and therefore has a potential role in tumorigenesis.

In this first study of the potential role of *NF1* in sporadic colon cancer, Čačev and colleagues investigated loss of heterozygosity at the *NF1* locus and NF1/mRNA expression in 100 samples of tumor and adjacent normal tissue obtained during routine surgery for colon adenocarcinoma.

Loss of heterozygosity of *NF1* was seen in only 20.7% of heterozygous samples, and the authors concluded that this event is not important in the development or progression of sporadic colon cancer. The differential expression of *NF1* isoforms during tumorigenesis, however, might be more important in the regulation of *NF1* function. There was a statistically significant increase in *NF1* mRNA expression in tumor tissue compared with normal tissue ($P = 0.04$), with *NF1* isoform type II predominantly expressed in normal tissue, and type I predominant in tumor tissues ($P = 0.0005$). A continuous transition from predominant type II expression in normal tissue to predominant type I expression in tumor tissue was also detected. Total neurofibromin expression increased as tumors advanced, but total wild-type neurofibromin remained the same.

The authors conclude that *NF1* might play a role in the development and progression of colon cancer and that this gene could be a potential tumor marker and new potential target for therapy.

Carol Lovegrove

Original article Čačev T *et al.* (2005) *NF1* gene loss of heterozygosity and expression analysis in sporadic colon cancer. *Gut* **54:** 1129–1135

CDH3 promoter hypomethylation and P-cadherin expression in invasive breast carcinoma

Around 30% of breast carcinomas show up-regulation of the cell–cell adhesion glycoprotein P-cadherin, which has been reported to be associated with proliferative high-grade tumors and poor outcome. Paredes and colleagues analyzed P-cadherin expression in a series of 150 cases of invasive breast cancer and found that P-cadherin expression strongly correlated with high histological grade, increased proliferation, c-erbB2 and p53 expression, lack of estrogen receptors and poor patient survival.

The authors also evaluated promoter methylation as a putative molecular mechanism for the transcriptional regulation of the P-cadherin gene (*CDH3*). When a breast cancer cell line expressing low levels of P-cadherin was treated with a demethylating agent, levels of P-cadherin mRNA and protein increased, suggesting that hypomethylation of the promoter accompanies transcriptional activation of *CDH3*. Analysis showed that 71% of P-cadherin-negative breast cancer cases exhibited promoter methylation, whereas 65% of the P-cadherin-positive cases were unmethylated. Most cases of partial methylation (tumors expressing both methylated and unmethylated alleles) were negative for P-cadherin expression. Normal, P-cadherin-negative breast epithelial cells showed consistent *CDH3* promoter methylation. The authors suggest that progressive hypomethylation of the *CDH3* allele occurs during breast carcinogenesis, inducing expression of P-cadherin, which in turn leads to cancer-cell invasion and motility.

These findings are consistent with the hypothesis that hypomethylation of critical