

identified 186 phage-peptide clones that bind to autoantibodies in serum samples from patients with prostate cancer. A genetic algorithm was then employed to select a panel of 22 peptides that would comprise the detector. In validation experiments using serum samples from 119 patients and 138 healthy controls, the detector was significantly more successful at identifying the presence of prostate cancer than the PSA test ($P < 0.001$). The difference in discriminatory power between the two tests was enhanced at PSA levels of $< 10 \mu\text{g/l}$. Of the 22 phage peptides in the detector, four were identified as being in-frame and derived from intracellular proteins involved in regulating transcription or translation.

The authors conclude that autoantibody tests could be used in combination with PSA screening to improve the early detection of prostate cancer, particularly in patients with lower PSA levels, thereby preventing unnecessary biopsies.

Alexandra King

Original article Wang X *et al.* (2005) Autoantibody signatures in prostate cancer. *N Engl J Med* 353: 1224–1235

Tumor protein D52: an early tumor marker in ovarian cancer?

Tumor protein D52 (TPD52) has been identified as a chromosome 8q21 amplification target in breast and prostate carcinoma. Given that recurrent chromosome 8q21 gain has been reported in ovarian cancer, Byrne and colleagues used a polyclonal anti-TPD52 antibody to examine the expression of TPD52 by immunohistochemistry in normal ovarian epithelium ($n=9$), benign serous adenomas ($n=11$), serous borderline tumors ($n=6$) and invasive carcinomas from all major histological subtypes ($n=57$). *In situ* TPD52 expression and TPD52 gene copy number were also established in an independent cohort of stage III serous carcinomas.

TPD52 was not expressed in normal ovarian tissue, and benign serous tumors were also predominantly negative. TPD52 was, however, overexpressed in the majority (77%) of ovarian carcinomas regardless of histological subtype. In general, expression of TPD52 was cytoplasmic as previously reported, but nuclear expression was seen in mucinous and clear-cell carcinomas. Comparison of *in situ* TPD52

expression and TPD52 copy number showed that dosage and expression were significantly and positively correlated (Spearman rank correlation coefficient; $r_s = 0.829$ and 0.837 , respectively). Upregulation of TPD52 therefore reflects increased TPD52 copy number.

The authors hypothesize that TPD52 represents a novel early tumor marker for ovarian cancer that could allow earlier detection of disease and also represent a potential therapeutic target. Further studies into the significance of TPD52 overexpression in ovarian and other cancers are required.

Carol Lovegrove

Original article Byrne JA *et al.* (2005) Tumor protein D52 (TPD52) is overexpressed and a gene amplification target in ovarian cancer. *Int J Cancer* 117: 1049–1054

High-intensity focused ultrasound shows promise for noninvasive tumor ablation

Studies from China and the Far East suggest that extracorporeal high-intensity focused ultrasound (HIFU) might have potential as a noninvasive method of tumor ablation. Illing *et al.* initiated a phase II study to determine whether HIFU might also be useful in a Western population.

Thirty patients with liver or kidney tumors were treated with a single session of HIFU under general anesthetic. Response was assessed by MRI 12 days post-treatment. Discrete zones of tumor ablation were seen in 25 of 27 evaluable patients, and ablation was more consistent in hepatic tumors than in renal tumors (100% vs 67%, respectively). Adverse events were local to the treatment site and were self-limiting. Although 80% of patients reported skin discomfort, this was generally described as mild. Around 13% of patients showed post-ablation syndrome, including low-grade fever, which resolved within 24 hours.

The advantages of HIFU include its non-invasive nature, which is associated with less morbidity than surgery, real-time imaging for evaluation of the treatment area, potential usefulness in a range of tumor types, favorable safety profile, and repeatability. Limitations of the method, however, include the need for general anesthesia, the length of time taken to perform the required ablation, and the effect of position on ability to access the tumor. Overall,

the authors conclude that HIFU holds promise in the curative setting and in palliation; further clinical development is ongoing at their unit.

Carol Lovegrove

Original article Illing RO *et al.* (2005) The safety and feasibility of extracorporeal high-intensity focused ultrasound (HIFU) for the treatment of liver and kidney tumors in a Western population. *Br J Cancer* **93**: 890–895

Pregnancy and breast cancer risk in women with *BRCA1* or *BRCA2* mutations

Many risk factors known to be associated with the development of breast cancer in the general population are linked to changes in the hormonal patterns to which the breast is exposed; early age at first birth and multiparity are both associated with a decreased breast cancer risk in the general population. Data from a previous study suggested that this association might be reversed in women at high risk of breast cancer, but patient numbers were small and confidence limits wide.

To extend this earlier study, Cullinane and colleagues performed a matched, case-controlled study of 1,260 paired women with *BRCA1* or *BRCA2* mutations. They found that, among *BRCA1* carriers, women with four or more children had a 38% decrease in breast cancer risk compared with matched nulliparous women. By contrast, women with the *BRCA2* mutation showed an increased risk of breast cancer with increasing parity; this increased risk was greatest in the 2-year period following a birth. The adjusted risk of breast cancer increased by 17% with each additional birth in women with the *BRCA2* mutation who were under 50 years of age; parity did not affect risk in women over 50 years of age.

The authors conclude that these results have important implications in risk assessment and management in this patient group.

Carol Lovegrove

Original article Cullinane CA *et al.* (2005) Effect of pregnancy as a risk factor for breast cancer in *BRCA1/BRCA2* mutation carriers. *Int J Cancer* **117**: 988–991

Novel nonmyeloablative conditioning regimen protects against GVHD

It has previously been reported that total lymphoid irradiation plus antithymocyte serum

administered before hematopoietic-cell transplantation prevents graft-versus-host disease (GVHD) in rodent models. A study by Lowsky *et al.* describes the first positive response to this therapy in humans.

Eligible patients with lymphoid malignant disease ($n=24$) or acute leukemia ($n=13$) underwent a nonmyeloablative conditioning regimen of 800 cGy irradiation, delivered in 10 fractions to all major lymphoid organs, together with antithymocyte globulin on the first 5 days of irradiation. Patients then received hematopoietic-cell transplantation from related or unrelated donors, followed by immunosuppressive therapy. For comparison, two groups of control patients conditioned with single-dose total-body irradiation (200 cGy) prior to transplantation, either alone or with fludarabine, were also studied.

Of the 37 patients who underwent total lymphoid irradiation plus antithymocyte conditioning, only 2 developed GVHD post-transplantation (both with lymphoid malignant disease). Sixty-seven percent of patients who were in partial remission before conditioning had attained complete remission when assessed for tumor status post-transplantation. In patients who underwent this conditioning regimen, the mean percentage of interleukin-4-positive CD4⁺ T cells was significantly higher than in control patients ($P=0.04$). The authors conclude that conditioning with total lymphoid irradiation plus antithymocyte globulin reduces the incidence of GVHD in patients with acute leukemia and lymphoid malignant disease, without affecting the efficacy of transplantation.

Alexandra King

Original article Lowsky R *et al.* (2005) Protective conditioning for acute graft-versus-host disease. *N Engl J Med* **353**: 1321–1331

Activated HER2 expression and resistance to taxane chemotherapy

Although preclinical studies have demonstrated that HER2 overexpression is associated with resistance to paclitaxel *in vitro*, previous clinical findings conflict with these data. Recent work has shown that the activated, phosphorylated form of HER2 (P-HER2) is expressed in a subset of HER2-overexpressing tumors, and is an indicator of poor prognosis in node-positive