the expression of this protein in a collection of renal cell carcinoma (RCC) tissues, Herrem and colleagues report that this may correlate with disease grade and could be a useful prognostic indicator in patients undergoing surgery.

The investigators obtained paraffin-embedded RCC and adjacent normal kidney tissues from 34 patients, all of whom had undergone radical or partial nephrectomy. Using a specific anti-EphA2 monoclonal antibody, they demonstrated that EphA2 expression varied markedly between different tumors and tended to be higher in more aggressive tumors. Expression was significantly greater in grade 3 and 4 tumors than in grade 2 tumors. Although not statistically significant, a trend was also shown between increased tumor volume and EphA2 expression. In addition, more vascularized tumors tended to show higher levels of expression of the protein.

Importantly, EphA2 overexpression was inversely correlated with disease-free interval and overall survival; patients with lowest expression of the EphA2 were more likely to remain disease-free after surgery, whereas those with highest expression were at greater risk of disease recurrence and tended to survive for a shorter period.

Commenting that the results seemed to apply not only to clear-cell RCC but also to the rarer forms, namely papillary and chromophobe RCC, Herrem *et al.* suggest that these findings could be useful in the clinical management of patients with this disease.

Original article Herrem CJ *et al.* (2005) Expression of EphA2 is prognostic of disease-free interval and overall survival in surgically treated patients with renal cell carcinoma. *Clin Cancer Res* **11:** 226–231

Defining risk in patients with renal cell carcinoma

In 2002, Motzer *et al.* proposed a prognostic model for survival in patients with previously untreated renal cell carcinoma, based on patient characteristics and biochemical parameters. In their recent study, Mekhail and colleagues from the Cleveland Clinic Foundation have validated the model and added two further prognostic factors.

The investigators analyzed the records of 308 patients with metastatic renal cell carcinoma who were included in clinical trials between 1987 and 2002. All patients were treated with immunotherapy and/or chemotherapy and most had prior nephrectomy. The team discovered that four of the five prognostic factors in the Motzer *et al.* model—time from diagnosis to treatment, hemoglobin, serum lactate dehydrogenase and corrected serum calcium—were independent predictors of survival in these patients. The corresponding favorable, intermediate and poor-risk groups had median survival times similar to those reported in Motzer *et al.*'s analysis.

Having considered an array of potential prognostic factors, Mekhail *et al.* showed that prior radiotherapy and the number of metastatic sites (none or one vs two or three) were also independent predictors of survival. The main effect of adding these two additional factors to the model was to reclassify some of the 'intermediate risk' patients into the favorable or poor-risk groups.

In conclusion, this study validates and extends the model proposed by Motzer *et al.* An international consortium has now been set up to continue the work and to agree a common approach.

Original article Mekhail TM *et al.* (2005) Validation and extension of the Memorial Sloan-Kettering prognostic factors model for survival in patients with previously untreated metastatic renal cell carcinoma. *J Clin Oncol* **23:** 832–841

Visceral fat may increase prostate cancer risk

Recent work by von Hafe *et al.* has shown a link between visceral fat and the risk of prostate cancer. Previous studies in this area have given conflicting results, possibly because visceral and subcutaneous fat accumulation have not been analyzed separately.

Von Hafe and colleagues from Portugal studied 63 patients with incident prostate cancer and 63 age-matched controls. Using a single CT scan of the abdomen at the level of the fourth lumbar vertebra, the investigators assessed the body fat distribution of each participant. Although the two groups were similar in terms of body mass index, the mean area of abdominal fat was significantly higher in men with prostate cancer than in the control participants, mainly because of a higher mean

area of visceral fat. Men whose ratio of visceral fat to subcutaneous fat lay in the upper tercile were more than 14 times more likely to have prostate cancer than those with lower ratios (odds ratio 14.5, 95% CI 4.45–47.19). No relationship was seen between disease stage and body fat distribution.

The authors suggest that the observed relationship between visceral fat and prostate cancer risk might be associated with cytokines secreted by visceral fat cells, steroid hormone imbalances or increased insulin levels. As all the participants in this study were white, von Hafe *et al.* note that the results may not apply to other ethnic groups.

Original article von Hafe P *et al.* (2004) Visceral fat accumulation as a risk factor for prostate cancer. *Obes Res* **12:** 1930–1935

Unstable DNA in cells obtained by prostatic massage associated with cancer

The standard diagnostic indicators of early prostate cancer—serum prostate-specific antigen (PSA) levels and ratios, and digital rectal examinations—are unreliable. In the search for better indicators of low-grade disease, cells manually liberated from the prostate have been examined for various markers. Unfortunately, the sensitivity of markers such as telomerase and ornithine decarboxylase is too low to be clinically useful. Now, a French group has shown that the presence of genetic lesions in prostate cells obtained by prostatic massage is correlated with positive biopsies.

Ninety-nine men with a serum PSA level between 4 and 10 ng/ml and/or abnormalities detected during digital rectal examination underwent prostatic massage. Prostatic cells sufficient for extraction of DNA were collected from the post-massage voided urine in 81 cases. Blood leukocyte DNA was also collected. DNA from these two cell types was comparatively examined for LOSS OF HETEROZYGOSITY (LOH) at six 'hotspot' loci.

At least one allelic deletion was detected in the prostatic DNA of 57 patients; 33 of these had biopsy-confirmed prostate cancer. Of the 25 men in whom no LOH was detected, 5 had prostate cancer. The sensitivity of LOH for detection of prostate cancer (87%), but not the specificity (44%), exceeded that of a free:total PSA ratio <15% (55% and 74%, respectively).

The validity of the LOH test using cells obtained via prostatic massage was confirmed by comparison with LOH of corresponding cells of tumors surgically excised from 19 men. Identical patterns of LOH were evident in 71% of samples, and similar patterns in 86%. The authors suggest that determination of LOH following prostatic massage is a useful, minimally invasive method of identifying candidates for prostate biopsy.

Original article Thuret R *et al.* (2005) Clinical relevance of genetic instability in prostatic cells obtained by prostatic massage in early prostate cancer. *Br J Cancer* **92:** 236–240

GLOSSARY

LOSS OF HETEROZYGOSITY (LOH) A 1.3× difference in relative intensity between an allele in genetic material from two different sources (e.g. prostatic cells and blood leukocytes)