**GLOSSARY**

**CELLULAR SENESCENCE**
A state of permanent cell-cycle arrest that may be induced by DNA damage or activated oncogenes

**PROSTATIC INTRAEPITHELIAL NEOPLASIA**
Cellular proliferations with cytologic changes mimicking cancer, including nuclear and nucleolar enlargement, without basement membrane disruption

Italian and Indigenous men were the least likely ethnicities to seek help.

The authors conclude that the high number of reproductive health disorders and concerns revealed by their study underlines the need for development of appropriate education strategies and services targeted at middle-aged and older men.

*Christine Kyme*

**Original article** Holden CA *et al.* (2005) Men in Australia Telephone Survey (MATeS): a national survey of the reproductive health and concerns of middle-aged and older Australian men. *Lancet* **366:** 218–224

## Cellular senescence suppresses prostate tumorigenesis in mice

Researchers at Memorial Sloan–Kettering Cancer Center have discovered that induction of CELLULAR SENESCENCE slows the development of prostate cancer in mice. The team also found evidence of senescence in human prostate tumors, demonstrating the therapeutic relevance of their findings.

Chen and colleagues engineered mice in which the tumor-suppressor genes *Pten* and/or *Trp53* (encoding the p53 protein) were inactivated in the prostate after puberty. Histopathologic analysis revealed that mice with an inactivated *Pten* gene developed high-grade PROSTATIC INTRAEPITHELIAL NEOPLASIA, which eventually developed into nonlethal prostate cancer, whereas those with an inactivated *Trp53* gene had healthy prostates. However, mice with both *Pten* and *Trp53* inactivated rapidly developed invasive prostate cancer and died within 7 months. From these observations, the authors postulated that loss of *Trp53* accelerates the progression of prostate cancers initiated by inactivation of *Pten*.

The researchers used mouse embryonic fibroblasts to explore the molecular basis of their observations, and found that acute homozygous loss of *Pten* arrests growth in prostate cancer cells via the p53-dependent cellular senescence pathway.

Immunohistochemical analysis of samples from 12 early-stage human prostate tumors showed strong staining for senescence in regions where premalignant changes were seen, but rarely in carcinomatous regions, providing further evidence that loss of p53 function is associated with prostate cancer progression.

In light of their findings, the authors suggest that drugs that potentiate activation of p53 could be developed to induce cellular senescence in *PTEN*-deficient prostate cancer, thus slowing its progression.

*Tamsin Osborne*

**Original article** Chen Z *et al.* (2005) Crucial role of p53-dependent cellular senescence in suppression of Pten-deficient tumorigenesis. *Nature* **436:** 725–730

## Gene expression profiling in prostate cancer

In prostate cancer patients, accurate estimation of the risk of disease recurrence following radical prostatectomy can aid decisions for primary and adjuvant treatment. This process is usually based on clinical variables such as tumor grade and serum PSA level, but there has also been interest in the use of molecular markers. Stephenson and colleagues have recently explored the differences in gene expression signatures between recurrent and nonrecurrent prostate tumor specimens. Their analysis suggests that the addition of gene expression profiling to an established, clinical nomogram, predictive model might allow improved risk stratification.

The investigators used a human gene array to find prognostic gene expression variables in 37 recurrent and 42 nonrecurrent primary prostate tumor samples. Overexpression of 57 genes was observed in the recurrent-tumor specimens; most of these genes had not previously been associated with prostate cancer. The next step was to use logistic regression modeling to compare the predictive accuracy of gene profiling with that of the clinical nomogram.

Using gene profiling alone, the samples were correctly classified as recurrent or nonrecurrent in 75% of cases. The corresponding predictive accuracy of the nomogram was significantly higher, at 84%. By combining the two methods, however, an accuracy of 89% was reached. The authors note that this dual method is likely to be particularly useful in patients whose nomogram-predicted risk of recurrence lies within the middle range.

*Ruth Kirby*

**Original article** Stephenson AJ *et al.* (2005) Integration of gene expression profiling and clinical variables to predict prostate carcinoma recurrence after radical prostatectomy. *Cancer* **104:** 290–298