Allele-specific expression of *TGFBR1* is linked to an increased risk of colorectal cancer

Genetic variation influences predisposition to colorectal cancer and, although alleles associated with an increased risk have been identified, much of the genetic basis of this predisposition remains unexplained. Evidence exists that a common variant of the transforming growth factor-β type I receptor (*TGFBR1*) gene could be associated with increased colorectal cancer risk. Valle and colleagues investigated the hypothesis that mutations in *TGFBR1* confer a predisposition to colorectal cancer either directly, or indirectly by modification of other genes.

The authors used three single-nucleotide polymorphisms to test for allele-specific expression of *TGFBR1*. Allele-specific expression of *TGFBR1* is dominantly inherited, occurs in sporadic colorectal cancer and results in reduced expression of the gene. The study included 242 patients with microsatellite-instability-negative colorectal cancer; of the 96 of patients who were heterozygous for the three single-nucleotide polymorphisms, 12 showed allele-specific expression variation ratios >1.5. A further 49 patients were heterozygous for one further single-nucleotide polymorphism and 17 of these individuals had allele-specific expression values >1.5. Of the 138 patients in whom this parameter was evaluated, 29 showed allele-specific expression of *TGFBR1*. The authors estimated that the population attributable risk of colorectal cancer contributed by allele-specific expression of *TGFBR1*, in the predominantly Caucasian population studied, was 10–21%.

In conclusion, allele-specific expression of *TGFBR1* is a major factor in genetic predisposition to colorectal cancer.

Original article Valle L *et al.* (2008) Germline allele-specific expression of *TGFBR1* confers an increased risk of colorectal cancer. *Science* **321:** 1361–1365

Premedication reduces discomfort during screening mammography

Fear of pain is a factor that affects many women who participate in screening mammography and little research has been conducted into how to reduce the discomfort associated with mammograms. Lambertz *et al*. carried out a prospective study in women who expected a high level of pain to investigate whether premedication with acetaminophen, ibuprofen and/or 4% lidocaine gel could reduce discomfort and improve satisfaction with screening mammography.

A total of 418 women aged between 32 and 89 years completed this double-blind, placebo-controlled study. The patients were randomly divided into 12 study groups, which covered all combinations of the study medications. A visual analog scale was used to rate discomfort and satisfaction.

Discomfort during mammography was significantly reduced with application of 4% lidocaine gel before the procedure. An experience of discomfort significantly decreased patients' satisfaction with their mammography and plans to undergo future mammograms were significantly affected by satisfaction levels. Interaction with the mammographic technologist and nurse examiner significantly affected discomfort and satisfaction.

Use of premedication with 4% lidocaine gel could reduce the fear of pain that leads patients to avoid screening mammography, and could potentially improve patients' willingness to undergo regular screening. In turn, the authors suggest that improved adherence to regular screening could lead to earlier detection of breast cancer.

Original article Lambertz *et al.* (2008) Premedication to reduce discomfort during screening mammography. *Radiology* **248:** 765–772

Intensive myeloablative chemoradiation improves response rates in melanoma

Interleukin (IL)-2 and dacarbazine have been approved for the treatment of metastatic melanoma and achieve objective response rates of 12–15%. Dudley and colleagues reported that in patients with metastatic melanoma, adoptive transfer of autologous tumor-infiltrating lymphocytes (TILs) after heavy pretreatment with lymphocyte-depleting chemotherapy, resulted in objective response rates of 51%. Dudley *et al.* now present updated results of that study and report the results of two pilot trials that investigated whether addition of 2 Gy or 12 Gy total-body irradiation to the chemotherapy conditioning regimen could improve the outcome of adoptive cell therapy.