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IN BRIEF

GENETICS

NUDT15 variants affect mercaptopurine tolerance in children

A new genome-wide association study has identified two genetic variants that influence tolerance of mercaptopurine chemotherapy in children with acute lymphoblastic leukaemia (ALL). Patients homozygous for the mutated T allele of rs116855232 in *NUDT15* tolerated 8.3% of the standard mercaptopurine dose; patients who were heterozygous for the T form of *NUDT15* had significantly reduced mercaptopurine tolerance (63% of planned dose) compared with patients expressing a wild-type genotype (83%, $P=0.024$). Association of the rs1142345 variant of *TPMT* with substantially lower mercaptopurine tolerance in patients who were homozygous or heterozygous for this allele was also confirmed. Patients who were heterozygous for both risk alleles had substantially lower mercaptopurine tolerance than those who were heterozygous for either risk allele. These findings have important implications for individualized ALL treatment.

Original article Yang, J. J. *et al.* Inherited *NUDT15* variant is a genetic determinant of mercaptopurine intolerance in children with acute lymphoblastic leukemia. *J. Clin. Oncol.* doi:10.1200/JCO.2014.59.4671

RISK FACTORS

Long-term statin use reduces pancreatic cancer risk in men

Data from a case-control study reveal that statin use reduces the risk of pancreatic cancer by 34% (OR 0.66; 95% CI 0.47–0.92); however in sex-stratified analyses, statistically significant effects were not detected in women. Furthermore, longer-term use of statins in men was found to be correlated with greater reductions in the risk of pancreatic cancer, regardless of age at commencement of statin use ($P_{trend}=0.006$). These data confirm tentative reports from epidemiological studies, which originally suggested this protective effect of statin use. This study provides the strongest evidence to date that statin use decreases the risk of pancreatic cancer.

Original article Walker, E. J. *et al.* Statin use and risk of pancreatic cancer: results from a large, clinic-based case-control study. *Cancer* doi:10.1002/cncr.29256

UROLOGICAL CANCER

Elevated TERT activity correlates with inferior survival

Research in urothelial cancer cell lines has shown that high telomerase activity is a better marker of aggressive urothelial cancer than mutations in the promoter of the telomerase reverse transcriptase gene (*TERT*). 23 different urothelial cancer cell lines were derived from both muscle-invasive and non-muscle invasive tumours with a wide range of different stages and grades. Copy-number variations (between two and six copies of *TERT*) were detected, and cell lines containing –126C>T or –142 C>T promoter mutations had significantly greater *TERT* mRNA expression than cell lines with other promoter mutations ($P=0.0067$); increased *TERT* mRNA generally resulted in greater telomerase protein expression and activity. Telomerase activity was correlated with telomere length, and ultimately disease-specific survival, although the presence of promoter mutations or copy-number variations was not, suggesting that telomerase activity is a better indicator of prognosis, in patients with urothelial cancer regardless of tumour grade or disease stage.

Original article Borah, S. *et al.* *TERT* promoter mutations and telomerase reactivation in urothelial cancer. *Science* doi:10.1126/science.1260200