12th AACR Frontiers in Cancer Prevention Research meeting

Methylation in cervical cancer

Erin Siegel (Moffitt Cancer Center, Tampa, FL, USA) showed data that reveals several methylated CpG loci and genomic regions in HPV-associated cancer and CIN3 lesions. Siegel and colleagues examined DNA from ten invasive cancers, five CIN3 lesions, and nine normal tissues to ascertain methylation status at more than 450 000 CpG loci. 321 CpG loci had different methylation patterns from normal tissues (false discovery rate corrected q<0·0005); with less stringent criteria, differential methylation was noted in 369 genes (q<0·01), 19 of which had sensitivity and specificity to distinguish between tumour, at least one CIN3 sample, and normal tissue. Siegel is now attempting to validate these findings in a larger, independent cohort. Methylated regions could have use as biomarkers for early detection of cervical cancer.

Biomarker for ovarian cancer

SP17, a cancer/testis antigen, could be used with CA125 to discriminate between ovarian cancer and benign ovarian lesions. Murizio Chiriva-Internati (Texas Tech University, Lubbock, TX, USA) and colleagues previously showed this discrimination with SP17 in preclinical and in-vitro models. Circulating concentrations of SP17 and CA125, and tissue expression of SP17 were measured in 136 ovarian cancers, 45 benign lesions, and 142 healthy tissue samples. SP17 expression was restricted to ovarian cancer, and serum concentrations were 3·7 ng/mL (95% CI 3·6–3·8) in controls, 3·9 ng/mL (3·7–4·1) in benign lesions, and 5·5 ng/mL (5·4–5·7) in ovarian cancer. Combining CA125 and SP17 data gave 86·2% sensitivity, 96·8% specificity, and a 96·1% positive predictive value for detecting ovarian cancer compared with controls or benign lesions.

NSAIDs in colorectal cancer

Polymorphisms affecting prostaglandin synthesis and related pathways affect preventive effects of non-steroidal anti-inflammatory drugs (NSAIDs) for colorectal cancer. Akke Botma (German Cancer Research Centre, Heidelberg, Germany) and colleagues investigated gene–NSAID interaction estimates in an analysis of four independent study populations that had previously been typed for polymorphisms in the prostaglandin synthesis and related pathways. Weighted averages of the interaction estimates were done. Three SNPs in *ALOX12* ($p_{interaction}$=0·02), *FLAP* ($p_{interaction}$=0·03), and *PTGS2* ($p_{interaction}$=0·02) affected NSAID effects on colorectal cancer occurrence. Four SNPs had significant effects on NSAID use and rectal cancer. These data could help to design tailored prevention.

Andy McLarnon

Cameron Davidson/Corbis

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Acute GVHD prophylaxis—atorvastatin for donor and recipient

Acute graft-versus-host disease (GVHD) is a leading cause of complications and death in patients receiving allogeneic haemopoietic cell transplantation (allo-HCT). GVHD occurs when donor T cells recognise recipient antigens as foreign and trigger a response that results in damage to recipient tissues. Of patients who receive an HLA-matched transplant from a related donor, 30–50% develop acute GVHD.

With a unique two-pronged approach, a prospective clinical phase 2 trial tested the effect of administering atorvastatin (a 3-hydroxy-3-methyl-glutaryl-coenzyme-A reductase inhibitor) to both donor and recipient before allo-HCT for protection against GVHD. 30 matched sibling donor and recipient pairs received oral atorvastatin (40 mg per day) for at least 14 days before allo-HCT; recipients also received standard tacrolimus and methotrexate prophylaxis, in addition to 180 days of atorvastatin. The cumulative incidence of grade 2–4 acute GVHD in recipients was 3·3% (95% CI 0·2–14·8) at day 100 and 11·1% (2·7–26·4) at day 180; at 1 year, it was 52·3% (27·6–72·1) for chronic GVHD. 25·4% of patients had relapsed at 1 year (10·9–42·9).

Senior investigator Michael Craig (West Virginia University, Morgantown, WV, USA) summarised, "Atorvastatin is a readily available statin; it is a relatively simple drug to take and has few side-effects." With this treatment, "there was a very low rate of acute GVHD, and the usual rate of chronic GVHD. There was no increase in relapse, and overall survival and progression-free survival were excellent."

Daniel Weisdorf (University of Minnesota, Minneapolis, MN) commented, "This was a very different approach to changing the immune response than others have used before, also a very safe approach. The results are promising, but atorvastatin did not affect the incidence of chronic GVHD. However, if statins can turn down the volume of acute GVHD and thus the clinical severity, patients will need less treatment."

Marco Mielcarek (Fred Hutchinson Cancer Research Center, Seattle, WA, USA) said, "Whether non-toxic statin treatment of donors or recipients prevents GVHD after allogeneic stem cell transplantation is a very interesting question. Unfortunately, the small sample size of the current study precludes conclusions that go much beyond what is already known. A larger phase 2 study and eventually a randomised controlled trial are needed to answer this intriguing question more definitively."

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