IN THE NEWS

Collaborative effort

A newly developed partnership between five pharmaceutical companies and the National Cancer Institute (NCI) will provide US \$6 million of funding to increase enrollment in early-phase clinical trials (<http://www3.cancer.gov/cancercenters/announcements/PA-03-501.pdf>).

In this unique public-private collaboration, the National Institutes of Health (NIH), along with the pharmaceutical companies, will provide selected cancer centres with funding to design and implement new approaches to increase patient participation in Phase I and Phase II cancer trials. NCI-funded cancer centres can apply for up to US \$600,000 of funding per year for two years. Half of the funding will be provided by the NCI and half will be provided by the industrial partners. The NCI expects to make 5–8 awards.

The funds are to be used by the cancer centres to develop new approaches for overcoming barriers to enrolling patients in early-phase trials. Some of these obstacles include inadequate understanding of the importance of clinical trials by the public and health-care professionals, inadequate compensation for participation, increasing regulatory requirements and over-burdened institutional review boards. Public wariness to clinical research, geographical barriers and inadequate peer recognition of physicians that conduct early-phase trials also prevent the enrollment of cancer patients.

The NCI plans to use what it learns from this pilot study to develop models that can be disseminated to other cancer centres and research institutions. The five pharmaceutical partners that will provide funding are Aventis, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline and Novartis.

Kristine Novak

TUMORIGENESIS

Hang on tight!

Helicobacter pylori infects the gastric mucosa of more than half of all people worldwide, and infection with these bacteria is an early risk factor for gastric cancer. Both *H. pylori* and the host inflammatory response that it elicits are believed to contribute to tumorigenesis, but this interaction is not well understood. Ironically, according to Thomas Borén and colleagues, this antibacterial inflammatory response promotes gastric-cell synthesis of sialylated glycoconjugates, which the bacteria exploit for adherence to the surface epithelium.

In *Science*, Borén's group reported that epithelial cells of inflamed gastric mucosa have sialylated glycosphingolipids (GSLs) on their surface, and they isolated a repetitive sialyl-di-Lewis x GSL (sLex/a) from human adenocarcinoma cells. The authors showed that *H. pylori* expresses an adhesin protein called sialic-acid-binding adhesin (SabA), which binds to sLex/a antigens and allows the bacteria to cling to the surface of the

GENOMIC INSTABILITY

Chromosome crisis

Crisis ensues when telomeres become critically short — the chromosome ends fuse with other chromosomes, which sets the stage for chromosomal breakage at cell division. These double-strand breaks provide a site for amplifications and deletions in the genome, which can result in tumorigenesis. Mice have much longer telomeres than humans and do not normally undergo significant telomere shortening — which occurs in premalignant cells and ageing tissues in humans — and crisis. However, engineered mice that do not possess *mTerc* — the RNA subunit of telomerase — display more gross chromosomal aberrations and have a shift in tumour spectrum to one that resembles that of aged humans. So which genes are affected by these chromosomal rearrangements, and are homologous genes affected in humans?

Rónán O'Hagan and colleagues, reporting in *Cancer Cell*, used array-comparative genomic hybridization (array-CGH) to investigate the mechanism by which loss of telomerase promotes genomic instability. To perform the analysis, arrays of bacterial artificial chromosomes (BACs) that spanned the mouse genomes were differentially hybridized with normal and tumour-cell DNA. Tumours from late-generation telomerase-deficient mice (*mTerc*^{-/-}, *Trp53*^{+/-}) showed alterations in 20.5% of the arrayed BACs, compared with only 2.5% from early-generation telomerase-deficient mice. A direct comparison between the amount of genomic instability in specific tumour types was difficult because of the different tumour spectrums of the early- and late-generation mice; however, an examination of osteosarcomas, lymphomas and breast carcinomas revealed that

late-generation mice have more chromosomal alterations than early-generation mice. So, this increase in genomic instability is independent of tumour type in those tumours that the mice have in common.

So where in the mouse genome do these alterations occur? Thirty-two alterations were recurrent — identified in more than 25% of the tumours examined — and the most common of these, which was observed in 8 out of 15 tumours, was an amplification of distal chromosome 6. A more careful analysis revealed that the minimal amplified region contained six genes — only one of which, *Kras*, is known to be involved in tumorigenesis. Although amplification of this region has been observed in viral-oncogene-induced skin tumours from late-generation telomerase-deficient mice, it has not been found in late-generation *mTerc*^{-/-} breast cancers that overexpress the *Wnt* oncogene, perhaps because *Wnt* expression can bypass the requirement for an activated *Kras*.