WEB WATCH

Buried treasure

• http://www.cancer.gov/

It's all-change at the United States National Cancer Institute (NCI): as well as a new Director, it has a new web site.

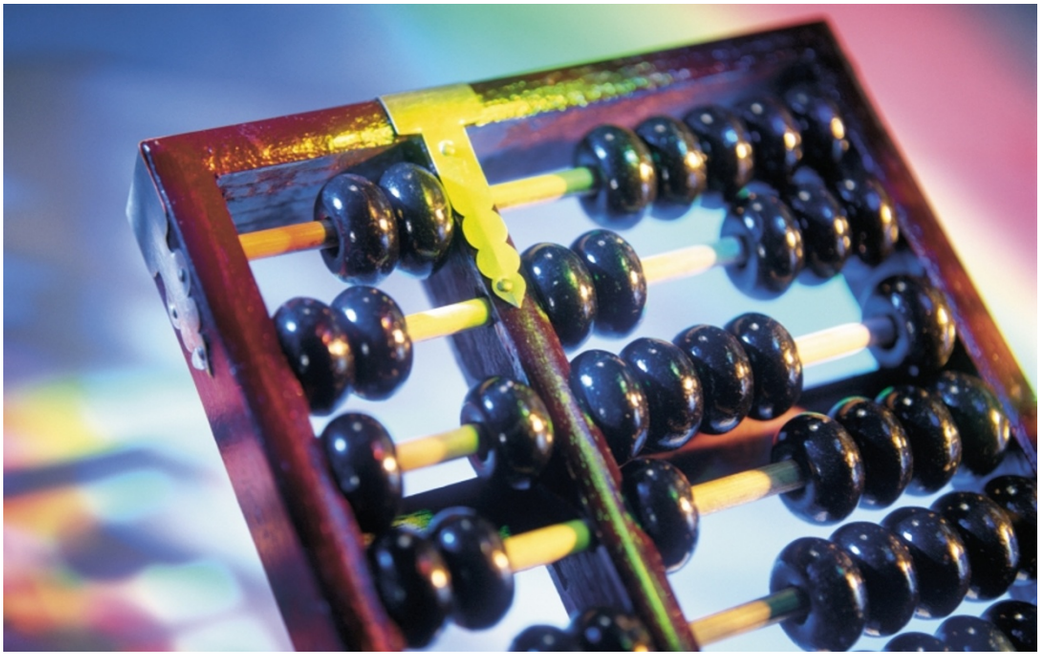
Navigation is now through a series of index tabs; this provides a welcome air of consistency throughout the site, but it's not obvious which information is directed at researchers and which is aimed at the general public. For researchers, finding funding opportunities is straightforward: the 'Research funding' tab takes you to a well-organized list of announcements and contact persons for grant applications. The 'Research programs' section is redundant with 'About NCI', but both sections provide a reasonable overview of NCI-funded research.

The problems come when you want to find a particular investigator or resource. The researcher directory is now hidden under 'Organizational structure' in 'About NCI', and the investigators' index, which doesn't have a search facility, is under 'Research programs'. A list of scientific resources is also located here, although it took me some time to track down old favourites such as the Cancer Genome Anatomy Project.

The acclaimed CancerNet site, which provides information on cancer diagnosis and treatment, is now housed in 'Cancer information'. Types of cancer are listed alphabetically, and it's easy to navigate between information for patients and that for health professionals, but, again, the free-text search facility has gone.

What's missing is a primer explaining the rationale for the reorganization, which maps the old resources onto the new site and describes new features. Without this, many of the NCI's treasures remain buried — to old and new visitors alike.

Cath Brooksbank



PROGNOSIS

Countdown to recurrence

What determines whether colorectal cancer will recur after surgery? Duke's system for histopathological staging has been the mainstay of colorectal cancer prognosis for many years. But patients with tumours of the same Duke's stage can have radically different outcomes.

Now, in the 19 January issue of *The Lancet*, Bert Vogelstein's group describe a new molecular technique called 'digital single-nucleotide polymorphism' (SNP), which they use to see how allelic imbalance of chromosomes 8p and 18q within tumour cells relates to disease progression. These chromosomes have previously been shown to exhibit allelic imbalance in colorectal cancer, but their relevance to disease progression is not understood.

The first step is to find an informative SNP on these chromosomes — one for which the patient is heterozygous — using DNA purified from normal tissue at the tumour margin. Once an informative marker has been found, purified DNA from microdissected tumour tissue is plated out robotically in 384-well plates at low concentrations, so that an average of one molecule containing the SNP lands in each well. After polymerase chain reaction (PCR) amplification, fluorescent probes that can distinguish the two alleles are used to count each allele one by one. Statistical algorithms are then used to determine whether there is an allelic imbalance in the sample. By this mechanism, the proportion of each allele in a patient's DNA can be assessed. This technique is more accurate than traditional methods of measuring allelic imbalance, which use microsatellite markers, in part because the PCR products obtained are identical in size, eliminating any artefacts caused by preferential degradation of larger alleles.

The authors studied 180 patients who had early-stage sporadic colorectal cancer with no sign of metastases. Digital SNP was used to test for imbalances of chromosomes 8p and 18q in surgically removed tumours. Tumour samples were divided into those with allelic imbalances in both chromosomes, those with imbalances in either (but not both) chromosome, and those that showed no imbalance at all on either chromosome. The five-year disease-free survival was remarkably different in the three groups: 100%, 74% and 58% in tumours with no allelic imbalance, imbalance in one chromosome, and imbalance in both chromosomes, respectively. These results were independent of other variables, including Duke's stage. So, a higher allelic imbalance correlates with a lower probability of disease-free survival.

How, then, does allelic imbalance affect prognosis? The authors propose three models. First, important tumour-suppressor genes on chromosomes 8p and 18q are lost. Second, allelic imbalance in these chromosomes might simply reflect instability within the cell as a whole. And third, if all colorectal cancers accumulate allelic imbalances at similar rates, allelic imbalance would simply represent a measure of how long the tumour has existed.

Although the authors do not favour a particular model, previous studies have correlated allelic imbalances in at least nine chromosomes with prognosis in colorectal cancer, which indicates that aneuploidy in general, rather than loss of specific tumour suppressors, might drive tumour progression. Similar correlations have been made for other cancers. So perhaps we'll eventually be able to use the same digital SNP-based assay to predict outcomes in every cancer patient.

Sandra Clark

References and links

ORIGINAL RESEARCH PAPER Zhou, W. *et al*. Counting alleles to predict recurrence of early-stage colorectal cancers. *Lancet* **359**, 219–225 (2002)

WEB SITE

Bert Vogelstein's lab:
http://www.hhmi.org/research/investigators/vogelstein.html