WEB WATCH

Meeting of minds

- http://www.cancer-researchuk.org/

Those of us in the United Kingdom cannot have failed to notice that its two leading cancer research charities — the Imperial Cancer Research Fund and the Cancer Research Campaign — have merged to form Cancer Research UK. The merging of their web sites is proof that two heads are better than one.

The front page is aimed squarely at the general public, with news, information on fundraising events and prominent links to patient resources. But a large 'science and research' button at the top of the page takes cancer researchers straight to the information that's most relevant to them.

Navigation within this 'science wing' is through five tabs. The 'researchers' section is a simple directory, searchable by name, keyword or free text. Information on individual researchers and their projects varies in detail; it would be useful to have key publications for all of them. There's also a clickable map that takes you to Cancer-Research-UK-funded institutes and labs around the United Kingdom. The 'research institutes' section is presented as a hypertext-linked list, each institute taking you to a list of group leaders; clinical centres are presented similarly but, unfortunately, are not yet clickable.

Cancer Research UK now awards an almost bewildering array of grants; these are organized into broad categories in the Grants application section, and sufficient information is given for you to work out whether you're eligible and when you should apply; forms are not available on the web, but there is information on how to send for application packs.

Finally, in the enigmatic 'other sites' section, don't miss the links list; this tracks cancer research across the globe, making it a useful resource for all cancer researchers.

Cath Brooksbank

GENOMIC INSTABILITY

Defective division

Centrosomes are frequently amplified in cancer cells, and this amplification has been proposed to contribute to tumorigenesis because cells with several spindles are genomically unstable. But what is the mechanism of amplification? Patrick Meraldi *et al.* report in *The EMBO Journal* that centrosome amplification is a consequence, rather than a cause, of defective division.

Overexpression of the mitotic kinase Aurora-A — which occurs in many cancers — causes centrosome amplification. Both wild-type Aurora-A and a kinase-dead (KD) mutant caused an increase in centrosome number when overexpressed in CHO cells, indicating that the kinase activity is not required for centrosome duplication. Addition of hydroxyurea (HU) — a drug that blocks cells in S phase, thereby allowing multiple rounds of centrosome duplication without DNA replication — also increased the percentage of cells with more than two centrosomes, but Aurora-A expression did not enhance this number above that of wild-type CHO cells.

So does Aurora-A induce centrosome amplification by mimicking HU and blocking cells in S phase? Overexpression of Aurora-A in HeLa cells — which are unable to duplicate their centrosomes during S-phase arrest — still increases centrosome number, but only in the absence of HU, indicating that Aurora-A overexpression does not induce S-phase arrest and that cells must pass through mitosis to increase their number of centrosomes.

Closer examination of the Aurora-A-overexpressing HeLa cells revealed that most cells (75%) with multiple centrosomes were also multinucleate, so could the increase in centrosome number be an indirect consequence of aberrant cell division? The number of multinucleate and tetraploid cells increases as Aurora-A is overexpressed, indicative of a cytokinesis defect. So can other defects that lead to an aberrant cytokinesis also cause centrosome amplification? Overexpression of the Aurora-B and PLK-1 mitotic kinases, which also result in multinucleate cells, leads to centrosome amplification, as does addition of the cytokinesis-inhibitory drug cytochalasin D.

TUMOUR SUPPRESSORS

More than meets the eye

Although most people don't think much of mucus, its important functions, such as lubricating the epithelia and protecting against infection, are undisputed. Recent findings, reported in the 1 March issue of *Science*, reveal a new function for this underappreciated substance — preventing the development of colorectal cancer.

A family of high-molecular-weight secreted glycoproteins known as mucins are a primary component of the mucus layer. So far, 13 different mucins have been discovered (MUC1–13), and found to be expressed in different tissues. Alterations in mucin expression and glycosylation pattern have been observed in human colon cancer samples, and MUC2 — the most abundant gastrointestinal mucin — is reportedly downregulated in human colorectal carcinomas. Little is known, however, about MUC2 function at the molecular level.

To evaluate the role of MUC2 in tumorigenesis, Anna Velcich *et al.* created *Muc2*-null mice. *Muc2* is highly expressed by the mucus-producing goblet cells of the intestine. The authors found that *Muc2*-null mice did not develop recognizable goblet cells in any region of the intestine, and were therefore defective in mucus production. *Muc2*-null mice are able to digest food and absorb nutrients, as they gained weight at the same rate as their heterozygous and wild-type littermates. But 65% of *Muc2*-null mice developed gastrointestinal tumours by the time they are 1 year old. These tumours were found in the small and large intestine and rectum, but not in the stomach, where *Muc2* is not normally expressed.

So what is the function of Muc2 in the intestinal epithelium? Velcich *et al.* believe that Muc2 is involved in regulating cell proliferation and migration, as intestinal epithelial cells of *Muc2*-null mice had a higher proliferation:apoptosis ratio than those of wild-type epithelium, resulting in elongated crypts. *Muc2*-null epithelial cells also migrated faster in the intestinal mucosa than did wild-type cells — in mice injected with bromodeoxyuridine, labelled epithelial cells of *Muc2*-null mice migrated more rapidly to proximal regions of intestinal villi. Tumours