WEB WATCH

Plant power

• http://www.mskcc.org/mskcc/html/11570.cfm

Several of the articles in *Nature Reviews Cancer* mention natural products with interesting biological effects against cancer. But — with so many of these products commercially available and so few stringent regulatory checks — how is it possible to evaluate these compounds and know how safe they are? The answers might only be a click away.

The 'About Herbs, Botanicals and Other Products' web site is the brainchild of the Memorial Sloan–Kettering Cancer Center, the mission of which was to provide an online resource with easy access to concise, clinically relevant information about botanicals, vitamin mixtures and other related products. Each entry is researched and written by an oncology-trained pharmacist, with expertise in botanical products, or by a cancer nutrition specialist. The entries are then peer-reviewed by at least two editors or panel advisors before being posted on the web site.

The web site is designed to be used by consumers and health-care professionals, and when you search for your favourite herb or botanical the results page provides a wealth of information. This includes a clinical summary and a list of constituents (where applicable), as well as facts about the mechanisms of actions, side effects, interactions and other potential problems or benefits. The entries are updated as often as relevant news is released and reviewed at least twice a year to ensure that the data are current.

So, with such high-quality information, it is hardly surprising this web site received a 2003 Sci/Tech Web Award in Medicine from the editors at *Scientific American*.

Emma Croager

more slowly, with lower proliferation rates and higher apoptotic rates than wild-type tumours. Unexpectedly, IC-VEGFko tumours had a similar phenotype to SC-VEGFko tumours and did not resemble IC-HIFko tumours at all. IC-VEGF-deficient tumours were focally localized, but did not form real tumour masses and contained a low density of distorted blood vessels. In fact, the density of blood vessels in IC-VEGFko tumours was about 50% less than in IC-VEGFwt tumours. So, it seems that loss of VEGF slows growth of IC tumours by impairing survival of the hijacked brain vasculature.

These results emphasize the importance of the microenvironment in determining tumour response, and have important implications for HIF-1α-targeted therapy. The use of this treatment in different tissues could produce diametrically opposing results — either tumour suppression or increased growth and invasion.

Emma Croager

References and links

ORIGINAL RESEARCH PAPER Blouw, B. *et al.* The hypoxic response of tumours is dependent on their microenvironment. *Cancer Cell* **4**, 133–146 (2003)

FURTHER READING Semenza, G. L. Targeting HIF-1 for cancer therapy. *Nature Rev. Cancer* **3**, 721–732 (2003)

WEB SITE

Gabriele Berger's lab:
http://www.som.ucsf.edu/departments/neuros/faculty_staff/department_faculty/bergers.html

ONCOGENES

One-man band

MYC is an all-singing, all-dancing oncogene. Not only does it induce cell proliferation, but there is evidence that it might also contribute to invasion, angiogenesis and genomic instability — all of which have implications for tumour formation. Dean Felsher and colleagues, reporting in the *Proceedings for the National Academy of Sciences*, have further investigated the role in genomic instability, and propose that MYC interferes with the repair of DNA double-strand breaks (DSBs).

Overexpression of *MYC* is known to lead to gene amplifications and fusions, which could be caused by defective DSB repair. To test this hypothesis, the authors generated normal human foreskin fibroblasts that contained a regulatable *MYC* gene. Overexpression of *MYC* was shown to increase the number of γ-H2AX foci — a marker of DSB repair. But does MYC cause the DSBs themselves or prevent their repair?

This was investigated by irradiating cells to introduce DSBs either in the presence or absence of MYC. Following this treatment, the number of γ-H2AX foci increased, regardless of whether or not *MYC* was expressed. However, in cells that did not express *MYC*, the γ-H2AX foci disappeared with an hour of treatment; in cells expressing *MYC*, the foci remained for up to 3 hours, indicating that MYC does not affect the generation of DSBs, but does interfere with their repair.

Felsher and colleagues next looked at the effect of *MYC* expression on the repair of a single DSB. The DRAA8 cell line has been engineered to contain the green fluorescent protein *(GFP)* gene, which is activated by a homologous recombination event following the introduction of a single DSB by the restriction enzyme I-*Sce*-I; repair can be monitored by expression of GFP. Transfection of I-*Sce*-I resulted in an increase in the number of GFP-positive cells, but expression of MYC reduced this back to background levels. A PCR-based assay confirmed that MYC could suppress DSB repair through non-homologous end joining and single-strand annealing, as well as through homologous recombination. The effect on DNA repair seems to be specific to DSBs though, as *MYC* expression has no effect on nucleotide excision repair of ultraviolet-light-induced lesions.

But can *MYC* expression result in genomic instability in normal cells by failing to repair DSBs that spontaneously occur? This was examined in a single cell cycle using synchronized normal human foreskin cells. Interestingly, *MYC* expression induced a high frequency of chromatid breaks (12%), deletions (3%) and translocations (3%), compared with only rare breaks and no deletions and translocations in cells that did not express *MYC*.

So, MYC seems to induce genomic instability by preventing DSB repair. What is left to determine is the precise mechanism by which this occurs, and the contribution that this makes to MYC-induced tumorigenesis.

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References and links

ORIGINAL RESEARCH PAPER Karlsson, A. *et al.* Defective double-strand DNA break repair and chromosomal translocations by *MYC* overexpression. *Proc. Natl Acad. Sci. USA* **100**, 9974–9979 (2003)

WEB SITE

Dean Felsher's lab:
http://www.med.stanford.edu/felsherlab/