CANCER GENETICS

EMSY forges a link

One of the recent puzzles in cancer genetics has been why the breast and ovarian cancer susceptibility genes *BRCA1* and *BRCA2* do not seem to be involved in sporadic cancer. The discovery of the BRCA2-interacting protein EMSY, by Tony Kouzarides and colleagues, might now allow part of this puzzle to be solved.

EMSY was identified in a yeast two-hybrid screen with the amino terminus of BRCA2. This protein is involved in several BRCA2-linked activities: transcriptional activation, DNA repair and chromatin remodelling. EMSY can repress BRCA2's ability to activate transcription of a reporter construct, it localizes to sites of DNA damage after γ-irradiation, and it interacts with chromatin-remodelling proteins.

The potential involvement in chromatin remodelling was discovered after *EMSY* was cloned. The sequence was novel, but contained an 80-amino-acid domain — named EMSY N-terminal domain — that was found in nine *Arabidopsis* proteins. These proteins also contained a new Royal family domain, designated Agenet, that can recognize lysine-methylated histones, hence the link with chromatin remodelling.

In two-hybrid screens with ENT, more than 80% of the interacting clones contained a Royal family domain. So, it is likely that one of EMSY's functions is in chromatin regulation.

But what about the connection with cancer? *EMSY* maps to chromosome 11q13.4-5, which is frequently amplified in sporadic breast cancer. Four different amplicons are found within this region and the authors used fluorescence *in situ* hybridization (FISH) to show that *EMSY* was amplified in 5/28 (18%) breast cancer cell lines and in 1/5 samples from newly diagnosed patients. The degree of amplification correlated with the expression level of *EMSY*, and the authors showed that *EMSY* could be amplified independently from other genes in the region.

To investigate the significance of this amplification, the authors next looked at how it affects prognosis by comparing expression in tissue samples from patients with sporadic breast cancer with their outcome. *EMSY* was shown to be amplified in 70/551 (13%) cases, and the median disease-specific survival for node-negative breast cancer was 6.4 years with the amplification, but 14 years without. So, *EMSY* amplification correlates with a poorer prognosis, specifically for node-negative breast cancer.

As *BRCA2* mutation increases susceptibility to ovarian cancer, as well as breast cancer, the authors investigated whether *EMSY* was amplified in sporadic ovarian cancer. They found amplification in 17% of high-grade carcinomas, but none in low-grade.

So, the BRCA2 pathway might be involved in sporadic breast and ovarian cancer after all. Although this is yet to be confirmed, the observation that EMSY and BRCA2 have overlapping functions and cause the same pathologies is encouraging. As EMSY inhibits the transcriptional activation function of BRCA2, it is certainly possible that *BRCA2* deletion and *EMSY* amplification have similar effects.

Emma Greenwood,
Senior Editor, Nature Reviews Cancer

References and links

ORIGINAL RESEARCH PAPER
Hughes-Davies, L. *et al. EMSY* links the BRCA2 pathway to sporadic breast and ovarian cancer. *Cell* **115**, 523–535 (2003)

WEB SITE
Tony Kouzarides' laboratory:
http://www.welc.cam.ac.uk/groups/kouzarides.html

WEB WATCH

Stem cells, anyone?

• http://www.isscr.org

The International Society for Stem Cell Research has launched a brand new web site so if you are a stem cell researcher — or simply curious about stem cells — and have not seen it yet, then I recommend you do so right now.

This sleek and easy-to-navigate site is sponsored by the Juvenile Diabetes Research Foundation International and promises to be a one-stop shop for scientists, students, media, policy-makers and the public. The homepage is updated regularly with news that is relevant to society members and to the stem-cell community. One attractive feature is the 'topic of the month' — a collection of primary papers and reviews on a selected topic. The first 'TOM' page was devoted to reproductive cloning and its inefficiency and featured a recent *Nature Reviews Genetics*' review by Ian Wilmut and colleagues.

For scientists, there is an up-to-date list of selected publications, upcoming meetings, a job bank and stem-cell FAQs. There is also a link to the society newsletter and a list of online stem-cell resources. For students, there is a Junior Investigator's Toolbox, which contains information about grants, jobs and other science-related links.

The public can access basic but timely information about stem cells and their use in research, including an explanation of the important differences between embryonic versus adult stem cells and therapeutic versus reproductive cloning.

And there is more: ethicists and policy makers can follow legislative and regulatory news and the media can check their facts by using the 'Find an expert' page.

Although the web site is freely accessible, members of the society are rewarded with special perks, such as stem-cell Endnote libraries.

Magdalena Skipper