IN BRIEF

CELL DIVISION

Dynamic localization of a cytoplasmic signal transduction response regulator controls morphogenesis during the *Caulobacter* cell cycle.

Jacobs, C. *et al. Proc. Natl Acad. Sci. USA* **98**, 4095–4100 (2001)

The bacterium *Caulobacter crescentus* divides asymmetrically to generate a small 'swarmer' cell and a larger 'stalked' cell. This asymmetry, it turns out, is generated and maintained by dynamic changes in the subcellular localization of components involved in a signal-transduction cascade. Whereas the DivK response regulator protein is found throughout the cytoplasm of the swarmer cell, it is localized to the pole of the stalked cell. And these localization patterns are controlled by the membrane-bound DivJ and PleC histidine kinases, which themselves are asymmetrically localized at opposite poles of the dividing cell.

SIGNAL TRANSDUCTION

p53 induction of heparin-binding EGF-like growth factor counteracts p53 growth suppression through activation of MAPK and PI3K/Akt signalling cascades.

Fang, L. *et al. EMBO J.* **20**, 1931–1939 (2001)

Transcriptional targets of p53 abound, and this paper reports the identification of a new one — the heparin-binding epithelial-growth-factor-like growth factor. Its expression is induced in response to DNA damage, in a p53-dependent way, and it in turn activates the mitogen-activated protein kinase and phosphatidyl-inositol 3-kinase/Akt pathways to promote cell survival.

DEVELOPMENT

Steroid regulation of autophagic programmed cell death during development.

Lee, C.-Y. & Baehrecke, E. H. *Development* **128**, 1443–1455 (2001)

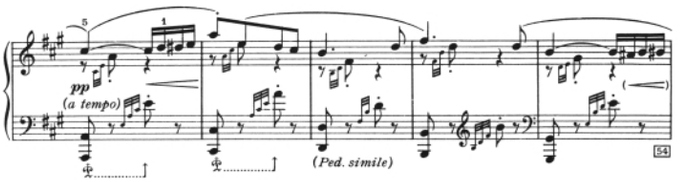
Steroid hormones activate programmed cell death during development to remove cells that are not needed. This study of *Drosophila* larval salivary glands reveals that developmental death involves genes involved in apoptosis — including caspases — yet the dying cells have morphological characteristics typical of autophagic cell death. These results indicate that there could be common regulatory mechanisms between the distinct processes of apoptosis and autophagy.

RIBOSOMES

Crystal structure of the ribosome at 5.5 Å resolution.

Yusupov, M. M. *et al. Science* March 29 2001 (epub ahead of print)

Harry Noller and colleagues report the crystal structure of the complete *Thermus thermophilus* 70S ribosome, complete with bound messenger and transfer RNAs, at a resolution of 5.5 Å. All of the ribosomal chains (16S, 23S and 5S) and most of the ribosomal proteins can be fitted to the electron-density map, and with this level of detail it is possible to formulate — and test — models for the mechanism of translation.



CANCER

Unwind with BACH

The product of the *BRCA1* gene — germline mutations in which confer an increased risk of breast or ovarian cancer — has been implicated in the repair of double-stranded DNA breaks (DSBs). How it does this is not clear, but a report in *Cell* by David Livingston and colleagues describes a new potential player in the process.

Although BRCA1 has little homology to known proteins, it is characterized by two carboxy-terminal BRCT domains, which are critical for its break-repair function. To try and understand how these domains function, Livingston and colleagues used a GST fusion protein to probe for proteins that interact with them. They pulled out and purified a 130-kDa protein that bound to BRCA1 only when its BRCT domains were intact.

Christened BACH1 — for BRCA1-associated carboxy-terminal helicase — this protein contains the seven helicase-specific motifs found in the DEAH family of helicases. Immunoprecipitations showed that BACH1 interacts with BRCA1 *in vivo*, and immunofluorescence experiments revealed a punctate nuclear staining pattern for the two proteins, which co-localized in many cells. Another protein known as BARD1 (BRCA1 RING-domain-associated protein) was also detected in the co-immunoprecipitations, but the authors believe that the BACH1–BARD interaction is indirect, probably occurring through BRCA1.

Livingston and co-workers next asked whether the interaction of BRCA1 with BACH1 contributes to its function in DSB repair. To do this they overexpressed a mutant form of BACH1— a key lysine residue conserved in many ATPases and helicases was mutated to arginine. This form of BACH1, designated K52R, could not hydrolyse ATP, and after irradiation cells overproducing K52R showed a considerable delay in break repair. Interestingly, though, overexpression of a double-mutant BACH1, which could neither hydrolyse ATP nor bind to BRCA1, had little effect on DSB repair. This means, conclude the authors, that K52R disrupts DSB repair in a dominant-negative fashion. And they suggest that the function of BRCA1 in DSB repair depends, at least in part, on its direct interaction with BACH1.

What does this all mean physiologically? To see whether mutations in *BACH1* might also be involved in cancer, Livingston and colleagues screened the germline DNAs of 65 patients with early-onset breast cancer, 35 of whom had no mutations in either *BRCA1* or *BRCA2*. They detected heterozygous missense mutations in two patients, and, in both cases, the mutations were found in the DEAH helicase region of BACH1. One mutation, P47A, was in a region homologous to the highly conserved nucleotide-binding box, and to investigate its effects further the authors incorporated it into an otherwise wild-type *BACH1* allele. Levels and stability of the mutant gene product were considerably lower than the wild-type protein, leading the authors to suggest that the P47A BACH1 change is a mutation as opposed to a simple polymorphism.

The involvement of a helicase in DSB repair is no surprise — localized unwinding of DNA at the site of a double-stranded break will allow the repair machinery to access the broken ends. However, the mystery of BRCA1 function is by no means solved, especially as it relates to tumour suppression, and the interplay between BRCA1 and BACH1 now needs to be investigated in greater depth.

Alison Mitchell

References and links

ORIGINAL RESEARCH PAPER Cantor, S. B. *et al.* BACH1, a novel helicase-like protein, interacts directly with BRCA1 and contributes to its DNA repair function. *Cell* **105**, 149–160 (2001)

FURTHER READING Deng, C. X. & Brodie, S. G. Roles of BRCA1 and its interacting proteins. *Bioessays* **22**, 728–737 (2000)