IN BRIEF

P53

C. elegans p53: Role in apoptosis, meiosis and stress resistance.

Derry, W. B., Putzke, A. P. & Rothman, J. H. *Science* 13 September (2001) (epub ahead of print)

Previous searches of the *Caenorhabditis elegans* genome had indicated that this organism does not have a *p53*-like gene. Now, however, using additional algorithms, Derry *et al.* have identified a *p53* homologue called *cep-1*, which is expressed in embryos. It promotes DNA-damage induced apoptosis, and is required for meiotic chromosome segregation in the germ line.

DEVELOPMENT

Argosomes: a potential vehicle for the spread of morphogens through epithelia.

Greco, V., Hannus, M. & Eaton, S. *Cell* **106**, 633–645 (2001)

Pattern formation in developing tissues occurs in response to morphogen gradients. But some morphogens are tightly associated with the plasma membrane, and Greco *et al.* now describe how these proteins might be distributed through the epithelium in *Drosophila* imaginal discs. They propose the existence of membrane exovesicles — called argosomes — which travel through adjacent tissue, acting as a vehicle for the spread of morphogens, such as Wingless.

RNA SPLICING

Crystal structure of the human nuclear cap binding complex.

Mazza, C. *et al. Mol. Cell* **8**, 383–396 (2001)

The nuclear cap binding complex binds the 5' cap of nascent RNA transcripts, and is involved in pre-messenger RNA splicing. The authors show that the CBP80 subunit contains three helical domains. The first is an MIF4G domain, found in other proteins involved in RNA maturation. The other two domains bind tightly to the CBP20 subunit. Four residues on CBP20 are crucial for cap binding, and the authors propose that both subunits might be required owing to "the poor stability of folded CBP20 in the absence of the CBP80".

TRANSLOCATION

Ssh1p determines the translocation and dislocation capacities of the yeast endoplasmic reticulum.

Wilkinson, B. M., Tyson, J. R. & Stirling, C. J. *Dev. Cell* **1**, 401–409 (2001)

Translocation across the endoplasmic reticulum (ER) membrane requires the Sec61 translocon. The largest component of this complex is the Sec61 protein, which spans the ER bilayer ten times. The Sec61 homologue Ssh1 has been shown to interact with ribosomes, leading to speculation that it could act as a cotranslational translocon. This study of *Δssh1* mutant cells supports such a function for Ssh1, identifying it as a component of a second, functionally distinct, translocon.

TRANSPORT PROTEINS

In the face of resistance

It's a depressingly familiar scenario. You have the right drug for the right target, you know how to deliver it to the right group of cells, but then you find that those same cells have developed resistance to the drug. The commonest cause of such 'multidrug' resistance (MDR) — which is being increasingly observed for antibiotics and anticancer drugs — is a family of transporter proteins that use the energy derived from hydrolysing ATP to pump drugs out of cells. Because proteins of this type share the common structural feature of an ATP-binding cassette (ABC), they are known as MDR–ABC transporters. Now, for the first time, Chang and Roth report the high-resolution X-ray structure of one of the 50 or so members of this protein class, the bacterial transporter Eco-msbA.

Eco-msbA is the closest bacterial homologue of the most studied human MDR–ABC transporter, P-glycoprotein, and prevents lethal accumulations of lipid A building up on the cytoplasmic face of the cell membrane in *Escherichia coli*. Chang and Roth's data indicate that Eco-msbA functions as a homodimer, with the two protein molecules interfacing in the outer membrane to form an inverted 'V' in the cell's lipid bilayer. The two ABC elements are cytoplasmic, as expected, and the two angled transmembrane domains form a chamber, which is closed at the top. The authors propose that, upon ABC activation, a conformational change leads hydrophobic lipid A to be carried into the lower part of the chamber by a substrate-specific binding site. Lipid A is then 'flipped' into the upper part by unfavourable electrostatic interactions in the chamber, before being translocated back into the outer cell membrane and out of the cell. Eco-msbA is therefore not a pore through the cell membrane, but a molecular machine.

Despite structural and functional similarities throughout the family, other MDR–ABC transporters — particularly those that transport hydrophilic substrates — could function differently. But importantly, we now have a snapshot of how some of these proteins might look.

Adam Smith, Editor,
Nature Reviews Drug Discovery

References and links

ORIGINAL RESEARCH PAPER Chang, G. & Roth, C. B. Structure of MsbA from *E. coli*: a homolog of the multidrug resistance ATP binding cassette (ABC) transporters. *Science* **293**, 1793–1800 (2001)
WEB SITE Chang laboratory:
http://www.scripps.edu/phd/mcsc/chang.html