IN BRIEF

CELL DIVISION

Role of the p53-homologue p73 in E2F1-induced apoptosis.

Stiewe, T. & Pützer, B. M. *Nature Genet.* **26**, 464–469 (2000)

The transcription factor E2F1 can suppress tumorigenesis by prolonging the half-life of p53, through induction of $p14^{ARF}$. Stiewe and Pützer now report a p53-independent mechanism of action for E2F: expression of the *TP53* homologue *TP73* is directly activated by E2F and can lead to the activation of pro-apoptotic genes in a p53-independent manner, providing an anti-tumorigenic 'safety catch' in the absence of functional p53.

CELL SIGNALLING

Quantitative imaging of lateral ErbB1 receptor signal propagation in the plasma membrane.

Verveer, P. J. *et al. Science* **290**, 1567–1570 (2000)

Ligand-driven ErbB1 activation is believed to occur through the formation of stable receptor dimers in which receptors cross-phosphorylate each other. Verveer *et al.* use an ingenious imaging technique based on FRET and fluorescence-lifetime imaging microscopy to measure the activation of ErbB1 in living cells. They find that receptor dimers are in fact transient. After focal stimulation of ErbB1, receptor phosphorylation rapidly propagates over the entire cell surface in a ligand-independent manner, leading to the full activation of all receptors.

PROTEIN-INTERACTION MAPPING

A network of protein–protein interactions in yeast.

Schwikowski, B., Uetz, P. & Fields, S. *Nature Biotechnol.* **18**, 1257–1261 (2000)

Proteins that associate with one another are likely to have similar functions. So if the function of one protein is known, those of its partners can be predicted. But first, a map of protein interactions must be built, and Fields and colleagues have done this in the yeast *Saccharomyces cerevisiae*. They analysed 2,709 published interactions and built up a network containing 2,358 interactions among over 1,500 proteins. Based on the functions of interacting partners, they then assigned possible functions to 364 previously uncharacterized proteins.

NUCLEAR TRANSPORT

Vesicular stomatitis virus matrix protein inhibits host cell gene expression by targeting the nucleoporin Nup98.

von Kobbe, C. *et al. Mol. Cell* **6**, 1243–1252 (2000)

Vesicular stomatitis virus is an RNA virus that causes acute infections in many mammalian hosts. Of particular importance during infection is the viral matrix protein (M) which has pleiotropic effects, shutting off transcription and inhibiting nuclear export of certain RNA species. In this paper, von Kobbe *et al.* identify the cellular target of M as the nucleoporin Nup98, indicating that M specifically blocks nuclear export of RNAs, the inhibition of transcription being a secondary effect.

CELL DIVISION

Dodging death at division?

Survivin is having an identity crisis. Is it an inhibitor of apoptosis (IAP), as suggested by its baculoviral IAP repeat (BIR) domain? Or is it necessary for cell division, like its closest relations in yeast and worms? Reporting in *Proceedings of the National Academy of Sciences*, Daniel O'Connor and colleagues present evidence that these two functions need not be mutually exclusive, whereas Anthony Uren and co-workers come down firmly on the side of a mitotic function for survivin.

O'Connor *et al.* found that survivin is unique among IAPs in that it has a consensus sequence for phosphorylation by the cyclin-dependent kinase CDC2, and is phosphorylated by CDC2 *in vitro* and *in vivo*. They could immunoprecipitate survivin phosphorylated on threonine 34 (T34) only from cells undergoing mitosis. Survivin could also be co-immunoprecipitated with CDC2, and this interaction doesn't depend on phosphorylation at T34 because it worked just as well when T34 was mutated to alanine (T34A). This suggests that the T34A mutant might act as a dominant-negative inhibitor. Sure enough, when T34A was overexpressed, mitotic cells died by apoptosis; but how does survivin prevent death during mitosis? The apoptotic protease caspase-9 could also be found in survivin immunoprecipitates, but the T34A mutant didn't associate with caspase-9, suggesting that this interaction, whether direct or indirect, requires phosphorylation of T34.

Uren and colleagues used antibodies to track survivin's behaviour thoughout the cell cycle, and found that survivin's movements closely mimicked those of a group of proteins known as chromosome passenger proteins. These hitch a ride on the centromeres to the spindle equator, where they remain until sister chromatids separate (see picture). Survivin bound to centromeres along the same axis as the inner centromere protein INCENP, which is needed to localize Aurora1 kinase to centromeres. To get a handle on what survivin might be doing at centromeres, the authors knocked it out in mice. At first glance, knockout embryos looked normal until embryonic day 4.5, but they then looked irregular, with cells that failed to separate and disorganized mitotic spindles. By day 5.5, the knockout embryos contained an average of only 13 nuclei, compared with around 200 in wild-type embryos.

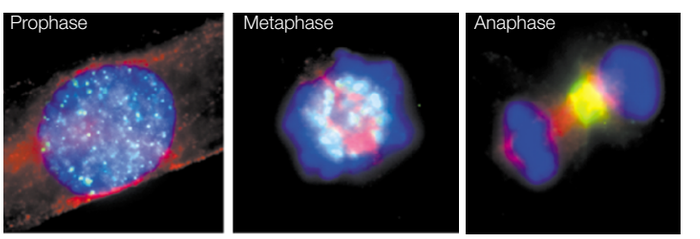
Is survivin a death defier, an orchestrator of division or something in between? We're still far from an answer but, whatever the final verdict, one thing is clear: dividing cells can't manage without it.

Cath Brooksbank

References and links

ORIGINAL RESEARCH PAPERS O'Connor, D. S. *et al.* Regulation of apoptosis at cell division by $p34^{cdc2}$ phosphorylation of survivin. *Proc. Natl Acad. Sci. USA* **97**, 13103–13107 (2000) | Uren, A. G. *et al.* Survivin and the inner centromere protein INCENP show similar cell-cycle localization and gene knockout phenotype. *Curr. Biol.* **10**, 1319–1328 (2000)

FURTHER READING Reed, J. C. & Bischoff J. R. BIRinging chromosomes through cell division — and survivin' the experience. *Cell* **102**, 545–548 (2000)



Localization of survivin (green; appears pale blue when colocalized with DNA and yellow when colocalized with tubulin), tubulin (red) and DNA (blue) at different stages of the cell cycle. Courtesy of Lee Wong and K. H. Andy Choo, The Murdoch Children's Research Institute, Parkville, Victoria, Australia.