IN BRIEF

TECHNIQUE

Profiling the global tyrosine phosphorylation site by Src homology 2 binding.

Nollau, P. & Mayer, B. J. *Proc. Natl Acad. Sci. USA* **98**, 13531–13536 (2001)

The reversible process of tyrosine phosphorylation creates binding sites for Src-homology-2 (SH2) domain-containing proteins. Here, the authors describe a far-Western blot technique for profiling the global tyrosine phosphorylation state in cell protein extracts, which involves probing membranes containing immobilized, electrophoresed proteins with purified recombinant glutathione-*S*-transferase–SH2-domain peptides. As this approach relies on protein–protein interactions, it could be extended to any protein-domain interaction.

ENDOCYTOSIS

Regulation of membrane-type matrix metalloproteinase 1 activity by dynamin-mediated endocytosis.

Jiang, A. *et al. Proc. Natl Acad. Sci. USA* **98**, 13693–13698 (2001)

Membrane-type matrix metalloproteinase 1 (MT1-MMP) has an important function in remodelling the extracellular matrix, but how the activity of this cell-surface enzyme is controlled remains poorly understood. In this study, Jiang *et al.* show that this control might be mediated through endocytosis. The authors found that the expression of MT1-MMP on the cell surface is regulated through its cytoplasmic domain by dynamin-mediated internalization into clathrin-coated pits.

CELL ADHESION

Taking cell–matrix adhesions to the third dimension.

Cukierman, E. *et al. Science* **294**, 1708–1712 (2001)

Most of our knowledge regarding the function of focal and fibrillar adhesions comes from studies of fibroblasts on two-dimensional (2D) tissue culture substrates, but fibroblast morphology and migration differ significantly within three-dimensional (3D) substrates. This report shows that cell adhesions in 3D cultures differ in structure, function and signalling compared to their 2D counterparts, implying that current 2D methods might not be entirely appropriate for studying cell–substrate adhesions.

CELLULAR MICROBIOLOGY

Extensive surface diversity of a commensal microorganism by multiple DNA inversions.

Krinos, C. M. *et al. Nature* **414**, 555–558 (2001)

Few studies have investigated how commensal organisms in the human intestine evade the host's immune response. Krinos *et al.* now show that *Bacteriodes fragilis* alters its surface antigenicity by producing at least eight different capsular polysaccharides — the most observed in a bacterium to date. Polysaccharide expression is subject to phase variation controlled by invertible promoter sequences upstream of the polysaccharide biosynthesis loci. This diversity might also have a role in the pathogenicity of *B. fragilis*.

DNA REPAIR

Damage limitation

If you've ever felt the pain of sunburn, you'll be convinced that the body puts up a feeble fight against exposure to the sun. But sunburn, in fact, is the best response, as it is the cue for the body to defend itself against any potentially harmful effects. A report by Schwarz and colleagues in *Nature Cell Biology* identifies an added complexity to this response, and their findings could pave the way to new areas of therapeutic intervention.

Exposure to ultraviolet-B (UVB) radiation induces the apoptotic cell death of keratinocytes, which leads to the appearance of sunburn cells (SCs) in the epidermis. The discovery that p53 is involved in this process led scientists to believe that the formation of SCs was a protective mechanism to destroy cells with irreparable DNA damage that could lead to skin cancer.

But does that mean the body just destroys cells and makes no effort to repair the DNA? Further studies suggested this might not be the case, as cytokines such as interleukin-1 were found to influence UV-induced apoptosis, although the mechanism was unknown.

So Schwarz and colleagues investigated the effects of various cytokines on UVB-induced apoptosis. They found that the immunomodulatory mediator interleukin-12 (IL-12) can inhibit this process in keratinocytes, as exposing epithelial cells to IL-12 *in vitro* before UVB-exposure significantly reduced apoptosis. This was due to a reduction of UVB-induced DNA damage, but this effect was not immediate — it occurred only after a period of time, which the authors suspected could be linked to the induction of DNA repair.

They tested this by looking for single-strand breaks created during nucleotide excision repair (NER) — the main repair mechanism for UVB-induced DNA damage in mammalian cells — using a 'comet' assay. This showed that IL-12 treatment enhances comet length, which meant that IL-12 might induce NER.

The researchers confirmed this by studying *Xpa*-knockout mice, which are severely deficient in NER. These mice had a higher number of SCs compared with wild-type mice that had received the same dose of UVB; and although IL-12 reduced SC numbers in UVB-irradiated wild-type mice, it had no effect on SCs in the knockout mice. This was further confirmed when cells taken from both a patient with xeroderma pigmentosum (which is caused by defects in various components of the NER) and a healthy control were exposed to UVB in the presence or absence of IL-12. IL-12 reduced UVB-induced DNA damage in the healthy cells but not in the cells from the patient.

So, this is the first demonstration that cytokines can protect cells from apoptosis in response to DNA damage from UVB by switching on the DNA repair machinery. It remains to be seen whether overexpression of IL-12 could reduce both the number of SCs in humans and the risk of UV-induced skin cancer. But it does offer the exciting therapeutic possibility that topically applied IL-12 could help prevent this disease.

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References and links

ORIGINAL RESEARCH PAPER Schwarz, A. *et al.* Interleukin-12 suppresses ultraviolet radiation-induced apoptosis by inducing DNA repair. *Nature Cell Biol.* **4**, 26–31 (2002)