Elsewhere in Biology

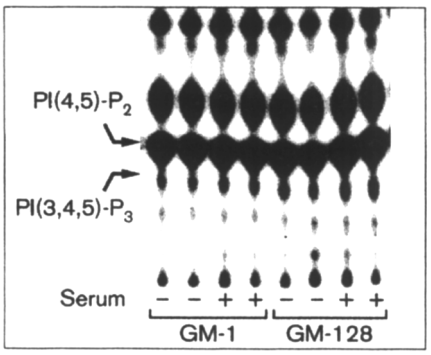
Chosen and summarized by the staff of *Chemistry & Biology*

A selection of interesting papers published last month in *Chemistry & Biology*'s sister journals, *Current Biology*, *Folding & Design* and *Structure*.

Chemistry & Biology November 1996, 3:957–959

☐ **Constitutive activation of protein kinase B and phosphorylation of P47^{phox} by a membrane-targeted phosphoinositide 3-kinase.** Svetlana A Didichenko, Bettina Tilton, Brian A Hemmings, Kurt Ballmer-Hofer and Marcus Thelen (1996). *Curr. Biol.* **6**, 1271–1278.

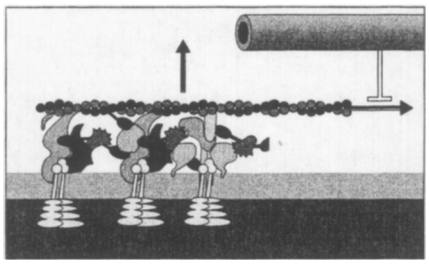
Phosphoinositide 3-kinase (PI 3-kinase) selectively phosphorylates the 3-OH position of phosphoinositides. Several mitogenic signal transduction and secretory response pathways appear to require PI 3-kinase activity. Its major substrate, phosphatidylinositol (4,5)-bisphosphate, is membrane-associated, but in resting cells the active enzyme is mainly associated with the cytosol. Cell activation is presumed to cause translocation of PI 3-kinase from the cytosol to the membrane, allowing it to interact with substrate. Here, a chimeric PI 3-kinase is constructed that contains the membrane-targeting sequence of Ha-Ras (which directs the addition of palmitoyl and farnesyl groups to the protein). Expression of the membrane-targeted enzyme resulted in constitutive activation of the downstream effector protein kinase B, and enhanced basal phosphorylation of p47^{phox}, a cytosolic factor that forms part of the phagocyte NADPH oxidase, required for the phagocyte respiratory burst. Thus, targeting of PI 3-kinase to the membrane is sufficient to generate signals through at least two different signal transduction pathways.



1 October 1996, Research Paper, *Current Biology*

☐ **Involvement of microtubules in the control of adhesion-dependent signal transduction.** Alexander Bershadsky, Alexander Chausovsky, Eitan Becker, Anna Lyubimova and Benjamin Geiger (1996). *Curr. Biol.* **6**, 1279–1289.

The adhesion of cells to the extracellular matrix (ECM) generates transmembrane signals that affect cell proliferation, differentiation and survival. The signals are triggered by interactions between cell-surface receptors (integrins) and ECM molecules, and lead to a rapid sequence of protein assembly and modification events in the cytoplasm, including tyrosine phosphorylation of focal adhesion kinase (FAK) and paxillin, culminating in the assembly of focal adhesions. Focal adhesions contain complexes of signal transduction proteins and are associated with bundles of actin filaments; they are thought to act as tension-sensing devices, and the tension developed by the actin cytoskeleton may thus affect the signal transduced by the integrins bound to the extracellular matrix. Here, the authors show that disruption of microtubules in ECM-adherent cells by nocodazole or vinblastine induces the rapid assembly of focal adhesions and micro-filament bundles, tyrosine phosphorylation of FAK and paxillin, and the subsequent enhancement of DNA synthesis. Thus, cytoskeletal modulation can trigger the integrin-dependent signaling cascade in the absence of external growth factor stimulation.



1 October 1996, Research Paper, *Current Biology*

☐ **Bypass of lethality with mosaic mice generated by Cre–*loxP*-mediated recombination.** Ulrich A.K. Betz, Christian A.J. Voßhenrich, Klaus Rajewsky and Werner Müller (1996). *Curr. Biol.* **6**, 1307–1316.

The generation of mutant mice by homologous recombination in embryonic stem cells is a powerful technique for gene function analysis. This approach cannot, however, be used for genes whose disruption causes embryonic lethality. It is often possible to bypass embryonic lethality by creating mosaic mice, which contain a certain proportion of mutant cells in all organs; it is thus possible to study which cell lineages require a given target gene for their development. The authors report a novel use of the Cre–*loxP* recombination system, normally used to generate mice that lack a target gene only in a specific cell lineage, to generate mice in which all the tissues are mosaics of normal cells and cells lacking a target gene. The genes chosen for analysis were the gene for the γ-chain of the interleukin-2 receptor (IL-2Rγ) and that for DNA polymerase β (polβ). Mice deficient in polβ die perinatally for unknown reasons; some of the mosaic mice were viable, but they were often reduced in size and weight. The proportion of polβ-deficient cells in all organs, and particularly the thymus, of the mosaic embryos decreased significantly after 10.5 days of development, showing that this enzyme is generally important in a wide range of cell types.

1 October 1996, Research Paper, *Current Biology*