Elsewhere in Biology

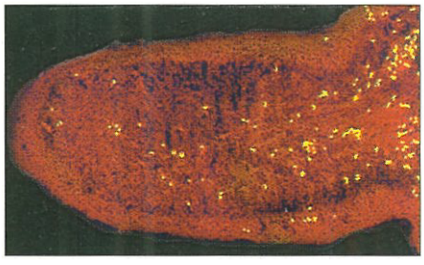
Chosen and summarized by the staff of *Chemistry & Biology*

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

Chemistry & Biology June 1996, **3**:499–501

☐ **Activation of a single retinoic acid receptor isoform mediates proximodistal respecification.** Lauren T. Pecorino, Alan Entwistle and Jeremy P. Brockes (1996). *Curr. Biol.* **6**, 563–569.

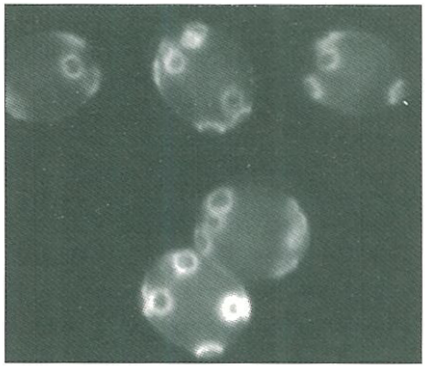
Newts can regenerate an amputated limb with the correct sequence of components: shoulder, elbow, wrist and hand. Retinoic acid (RA) can cause the regenerating region to adopt a more proximal fate, resulting in the duplication of a feature. Here the authors address the identity of the retinoic acid receptor (RAR) responsible for this activity by transfecting regenerating limb tissue with plasmid DNA by particle bombardment. The plasmids encode chimeric receptors that



are activated by the addition of thyroid hormone, but retain the binding specificity of one of the five RAR isoforms. Only a single isoform, δ2, leads to thyroid-hormone-stimulated respecification. As the level of transfection is very low, it is likely that the RAR δ2 isoform can result in respecification in a cell-autonomous manner. The identification of a single receptor isoform responsible for this phenomenon should help in the identification of the molecular and cellular bases of the developmental changes observed.
1 May 1996, Research Paper, *Current Biology*

☐ **Bud10p directs axial cell polarization in budding yeast and resembles a transmembrane receptor.** Adrian Halme, Merrilyn Mitchelitch, Elizabeth L. Mitchell and John Chant (1996). *Curr. Biol.* **6**, 570–579.

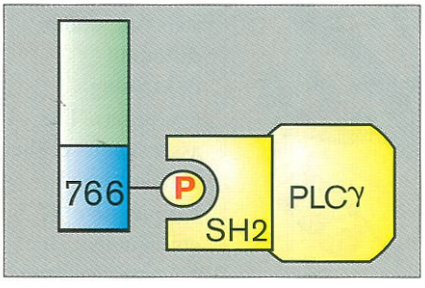
The direction in which a cell divides is critical in the development of multicellular organisms, but it is in the unicellular budding yeast *Saccharomyces cerevisiae* that we have the clearest idea of how such a choice is made. Diploid budding yeast cells divide in a polar pattern, in which new buds are placed at the opposite end of the cell from the previous site of cell separation, whereas haploid cells place their new bud next to the previous site of division, forming an axial pattern. Proteins have been identified that are required for either axial, or polar, or both types of budding. This paper investigates the role of Bud10p, which, with Bud3p, Bud4p and Axl1p, is required only for axial budding. Bud10p is found



to be a transmembrane protein with a large extracellular domain but no similarities to known proteins. It is therefore most likely to be a transmembrane receptor with no intrinsic catalytic activity. Bud10p is localized to the presumptive site of division early in the cell cycle, and remains there as the bud grows and Bud3p and Bud4p accumulate at the same site. When the cells divide, the Bud10p ring splits into two rings, one in each progeny cell; these rings remain until a new axial bud site develops adjacent to the old ring. Some aspects of Bud10p localization are dependent on the gene for Bud3p, suggesting that there is a functional interaction between Bud3p and Bud10p. It appears that one or more of the proteins proteins required for axial budding must be necessary for the clustering (but not the gross localization) of the downstream factors that direct cytoskeletal attachment.
1 May 1996, Research Paper, *Current Biology*

☐ **Inhibition of FGF-stimulated phosphatidylinositol hydrolysis and neurite outgrowth by a cell-membrane permeable phosphopeptide.** Heike Hall, Emma J. Williams, Stephen E. Moore, Frank S. Walsh, Alain Prochiantz and Patrick Doherty (1996). *Curr. Biol.* **6**, 580–587.

Dissecting pathways of signal transduction is never simple, as often the stimulation of a single receptor leads to the activation of several different pathways. To dissect the signalling pathway of the fibroblast growth factor receptor (FGFR), the authors used a fusion between a peptide from FGFR and one from the third helix of the Antennapedia homeodomain protein. The FGFR peptide includes a tyrosine that is

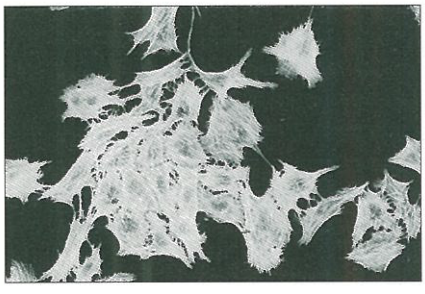


normally phosphorylated in response to FGF binding, forming the binding site for phospholipase Cγ (PLCγ), while the Antennapedia peptide has previously been shown to act as an internalization vector that can deliver other peptides into cells. The composite peptide, when phosphorylated on tyrosine, inhibited phospholipid hydrolysis

stimulated by basic FGF with a maximal effect at 1 μg ml^{-1}, although phospholipid hydrolysis stimulated by other growth factors (platelet-derived growth factor and bradykinin) were not affected. The phosphorylated peptide inhibited neurite outgrowth stimulated by FGF. This study suggests that a novel family of peptides can be designed as tools for studying the biological consequences of receptor activation.
1 May 1996, Research Paper, *Current Biology*

☐ **Stimulation of actin stress fibre formation mediated by activation of phospholipase D.** Michael J. Cross, Sally Roberts, Anne J. Ridley, Matthew N. Hodgkin, Allison Stewart, Lena Claesson-Welsh and Michael J.O. Wakelam (1996). *Curr. Biol.* **6**, 588–597.

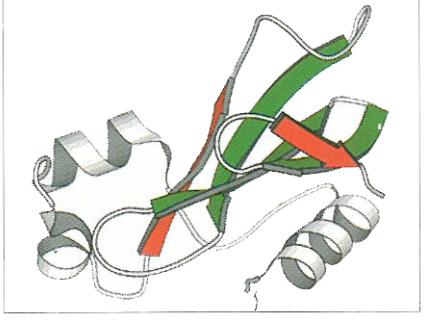
Phospholipase D (PLD) has not been assigned a specific physiological function, in part because it has not been possible to activate it without the concomitant activation of other signalling pathways. Here, the authors show that in porcine aortic endothelial cells the agonist lysophosphatidic acid stimulates



only PLD activation, resulting in the production of the putative messenger phosphatidate (PA) and the formation of actin stress fibres. It was thus possible to show that PA is indeed a messenger and that the small GTPase Rho is downstream of PA in the signaling pathway. Tyrosine kinases are involved in the activation of PLD, and also in the subsequent induction of stress fibre formation by signals downstream of Rho.
1 May 1996, Research Paper, *Current Biology*

☐ **An NMR study on the β-hairpin region of barnase.** José I. Neira and Alan R. Fersht (1996). *Folding & Design* **1**, 231–241.

The β-hairpin of barnase, a small monomeric protein often used as a model for folding studies, has been proposed to be an initiation site for the folding of the protein. Consistent with this notion, there is some evidence from NMR studies that this

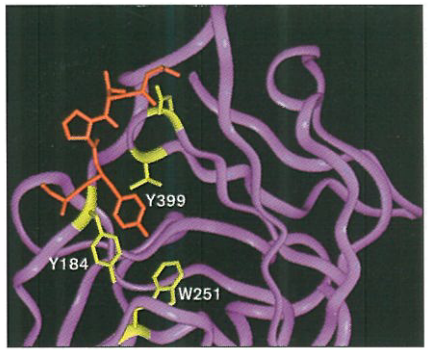


region of the protein has residual structure under different denaturing conditions. The assignments of the NOEs to this hairpin were ambiguous, however, because of overlap of signals. Here, several large carboxy-terminal fragments of barnase, comprising the β-turn region, are characterized in detail. The results clearly show hydrophobic clustering of residues centered around Trp94 even i presence of 6M urea. Although the structure is non- possibly reflecting the conformational search in the stages of the folding reaction, it could nucleate the β
31 May 1996*, Research Paper, *Folding & Design*

☐ **Aromatic interactions define the binding o alphavirus spike to its nucleocapsid.** Ulrica Mauno Vihinen, Lennart Nilsson and Peter Liljes (1996). *Structure* **4**, 519–529.

☐ **Identification of a protein binding site on t of the alphavirus nucleocapsid and its impl virus assembly.** Sukyeong Lee, Katherine E O Hok-Kin Choi, Heuiran Lee, Guoguang Lu, Gerd Dennis T Brown, Michael G Rossmann and Rich (1996). *Structure* **4**, 531–541.

Many enveloped viruses exit cells by budding from membrane, a complex and poorly-understood proces driving force for budding involves the interaction of protein nucleocapsid core, containing the capsid pro transmembrane glycoprotein spikes. These papers a interactions involved in the assembly of two membe alphavirus family. Skoking *et al.* use molecular dynar docking calculations followed by a biochemical analy



mutant S Forest vi proteins a hydrop pocket i protein t involved binding essential within th glycopro *al.* deter high-resolution structure of the Sindbis virus capsid which shows that amino acids 108 to 111 bind to an a identical hydrophobic pocket in neighboring capsid molecules. But the amino-terminal arm containing th residues is not long enough to reach from one capsid to another in the intact virus, so Lee *et al.* suggest tha process of assembly this arm is displaced by residues integral membrane E2 spike glycoprotein in the inte identified by Skoking *et al.* This interaction should n hydrophobic surfaces of the capsid protein and the E terminal residues inaccessible to water, explaining th the driving force for budding. Disruption of this inte when the virus enters a new cell and uncoats should the core and lead to its disassembly.
15 May 1996, Research Papers, *Structure*

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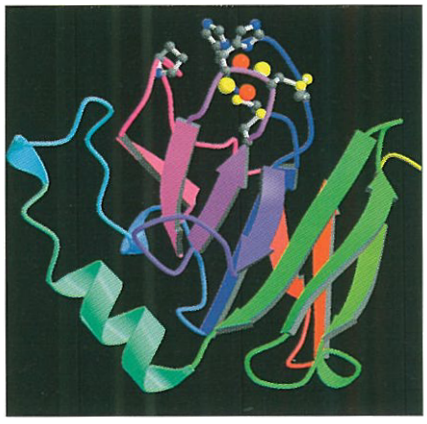
☐ **Structure of a water soluble fragment of the 'Rieske' iron–sulfur protein of the bovine heart mitochondrial cytochrome bc_1 complex determined by MAD phasing at 1.5 Å resolution.** So Iwata, Monica Saynovits, Thomas A Link and Hartmut Michel (1996). *Structure* **4**, 567–579.

The Rieske iron-sulfur protein is the primary electron acceptor during hydroquinone oxidation in cytochrome *bc* complexes; it accepts electrons from the donor hydroquinone and passes them on to cytochrome c_1 or *f*. Most known iron–sulfur proteins have their iron atoms coordinated by the thiolates of cysteine residues, but the Rieske-type [2Fe–2S] cluster involves two histidine ligands. As shown by the structure determined here,

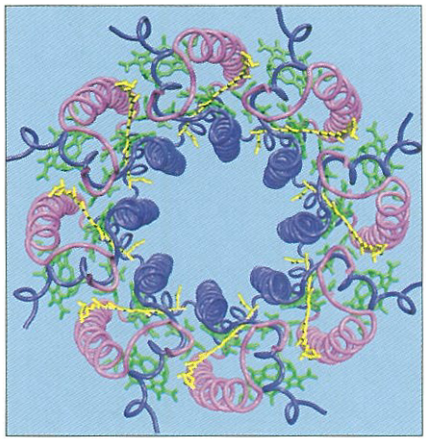


these are instrumental in maintaining the high redox potential of the Rieske cluster, in part because they are exposed at the surface of the protein and the hydrogens at their Nε atoms are not involved in any hydrogen bond. The high stability of the protein is a result of a strong salt bridge/hydrogen-bonding network and a fully exposed disulfide bridge very close to the iron–sulfur cluster. The latter feature is unprecedented.

15 May 1996, Research Paper, *Structure*

☐ **The crystal structure of the light-harvesting complex II (B800–850) from *Rhodospirillum molischianum*.** Juergen Koepke, Xiche Hu, Cornelia Muenke, Klaus Schulten and Hartmut Michel (1996). *Structure* **4**, 581–597.

By their deployment of many chromophores in varying environments, light-harvesting complexes (LHs) in plants and photosynthetic bacteria can increase the efficiency of energy use by photosynthetic reaction centers by two orders of magnitude and broaden the spectral range of light used. The LH-2 complex in purple bacteria harvests light energy using two bacteriochlorophyll a (BChl-a) molecules, termed B800 and B850 here to denote their wavelength of maximal absorption. Transfer of energy occurs from both B800 and from one of the BChl-as of LH-3 to B850, and from B850 to the B880 of the reaction center, LH-1. The structure of the octameric LH-2 from *Rhodospirillum molischianum* reported here displays two concentric cylinders of 16 membrane-spanning helical subunits; the inner 8 are α-subunits, the outer 8 β-subunits. The 16 B850 BChl-as are oriented perpendicular to the membrane and are in a ring sandwiched between the α and β subunits, and the 8 B800 BChl-as are nearly parallel to the membrane and located between the outer, β subunits. Energy transfer could occur between the two BChl-as by the concerted action of two mechanisms: the Dexter mechanism



relies on close contact, which could be mediated by a bridging carotenoid (lycopene), while the Förster mechanism allows the bridging of large distances if Q_y dipole moments are lined up, as is the case here for B800 and B850 BChl-as even though the planes of the rings are not parallel. Finally, the finding that the binding environment of the B850 BChl-a is non-polar, whereas that of the B800 BChl-a is polar, may help in elucidating how proteins cause the spectral shifts of chromophores that are so vital for the functioning of cascades of excitation energies.

15 May 1996, Research Paper, *Structure*