Calendar

If you know of any meetings other than those listed below, or of changes to this information, please let *Chemistry & Biology* know by fax (44 (0)171 580 8167) or e-mail (chembiol@current-biology.com).

Chemistry & Biology May 1999, 6:R150–R151

22–27 May, 1999
Biology of molecular chaperones, Acquafredda di Maratea, Italy.
Contact: Dr Josip Hendekovic.
Tel: +33 3 88 76 71 35
Fax: +33 3 88 36 69
http://www.esf.org/euresco/PC99121A.HTM.

30 May – 4 June, 1999
Gordon research conference on immunochemistry & immunobiology, Barga, Italy.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/immuno.htm

6–11 June, 1999
Gordon research conference on computational aspects of biomolecular NMR, Barga, Italy.
Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.rowland.org/hoch/grc.html

6–11 June, 1999
Gordon research conference on second messengers and protein phosphorylation, Meriden, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/second.htm

7–9 June, 1999
High throughput screening – the next generation, Guildford, UK.
Contact: Conference Secretariat, Society of Chemical Industry, 14/15 Belgrave Square, London, SW1X 8PS, UK.
Tel: +44 (0) 171 235 3681
Fax: +44 (0) 171 235 7743
e-mail: conferences@chemind.demon.co.uk
http://sci.mond.org/

13–17 June, 1999
Gordon research conference on molecular and cell biology , Tilton, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/molcell.htm

13–18 June, 1999
Bioorganic Gordon conference, Andover, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/bioorgch.htm

23–27 June, 1999
RNA '99 – Fourth annual meeting of the RNA society, Edinburgh, Scotland.
Contact: The RNA Society, 9650 Rockville Pike, Bethesda, MD 20814-3998, USA.
Phone: +1 301 530 7120
Fax: +1 301 530 7049
e-mail: rna@faseb.org

26 June – 1 July, 1999
16th American peptide symposium, Minneapolis, MN, USA.
Contact: Mary Kay Ferguson, Administrative Assistant, 16th American Peptide Symposium, c/o University of Minnesota, PO Box 64780, St Paul, Minnesota, MN 55164-0780, USA.
Tel: + 1 612 624 7505
e-mail: 16aps@chem.umn.edu
http://www.chem.umn.edu/16aps/

30 June – 1 July, 1999
Combinatorial approaches to chemistry and biology II, Cambridge, UK.
Contact: Elaine Wellingham, Conference Secretariat, Bude Close, Nailsea, Bristol BS48 2FQ, UK.
Tel: +44 (0)1275 853311
Fax: +44 (0)1275 853311
e-mail: confsec@dial.pipex.com
http://www.rsc.orgs/confs.htm

4–9 July, 1999
Gordon Research conference on purines, pyrimidines and related substances, Newport, RI, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984 West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/purine.htm

10–15 July, 1999
NMR in Molecular biology structure, binding and molecular recognition, Granada, Spain.
Contact: Dr Josip Hendekovic.
Tel: +33 3 88 76 71 35
Fax: +33 3 88 36 69 87
http://www.esf.org/euresco/Lc99015a.htm

11–15 July 1999
RSC Perkin division – 2nd international conference: biological challenges for organic chemistry II, S Andrews, Fife, UK.
Contact: Nicola Durkan, The Royal Society of Chemistry, Conferences & Divisional Affairs, Burlington House, London W1V 0BN, UK.
Tel: + 44 (0)171 437 8656
Fax: + 44 (0)171 734 1227
e-mail conferences@rsc.org
http://www.rsc.org/conferences

18–23 July, 1999
Gordon Research conference on tissue engineering, biomaterials and biocompatibility, Holderness, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.pittsburgh-tissue.net/brochure/Outreach/Gordon.html

24–28 July, 1999
13th Symposium of the protein society, Boston, MA, USA.
Contact: The Protein Society Symposium Office, 9650 Rockville Pike, Bethesda, MD 20814-3998, USA.
Tel: +1 301 530 7010
Fax +1 301 530 7014
e-mail: prot99mtg@faseb.org
http://www.faseb.org/meetings/protein99/

25–30 July, 1999
Gordon Research conference on quantitative structure–activity relationships, Tilton, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/qsar.htm

8–13 August, 1999
Gordon Research conference on matrix metalloproteinases, New London, NH, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/matrix.htm

14–19 August, 1999
37th IUPAC Congress – frontiers in chemistry: molecular basis of the life sciences, Berlin, Germany.
Contact: Professor Heindirck tom Dick, Gesellschaft Deutcher Chemiker - IUPAC/GDCh99, PO Box 90 04 40, Frankfurt-am-Main D 60444 , Germany.
Tel: + 49 69 7917 358
Fax: + 49 69 7917 425
e-mail: tg@gdch.dc

15–20 August, 1999
Gordon Research conference on biological structure and gene expression, Meriden, New Hampshire, USA.
Contact: Gordon Research Conferences, University of Rhode Island, PO Box 984, West Kingston, RI 02892-0984, USA.
Tel: +1 401 783 4011
Fax: +1 401 783 7644
e-mail: app@grcmail.grc.uri.edu
http://www.grc.uri.edu/programs/1999/biostruc.htm

16–19 August, 1999
Drug discovery technology, Boston, MA, USA.
Contact: Michael Keenan, IBC USA, 225 Turnpike Road, Southboro, MA 01772, USA.
Tel: +1 508 481 6400
Fax: + 1 508 481 7911
e-mail: mkeenan@ibcusa.com
http://www.ibcusa.com/usc2269/

22–26 August, 1999
218th American Chemical society national meeting, New Orleans, USA.
Contact: ACS, American Chemical Society Meetings Department, 1155 Sixteenth Street, N.W. Washington, DC 20036 USA.
Tel: +1 202 872 4396
Fax: + 1 202 872 6128
e-mail: natlmtgs@acs.org

29 August – 4 September, 1999
13th International congress on flavin and flavoproteins, University of Konstanz, Germany.
Contact: Sandro Ghisla, Universität Konstanz, Fak. Biologie M644, D-78457 Konstanz, Germany.
Tel: +49 7531 88 2291
Fax: +49 7531 88 4161
http://www.uni-konstanz.de/FuF/Bio/tagung/flavin.html
e-mail: Sandro.Ghisla@uni-konstanz.de

5–7 September, 1999
An international symposium on chirality, Cambridge, UK.
Contact: Dr Claire Davey, Scientific Update, Wyvern Cottage, High Street, Mayfield, East Sussex, TN20 6AE, UK.
Tel: +44 1435 873062
Fax: +44 1435 872734
e-mail: sciup@scientificupdate.co.uk
http://www.scientificupdate.co.uk/

10–16 September, 1999
Isoprenoids, 18th Conference, Prachatice, Czech Republic.
Contact: Dr L Kohout, UOCHB AV CR, Flemingovo 2, 166 10 Praha 6, Czech Republic.
Tel: +420 2 20183 200
Fax: +420 2 24310090
e-mail: kohout@uochb.cas.cz

19–22 September, 1999
3rd European symposium of the protein society, Garmisch-Partenkirchen, Germany
Contact: Third European Symposium of the Protein Society Meeting Office, 9650 Rockville Pike, Bethesda, MD 20814-3998, USA
Tel: +1 301 530 7010
Fax: +1 301 530 7014
e-mail: europrot99@faseb.org
www.faseb.org/meeting/europro99

3–6 October, 1999
International combinatorial chemistry symposium, Tuebingen, Germany
Contact: Professor Günther Jung, Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle 18, D-72076 Tübingen, Germany.
Tel: +49 7071 29 76925
Fax: +49 7071 29 5560
e-mail: guenther.jung@uni-tuebingen.de
http://www.gdch.de/tagung/1999/iccs/index.htm

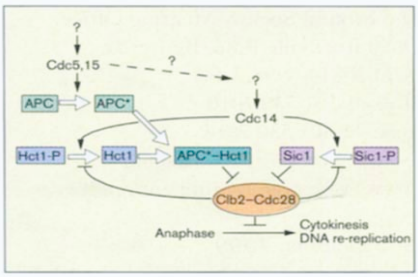
Elsewhere in biology

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

Chemistry & Biology May 1999, 6:R152–R155
 ISSN 1074-5521

☐ **Inhibitory phosphorylation of the APC regulator Hct1 is controlled by the kinase Cdc28 and the phosphatase Cdc14.**
Sue L Jaspersen, Julia F Charles and David O Morgan (1999). *Curr. Biol.* 9, 227–236.

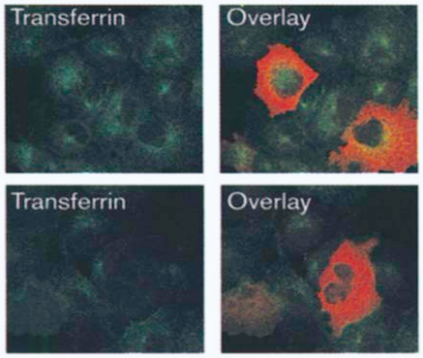
Exit from mitosis requires inactivation of mitotic cyclin-dependent kinases (CDKs). A key mechanism of CDK inactivation is ubiquitin-mediated cyclin proteolysis, which is triggered by the late mitotic activation of a ubiquitin ligase known as the anaphase-promoting complex (APC). Activation of the APC requires its



association with substoichiometric activating subunits termed Cdc20 and Hct1 (also known as Cdh1). Here, the authors explore the molecular function and regulation of the APC regulatory subunit Hct1 in *Saccharomyces cerevisiae*, and conclude that Hct1 phosphorylation is a key regulatory mechanism in the control of cyclin destruction. Phosphorylation of Hct1 provides a mechanism by which Cdc28 blocks its own inactivation during S phase and early mitosis. Following anaphase, dephosphorylation of Hct1 by Cdc14 may help initiate cyclin destruction.
19 February 1999, Research Paper, *Current Biology*.

☐ **Importance of the pleckstrin homology domain of dynamin in clathrin-mediated endocytosis.**
Yvonne Vallis, Patrick Wigge, Bruno Marks, Philip R Evans and Harvey T McMahon (1999). *Curr. Biol.* 9, 257–260.

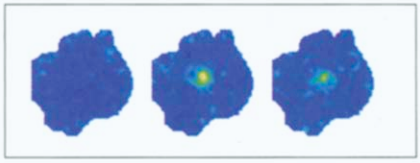
The GTPase dynamin plays an essential role in clathrin-mediated endocytosis. Substantial evidence suggests that dynamin oligomerisation around the necks of endocytosing vesicles and subsequent dynamin-catalysed GTP hydrolysis is responsible for membrane fission. The pleckstrin homology (PH) domain of dynamin has previously been shown to



interact with phosphoinositides, but it has not been determined whether this interaction is essential for dynamin's function in endocytosis. In this study, the authors address the *in vivo* function of the PH domain of dynamin by assaying the effects of deletions and point mutations in this region on transferrin uptake in COS-7 fibroblasts, and demonstrate that dynamin's interaction with phosphoinositides through its PH domain is essential for endocytosis. The results also support the hypothesis that proline-rich domains (PRD)–SH3 domain interactions are important in the recruitment of dynamin to sites of endocytosis.
1 March 1999, Brief Communication, *Current Biology*.

☐ **Dominant-negative inhibition of receptor-mediated endocytosis by a dynamin-1 mutant with a defective pleckstrin homology domain.**
Anthony Lee, David W Frank, Michael S Marks and Mark A Lemmon (1999). *Curr. Biol.* 9, 261–264.

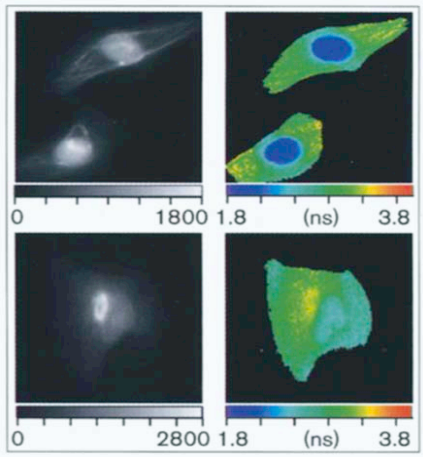
The dynamins are 100 kDa GTPases involved in the scission of endocytic vesicles from the plasma membrane. Dynamin-1 is present in solution as a tetramer, and undergoes further self-assembly following its recruitment to coated pits to form higher-order oligomers that resemble 'collars' around the necks of nascent coated buds. GTP hydrolysis by dynamin in these collars is thought to accompany the 'pinching off' of endocytic vesicles. Dynamin contains a pleckstrin homology (PH) domain that binds phosphoinositides, which in turn enhance both the GTPase activity and self-assembly of dynamin. The authors showed recently that the dynamin PH domain binds phosphoinositides only when it is oligomeric. Here, the authors demonstrate that interactions between



the dynamin PH domain and phosphoinositides are important for dynamin function *in vivo*, and propose that high-avidity binding to phosphoinositide-rich regions of the membrane by the multiple PH domains in a dynamin oligomer is critical for dynamin's ability to complete vesicle budding.
1 March 1999, Brief Communication, *Current Biology*.

☐ **Simultaneous detection of multiple green fluorescent proteins in live cells by fluorescence lifetime imaging microscopy.**
Rainer Pepperkok, Anthony Squire, Stephan Geley and Philippe IH Bastiaens (1999). *Curr. Biol.* 9, 269–272.

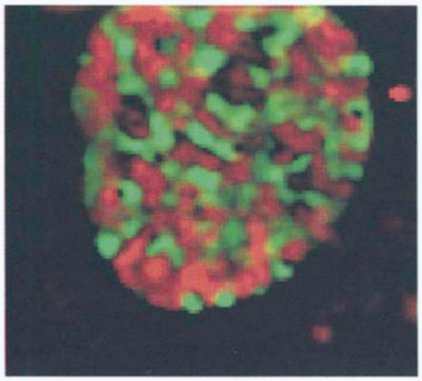
The green fluorescent protein (GFP) has proven to be an excellent fluorescent marker for protein expression and localisation in living cells. Several mutant GFPs with distinct fluorescence excitation and emission spectra have been engineered for intended use in multilabelling experiments. Discrimination of these co-expressed GFP variants by wavelength is hampered, however, by a high degree of spectral overlap, low quantum efficiencies and extinction coefficients, or rapid photobleaching. Using fluorescence lifetime imaging microscopy (FLIM), four GFP variants were shown to have distinguishable fluorescence lifetimes. Among these



was a new variant (YFP5) with spectral characteristics reminiscent of yellow fluorescent protein and a comparatively long fluorescence lifetime. The fluorescence intensities of co-expressed spectrally similar GFP variants (either alone or as fusion proteins) were separated using lifetime images obtained with FLIM at a single excitation wavelength and using a single broad band emission filter. Fluorescence lifetime imaging opens up an additional spectroscopic dimension to wavelength through which novel GFP variants can be selected to extend the number of protein processes that can be imaged simultaneously in cells.
1 March 1999, Brief Communication, *Current Biology*.

☐ **Movement of nuclear poly(A) RNA throughout the interchromatin space in living cells.**
Joan C Politz, Richard A Tuft, Thoru Pederson and Robert H Singer (1999). *Curr. Biol.* 9, 285–291.

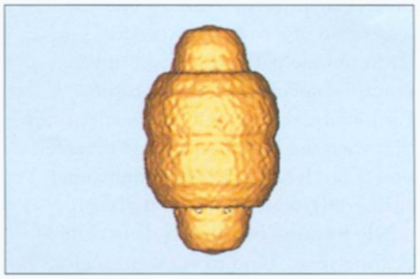
Messenger RNA (mRNA) is transcribed and processed in the nucleus of eucaryotic cells and then exported to the cytoplasm through nuclear pores. It is not known whether the movement of mRNA from its site of synthesis to the nuclear pore is directed or random. Directed movement would suggest that there is an energy-requiring step in addition to the step required for active transport through the pore, whereas random movement would indicate that mRNAs can make their way to the nuclear envelope by diffusion. The authors devised a method to visualize movement of endogenous polymerase II transcripts in the nuclei of living cells. Oligo(dT) labelled with chemically masked (caged) fluorescein was allowed to penetrate cells and hybridize to nuclear poly(A) RNA. Laser spot photolysis then uncaged the



oligo(dT) at a given intranuclear site and the resultant fluorescent, hybridized oligo(dT) was tracked using high-speed imaging microscopy. Poly(A) RNA moved away from the uncaging spot in all directions with a mean square displacement that varied linearly with time, and the same apparent diffusion coefficient was measured for the movement at both 37°C and 23°C. These properties are characteristic of a random diffusive process. High-resolution three-dimensional imaging of live cells containing both Hoechst-labelled chromosomes and uncaged oligo(dT) showed that, excluding nucleoli, the poly(A) RNA could access most, if not all, of the nonchromosomal space in the nucleus. Poly(A) RNA can move freely throughout the interchromatin space of the nucleus with properties characteristic of diffusion.
5 March 1999, Research Paper, *Current Biology*.

☐ **Structure of the vault, a ubiquitous cellular component.**
Lawrence B Kong, Amara C Siva, Leonard H Rome, Phoebe L Stewart (1999). *Structure* 7, 371–379.

The vault is a ubiquitous and highly conserved ribonucleoprotein particle of ~13 MDa. This particle has been shown to be upregulated in certain multidrug-resistant cancer cell lines and to share a protein component with the telomerase complex. Determination of the structure of the vault was undertaken to provide a first step towards understanding the role of this cellular component in normal metabolism and perhaps to shed some light on its role in mediating drug resistance. Over 1300 particle images were combined to calculate an ~31 Å resolution structure of the vault. Rotational power spectra did not yield a clear symmetry peak, either because of the thin, smooth walls or inherent flexibility of the vault. The authors'

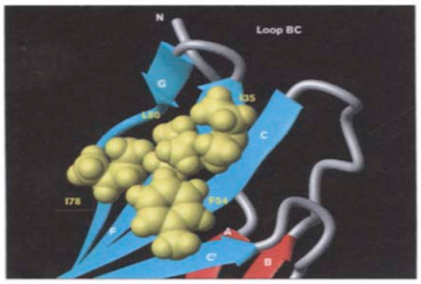


results reveal the vault to be a hollow, barrel-like structure with two protruding caps and an invaginated waist. Although the normal cellular function of the vault is as yet undetermined, the structure of the vault is consistent with either a role

in subcellular transport, as previously suggested, or in sequestering macromolecular assemblies.
24 March 1999, Research Paper, *Structure*.

☐ **NMR structure of the human oncofoetal fibronectin ED-B domain, a specific marker for angiogenesis.**
Roberto Fattorusso, Maurizio Pellecchia, Francesca Viti, Paolo Neri, Dario Neri and Kurt Wüthrich (1999). *Structure* **7**, 381–390.

The process of angiogenesis (i.e. the formation of new blood vessels from pre-existing ones) is fundamental to physiological processes such as reproduction, development and repair, as well as to pathological conditions such as tumor progression, rheumatoid arthritis and ocular disorders. The oncofoetal ED-B domain, a specific marker of angiogenesis, consists of 91 amino-acid residues that are inserted by alternative splicing into the fibronectin (FN) molecule. The NMR structure of the ED-B domain is reported and reveals important differences from other FN type III domains. A comparison of the ED-B domain with the crystal structure of a four-domain FN fragment shows the novel features of ED-B to be located in loop regions that are buried at interdomain interfaces, which therefore largely determine the global shape of the FN molecule. The negatively charged amino acids in this highly acidic protein are uniformly distributed over the molecular surface, with the sole exception of a solvent-exposed hydrophobic patch that represents a potential specific recognition site. Epitope mapping with 82 decapeptides that span the ED-B sequence revealed that three ED-B-specific monoclonal antibodies, which selectively target newly forming blood vessels in tumor-bearing mice, bind to adjacent regions on the ED-B surface. The NMR structure enables the identification of a large surface area of the ED-B domain that appears to be accessible *in vivo*, opening up new diagnostic and therapeutic opportunities. Furthermore, the mapping of specific monoclonal antibodies to the three-dimensional structure of the ED-B domain, and their use in angiogenesis inhibition experiments, provides a basis for further investigation of the role of the



ED-B domain in the formation of new blood vessels.
25 March 1999, Research Paper, *Structure*.

☐ **The crystal structure of pyroglutamyl peptidase I from *Bacillus amyloliquefaciens* reveals a new structure for a cysteine protease.**
Y Odagaki, A Hayashi, K Okada, K Hirotsu, T Kabashima, K Ito, T Yoshimoto, D Tsuru, M Sato and J Clardy (1999). *Structure* **7**, 399–412.

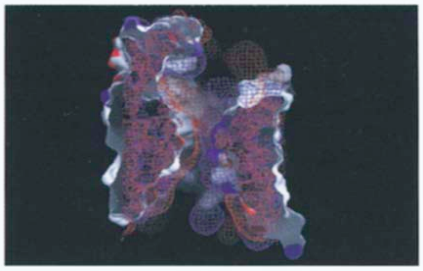
The amino-terminal pyroglutamyl (pGlu) residue of peptide hormones, such as thyrotropin-releasing hormone (TRH) and luteinizing hormone releasing hormone (LH-RH), confers resistance to proteolysis by conventional aminopeptidases. Specialized pyroglutamyl peptidases (PGPs) are able to cleave an amino-terminal pyroglutamyl residue and thus control hormonal signals. The authors have determined the crystal structure of pyroglutamyl peptidase I (PGP-I) from *Bacillus amyloliquefaciens*, the first structure of argPGP. The structure allows the function of most of the conserved residues in the PGP-I family to be identified. The catalytic site has an S1 pocket lined with conserved hydrophobic residues to accommodate the pyroglutamyl residue. Aside from the S1 pocket, there is no clearly defined mainchain substrate-binding region, consistent with the lack of substrate specificity. Although the overall structure of PGP-I resembles some other α/β twisted open-sheet structures, such as purine nucleoside phosphorylase and cutinase, there are important differences in the location and organization of the active-site

residues. Thus, PGP-I belongs to a new family of cysteine proteases.
30 March 1999, Research Paper, *Structure*.

☐ **Crystal structure and functional characterization of OmpK36, the osmoporin of *Klebsiella pneumoniae*.**
R Dutzler, G Rummel, S Albertí, S Hernández-Allés, PS Phale, JP Rosenbusch, VJ Benedí and T Schirmer (1999). Structure **7**, 425–434.

Porins are channel-forming membrane proteins that confer solute permeability to the outer membrane of Gram-negative bacteria. In *Escherichia coli*, major nonspecific porins are matrix porin (OmpF) and osmoporin (OmpC), which show high sequence homology. In response to high osmolarity of the medium, OmpC is expressed at the expense of OmpF porin. Here, we study osmoporin of the pathogenic *Klebsiella pneumoniae* (OmpK36), which shares 87% sequence identity with *E. coli* OmpC, in an attempt to establish why osmoporin is best suited to function at high osmotic pressure. The crystal structure of OmpK36 has been determined, and closely resembles that of the search model. The homotrimeric structure is composed of three hollow 16-stranded antiparallel β barrels, each delimiting a separate pore. Most insertions and deletions with respect to OmpF are found in the loops that protrude towards

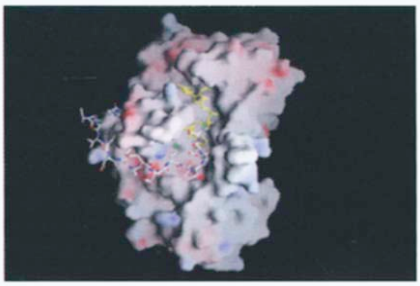
the cell exterior. Functionally, as characterized in lipid bilayers and liposomes, OmpK36 resembles OmpC with decreased conductance and increased cation selectivity in comparison with OmpF. The osmoporin structure suggests that an increase in charge density rather than an altered pore size is the basis for the distinct



physicochemical properties of this porin that are relevant for its preferential expression at high osmotic strength.
31 March 1999, Research Paper, *Structure*.

☐ **Chloroplast NADP-malate dehydrogenase: structural basis of light-dependent regulation of activity by thiol oxidation and reduction.**
Paul D Carr, Denis Verger, Anthony R Ashton and David L Ollis (1999). *Structure* **7**, 461–475.

NADP-dependent malate dehydrogenase (EC 1.1.1.82) is a light-activated chloroplast enzyme that functions in the C_4 pathway of photosynthesis. The light regulation is believed to be mediated *in vivo* by thioredoxin-catalyzed reduction and re-oxidation of cystine residues. The rates of reversible activation and inactivation of the enzyme are strongly influenced by the coenzyme substrates that seem to ultimately determine the steady-state extent of activation *in vivo*. The core structure is homologous to NAD-dependent malate dehydrogenases. Two surface-exposed and thioredoxin-accessible disulfide bonds are present — one in the amino-terminal extension and the other in the carboxy-terminal extension. The carboxy-terminal peptide of the inactive, oxidized enzyme is constrained by its disulfide bond to fold into the active site over NADP+, hydrogen bonding to the catalytic His225, as well as obstructing access of the C_4 acid substrate. Two loops flanking the active site, termed the Arg_2 and Trp loops, that contain the C_4 acid substrate binding residues are prevented from closing by the carboxy-terminal extension. The structure explains the role of the carboxy-terminal extension in inhibiting activity. The negative carboxyl terminus will interact more strongly with the positively charged nicotinamide of NADP+ than NADPH, explaining why the coenzyme-binding affinities of the enzyme differ so markedly from those of all other homologous α-hydroxy acid dehydrogenases. NADP+ may also slow dissociation of the carboxyl terminus upon reduction, providing a mechanism



for the inhibition of activation by NADP+ but not NADPH.
1 April 1999, Research Paper, *Structure*.