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Paper Alert

Chosen by Robert Liddington[1], Christin Frederick[2], Jane Clarke[3] and Sophie Jackson[3]

A selection of interesting papers that were published in the month before our press date in major journals most likely to report significant results in structural biology, protein and RNA folding.

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Structure 1999, Vol 7 No 12:000–000

☐ Core-directed protein design. I. An experimental method for selecting stable proteins from combinatorial libraries. MD Finucane, M Tuna, JH Lees and DN Woolfson (1999). *Biochemistry* 38, 11604–11612.

A major obstacle in the design of proteins is the specification of well-packed hydrophobic cores to drive the folding and stabilization of the target. Computational approaches have been used to alleviate this by testing alternate sequences prior to the production and characterization of a few proteins. In this paper an experimental counterpart of this approach is used. Stable variants from a library of ubiquitin hydrophobic-core mutants were selected as follows. Hexahistidine-tagged proteins were displayed on the surface of phage. These protein–phage were immobilized onto Ni-coated surfaces and treated with protease to remove unstable or poorly folded proteins. Stable phage fusions were eluted and infected into *Escherichia coli*, which allowed amplification for further selection, sequencing or protein expression. Two Ni-derivatized supports were tested: Ni–NTA chips for surface plasmon resonance (SPR) and Ni–NTA agarose beads. SPR had an advantage in that the selection process could be monitored directly. This allowed individual clones and experimental conditions to be tested rapidly prior to preparative panning of the library, which was carried out using Ni–NTA agarose beads. This method is demonstrated by the selection of stable core mutants of ubiquitin. As the method selects only on the basis of structure and stability, it will be of use in improving the stabilities and structural specificities of proteins of *de novo* design, and in establishing rules that link sequence and structure.
7 September 1999, *Biochemistry*

☐ Core-directed protein design. II. Rescue of a multiply mutated and destabilized variant of ubiquitin. MD Finucane and DN Woolfson (1999). *Biochemistry* 38, 11613–11623.

Stability-based selection using phage display was used to explore the sequence requirements for packing in the hydrophobic core of ubiquitin. In contrast to the parent protein, which was a structurally compromised mutant, the selected variants could be overexpressed and purified in yields for structural studies. In particular, circular dichroism and NMR measurements showed that the selectants folded correctly to stable native-like structures. These points demonstrate the utility of the core-directed method for stabilizing and redesigning proteins. In addition and in contrast to foregoing studies on other proteins, which suggest that hydrophobic cores permit substitutions provided that hydrophobicity and core volumes are generally conserved, the core of ubiquitin is found to be surprisingly intolerant of amino acid substitutions; variants that survived the selection showed a clear consensus for the wild-type sequence. It is probable that these results differed from those from other groups for two reasons. First, ubiquitin may be unusual in that it has strict sequence requirements for its structure and stability. Second, the mutants were selected solely on the basis of stability, in contrast to the other studies that rely on function-based selection. The latter may lead to proteins that are more plastic and tolerant of substitutions.
7 September 1999, *Biochemistry*

☐ Basis of substrate binding by the chaperonin GroEL. Zholun Wang, Hwa-ping Feng, Samuel J Landry, Jennifer Maxwell and Lila M Gierasch (1999). *Biochemistry* 38, 12537–12546.

The authors have characterized by NMR methods the interactions of GroEL with synthetic peptides that mimic segments of unfolded proteins. By extending the study to a variety of peptides with differing sequence motifs, they observed that peptides can adopt conformations other than α helix when bound to GroEL. Furthermore, peptides of the same composition exhibited significantly different affinities for GroEL as manifested by the magnitude of transferred nuclear Overhauser effects (trNOEs). The authors conclude that the molecular basis of GroEL substrate recognition is the presentation of a hydrophobic surface by an incompletely folded polypeptide and that many backbone conformations can be accommodated.
28 September 1999, *Biochemistry*

☐ The structure of the ligand-binding domain of neurexin Iβ: regulation of LNS domain function by alternative splicing. Gabby Rudenko, Thai Nguyen, Yogarany Chelliah, Thomas C Südhof and Johann Deisenhofer (1999). *Cell* 99, 93–101.

Neurexins are expressed in hundreds of isoforms on the neuronal cell surface, where they may function as cell recognition molecules. Neurexins contain LNS domains, folding units found in many proteins like the G domain of laminin A, agrin, and slit. The crystal structure of neurexin Iβ, a single LNS

domain, reveals two seven-stranded β sheets forming a jelly-roll fold with unexpected structural similarity to lectins. The LNS domains of neurexin and agrin undergo alternative splicing that modulates their affinity for protein ligands in a neuron-specific manner. These splice sites are localized within loops at one edge of the jelly roll, suggesting a distinct protein interaction surface in LNS domains that is regulated by alternative splicing.
1 October 1999, *Cell*

☐ **Building a replisome from interacting pieces: sliding clamp complexed to a peptide from DNA polymerase and a polymerase editing complex.** Yousif Shamoo and Thomas A Steitz (1999). *Cell* **99**, 155–166.
The authors have solved the crystal structures of the bacteriophage RB69 sliding clamp, its complex with a peptide essential for DNA polymerase interactions, and the DNA polymerase complexed with primer–template DNA. The editing complex structure shows a partially melted duplex DNA exiting from the exonuclease domain at an unexpected angle, and significant changes in the protein structure. The clamp complex shows the C-terminal 11 residues of polymerase bound in a hydrophobic pocket, and it allows docking of the editing and clamp structures together. The peptide binds to the sliding clamp at a position identical to that of a replication inhibitor peptide bound to PCNA.
15 October 1999, *Cell*

☐ **Crystal structure of the helicase domain from the replicative helicase–primase of bacteriophage T7.** Michael R Sawaya, Shenyuan Guo, Stanley Tabor, Charles C Richardson and Tom Ellenberger (1999). *Cell* **99**, 167–177.
Helicases that unwind DNA at the replication fork are ring-shaped oligomeric enzymes that move along one strand of a DNA duplex and catalyze the displacement of the complementary strand in a reaction that is coupled to nucleotide hydrolysis. The helicase domain of the replicative helicase–primase protein from bacteriophage T7 crystallized as a helical filament that resembles the *Escherichia coli* RecA protein, an ATP-dependent DNA strand exchange factor. When viewed in projection along the helical axis of the crystals, six protomers of the T7 helicase domain resemble the hexameric rings seen in electron microscopic images of the intact T7 helicase–primase. Nucleotides bind at the interface between pairs of adjacent subunits and stabilize the folded conformation of a DNA-binding motif located near the center of the ring.
15 October 1999, *Cell*

☐ **Crystal structure of the PTEN tumor suppressor: implications for its phosphoinositide phosphatase activity and membrane association.** Jie-Oh Lee, Haijuan Yang, Maria-Magdalena Georgescu, Antonio Di Cristofano, Tomohiko Maehama, Yigong Shi, Jack E Dixon, Pier Pandolfi and Nikola P Pavletich (1999). *Cell* **99**, 323–334.
The PTEN tumor suppressor is mutated in diverse human cancers and in hereditary cancer predisposition syndromes. PTEN is a phosphatase that can act on both polypeptide and phosphoinositide substrates *in vitro*. The PTEN structure reveals a phosphatase domain that is similar to protein phosphatases but has an enlarged active site important for the accommodation of the phosphoinositide substrate. The structure also reveals that PTEN has a C2 domain. The PTEN C2 domain binds phospholipid membranes *in vitro*, and mutation of basic residues that could mediate this reduces PTEN's membrane affinity and its ability to suppress the growth of glioblastoma tumor cells. The phosphatase and C2 domains associate across an extensive interface, suggesting that the C2 domain may serve to productively position the catalytic domain on the membrane.
October 1999, *Cell*

☐ **Adhesion mechanism of human β_2-glycoprotein I to phospholipids based on its crystal structure.** Barend Bouma, Philip G de Groot, Jean MH van den Elsen, Raimond BG Ravelli, Arie Schouten, Marleen JA Simmelink, Ronald HWM Derksen, Jan Kroon and Piet Gros (1999). *EMBO J.* **18**, 5166–5174.
Human β_2-glycoprotein I is a heavily glycosylated five-domain plasma membrane adhesion protein, which has been implicated in blood coagulation and clearance of apoptotic bodies from the circulation. The crystal structure of β_2-glycoprotein I isolated from human plasma reveals an elongated fish-hook-like arrangement of the globular short consensus repeat domains. Half of the C-terminal fifth domain deviates strongly from the standard fold and forms a specific phospholipid-binding site. A large patch of 14 positively charged residues provides electrostatic interactions with anionic phospholipid headgroups and an exposed membrane-insertion loop yields specificity for lipid layers.
1 October 1999, *The EMBO Journal*

☐ **Crystal structure and induction mechanism of AmiC–AmiR: a ligand-regulated transcription antitermination complex.** Bernard P O'Hara, Richard A Norman, Paul TC Wan, S Mark Roe, Tracey E Barrett, Robert E Drew and Laurence H Pearl (1999). *EMBO J.* **18**, 5175–5186.
Inducible expression of the aliphatic amidase operon in *Pseudomonas aeruginosa* is controlled by an antitermination mechanism which allows production of the full-length transcript only in the presence of small-molecule inducers, such as acetamide. Ligand-regulated antitermination is provided by AmiC, the ligand-sensitive negative regulator, and AmiR, the RNA-binding positive regulator. Under non-inducing or repressing growth conditions, AmiC and AmiR form a complex in which the activity of AmiR is silenced. The crystal structure of the AmiC–AmiR complex identifies AmiR as a new and highly unusual member of the response-regulator family of bacterial signal-transduction proteins, regulated by sequestration rather than phosphorylation. Comparison with the structure of free AmiC reveals the subtle mechanism of ligand-induced release of AmiR.
1 October 1999, *The EMBO Journal*

☐ GroEL recognises sequential and non-sequential linear structural motifs compatible with extended β-strands and α-helices. Jean Chatellier, Ashley M Buckle and Alan R Fersht (1999). *J. Mol. Biol.* 292, 163–172.

The authors have analysed characteristics of the motifs that bind to GroEL by using affinity panning of immobilised GroEL minichaperones for a library of bacteriophages that display the fungal cellulose-binding domain of the enzyme cellobiohydrolase I. This protein has seven non-sequential residues in its binding site that form a linear binding motif with similar dimensions and characteristics to the peptide tag that was bound to the minichaperone GroEL(191–376). The seven residues thus form a constrained scaffold. The results imply that GroEL can bind a wide range of structures, from extended β strands and α helices to folded states with exposed sidechains. The data support two activities of GroEL: the ability to act as a temporary parking spot for sticky intermediates by binding many motifs; and an unfolding activity of GroEL by binding an extended sequential conformation of the substrate.
10 September 1999, *Journal of Molecular Biology*

☐ Identification of substrate binding site of GroEL minichaperone in solution. Naoki Tanaka and Alan R Fersht (1999). *J. Mol. Biol.* 292, 173–180.

The authors have located the substrate-binding site of the minichaperone GroEL(193–335) in solution by labelling it at various positions with a fluorescent probe and detecting which positions are perturbed on binding a denatured substrate. The dissociation constants between substrates and minichaperone were evaluated from fluorescence anisotropy. Intriguingly, the same site is involved in the binding of GroES. Thus, an important function of GroES in the regulation of the activity of GroEL for substrates is to displace the bound substrate by competing for its binding site.
10 September 1999, *Journal of Molecular Biology*

☐ A day in the life of Dr K. or how I learned to stop worrying and love lysozyme: a tragedy in six acts. Gunnar von Heijne (1999). *J. Mol. Biol.* 293, 367–379.

In modern drama, the agonizing nature of membrane protein work has not been adequately acknowledged. The play features, *inter alia*, Dr C., a young, hungry crystallographer. This is a play that is brutally honest, yet full of empathy for the poor souls that get caught between the Scylla of unreachable scientific glory and the Charybdis of helpless mediocrity.
22 October 1999, *Journal of Molecular Biology*

☐ Crystal structures of the XLP protein SAP reveal a class of SH2 domains with extended, phosphotyrosine-independent sequence recognition. Florence Poy, Michael B Yaffe, Joan Sayos, Kumkum Saxena, Massimo Morra, Janos Sumegi, Lewis C Cantley, Cox Terhorst and Michael J Eck (1999). *Mol. Cell* 4, 555–561.

SAP, the product of the gene mutated in X-linked lymphoproliferative syndrome (XLP), consists of a single SH2 domain that has been shown to bind the cytoplasmic tail of the lymphocyte coreceptor SLAM. The authors describe structures that show that SAP binds phosphorylated and nonphosphorylated SLAM peptides in a similar mode, with the tyrosine or phosphotyrosine residue inserted into the phosphotyrosine-binding pocket. Specific interactions with residues N-terminal to the tyrosine, in addition to more characteristic C-terminal interactions, stabilize the complexes. A phosphopeptide library screen and analysis of mutations identified in XLP patients confirm that these extended interactions are required for SAP function.
October 1999, *Molecular Cell*

☐ Triggering cell death: the crystal structure of Apo2L/TRAIL in a complex with death receptor 5. Sarah G Hymowitz, Hans W Christinger, Germaine Fuh, Mark Ultsch, Mark O'Connell, Robert F Kelley, Avi Ashkenazi and Abraham M de Vos (1999). *Mol. Cell* 4, 563–571.

Formation of a complex between Apo2L (also called TRAIL) and its signaling receptors, DR4 and DR5, triggers apoptosis by inducing the oligomerization of intracellular death domains. The authors report the crystal structure of the complex between Apo2L and the ectodomain of DR5. The structure shows three elongated receptors snuggled into long crevices between pairs of monomers of the homotrimeric ligand. The interface is divided into two distinct patches, one near the bottom of the complex close to the receptor cell surface and one near the top. Both patches contain residues that are critical for high-affinity binding.
October 1999, *Molecular Cell*

☐ Atomic structure of the GCSF—receptor complex showing a new cytokine–receptor recognition scheme. Masaharu Aritomi, Nauki Kunishima, Tomoyuki Okamoto, Ryota Kuroki, Yoshimi Ota and Kosuke Morikawa (1999). *Nature* 401, 713–717.

Granulocyte colony-stimulating factor (GCSF) is a member of the class 1 cytokine superfamily. The crystal structure of GCSF complexed to the BN–BC domains of the GCSF receptor presents a new molecular basis for cytokine–receptor recognition.
14 October 1999, *Nature*

☐ The reaction cycle of isopenicillin *N* synthase observed by X-ray diffraction. Nicotal I Burzlaff, Peter J Rutledge, Ian J Clifton, Charles MH Hensgens, Michael Pickford, Robert M Adlington, Peter L Roach and Jack Baldwin (1999). *Nature* 401, 721–724.

Isopenicillin *N* synthase (IPNS), a non-haem iron-dependent oxidase, catalyses the biosynthesis of isopenicillin *N* (IPN). The key intermediates in the reaction cycle were elucidated by high-resolution crystallographic analysis of frozen intermediates and substrate analogues. These monocyclic and bicyclic structures support the hypothesis of a two-stage reaction sequence leading to penicillin. The formation of a monocyclic sulphoxide product from the substrate analogue

ACmC is most simply explained by the interception of a high-valency iron-oxo species.
14 October 1999, *Nature*

☐ **Structural evidence for dimerization-regulated activation of an integral membrane phospholipase**. HJ Snijder, I Ubarretxena-Belandia, M Blaauw, KH Kalk, HM Verheij, MR Egmond, N Dekker and BW Dijkstra (1999). *Nature* **401**, 717–721.

Dimerization is a biological regulatory mechanism employed by both soluble and membrane proteins. Outer membrane phospholipase A (OMPLA) is an integral membrane enzyme which participates in secretion of colicins in *Escherichia coli*. Its activity is regulated by reversible dimerization. Crystal structures of monomeric and dimeric OMPLA show that dimerization results in functional oxyanion holes and substrate-binding pockets, which are absent in monomeric OMPLA. Dimer interactions occur almost exclusively in the apolar membrane-embedded parts.
14 October 1999, *Nature*

☐ **High-resolution X-ray structure of an early intermediate in the bacteriorhodopsin photocycle**. Karl Edman, Peter Nollert, Antoine Royant, Hassan Belrhali, Eva Pebay-Peyroula, Janos Hajdu, Richard Neutze and Ehud M Landau (1999). *Nature* **401**, 822–826.

Bacteriorhodopsin is the simplest known photon-driven proton pump. To elucidate the inital structural changes coupled to the proton-pumping mechanism the authors trapped at low temperature an early intermediate of the photocycle within wild-type bacteriorhodopsin crystals grown in a lipidic cubic phase. The high-resolution X-ray structure reveals that a key water molecule is dislocated, allowing the primary proton acceptor, Asp85, to move. Movement of the mainchain Lys216 locally disrupts the hydrogen-bonding network of helix G, facilitating structural changes later in the photocycle. (The structure of a trapped photoproduct of bacteriorhodopsin is described by H Luecke, B Schobert, H-T Richter, J-P Cartailler and JK Lanyi in *Science* **286**, 255–261.)
21 October 1999, *Nature*

☐ **A triple β-spiral in the adenovirus fibre shaft reveals a new structural motif for a fibrous protein**. Mark J van Raaij, Anna Mitraki, Gilles Lavigne and Stephen Cusack (1999). *Nature* **401**, 935–938.

Human adenovirus particles have a protruding trimeric fibre that is responsible for receptor attachment. The fibres are homo-trimeric proteins containing an N-terminal penton base attachment domain, a long, thin central shaft and a C-terminal cell attachment or head domain. The crystal structure of the four distal repeats of the adenovirus type 2 fibre shaft plus the receptor-binding head domain reveals a novel triple β-spiral fibrous fold for the shaft. Implications for folding of fibrous proteins and for the design of a new class of artificial, silk-like fibrous materials are discussed.
28 October 1999, *Nature*

☐ **Crystal structure of hemopexin reveals a novel high-affinity heme site formed between two β-propeller domains**. Massimo Paoli, Bryan F Anderson, Heather M Baker, William T Morgan, Ann Smith and Edward N Baker (1999). *Nat. Struct. Biol.* **6**, 926–931.

Hemopexin binds heme with the highest affinity of any known protein, but releases it into cells via specific receptors. It is necessary for cellular protection during trauma, inflammation and hemolysis, and to maintain iron homeostasis. The crystal structure of the heme–hemopexin complex reveals a novel heme-binding site, formed between two similar four-bladed β-propeller domains and bounded by the interdomain linker. The ligand is bound to two histidine residues in a pocket dominated by aromatic and basic groups. Further stabilization is achieved by the association of the two β-propeller domains, which form an extensive polar interface that includes a cushion of ordered water molecules.
October 1999, *Nature Structural Biology*

☐ **Crystal structure of the RNA-dependent RNA polymerase from hepatitis C virus reveals a fully encircled active site**. Charles A Lesburg, Michael B Cable, Eric Ferrari, Zhi Hong, Anthony F Mannarino and Patricia C Weber (1999). *Nat. Struct. Biol.* **6**, 937–943.

Various classes of nucleotidyl polymerases with different transcriptional roles contain a conserved core structure. The crystal structure of hepatitis C virus (HCV) nonstructural protein 5B (NS5B) provides the first complete and detailed view of an RNA-dependent RNA polymerase. While canonical polymerase features exist in the structure, NS5B adopts a unique shape due to extensive interactions between the fingers and thumb polymerase subdomains that serve to encircle the enzyme active site. The apoenzyme can accommodate a template–primer duplex without global conformational changes, supporting the hypothesis that this structure is essentially preserved during the reaction pathway. This NS5B template–primer model also allows identification of a new structural motif involved in stabilizing the nascent base pair.
October 1999, *Nature Structure Biology*

☐ **Prediction of protein-folding mechanisms from free-energy landscapes derived from native structures**. E Alm and D Baker (1999). *Proc. Natl Acad. Sci. USA* **96**, 11305–11310.

Guided by recent experimental results suggesting that protein-folding rates and mechanisms are determined largely by native-state topology, a simple model for protein folding free-energy landscapes based on native-state structures has been developed. The configurations considered by the model contain one or two contiguous stretches of residues ordered as in the native structure with all other residues completely disordered; the free energy of each configuration is the difference between the entropic cost of ordering the residues, which depends on the total number of residues ordered and the length of the loop between the two ordered segments, and the favourable attractive interactions, which are taken to be

proportional to the total surface area buried by the ordered residues in the native structure. Folding kinetics are modelled by allowing only one residue to become ordered/disordered at a time, and a rigorous and exact method is used to identify free-energy maxima on the lowest free-energy paths connecting the fully disordered and fully ordered configurations. The distribution of structure in these free-energy maxima, which comprise the transition-state ensemble in the model, are reasonably consistent with experimental data on the folding transition state for five of seven proteins studied. Thus, the model appears to capture, at least in part, the basic physics underlying protein folding and the aspects of native-state topology that determine protein-folding mechanisms.
28 September 1999, *Proceedings of the National Academy of Science USA*

☐ A simple model for calculating the kinetics of protein folding from three-dimensional structures. Victor Muñoz and William A Eaton (1999). *Proc. Natl Acad. Sci.* 96, 11311–11316.
An elementary statistical mechanical model was used to calculate the folding rates for 22 proteins from their known three-dimensional structures. In this model, residues come into contact only after all of the intervening chain is in the native conformation. An additional simplifying assumption is that native structure grows from localized regions that then fuse to form the complete native molecule. The free-energy function for this model contains just two contributions, conformational entropy of the backbone and the energy of the inter-residue contacts. The matrix of inter-residue interactions is obtained from the atomic coordinates of the three-dimensional structure. For the 18 proteins that exhibit two-state equilibrium and kinetic behaviour, profiles of the free energy versus the number of native peptide bonds show two deep minima, corresponding to the native and denatured states. For four proteins known to exhibit intermediates in folding, the free energy profiles show additional deep minima. The calculated rates of folding the two-state proteins, obtained by solving a diffusion equation for motion on the free energy profiles, reproduce the experimentally determined values surprisingly well. The success of these calculations suggests that folding speed is largely determined by the distribution and strength of contacts in the native structure. The effect of mutations on the folding kinetics of chymotrypsin inhibitor 2, the most intensively studied two-state protein, was also modelled with some success.
28 September 1999, *Proceedings of the National Academy of Science USA*

☐ Crystal structure of the DNA nucleotide excision repair enzyme UvrB from ***Thermus thermophilus***. Mischa Machius, Lisa Henry, Maya Palnitkar and Johann Deisenhofer (1999). *Proc. Natl Acad. Sci. USA* 96, 11717–11722.
In prokaryotes, three enzymes forming the UvrABC system initiate nucleotide excision repair (NER) of a variety of structurally different DNA lesions. UvrB, the central component of this system, is responsible for the ultimate DNA damage recognition and participates in the incision of the damaged DNA strand. The crystal structure of *Thermus thermophilus* UvrB reveals a core that is structurally similar to core regions found in helicases, where they constitute molecular motors. Additional domains implicated in binding to DNA and various components of the NER system are attached to this central core. The architecture and distribution of DNA-binding sites suggest a possible model for the DNA damage recognition process.
26 October 1999, *Proceedings of the National Academy of Science USA*

☐ Structure of a soluble secreted chemokine inhibitor vCCI (p35) from cowpox virus. Andrea Carfí, Craig A Smith, Pamela J Smolak, Jeffrey McGrew and Don C Wiley (1999). *Proc. Natl Acad. Sci. USA* 96, 12379–12383.
Most poxviruses, including variola, the causative agent of smallpox, express a secreted protein of 35 kDa, vCCI, which binds CC-chemokines with high affinity. This viral protein competes with the host cellular CC-chemokine receptors, reducing inflammation and interfering with the host immune response. The authors have determined the crystal structure to 1.85 Å resolution of vCCI from cowpox virus, the prototype of this poxvirus virulence factor. The molecule is a β sandwich of topology not previously described.
26 October 1999, *Proceedings of the National Academy of Science USA*

☐ X-ray crystal structures of a severely desiccated protein. Jeffrey A Bell (1999). *Protein Sci.* 8, 2033–2040.
Unlike most protein crystals, form IX of bovine pancreatic ribonuclease A diffracts well when severely dehydrated. High-resolution crystal structures of two desiccated structures are very similar. A root mean square displacement of 1.6 Å is observed for mainchain atoms in each structure when compared with the hydrated crystal structure, with some large rearrangements observed in loop regions. The structural changes are the result of intermolecular contacts formed by strong electrostatic interactions in the absence of a high dielectric medium. These results help explain conformational changes during the lyophilization of protein and the associated phenomena of denaturation and molecular memory.
8 October 1999, *Protein Science*

☐ X-ray crystallographic structure of the Norwalk virus capsid. BVV Prasad, Michele E Hardy, Terje Dokland, Jordi Bella, Michael G Rossmann and Mary K Estes (1999). *Science* 286, 287–290.
Norwalk virus, a noncultivatable human calicivirus, is the major cause of epidemic gastroenteritis in humans. The first X-ray structure of a calicivirus capsid, which consists of 180 copies of a single protein, has been determined by phase extension from a low-resolution electron-microscopy structure. The capsid protein has a protruding (P) domain connected by a flexible hinge to a shell (S) domain that has a classical eight-stranded β-sandwich motif. The structure of the P domain,

thought to contain the determinants of strain specificity and cell binding, is unlike that of any other viral protein, with a subdomain exhibiting a fold similar to that of the second domain in the eukaryotic translation elongation factor Tu.
8 October 1999, *Science*

☐ Crystal structure of invasin: a bacterial integrin-binding protein. Zsuzsa A Hamburger, Michele S Brown, Ralph R Isberg and Pamela J Bjorkman (1999). *Science* 286, 291–295.

The *Yersinia pseudotuberculosis* invasin protein promotes bacterial entry by binding to host cell integrins with higher affinity than natural substrates such as fibronectin. The crystal structure of the invasin extracellular region reveals five domains that form a 180 Å rod with structural similarities to tandem fibronectin type III domains. The integrin-binding surfaces of invasin and fibronectin include similarly located key residues, but in the context of different folds and surface shapes. The structures of invasin and fibronectin provide an example of convergent evolution, in which invasin presents an optimized surface for integrin binding, in comparison with host substrates.
8 October 1999, *Science*

☐ Crystal structure of the ectodomain of human transferrin receptor. C Martin Lawrence, Sanjoy Ray, Marina Babyonyshev, Renate Galluser, David W Borhani and Stephen C Harrison (1999). *Science* 286, 779–782.

The transferrin receptor (TfR) undergoes multiple rounds of clathrin-mediated endocytosis and reemergence at the cell surface, importing iron-loaded transferrin (Tf) and recycling apotransferrin after discharge of iron in the endosome. The crystal structure of the dimeric ectodomain of the human TfR reveals a three-domain subunit. One domain closely resembles carboxypeptidases and aminopeptidases, and features of membrane glutamate carboxypeptidase can be deduced from the TfR structure. A model is proposed for Tf binding to the receptor.
22 October 1999, *Science*

☐ The structure of bacteriophage T4 gene product 9: the trigger for tail contraction. Victor A Kostyuchenko, Grigorii A Navruzbekov, Lidia P Kurochkina, Sergei V Strelkov, Vadim V Mesyanzhinov, Michael G Rossmann (1999). *Structure* 7, 1213–1222.

The T4 bacteriophage consists of a head and a complex contractile tail required for the ejection of the viral genome into the *Escherichia coli* host. The tail has a baseplate to which are attached six long and six short tail fibers. Gene product 9 (gp9) is the protein that connects the long tail fibers to the baseplate and triggers the tail contraction after virus attachment to a host cell. The crystal structure of recombinant gp9 reveals a homotrimer. The monomer consists of three domains: the N-terminal domain generates a triple coiled coil; the middle domain is a mixed, seven-stranded β sandwich associated with the long tail fibers; and the C-terminal domain is an antiparallel β sandwich, which binds to the baseplate. The protein contains flexible interdomain hinges, which are presumably required to facilitate signal transmission between the long tail fibers and the baseplate.
30 September 1999, *Structure*

☐ The structure of the outer membrane protein OmpX from ***Escherichia coli*** reveals possible mechanisms of virulence. Joachim Vogt and Georg E Schulz (1999). *Structure* 7, 1301–1309.

The integral outer membrane protein X (OmpX) from *Escherichia coli* belongs to a family of highly conserved bacterial proteins that promote bacterial adhesion to and entry into mammalian cells. The crystal structure of OmpX from *E. coli* consists of an eight-stranded antiparallel all-next-neighbor β barrel and resembles an inverse micelle. Extracellular loops form a protruding β sheet, the edge of which presumably binds to external proteins. Although OmpX has the same β-sheet topology as the structurally related outer membrane protein A (OmpA), their barrels differ with respect to the shear numbers and internal hydrogen-bonding networks.
1 October 1999, *Structure*