# Paper Alert

## Chosen by Robert Liddington[1] and Christin Frederick[2]

**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.**

Addresses: [1]Department of Biochemistry, University of Leicester, Leicester LE1 7RH, UK and [2]Laboratory of X-ray Crystallography, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA.

**Structure** 15 March 1996, **4**:353–355



□ **The crystal structure of ribonuclease Rh from *Rhizopus niveus* at 2.0 Å resolution**. Hiroyuki Kurihara, Takamasa Nonaka, Yukio Mitsui, Kazuko Ohgi, Masachika Irie and Kazuo T Nakamura (1996). *J. Mol. Biol.* **255**, 310–320.

Ribonuclease Rh (RNase Rh) is one of the 2′3′-cyclizing RNases which hydrolyze phosphodiester bonds of RNA to 3′-nucleotides via 2′,3′-cyclic nucleotides. The crystal structure was determined at 2.0 Å resolution. The overall structure of RNase Rh is completely different from those of other previously studied RNases, such as RNase A from bovine pancreas and RNase $T_1$ from *Aspergillus oryzae*. In the structure of RNase Rh, two histidine residues and one glutamic acid residue form the active site. There is a hydrophobic pocket around the active site which is presumed to be the base binding site of the substrate.

19 January 1996, *Journal of Molecular Biology*

□ **Crystal structure of *Citrobacter freundii* restriction endonuclease *Cfr*10I at 2.15 Å resolution**. Damir Bozic, Saulius Grazulis, Virginijus Siksnys and Robert Huber (1996). *J. Mol. Biol.* **255**, 176–186.

The crystal structure of *Citrobacter freundii* restriction endonuclease *Cfr*10I, determined at a resolution of 2.15 Å, represents the first structure of a restriction endonuclease recognizing a degenerate nucleotide sequence. The arrangement of the putative active-site residues shows some striking differences from previously described restriction endonucleases and supports a two-metal-ion mechanism of catalysis.

12 January 1996, *Journal of Molecular Biology*

■ **Structure and mechanism of DNA topoisomerase II**. James M Berger, Steven J Gamblin, Stephen C Harrison and James C Wang (1996). *Nature* **379**, 225–232.

Type II DNA topoisomerases are enzymes that function in the segregation of newly replicated chromosome pairs, in chromosome condensation, and in altering DNA superhelicity. The crystal structure of a large fragment of yeast type II DNA topoisomerase reveals a heart-shaped dimeric protein with a large central hole. It provides a molecular model of the enzyme as an ATP-modulated clamp with two sets of jaws at opposite ends, connected by multiple joints. An enzyme with bound DNA can admit a second DNA duplex through one set of jaws, transport it through the cleaved first duplex, and expel it through the other set of jaws.

18 January 1996, *Nature*

□ **Spatial constraints on the recognition of phosphoproteins by the tandem SH2 domains of the phosphatase SH-PTP2**. Michael J Eck, Scott Pluskey, Thomas Trüb, Stephen C Harrison and Steven E Shoelson (1996). *Nature* **379**, 277–280.

The mammalian SH2 domain protein tyrosine phosphatases (PTPs) contain tandem SH2 domains and a single C-terminal catalytic domain. SH-PTP1 and SH-PTP2 function downstream from tyrosine kinase-linked receptors. As well as directing subcellular localization by binding to receptors and their substrates, the two SH2 domains of these PTPs function together to regulate catalysis. Here the authors report the structure of the tandem SH2 domains of SH-PTP2 in complex with monophosphopeptides. A fixed relative orientation of the two domains separates the peptide-binding sites by ~40 Å, suggesting that spatial constraints are important in this multidomain protein–protein interaction.

18 January 1996, *Nature*

● **The crystal structure of the GroES co-chaperonin at 2.8 Å resolution**. John F Hunt, Arthur J Weaver, Samuel J Landry, Lila Gierasch and Johann Deisenhofer (1996). *Nature* **379**, 37–45.

Chaperonins are proteins that control the folding of other proteins. The most thoroughly studied chaperonin system is the GroEL:GroES complex from *Escherichia coli* and here the authors describe the crystal structure of GroES. The GroES heptamer forms a dome, approximately 75 Å in diameter and 30 Å high, with an 8 Å orifice in the centre of its roof. The 'mobile loop' segment, previously identified as a GroEL binding determinant, is disordered in the crystal structure in six subunits; the single well-ordered copy extends from the bottom outer rim of the GroES dome, suggesting that the cavity within the dome is continuous with the polypeptide binding chamber of GroEL in the chaperonin complex.

4 January 1996, *Nature*

---

■ See the Minireview article by Dale B Wigley in the 15 February issue of *Structure* (volume **4**:117–120).

● See the Minireview article by Helen Saibil in the 15 January issue of *Structure* (volume **4**:1–4).

□ **Binding of the antitumor drug nogalamycin to bulged DNA structures**. Janet Caceres-Cortes and Andrew H-J Wang (1996). *Biochemistry* **35**, 616–625.

Two DNA heptamers, $CT_b$-GTACG and $CGTACT_bG$, each containing a bulged T nucleotide embedded in the C–G step, have been studied by NMR. Both duplexes are significantly destabilized, and the bulged T remains intrahelical. Binding of the anthracycline antitumor antibiotic nogalamycin (Ng) to these two heptamers stabilizes the duplex structure. The bulged T behaves differently upon the binding of Ng. In Ng-$CT_bGTACG$ wobble $G_6$:$T_b$ base pairs are formed, leaving two dangling 5′-$C_1$ nucleotides: whereas in Ng-$CGTACT_bG$ weak $C_1$:$T_b$ base pairs are formed, leaving two dangling 3′-$G_6$ nucleotides. Thus, Ng induces the bulged T and the opposing base in the duplex to stack on the aglycon and causes the base next to $T_b$ to unpair, mimicking a 'frame shift'.
16 January 1996, *Biochemistry*

□ **The crystal structure of ribosomal protein L14 reveals an important organizational component of the translational apparatus**. Christopher Davies, Stephen W White and V Ramakrishnan (1996). *Structure* **4**, 55–66.

L14 is one of the most conserved ribosomal proteins and occupies a central location between the peptidyl transferase and GTPase regions of the large ribosomal subunit. The crystal structure of L14 from *Bacillus stearothermophilus* comprises a five-stranded β-barrel, a C-terminal loop region that contains two small α-helices, and a β-ribbon that projects from the β-barrel. Three surface patches probably mediate L14–RNA and L14–protein interactions within the ribosome.
15 January 1996, *Structure*

□ **Crystal structures of nucleoside 2-deoxyribosyltransferase in native and ligand-bound forms reveal architecture of the active site**. Shelly R Armstrong, William J Cook, Steven A Short and Steven E Ealick (1996). *Structure* **4**, 97–107.

Nucleoside 2-deoxyribosyltransferase plays an important role in the salvage pathway of nucleotide metabolism in certain organisms, catalyzing the cleavage of β-2′-deoxyribonucleosides and the subsequent transfer of the deoxyribosyl moiety to an acceptor base. The paper describes the crystal structure of the enzyme with and without bound ligand at 2.5 Å. The enzyme comprises a single domain that belongs to the class of doubly-wound α/β proteins and contains a unique nucleoside-binding motif. A comparison of the enzyme interactions with both a purine and pyrimidine ligand provides insight into the structural basis for enzyme specificity.
15 January 1996, *Structure*

□ **2.0 Å crystal structure of a four-domain segment of human fibronectin encompassing the RGD loop and synergy region.** Daniel J Leahy, Ikramuddin Aukhil and Harold P Erickson (1996). *Cell* **84**, 155–164.

Fibronectin (FN) is a component of extracellular matrices and is present at high concentrations (~300 μg $ml^{-1}$) in plasma. The authors determined the 2.0 Å crystal structure of a fragment of human fibronectin extending from the seventh to the tenth (RGD-containing) type III repeat (FN7–10). The structure reveals an extended rod-like molecule with a long axis of ~140 Å and highly variable relationships between adjacent type II repeats or domains. An unusually small rotation between domains 9 and 10 creates a distinctive binding site, in which the RGD loop from domain 10 and the 'synergy' region from domain 9 are on the same face of FN7–10 and thus easily accessible to a single integrin molecule. The cell-binding RGD loop is well-ordered in this structure and extends ~10 Å away from the FN7–10 core.
12 January 1996, *Cell*

□ **Structure of the heat shock protein chaperonin-10 of *Mycobacterium leprae***. Shekhar C Mande, Vijay Mehra, Barry R Bloom and Wim GJ Hol (1996). *Science* **271**, 203–207.

Members of the chaperonin-10 (cpn10) protein family, also called heat shock protein 10 and in *Escherichia coli* GroES, play an important role in ensuring the proper folding of many proteins. The crystal structure of the *Mycobacterium leprae* cpn10 (Ml-cpn10) oligomer has been elucidated at a resolution of 3.5 Å. The architecture of the Ml-cpn10 heptamer resembles a dome with an oculus in its roof. The inner surface of the dome is hydrophilic and highly charged. A flexible region, known to interact with cpn60, extends from the lower rim of the dome. With the structure of a cpn10 heptamer now revealed and the structure of the *E. coli* GroEL previously known, models of cpn10:cpn60 and GroEL:GroES complexes are proposed.
12 January 1996, *Science*

▲ **Direct observation of protein solvation and discrete disorder with experimental crystallographic phases**. F Temple Burling, William I Weis, Kevin M Flaherty and Axel T Brünger (1996). *Science* **271**, 72–77.

A complete and accurate set of experimental crystallographic phases to a resolution of 1.8 Å was obtained for a 230-residue dimeric fragment of rat mannose-binding protein A with the use of multiwavelength anomalous dispersion (MAD) phasing. Partially reduced disulfide bonds, local disorder, and differences in the mobility of chemically equivalent molecules are apparent in the experimental electron-density map. A solvation layer is visible that includes well-ordered sites of hydration around polar and charged protein atoms, as well as diffuse, partially disordered solvent shells around exposed hydrophobic groups. Because the experimental phases and the resulting electron-density map are free from the influence of a model, they provide a stringent test of theoretical models of macromolecular solvation, motion and conformational heterogeneity.
5 January 1996, *Science*

▲ See the Minireview article by Randy J Read in the 15 January issue of *Structure* (volume **4**:11–14).

☐ **Crystal structure of *S*-adenosylmethionine synthetase**. Fusao Takusagawa, Shigehiro Kamitori, Shintaro Misaki and George D Markham (1996). *J. Biol. Chem.* **271**, 136–147.

Methylation reactions involving *S*-adenosylmethionine are involved in the regulation of a variety of cellular functions. The structure of *S*-adenosylmethionine synthetase from *Escherichia coli* has been determined at 3.0 Å resolution. The enzyme consists of four identical subunits; two subunits form a spherical tight dimer, and pairs of these dimers form a peanut-shaped tetrameric enzyme. Each dimer has two active sites which are located between the subunits. Each subunit consists of three domains that are related to each other by pseudo-threefold symmetry.

5 January 1996, *Journal of Biological Chemistry*

☐ **The structure of r(UUCGCG) has a 5′-UU-overhang exhibiting Hoogsteen-like *trans* U·U base pairs**. Markus C Wahl, Sambhorao T Rao and Muttaiya Sundaralingam (1996). *Nature Struct. Biol.* **3**, 24–31.

The crystal structure of the RNA fragment, 5′-r(UUCGCG)-3′, has been determined at 1.4 Å resolution. The 3′-terminal CGCG portion of the hexamer engages in Watson–Crick hydrogen bonding while the 5′-terminal UU-overhang forms novel Hoogsteen-like U·U self-base pairs with the overhang of an adjacent duplex. An unusual arrangement of one of the bases results in a *trans* U·U pair on antiparallel strands in contrast to the usual *cis* base pairs. The structure emphasizes the pronounced polymorphism of U·U pairs and has implications for folding of RNA molecules.

January 1996, *Nature Structural Biology*

☐ **Structure of a novel extracellular $Ca^{2+}$-binding module in BM-40**. Erhard Hohenester, Patrik Maurer, Christine Hohenadl, Rupert Timpl, Johan N Jansonius and Jürgen Engel (1996). *Nature Struct. Biol.* **3**, 67–73.

The EF-hand is a highly conserved $Ca^{2+}$-binding motif found in many cytosolic $Ca^{2+}$-modulated proteins. The authors report the crystal structure at 2.0 Å resolution of the C-terminal domain of human BM-40 (SPARC, osteonectin), an extracellular matrix protein containing an EF-hand pair. The two EF-hands interact canonically but their detailed structures are unusual. In the first EF-hand a one-residue insertion is accommodated by a *cis*-peptide bond and by substituting a carboxylate by a peptide carbonyl as a $Ca^{2+}$ ligand. The second EF-hand is stabilized by a disulphide bond. The EF-hand pair interacts tightly with an amphiphilic N-terminal helix, reminiscent of target peptide binding by calmodulin. The present structure defines a novel protein module occurring in several other extracellular proteins.

January 1996, *Nature Structural Biology*

☐ **The crystal structure of GMP synthetase reveals a novel catalytic triad and is a structural paradigm for two enzyme families**. John JG Tesmer, Thomas J Klem, Michael L Deras, V Jo Davisson and Janet L Smith (1996). *Nature Struct. Biol.* **3**, 74–86.

GMP synthetase is a glutamine amidotransferase from the *de novo* purine biosynthetic pathway. The crystal structure of GMP synthetase serves as a prototype for two families of metabolic enzymes. The Class I glutamine amidotransferase domain of GMP synthetase is found in related enzymes of the purine, pyrimidine, tryptophan, arginine, histidine and folic acid biosynthetic pathways. This domain includes a conserved Cys-His-Glu triad and is representative of a new family of enzymes that use a catalytic triad for enzymatic hydrolysis. The structure and conserved sequence fingerprint of the nucleotide-binding site in a second domain of GMP synthetase are common to a family of ATP pyrophosphatases, including NAD synthetase, asparagine synthetase and argininosuccinate synthetase.

January 1996, *Nature Structural Biology*