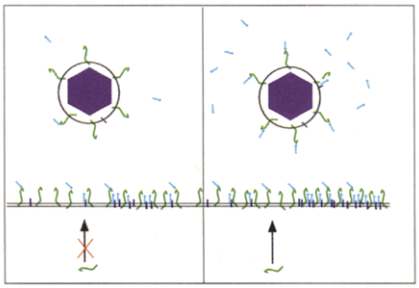
☐ **Cell-surface expression of CD4 reduces HIV-1 infectivity by blocking Env incorporation in a Nef- and Vpu-inhibitable manner.**
Juan Lama, Aram Mangasarian and Didier Trono (1999). *Curr. Biol.* **9**, 622–631.

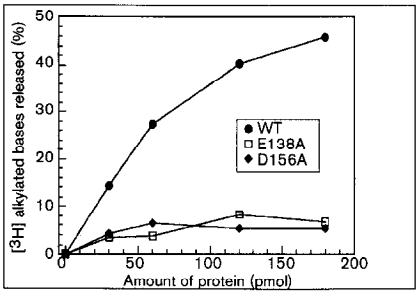
HIV-1 infection decreases the cell-surface expression of its cellular receptor, CD4, through the combined actions of three viral proteins: Nef, Env (envelope) and Vpu. Such functional convergence strongly suggests that CD4 downregulation is essential for optimal viral replication, but the significance of this phenomenon has so far remained a mystery. The authors show that high levels of CD4 on the surface of



HIV-infected cells induce a dramatic reduction in the infectivity of released virions by the sequestering of the viral envelope by CD4. CD4 is able to accumulate in viral particles while at the same time blocking incorporation of Env into the virion. Nef and Vpu, through their ability to downregulate CD4, counteract this effect. The CD4-mediated 'envelope interference' probably explains why HIV has developed more than one mechanism to downregulate the cell-surface expression of its receptor.
3 June 1999, Research Paper, *Current Biology*.

☐ **A new member of the endonuclease III family of DNA repair enzymes that removes methylated purines from DNA.**
Thomas J Begley, Brian J Haas, Jerry Noel, Alexander Shekhtman, William A Williams and Richard P Cunningham (1999). *Curr. Biol.* **9**, 653–656.

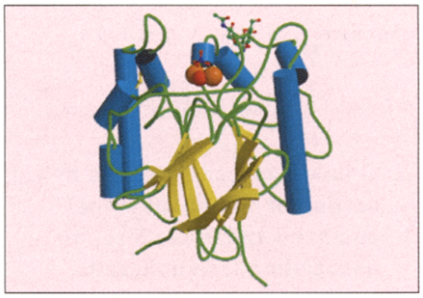
DNA is constantly exposed to endogenous and exogenous alkylating agents that can modify its bases, resulting in mutagenesis in the absence of DNA repair. DNA glycosylases remove alkylation damage by initiating the base-excision repair pathway and protecting the sequence information of the genome. The authors have identified a new class of methylpurine DNA glycosylase, designated MpgII, that is a member of the endonuclease III family of DNA repair enzymes. The authors showed that the enzyme releases both 7-methylguanine and 3-methyladenine from DNA. The MpgII genes from *T. maritima* and *Aquifex aeolicus* could restore methylmethanesulfonate (MMS) resistance to *Escherichia coli alkA tagA*



double mutants, which are deficient in the repair of alkylated bases. MpgII is the fifth member of the endonuclease III family of DNA repair enzymes, suggesting that the endonuclease III protein scaffold has been modified during evolution to recognize and repair a variety of DNA damage.
7 June 1999, Brief Communication, *Current Biology*.

☐ **Crystal structure of mammalian purple acid phosphatase.**
Luke W Guddat, Alan S McAlpine, David Hume, Susan Hamilton, John de Jersey and Jennifer L Martin (1999). *Structure* **7**, 757–768.

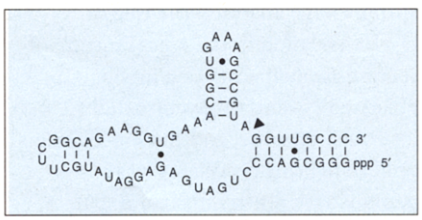
Mammalian purple acid phosphatases are highly conserved binuclear metal-containing enzymes produced by osteoclasts, the cells that resorb bone. There is strong evidence that the enzyme is involved in bone resorption, so it is a target for drug design. The structure of pig purple acid phosphatase has been solved. Despite less than 15% sequence identity, the protein fold resembles that of the catalytic domain of plant purple acid phosphatase and some serine/threonine protein phosphatases. The active-site regions of the mammalian and plant purple acid phosphatases differ significantly, however. The internal symmetry suggests that the binuclear centre



evolved as a result of the combination of mononuclear ancestors. The structure of the mammalian enzyme provides a basis for the design of drugs for bone resorptive diseases.
22 June 1999, Research Paper, *Structure*.

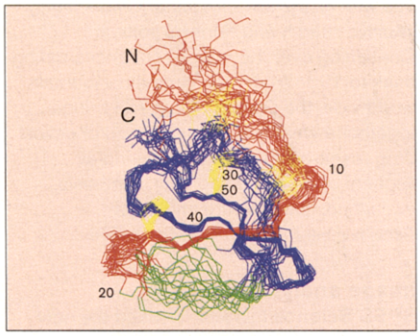
☐ **Design of allosteric hammerhead ribozymes activated by ligand-induced structure stabilization.**
Garrett A Soukup and Ronald R Breaker (1999). *Structure* **7**, 783–791.

Ribozymes can function as allosteric enzymes that undergo a conformational change upon ligand binding to a site other than the active site. Although allosteric ribozymes are not known to exist in nature, modular rational design has been used to engineer artificial ribozymes that act as allosteric enzymes. In this study, the authors exploit the modular nature of certain functional RNAs to engineer allosteric ribozymes that are activated by flavin mononucleotide (FMN) or



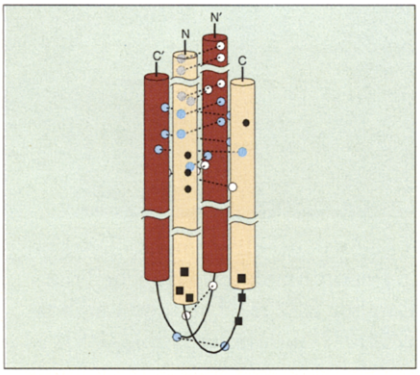
theophylline. The authors joined an FMN- or theophylline-binding domain to a hammerhead ribozyme by different stem II elements and identified a minimal connective bridge comprised of a G·U wobble pair that is responsive to ligand binding. Binding of FMN or theophylline to its allosteric site induces a conformational change in the RNA that stabilizes the wobble pair and favors the active form of the catalytic core. These ligand-sensitive ribozymes exhibit rate enhancements of more than 100-fold in the presence of FMN and of ~40-fold in the presence of theophylline. Conceivably, similar engineering strategies and allosteric mechanisms could be used to create a variety of novel allosteric ribozymes that function with other effector molecules.
23 June 1999, Research Paper, *Structure*.

☐ **Structure of a putative ancestral protein encoded by a single sequence repeat from a multidomain proteinase inhibitor gene from *Nicotiana alata*.**
Martin J Scanlon, Marcus CS Lee, Marilyn A Anderson and David J Craik (1999). *Structure* **7**, 793–802.
The ornamental tobacco *Nicotiana alata* produces a series of proteinase inhibitors (PIs) that are derived from a 43 kDa precursor protein, NaProPI. NaProPI contains six highly



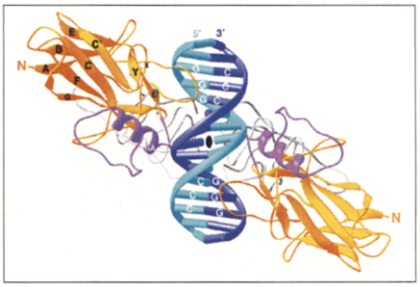
homologous repeats that fold to generate six separate structural domains. Unusually, the structural domains lie across adjacent repeats and the sixth PI domain is generated from fragments of the first and sixth repeats. Although the homology of the repeats suggests that they might have arisen from gene duplication, the observed folding does not appear to support this hypothesis. This structure of a single NaProPI repeat (aPI1) forms a basis for unravelling the mechanism by which this protein might have evolved. The structure of aPI1 closely resembles the triple-stranded antiparallel sheet observed in each of the native PIs. A single repeat from NaProPI is capable of folding into a compact globular domain that displays native-like PI activity. It is therefore possible that a similar single-domain inhibitor represents the ancestral protein from which NaProPI evolved.
24 June 1999, Research Paper, *Structure*.

☐ **The aspartate receptor cytoplasmic domain: *in situ* analysis of structure, mechanism and dynamics.**
Randal B Bass and Joseph J Falke (1999). *Structure* **7**, 829–840.
Site-directed sulfhydryl chemistry and spectroscopy can be used to probe



protein structure, mechanism and dynamics *in situ*. The aspartate receptor of bacterial chemotaxis belongs to a large family of prokaryotic and eukaryotic receptors that regulate histidine kinases in two-component signaling pathways, and has become one of the best characterized transmembrane receptors. The authors use cysteine and disulfide scanning to probe the helix-packing architecture of the cytoplasmic domain of the aspartate receptor. The results have led to a four-helix bundle model for the domain, and have provided constraints on the signalling mechanism and insights into backbone dynamics. The model should be relevant to to other receptors that regulate histidine kinases. The techniques used should continue to be useful for probing a range of systems, particularly complex protein systems.
28 June 1999, Research Paper, *Structure*.

☐ **Structure of the specificity domain of the Dorsal homologue Gambif1 bound to DNA.**
Patrick Cramer, Annabelle Varrot, Carolina Barillas-Mury, Fotis C Kafatos and Christoph W Müller (1999). *Structure* **7**, 841–852.
NF-κB/Rel transcription factors play important roles in immunity and development in mammals and insects. Their activity is regulated by their cellular localization, homo- and heterodimerization and association with other factors on their target gene promoters. Gambif1 from *Anopheles gambiae* is a member of the Rel family



and a close homologue of the morphogen Dorsal, which establishes dorsoventral polarity in the *Drosophila* embryo. The authors present the crystal structure of the amino-terminal specificity domain of Gambif1 bound to DNA. The Gambif1–DNA complex structure illustrates how differences in Dorsal affinity to binding sites in developmental gene promoters are achieved. Comparison with other Rel–DNA complex structures leads to a general model for DNA recognition by Rel proteins.
29 June 1999, Research Paper, *Structure*.