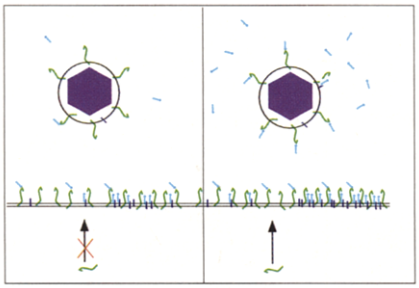
☐ **Cell-surface expression of CD4 reduces HIV-1 infectivity by blocking Env incorporation in a Nef- and Vpu-inhibitable manner.**
Juan Lama, Aram Mangasarian and Didier Trono (1999). *Curr. Biol.* **9**, 622–631.

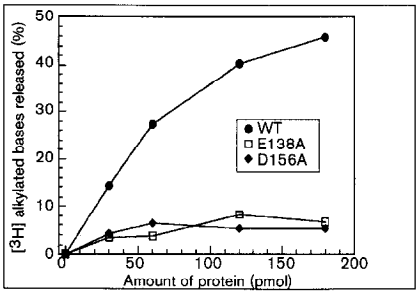
HIV-1 infection decreases the cell-surface expression of its cellular receptor, CD4, through the combined actions of three viral proteins: Nef, Env (envelope) and Vpu. Such functional convergence strongly suggests that CD4 downregulation is essential for optimal viral replication, but the significance 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.

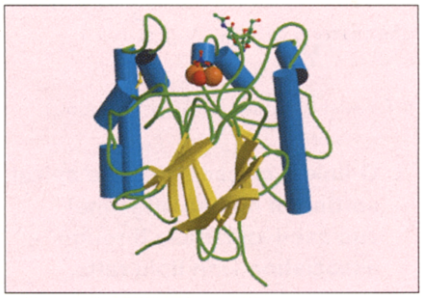
DNA is constantly exposed to endogenous and exogenous alkylating agents that can modify its bases, resulting in mutagenesis in the absence of DNA repair. DNA glycosylases remove alkylation damage by initiating the base-excision repair pathway and protecting the sequence information of the genome. The 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