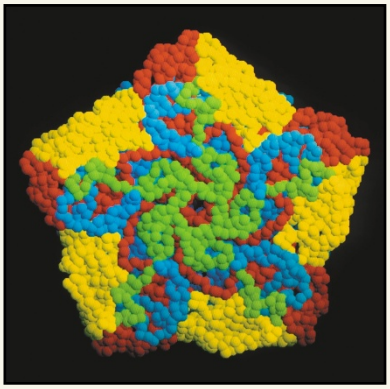
Synthetic polio to go



For the first time, researchers have shown that it is possible to generate a simple organism *de novo* from its genetic blueprint alone. Eckard Wimmer and colleagues at the State University of New York at Stony Brook generated infectious poliovirus from basic chemical building blocks (*Science* **297**, 1016–1018, 2002). Viral particles are composed of RNA rather than DNA, so the researchers took commercially available cDNA and used RNA polymerase to generate the necessary viral RNA. In a cell-free extract, the viral RNA was translated into proteins, which self-assembled into viral particles that can replicate. The synthetic virus proved to be infectious, generating polio-like symptoms in transgenic mice rendered susceptible to the disease. The research shows that it is possible to create life from simple chemicals. Because the genetic code of many other pathogens is publicly available, there are concerns that terrorists could create a range of deadly bioweapons. However, the poliovirus is a particularly rudimentary structure, and the ability to construct more sophisticated organisms such as bacteria is some way off. *LF*

Disulfide bond switches

Building and breaking phosphate bonds switches proteins on and off, and modifiers of phosphate bonds—such as the kinase inhibitor Gleevec—interest drug developers. To date, the disulfide bond, which forms bridges between distant protein domains, has courted little attention. Now, Philip Hogg at the University of New South Wales (Sydney, Australia) has shown that tampering with disulfide bonds on the CD4 receptors of T cells might prevent infection by HIV (*Nat. Immunol.* **3**, 727–732, 2002). The crystal structure of the CD4 receptor, onto which HIV latches, suggested that a disulfide bond in the extracellular domain was strained and could readily snap. Tests with a chemical that can label free thiol groups confirmed Hogg's hunch. The shearing of the sulfide bonds happened physiologically—free thiol groups appeared when T cells were challenged with a viral mimic. When Hogg chemically clamped together free thiols using a novel arsenic-containing compound, GSAO, HIV failed to enter T cells. GSAO seems nontoxic in mice and so could be used as an anti-HIV therapeutic. Hogg has shown that other extracellular proteins—angiostatin and the clotting agent von Willebrand Factor—are also regulated via sulfide bonds, suggesting that modulators of sulfide bonds may have wider applications. *EF*

Research news briefs written by Ella Finkel, Liz Fletcher, Judy Jamison, and Christopher Martino.

Prophylactic for prions

Prions—infectious protein particles—cause a variety of transmissible spongiform encephalopathies including scrapie, mad cow disease (bovine spongiform encephalopathy), and Creutzfeldt–Jakob disease. At present, there is neither cure nor prophylaxis for people accidentally exposed to prions. However, hope now comes from researchers in Germany working in collaboration with Coley Pharmaceuticals (Lagenfield, Germany), who show that CpG oligodeoxynucleotides (CpGs) might prolong prion incubation and extend life (*Lancet* **360**, 229–230, 2002). Unlike other infectious agents, prions lack nucleic acids, the usual triggers for a protective immune response. However, CpGs stimulate innate immunity in the host and could therefore slow the spread of infection. To test this theory, researchers injected mice with a mouse variant of scrapie and within seven hours treated the mice with saline or CpG daily for 4 or 20 days. All control mice died of scrapie within 183 days, whereas those given CpG daily for 4 days survived 38% longer. All mice treated for 20 days were still alive after 330 days. Although the exact mode of action is not known, CpG prophylaxis could reassure those unwittingly exposed to prion-infected material. Coley is currently testing CpGs as treatment for asthma, allergies, and other infectious diseases, and so far they have proven safe for use in humans. *LF*

Let there be light

Brent S. Gaylord and colleagues at the University of California (Santa Barbara, CA) have developed a sensitive and robust DNA-detection technique that exploits peptide nucleic acids (PNAs) and light-harvesting conjugated polymers (*Proc. Natl. Acad. Sci.*; published online August 7, 2002, doi:10.1073/pnas.162375999). The researchers created a PNA molecule complementary to a single strand of DNA, attaching a fluorescent dye to the PNA strand. Because PNA molecules have neutral charge, they bind rapidly and strongly to negatively charged, single-stranded DNA. The negatively charged DNA–PNA complexes can then bind to the positively charged conjugated polymer, drawing the PNA fluorescent group close enough for fluorescence resonance energy transfer (FRET) between the two. PNA that does not associate with DNA cannot associate with the polymer, and FRET does not take place. The major advantages of the technique include its sensitivity (10 pM of DNA can be detected) and robustness (the PNA molecules are very stable). The researchers say that PNA could also bind to double stranded DNA. *CM*

Plant sterility gene exposed

Sterile male plants may allow for production of hybrid seeds, boost flowering of ornamental plants, and generate genetically modified crops with a low risk of cross-pollination. Now a team of biologists at Penn State University (Philadelphia, PA) led by Hong P. Ma has discovered a gene—vital for normal pollen production—that might provide some leverage (*Genes Dev.* **16**, 2021–2031, 2002). Through random mutations, Ma and his team isolated a line of male-sterile *Arabidopsis thaliana* plants. Phenotypic and molecular analysis revealed that several aspects of anther cell division and differentiation had gone awry. During normal anther development, various cells differentiate on cue to produce mature pollen grains. However, although the male-sterile mutants' anthers started to develop normally, special cells called microsporocytes failed to complete their maturation, aborting pollen formation. Because these mutants produced an excess of microsporocytes, the gene subsequently identified was dubbed *EMS1*. *EMS1* appears to be a receptor protein kinase that could define a new signaling pathway controlling pollen production in the anthers. *JJ*