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nicked DNA molecules

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COVER

Crystal structure of the T cell receptor (TCR) (blue), showing its orientation bound to a major histocompatibility complex (MHC) molecule (red). The classic model (background, from *Immunobiology*, C. A. Janeway and P. Travers, Garland Press and Current Biology, London) placed the TCR over the MHC groove, but in an unknown orientation. The TCR interacts with the MHC bound to a peptide antigen (yellow) through its hypervariable loops (red, blue, and yellow). See page 209 and the News story on page 176. [Image: M. Pique, K. C. Garcia, and I. A. Wilson]

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This Week in Science

edited by PHIL SZUROMI

Cometary x-rays

When comet Hyakutake made its close approach to Earth, perhaps the most unexpected observation was that of x-ray and ultraviolet emission detected by the Roentgen X-ray Satellite and the Rossi X-ray Timing Explorer. Lisse et al. (p. 205) suggest that the emission might be due to the interaction of the comet with the solar wind, the solar magnetic field, or both. Although the exact mechanism that produced these cometary x-rays remains unclear, the next cometary interloper into our solar system will likely be scrutinized in these higher frequency ranges.

Roots of the Urals

The Ural Mountains mark the collision of Asia and Europe that began about 300 million years ago during the assembly of the Pangea supercontinent. Unlike the sutures in the Appalachians or Alps, the suture created by this collision was preserved in the continental interior during the subsequent breakup of Pangea. Four reports (beginning on p. 220; see the news story by Kerr, p. 181) highlight results from an international seismic experiment to investigate the nature of this crustal suture at depth. The crust in the Urals may extend to depths of up to 60 kilometers and the mantle lithosphere (the region without melt) may extend to 150 kilometers.

Surging ahead

Knowledge of the variability in the discharge of the large Greenland and Antarctic ice sheets is critical for evaluating their stability. Rapid transient

Role of cholesterol in development

Cholesterol has yet another essential role in biology. Porter *et al.* (p. 255; see the Perspective by Martin, p. 203) show that it is attached to the Hedgehog (Hh) proteins, which are key regulators of pattern formation, during embryogenesis. The Hh precursor undergoes autoproteolysis to form an amino-terminal domain (Hh-N) that has Hh signaling activity and a carboxyl-terminal (Hh-C) domain. During this process, Hh-C mediates the attachment of cholesterol to Hh-N. This cholesterol tag minimizes diffusion of the Hh-N signal and may control its short-range versus long-range effects in embryonic development.

increases in the speed (surges) of small glaciers have been identified for some time, but the variability in the recent discharge of the larger ice sheets has been uncertain. Joughin *et*



al. (p. 228) now show, using satellite radar interferometry observations, that the speed of an outlet glacier of the Greenland Ice Sheet, the Ryder Glacier, increased abruptly by a factor of 3 near the end of 1995.

Ultrashort x-ray pulses

Although x-ray methods can provide very high structural resolution, it has been difficult to generate ultrashort x-ray pulses, and high-resolution dynamical studies (on the order of 100 femtoseconds, or roughly one molecular vibration) have generally been limited to optical spectroscopy. Schoenlein *et al.* (p. 236) have demonstrated the production of 300-femtosecond x-rays with a wavelength of 0.4 angstroms. They scattered intense infrared laser pulses off a beam of highly relativistic electrons in an accelerator. In a Perspective, Eisenberger and Suckewer (p. 201) discuss how these results relate to other approaches for generating short x-ray pulses.

TCR structure, alone and with MHC

The interaction of the α and β chains of the T cell receptor (TCR) with peptides bound by the major histocompatibility complex (MHC) governs the recognition of foreign antigens by T cells. Previous structural studies of the β chain and part of the α chain showed that these molecules resemble immunoglobulins, but crystals revealing the interactions within the intact $\alpha\beta$ receptor have been difficult to obtain. Garcia et al. (p. 209; see cover and the news story by Service, p. 176) overexpressed a fully glycosylated form of a particular $\alpha\beta$ TCR, TCR 2C. The high-resolution structure of this receptor resembles that of an antibody except for the constant (C) domain of the α chain (C α) and the interactions between $C\alpha$ and C β . An analysis at lower resolution of crystals of this receptor with the MHC molecule H-2K^b shows how different TCR domains are positioned relative to the MHC peptide binding groove.

-

Means to a chromosome end

Telomeres, the structures at the ends of chromosomes, must be maintained by the telomerase enzyme during cycles of cell division or else the telomeres gradually shorten, which leads to aging of the cells. Nugent et al. (p. 249) identified yeast mutants that exhibited the telomerase-defect phenotype. One of the responsible genes, EST4 (EST, ever shorter telomeres), is actually an allele of CDC13, which has been previously implicated in telomere function. The authors show that the CDC13 protein binds to single-stranded telomere DNA and has two functions: one is to protect the end of the chromosome from degradation and the other is to mediate access of telomerase to the chromosome terminus.

Budding caveolae

The role of caveolae (membrane invaginations on the plasma membrane of mammalian cells) in membrane traffic and the mechanism by which caveolae promote the internalization of a variety of extracellular ligands have been controversial. Schnitzer et al. (p. 239) now show that caveolae are released from isolated plasma membranes in vitro and from the plasma membranes of permeabilized cells in the presence of guanosine triphosphate and cytosol.

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1. Science 257: 1906 (1992) 2. Cancer Research 55: 5642 (1995) 3. PNAS 92: 2750 (1995)

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Summer 1996

NEW ADVANCES EASE IN-SITU PCR*; SLIDE SEALING ALMOST EFFORTLESS



PTC-200 DNA Engine with Interchangeable Twin Towers[™] In Situ Block

Frame-Seal Chambers Offer Alternative for Sealing

One approach to sealing slides against vapor loss is the use of Frame-Seal[™] chambers. First



an adhesive "frame" is attached to a slide with mounted tissue and a release liner is removed. Reaction cocktail is added, a polyester cover slip is adhered, and the slide is then cycled. Afterwards, the 3) Attach coverslip whole assembly is pulled from **Twin Towers System Works** Well for Hybridizations Too

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This technique allows the use of ordinary slides and cover glasses, large areas of the slide can be utilized, cover glasses are easily removed without leaving residue, and the stuff works well with archival slides. Best of all, it's easy.

¹Bagasra, Omar et al., NEJM (326) 1385-1391; 1992 ²Embretson, Janet et al., Nature (362) 359-362; 1993 ³Hindkjaer, J et al., Chromosome Res (3) 41-44; 1995 FOR A DETAILED PROTOCOL

Bagasra, Omar et al., "In-Situ PCR and Hybridization to Detect Low-Abundance Nucleic Acid Targets," Current Protocols in Molecular Biology, Sec. 14.8.1-14.8.23; 1995

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NEW TWIN TOWERS BLOCK FITS EXISTING DNA ENGINES

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has revolutionized understanding of HIV-1 pathogenesis,^{1,2} as well as other disease and genetic processes.³ Now a new system is available that addresses many of the technical difficulties that researchers have experienced. Its slide and sealing components even work well with most other makes of thermal cycler.

The system is centered around the new Twin Towers[™] in situ block, which fits any new or existing DNA Engine[™] or Tetrad[™] thermal cycler chassis. This interchangeable block assembly features two independent towers, each of which can hold up to sixteen standard glass slides. Each tower can ramp at speeds up to 1.2°/sec, each has a thermal homogeneity within ±0.4°C slot-to-slot, and each features Peltier-Joule heat pumps with a range of 4°-105°C.

Better still are the multiplicity of sealing technologies that work well with this instrument. Of course one can use the tried-and-true method of a coverslip adhered with nail polish or rubber cement, but now two superior alternatives are available. The first, Frame-Seal chambers, employ an adhesive "frame" and polyester coverslip to create vapor-tight chambers on a slide. Even more novel is Self-Seal reagent, which is added to the reaction cocktail to seal slides and cover glasses automatically during the initial denaturation step. Both work well and outperform any other existing product.

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