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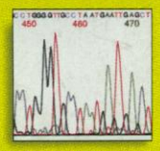

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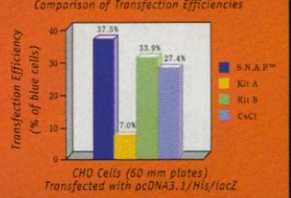

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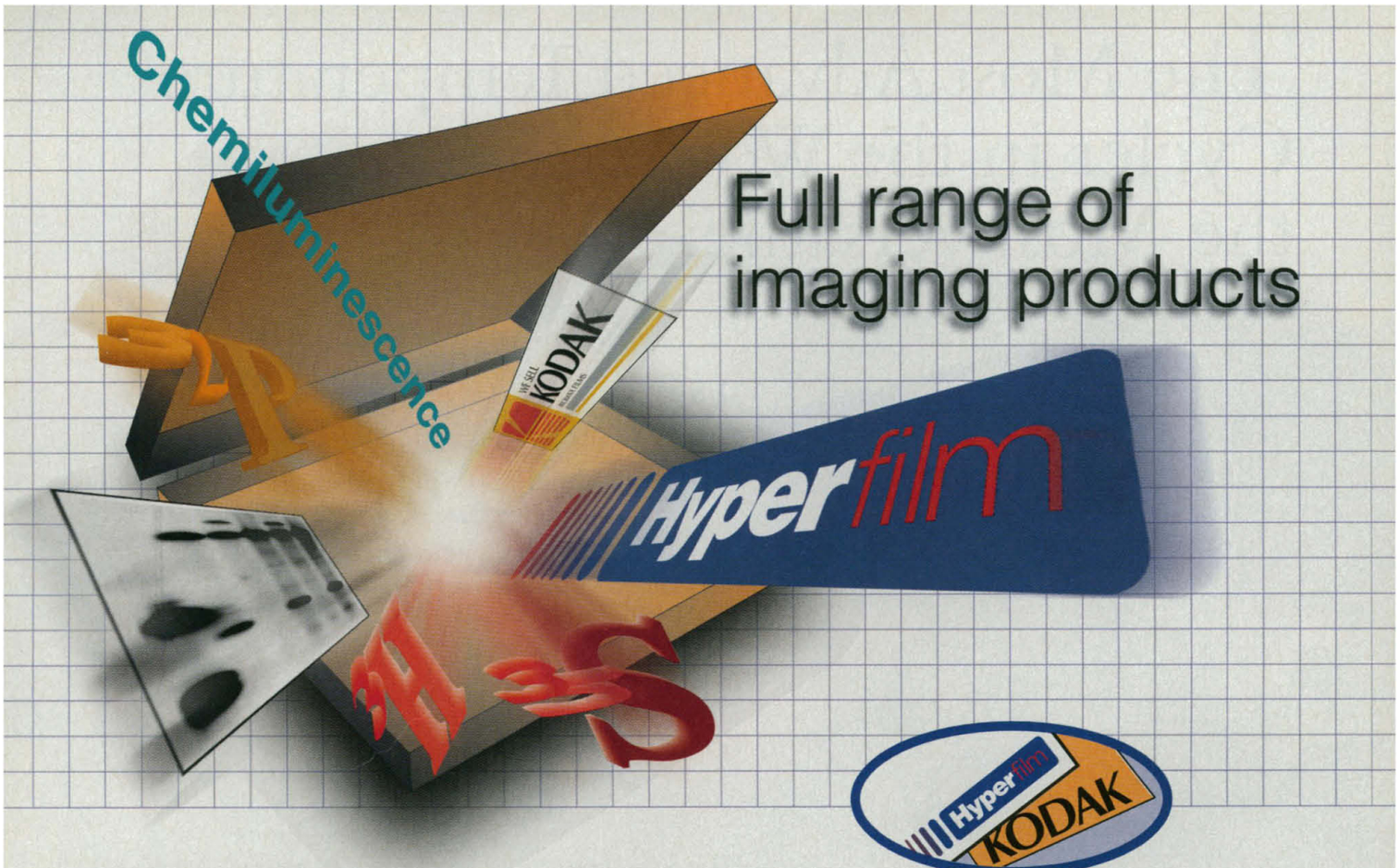

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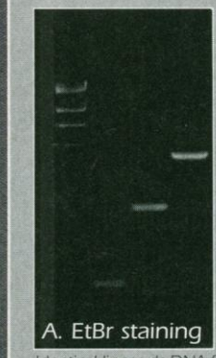
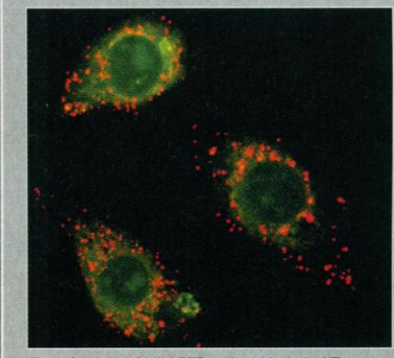


Identical linear ds DNA fragments, either unlabeled (A), or labeled with the *Label* IT™ Rhodamine* Labeling Kit (B), were analyzed by gel electrophoresis and visualized under UV illumination. Gel A was stained with EtBr; the labeled fragments on Gel B were visualized WITHOUT EtBr staining. This demonstrates the high labeling efficiency and non-destructiveness of the *Label* IT method.



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COVER

The high Andes near La Paz, Bolivia. The great Andean plateau has been forming for millions of years as the South American continent shortens as a result of the subduction of the oceanic Nazca plate beneath it. The global positioning system, which can measure the relative positions of sites thousands of kilometers apart to precisions of less than a centimeter, allows the shortening to be measured over only a few years. See page 358. [Image: S. Stein]

REPORTS

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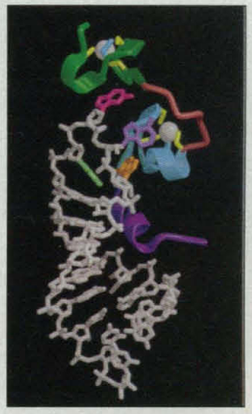
Pyramids and domes



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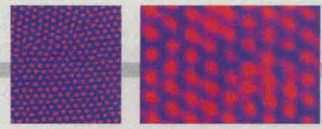
Recognition via backbone and knuckles



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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Overcoming error

Quantum computing has been proposed as a more powerful way to do computing than present approaches; the evolution over time of coherent quantum states that have become "entangled" corresponds to basic computing operations. One difficulty, however, is that an actual computational device would interact with the environment, which would lead to decoherence of the quantum states. Knill *et al.* (p. 342) show how the introduction of decoherence and operational errors can be overcome in quantum computing, provided the errors are sufficiently small.

■

Collapsing spin gap

Superconducting ladder compounds ($Sr_2Ca_{12}Cu_{24}O_{41}$, for example) have, instead of a CuO_2 layer structure, isolated CuO_2 chains and Cu_2O_3 "ladders," which are pairs of CuO_2 chains linked by oxygen atoms. Mayaffre *et al.* (p. 345) present transport and copper-63 nuclear magnetic resonance measurements, which show that at sufficiently high pressures (29 kilobar), the normal state no longer exhibits a spin gap (that is, energy is no longer needed to promote the singlet spin state to the triplet). This collapse corresponds to the onset of the high-temperature superconducting state.

■

Speeding up

Charge density distributions in molecules determine properties such as the reactivity of the molecule, which may in turn become important for molecular design. However, experimental determination of charge density distributions requires high-accuracy x-ray diffraction data, and even for a small molecule such as a single amino acid, it may take 6 weeks to collect adequate data with conventional methods. Koritsánszky *et al.* (p. 356) show that by using area detectors and synchrotron radiation, equivalent data can be collected in 1 day. Future determinations of charge densities with area detectors may become limited less by the number of reflections (that is, the molecule size), the main limitation for traditional methods, but rather by crystal size and quality.

Receptors and HIV resistance

Variations in the genes encoding coreceptors for human immunodeficiency virus (HIV), CCR5 and CCR2, have been associated with a delay in the rate of progression to AIDS. Winkler *et al.* (p. 389; see the news story by Balter, p. 327) have identified a polymorphism in a conserved part of the 3′ untranslated region of the ligand for the CXCR4 coreceptor, SDF-1, that (when it occurs homozygously) delays the onset of AIDS. SDF-1 down-regulates CXCR4 and may be involved in changes in tropism of HIV that occur during progression. Although this variant is found in only a small number of people, the protection was twice as strong as that offered by the previously identified alleles of CCR5 or CCR2. Analysis of the basis of natural resistance to the development of AIDS can identify genes that will be important targets for therapeutics.

■

Getting in shape

The growth of germanium on the (001) surface of silicon is know to lead to the formation of nanocrystals. Medeiros-Ribeiro *et al.* (p. 353) grew such structures by physical vapor deposition at 600°C and found that only two structures formed, smaller square-based pyramids 6 nanometers in height and larger multifaceted domes that were approximately 15 nanometers high. They present a thermodynamic model to account for the abrupt change in morphology as more germanium is deposited.

■

Raising South America

Subduction of an oceanic plate beneath South America at a rate of about 75 millimeters per year is responsible for the worlds highest volcanic arcs, the Andes, and several major faults to the east side within South America. Norabuena *et al.* (p. 358; see the cover) used several space geodetic measurements to examine how deformation resulting from the subduction is distributed across the continent. The data imply that about half of the convergence rate is accumulating on the plate boundary. About 10 to 15 millimeters per year is accumulating along the thrust faults to the east; the rest is likely occurring aseismically.

■

Lack of life?

The possibility that martian meteorite ALH84001 contains evidence of biologic activity on Mars remains controversial. Two reports focus on studies of carbonate minerals and organic carbon components from small samples of ALH84001 to determine if the amount of terrestrial contamination can account for the carbonaceous material. Jull *et al.* (p. 366) measured the amount of carbon-14 and carbon-13 extracted from step-heating experiments. They found a large component of high carbon-14 material combusted at low temperatures between 200° to 400°C, which probably represents terrestrial contamination, and a smaller component of low carbon-14 material combusted at 400° to 600°C, which probably represents extraterrestrial material. Bada *et al.* (p. 362) used liquid chromatography to measure the composition and chirality of amino acids in ALH84001 and found that most of the measured amino acids probably represent terrestrial contamination, although a small portion of the amino acids could be endogenous. They propose that the terrestrial contamination was produced by water that permeated through the meteorite during its ~13,000-year residence on Antarctica. The mechanism for concentrating and retaining the amino acids by water percolation remains unknown, and the origin of a portion of the carbonaceous material in ALH84001 remains undetermined.

■

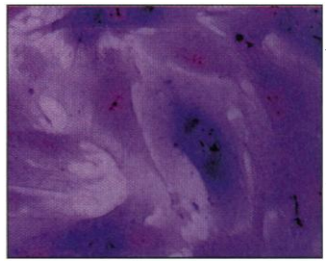
Memory and inhibition

Many biological systems are both positively and negatively regulated; for example, tumor formation can occur through expression of active oncogenes but also through the loss of tumor suppressor genes. In a review, Abel *et al.* (p. 338) discuss how memory formation requires not only the activation of positive regulators but also the removal of inhibitors, and how normal long-term memory formation involves a balance of these two effects.

■

Forever young

Shortening of telomeres, the DNA sequences that cap chromosome ends, has been postulated to be a molecular clock that limits cell proliferation. Bodnar *et al.* (p. 349; see the commentary by de Lange, p. 334) have tested this hypothesis by introducing the catalytic subunit of telomerase,



(Continued on page 299)

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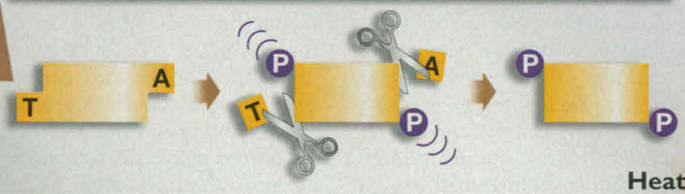

Heat Inactivation (10 minutes)

Homogeneous Product, Blunt and Phosphorylated

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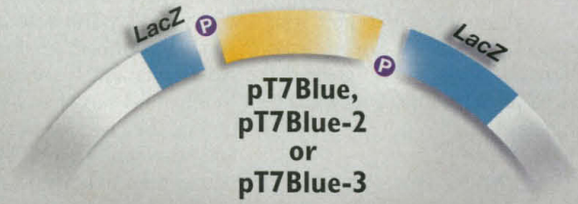

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References

1. Brownstein, J.M., *et al.* (1996) *BioTechniques* **20**, 1004–1010.
2. Magnuson, V.L., *et al.* (1996) *BioTechniques* **21**, 700–709.
3. Novy, R.E., Yaeger, K.W., and Kolb, K.M. (1996) *In**Nova**tions* **6**, 7–11.

*The Polymerase Chain Reaction (PCR) process is covered by patents owned by Hoffmann-La Roche.

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(Continued from page 297)

the enzyme that synthesizes telomeres, into cultured human cells that normally do not express the enzyme. The resultant cells had a significantly longer life-span, with no evidence of karyotypic abnormalities. The ability to extend the life-span of normal human cells is likely to have important applications in medicine as well as in basic biological research.

■

Mitochondrial import

The mitochondrion, the power house of the cell, is characterized by a double membrane. The inner membrane contains metabolite carrier proteins, which are multispanning membrane proteins. These proteins, however, lack identified signal peptides that mediate their targeting to and within the mitochondrion, and their import mechanism has remained obscure. Koehler *et al.* (p. 369) have found a pair of proteins that act to chaperone the insoluble carrier proteins during their transport across the intermembrane space prior to insertion into the inner mitochondrial membrane.

■

Homing in on drug delivery

A major limitation of cancer chemotherapeutic drugs is their toxicity to normal tissues; hence, there is much interest in new strategies for targeted delivery of these drugs to tumor cells. Arap *et al.* (p. 377; see the news story by Barinaga, p. 323) studied one such strategy in a mouse model, conjugation of the drug doxorubicin to peptides that, upon intravenous injection, home selectively to tumor blood vessels. In comparison to free doxorubicin, the conjugates showed much greater efficacy and lower toxicity in mice bearing human tumor xenografts.

Hidden duplicate genes

Helicobacter pylori is thought to cause many ulcers and is an early risk factor for stomach cancer. These microbes bind to the lining of the stomach through the mammalian carbohydrate complex known as Lewis b (Le^b) blood group antigen. Ilver *et al.* (p. 373) have now characterized, cloned, and examined the genetics of the protein from pathogenic *H. pylori* strains that bind to Le^b, by using receptor activity—directed affinity tagging. The adhesin that they identified is part of a family of duplicated genes and was not identified in the published genomic sequence of *H. pylori*, which demonstrates that functional approaches are necessary to refine the information from genomic sequencing. The identification of this adhesin opens up the possibility of developing vaccines to prevent colonization by this microbe.

■

The knees have it

The circadian clock of humans is approximately a 24-hour period, but is kept synchronized with the solar days by daily entrainment to our natural light dark cycle. It has always been supposed that this entrainment occurs through light stimulation of the retina, but Campbell *et al.* (p. 396; see the commentary by Oren, p. 333) now demonstrate the surprising finding that application of light to the back of the knees only can entrain endogenous circadian rhythms in temperature and melatonin.

■

Stops on a chemokine

Lymphocytes in the bloodstream go through a multistep adhesion process to slow down, move through the blood vessel wall, and enter the tissue. It has been hypothesized that chemokines produced at the target site may be the signal that activates the strong adhesion system, the integrins, on the lymphocytes and causes the cells to stop rolling at the appropriate spot. Campbell *et al.* (p. 381) now show that particular chemokines—MIP-3β, SDF-1α, and 6-C-kine—can cause flowing lymphocytes to decelerate and adhere to an integrin target protein within about 500 milliseconds. Another chemokine, MIP-3α, seemed selective for T cells that had characteristics of "memory" cells. Thus, specific chemokines that are produced at particular sites may actively recruit the appropriate T cells.

■

Membrane fusion and LTP

The strengthening of specific synapses that occurs in long-term potentiation (LTP) has been thought to be the cellular correlate of memory. Lledo *et al.* (p. 399) suggest a new role for the postsynaptic cell in LTP. They found that loading the postsynaptic cell with substances that block membrane fusion also blocked LTP, whereas agents that promote membrane fusion enhanced synaptic transmission.

■

Packaging HIV

An early step in the packaging of the human immunodeficiency virus genome is the interaction of the stem-loop structures of the genomic RNA with the nucleocapsid protein. De Guzman *et al.* (p. 384) have used nuclear magnetic resonance spectroscopy to resolve the structure of the protein-nucleic acid complex. The two zinc knuckles of the nucleocapsid protein, which are conserved in most retroviruses, each surround guanine bases in the loop portion of the stem-loop with the carbonyl and amide backbone functionalities, as opposed to side chains. This arrangement provides specific recognition of the nucleotide by means of hydrogen bonds.

Trying to stay ahead of influenza

New strains of influenza can develop through genetic reassortment between human viruses and animal viruses, and following new strains as they develop is critical for influenza surveillance. Subbarao *et al.* (p. 393; see the news story by Vogel, p. 324) present a molecular analysis of a strain of influenza that is believed to be responsible for the death of a child in Hong Kong. This avian influenza A virus had hemagglutinin that contained cleavage sites characteristic of highly pathogenic strains. Whether this case is an early stage in the development of a new epidemic remains to be seen.

■

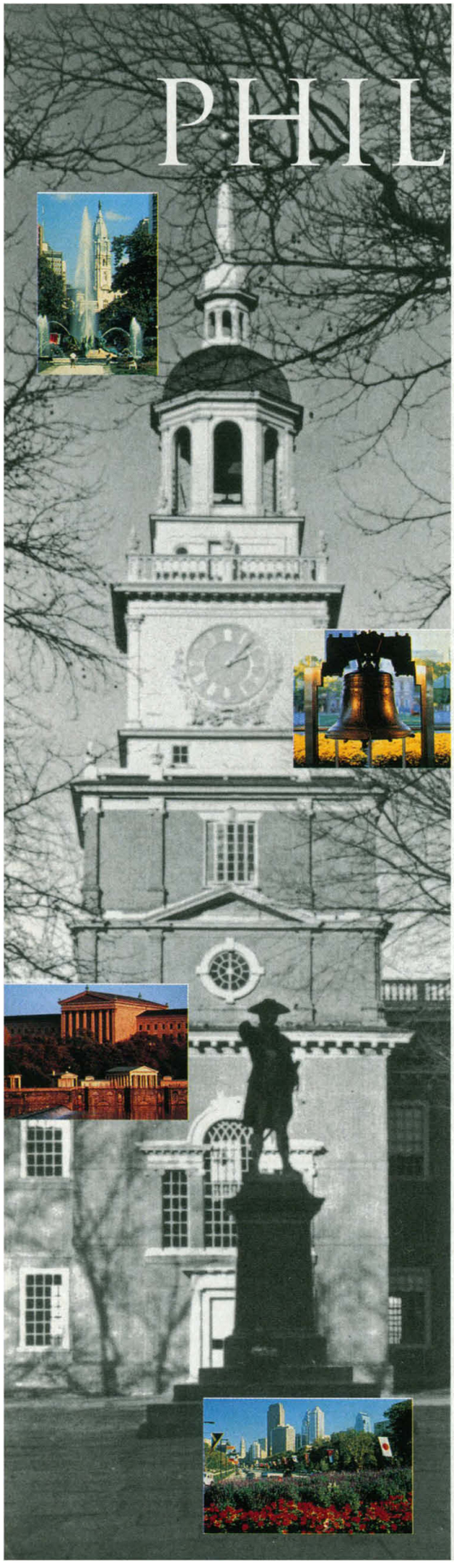
Knows its nitrates

Plant root structures form under the direction of a general developmental program, but their final shape is a result of responding to information from their environment as the root tips search out and grow into pockets of useful nutrients. Zhang and Forde (p. 407) have cloned a putative transcription factor, ANR1, from *Arabidopsis* that is induced in response to locally increased concentrations of nitrate. ANR1 mediates the growth response of lateral roots to the nitrate signal from the local environment.

■

Epilepsy and potassium

Benign familial neonatal convulsions is a congenital neonatal human epilepsy linked to chromosomes 8 and 20. Biervert *et al.* (p. 403) have identified a potassium channel defect on chromosome 20 as the likely cause of this disease. The function of the mutant channel is abolished due to a large carboxyl-terminal truncation that would interfere with potassium-dependent repolarization of stimulated neurons.



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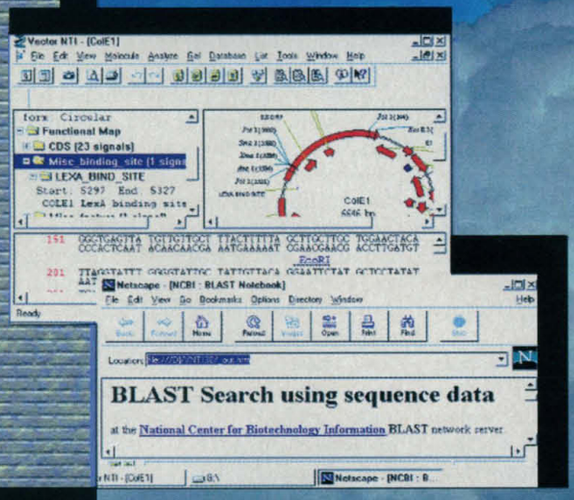

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