

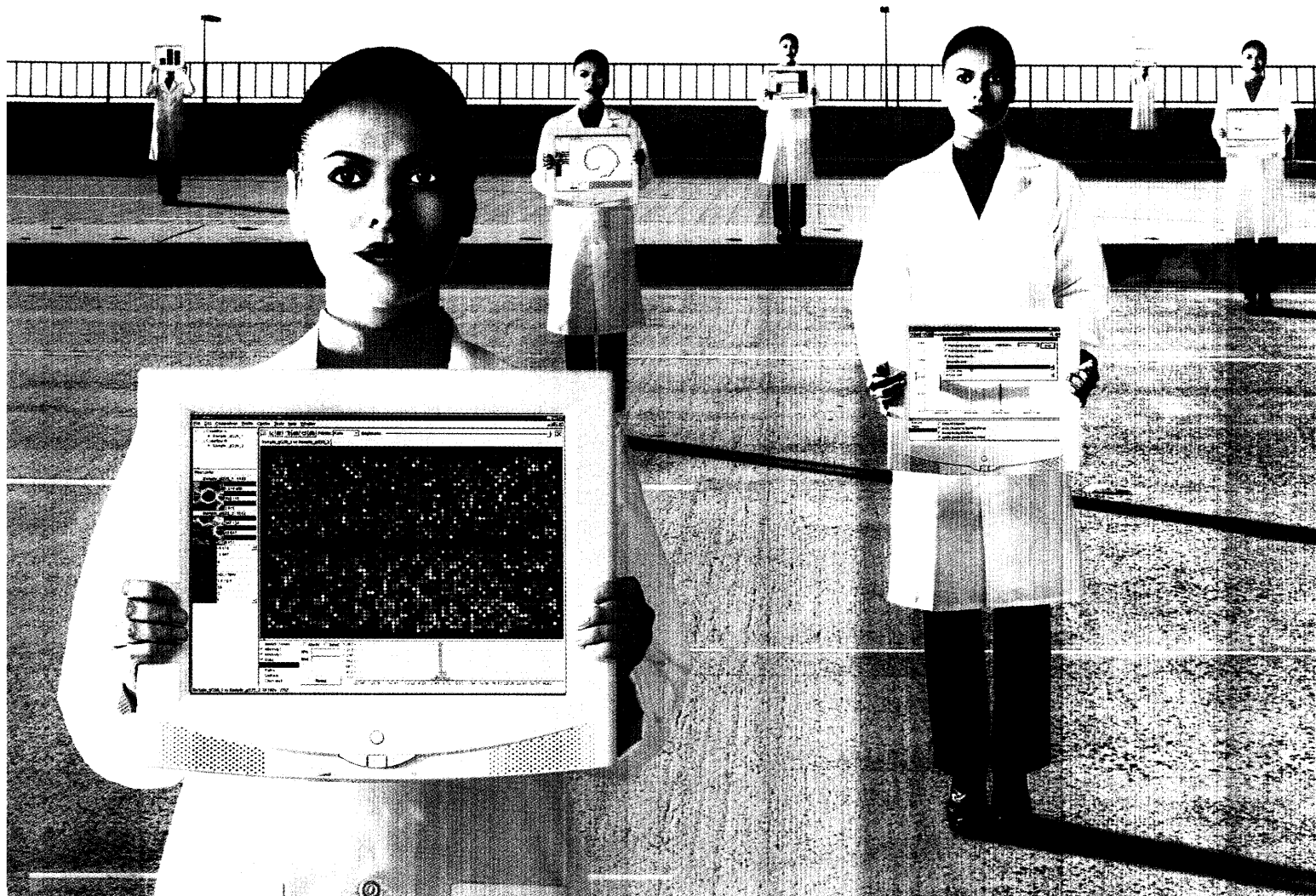
21 September 2001

Science

Vol. 293 No. 5538
Pages 2157-2336 \$9



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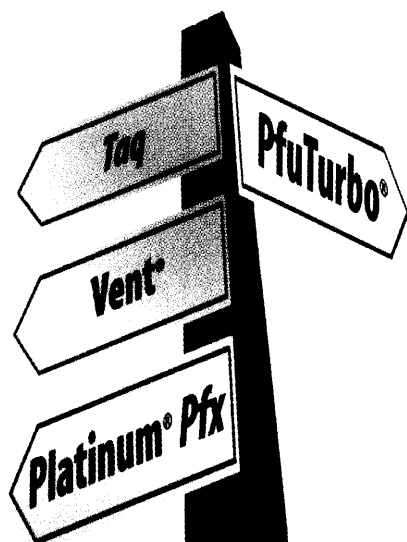
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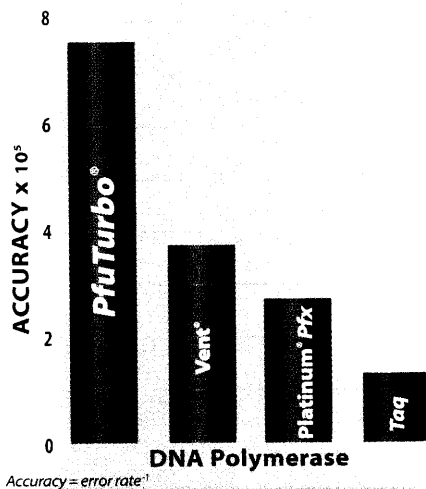
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To Our Colleagues

In the aftermath of the dreadful events of 11 September, *Science* and our publisher, AAAS, extend heartfelt condolences to those among its readers, members, and business partners who have suffered personal losses. We hope that the international community of scientists we serve can help reshape the world into one in which such things will never happen again.

SCIENCE'S COMPASS

2203 LETTERS

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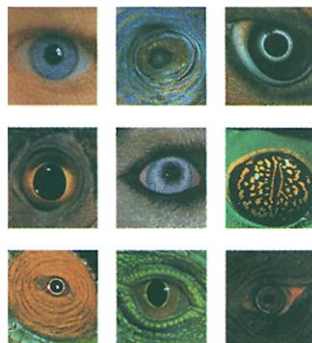
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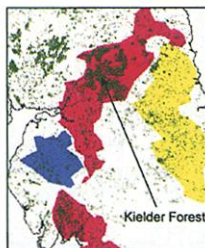
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Genetic history
in shifting
habitats



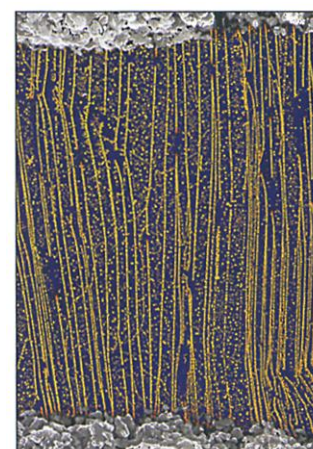
COVER 2239

Rodhocetus, a whale that lived 47 million years ago, visualized on the basis of new Eocene fossils from Pakistan. The ankle bones indicate a close relationship of early whales to hooved land mammals such as hippopotami and pigs. Forefeet retain hooves on the central digits, but hind feet with slender webbed toes indicate that *Rodhocetus* was predominantly aquatic. [Painting by John Klausmeyer, University of Michigan Exhibit Museum]

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by fixing breaks

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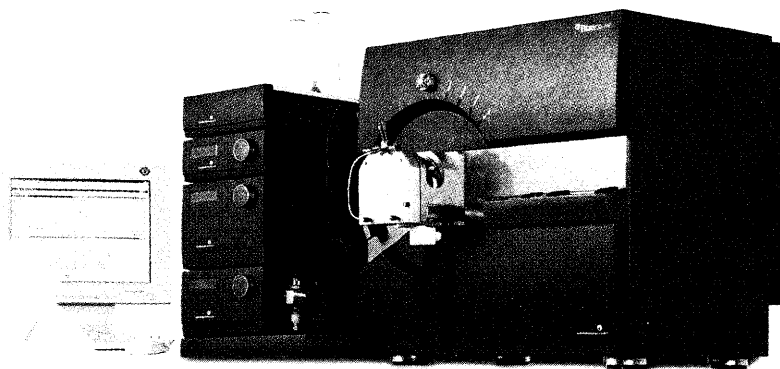
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Patterning of the Neocortex by the Secreted Signaling Molecule FGF8 T. Fukuchi-Shimogori and E. A. Grove

Patterns of cortical structures in the developing mammalian brain form in response to signals of FGF8 from the anterior cortical primordium.

Regulation of Cutaneous Malignancy by $\gamma\delta$ T Cells M. Girardi *et al.*

PERSPECTIVE: Stress, NK Receptors and Immune Surveillance of Cancer D. M. Pardoll

Studies in genetically deficient mice suggest a significant role for $\gamma\delta$ T cells in monitoring and preventing cutaneous tumorigenesis, in part through the recognition of a novel ligand, Rae-1.

TECHNICAL COMMENTS

Roots of Clinical Resistance to STI-571 Cancer Therapy

Studying 11 patients with chronic myeloid leukemia who had relapsed after initially successful treatment with the kinase inhibitor STI-571, Gorre *et al.* (Reports, 3 August 2001) tied drug resistance to "progressive BCR-ABL gene amplification" in three patients and to a point mutation in the BCR-ABL kinase domain in six patients. In separate comments, Barthe *et al.* and Hochhaus *et al.* report the results of two studies that were unable to find the point mutation cited by Gorre *et al.* in any of a total of 44 relapsed patients. Gambacorti-Passerini *et al.*, in a third comment, argue that the Gorre *et al.* focus on "cellular" mechanisms gave insufficient weight to "organismic" explanations of STI-571 resistance, such as the binding and inactivation of the drug by $\alpha 1$ acid glycoprotein. Gorre *et al.*, in their response, raise questions about the alternative model suggested by Gambacorti-Passerini *et al.*, and suggest that the alternative results reported by Barthe *et al.* and Hochhaus *et al.* may trace to "differences in the patient population studied or the methods used to detect the mutation."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/293/5538/2163a

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Perspective: Wnts, Signaling and Sulfates S. S. Blair

A candidate sulfatase for regulating sulfation of proteoglycans that influence Wnt signaling.

science's next wave

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UK: Shotgun Thesis Composition P. H. Dee

Next Wave's "Yours Transferably" columnist describes his unorthodox approach to the dreaded thesis write-up: Touch everything—every result, every paper—only once.

US: Small Mistakes with Big Consequences D. Jensen

In "Tooling Up," some common snafus that might impede your search for an industry job.

US: Images of Athena L. Pray

Athena, the first mentor and counselor, serves as a model for two faculty members who recently became leaders of offices of postdoctoral education.

Canada: Photon Opportunities L. Lilge

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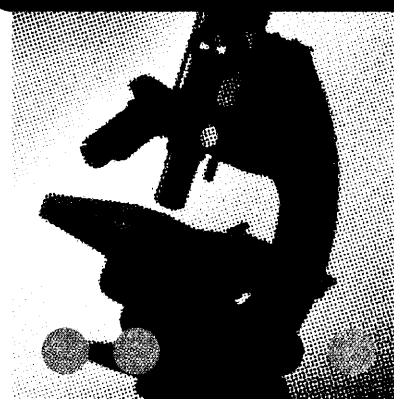
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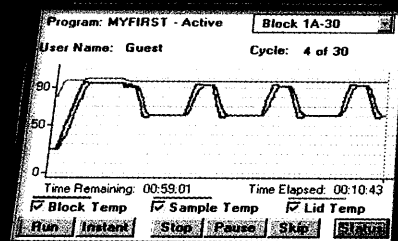
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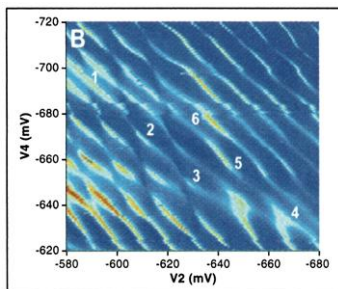
edited by Phil Szuromi

Mesowires for Hydrogen Detection

Submicrometer wires of palladium embedded in a polymer matrix are shown to decrease their resistance at room temperature in the presence of hydrogen, unlike bulk palladium, which becomes more resistive as the hydride forms. Favier *et al.* (p. 2224) find that hydrogen adsorption lowers the resistance by expanding microcrystallites in the wires, which then heals tiny "break junctions" in the wire. These effects are seen even when gases that normally poison hydrogen sensing were present, including O₂, CO, and CH₄. The rapid response and low power requirements suggest their use as sensors and switches.

Coupled Kondo Systems

Quantum dots provide an ideal system for investigating the many-body Kondo effect, in which the interaction of a magnetic impurity with a surrounding sea of electrons enhances conduction through the dot that would otherwise be suppressed by Coulomb blockade. However, when quantum dots are coupled, the Kondo effect must compete with spin-spin interactions. Jeong *et al.* (p. 2221) present an experimental study of a coupled pair of quantum dots which shows that the transport through the system can be explained through a simple model involving the spin configuration on each dot. They also observed a splitting of the Kondo resonance peak at zero bias which suggests that many-body bonding-antibonding Kondo states form in this artificial molecule.



A Primitive Messenger

The Tagish Lake meteorite is an unusual carbonaceous chondrite that was recovered from a frozen lake in Canada soon after its fall and before significant terrestrial alteration could occur. Two reports now provide important information about the origin of the meteorite and its well-preserved carbonaceous material. Hiroi *et al.* (p. 2234) compared reflectance spectra of the Tagish Lake meteorite with those of different types of asteroids. The D-type asteroids provided the best spectral fit; these asteroids are located near the Kirkwood gaps in the main asteroid belt. Some of these asteroids may be driven into the gaps as a consequence of gravitational interactions with Jupiter. As a result, their orbits would become chaotic, leading to collisions that could transfer material to the inner solar system and eventually to Earth. Pizzarello *et al.* (p. 2236)

2224 All-in-One Dot Characterization

The nanoscopic size and discrete energy levels of quantum dots make them attractive candidates for very high density optical components. However, obtaining information simultaneously on both the spatial location of excitations in a quantum dot and their spectral properties can be challenging. Guest *et al.* (p. 2224; see the Perspective by Koch and Knorr) have overcome this limitation by combining the spatial sensitivity of scanning near-field optical microscopy with the spectral sensitivity of a nonlinear optical pump-probe technique. They can access and excite individual energy levels of the quantum dot and monitor the dynamics of such excitation processes.

analyzed the organic matter in the Tagish Lake meteorite and found it to be dominated by water-soluble carboxyl and dicarboxyl compounds, to be relatively low in amino acids, and to contain insoluble carbon with aromatic character. This composition is distinct from those of other carbonaceous chondrites and implies an origin on a primitive parent body that had accreted solar nebular and interstellar material. Thus, the organic matter may represent the least altered material from the early solar nebula currently accessible to terrestrial scientists. ✕

ula currently accessible to terrestrial scientists. ✕

Whale Ankles

Whales, the largest marine mammals, are thought to have evolved from the land to the sea about 40 to 50 million years ago. Gingerich *et al.* (p. 2239; see the cover and the Perspective by Rose) have found two new species of early whales, *Artiocetus clavis* and *Rodhocetus balochistanensis*, in marine deposits from the Tethys Sea in Pakistan. The ankle bones of these species are similar to those found in artiodactyls, suggesting that the whales belong to Artiodactyla rather than Mesonychia. In addition, the fore and hind limbs of *Rodhocetus* indicate that it was a paddler in the shallow seas of the Tethys.

Climate and Tropical Speciation

Early models suggested that the high species richness of the tropics was the result of a gradual accumulation of species in a stable climate. Evidence that tropical climates have not remained stable, especially during the last 2 million years of the Pleistocene, led to the idea that tropical diversity might have originated recently and that speciation has been driven by environmental instability. Richardson *et al.* (p. 2242; see the Perspective by Bermingham and Dick) show that the model of recent speciation is far more accurate for *Inga*, a species-rich genus of neotropical rain forest trees. Nuclear and plastid DNA sequences and a molecular clock approach suggest recent, rapid diversification in *Inga* that resemble recent radiations of plant species on oceanic islands.

One Out of Many

Can many small patches of suitable habitat really act as a large patches if they are connected by corridors and "stepping stone" patches? Hale *et al.* (p. 2246; see the news story by Kaiser) analyzed DNA microsatellite variation to show the use of stepping stone patches of habitat by the red squirrel in northern Britain and dispersal through a patchy habitat during a 50-year period by a species that evolved in an unfragmented landscape. Samples of red squirrels were obtained before and after patches of a new forest were planted to connect isolated populations from northern England and

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CONTINUED ON PAGE 2167

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southern Scotland. The squirrels used the patches of new forest as stepping stones for dispersal from the southeast of Scotland to the northwest of England.

Burning Evenly

From sloths to squirrels, from weed to hibernating polar bears, the world of bioorganisms seems to present a wide diversity of metabolic rates. Gillooly *et al.* (p. 2248; see the news story by Brown) have analyzed measurements of metabolism among plants, animals, and microbes to derive a general model that describes the factors determining metabolic rate. Within a range of biologically relevant temperatures, metabolic rates are predominantly determined by temperature and body mass. Even unusual states, such as hibernation, thus need not invoke additional mechanisms for adjustment of metabolic rates.

Phantom Mendelian Inheritance

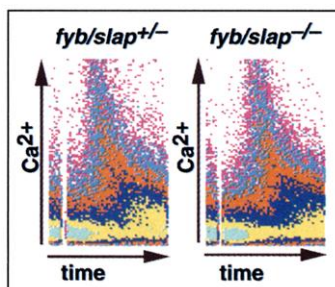
Bardet-Biedl syndrome (BBS) is an inherited disorder characterized by a variable phenotype that can include defects in vision, polydactyly, obesity, and learning disabilities. Historically, BBS has been viewed as a classical Mendelian recessive trait in which mutations at a single genetic locus suffice to cause disease. Katsanis *et al.* (p. 2256; see the Perspective by Burghes *et al.*) now show that in at least 40% of BBS patients, manifestation of the syndrome requires mutation of three alleles at two different genetic loci. This work blurs the well-defined boundary between Mendelian traits and complex traits such as diabetes, which are caused by the interaction of multiple genes, and will likely stimulate a re-examination of theoretical models of inheritance.

Analyzing the Staph

Staphylococcus aureus is a common cause of infection for which there are diminishing therapeutic options. By combining two existing technologies in a new way, Ji *et al.* (p. 2266) developed a library of antisense RNAs that are inducible with tetracycline, which means the respective genes can be turned on and off not just in vitro but also in infected mice. The roles played by specific genes in bacterial growth and behavior can be examined in complex ecologies, such as at the site of infection, and thereby clinically relevant drug or vaccine targets can be identified.

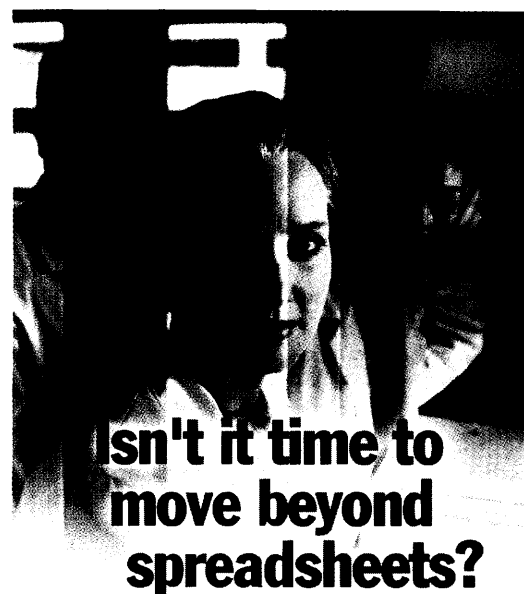
Making Signals Stick

In T cells, adapter proteins couple the T cell receptor (TCR) to multiple cellular signaling pathways. T cells also depend on cellular adhesion through integrins to perform many of their tasks, and Peterson *et al.* (p. 2263) and Griffiths *et al.* (p. 2260) show that the adapter SLAP-130/Fyb is directly involved in this process. Using mice genetically deficient SLAP-130/Fyb, both groups observed that this protein was not required for inducing TCR-mediated calcium flux and protein tyrosine kinase activation, but was needed for clustering and activation of the integrin, LFA-1, which led to cellular adhesion. This process occurred in the presence of normal TCR-induced actin polymerization, which suggests that SLAP-130/Fyb couples TCR-dependent motility of the cytoskeleton with integrin activation.



The Independent Dendrite

The extensive dendritic trees of neurons are by no means passive receivers but are actively involved in processing and transforming synaptic inputs. Wei *et al.* (p. 2272) examined the passive and active transformations that an individual dendritic terminal segment performs on its excitatory inputs. By combining electrophysiological recordings at the cell bodies of hippocampal pyramidal neurons in organotypic cultures and visually guided local application of caged glutamate over dendritic arbors, they showed that distal arbors may generate an all-or-none regenerative response that spreads in a restricted dendritic region. These results now demonstrate directly that dendritic trees can be partitioned into independent functional subunits and that voltage-dependent calcium channels play a crucial role in this compartmentalization.

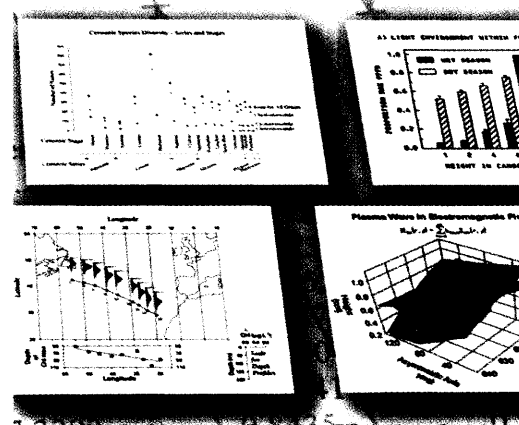


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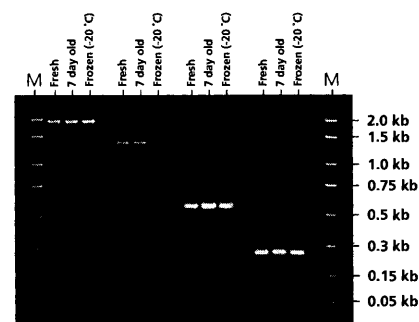
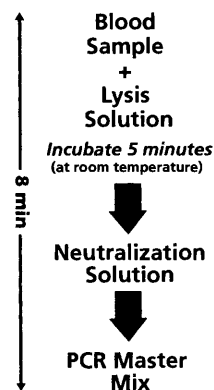
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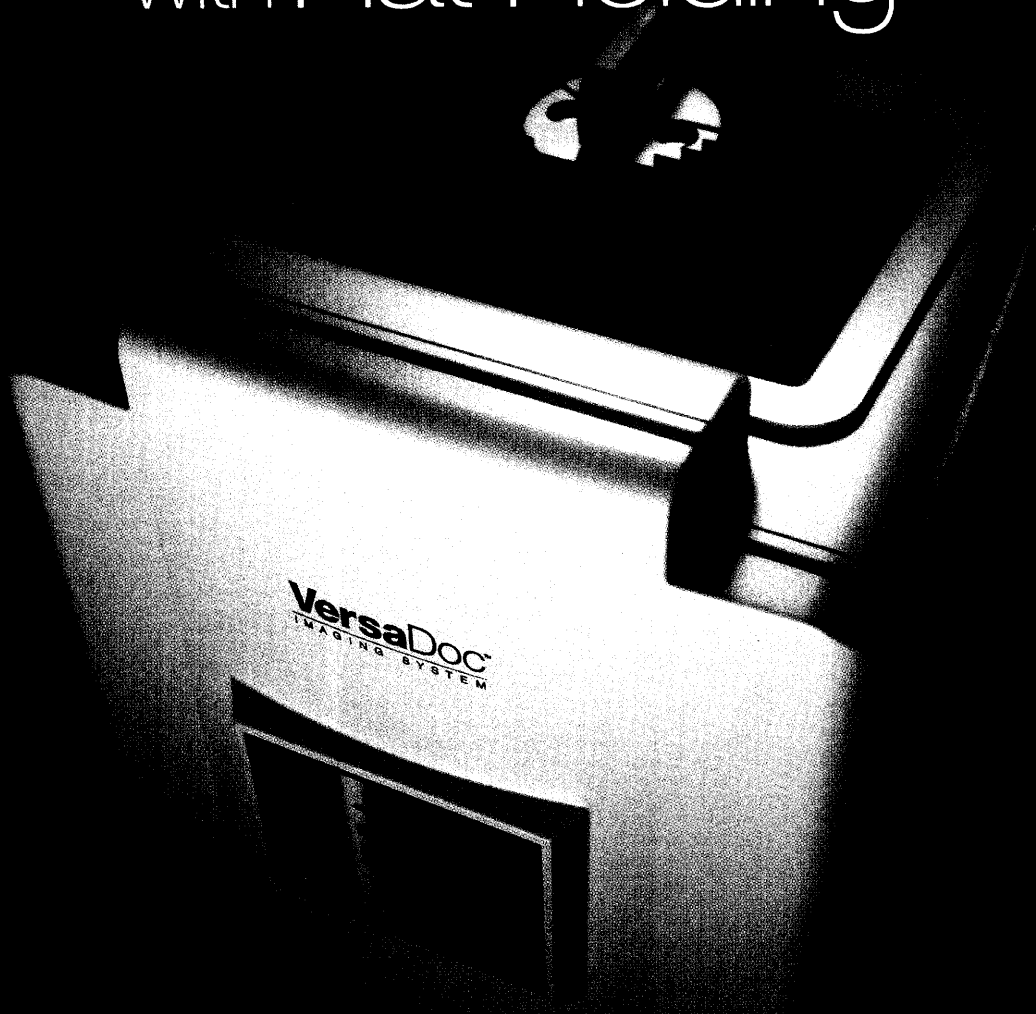
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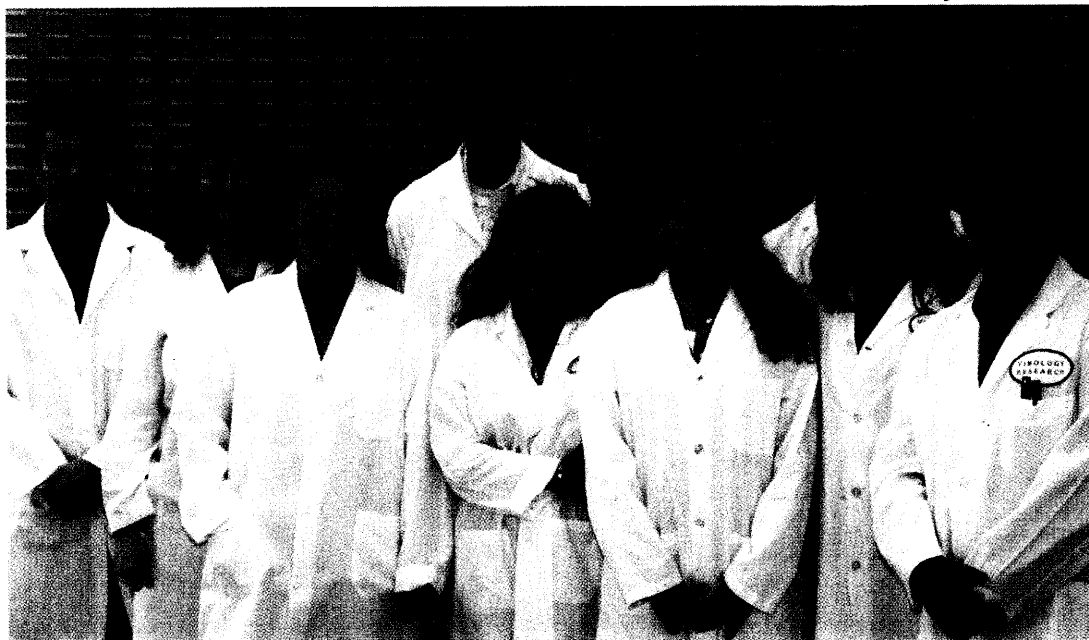
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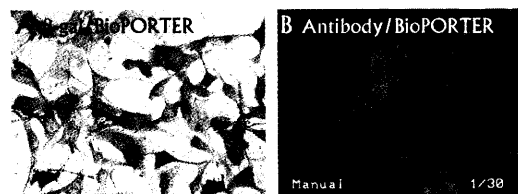


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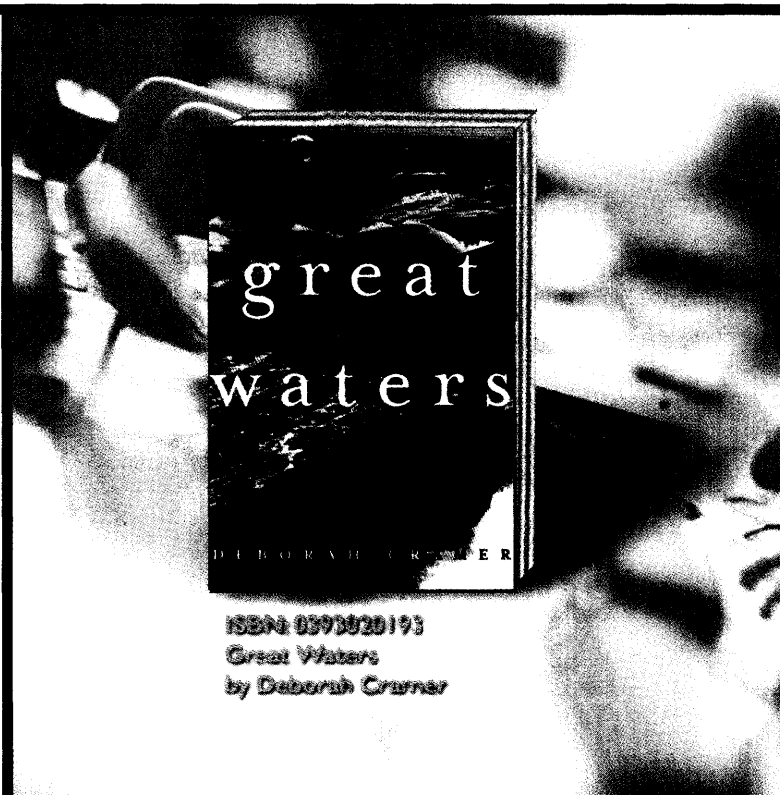
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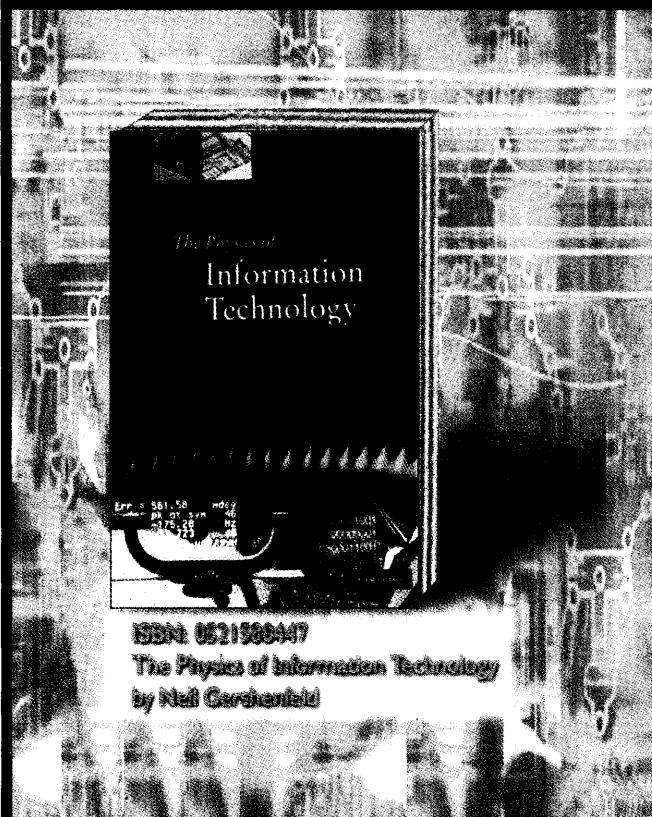
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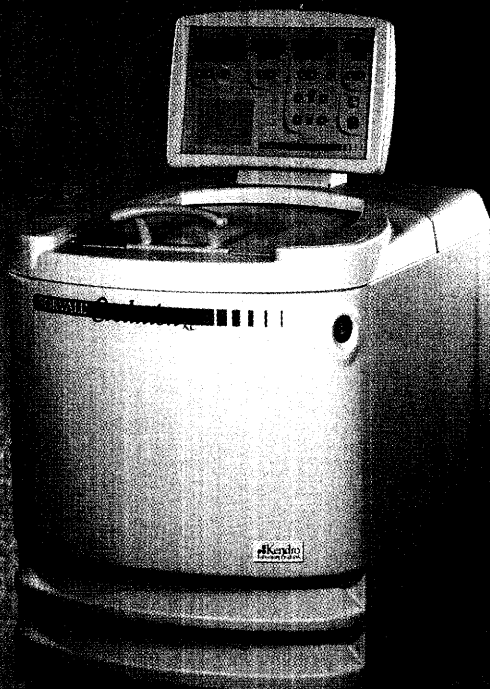


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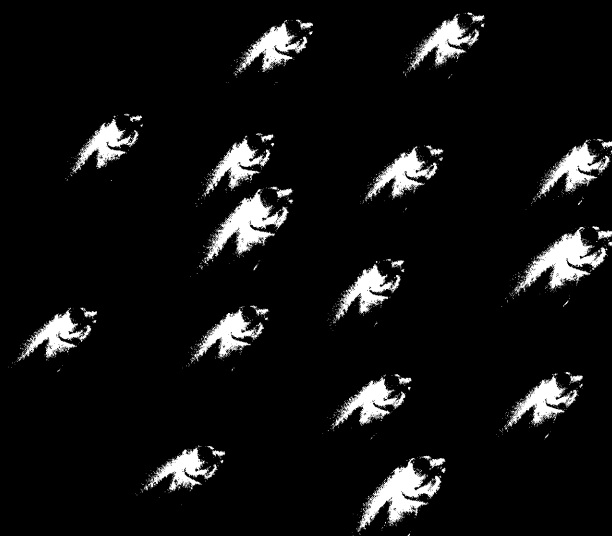
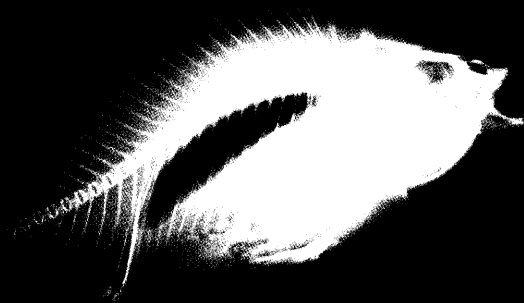
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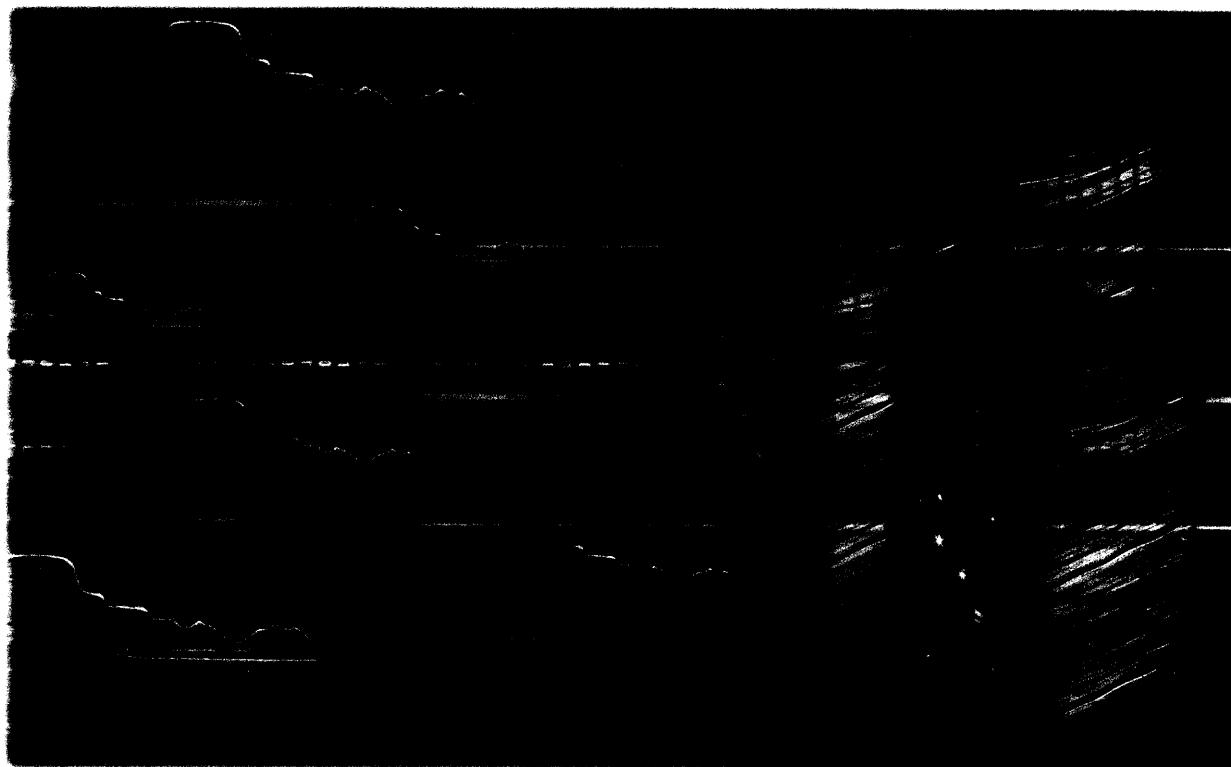
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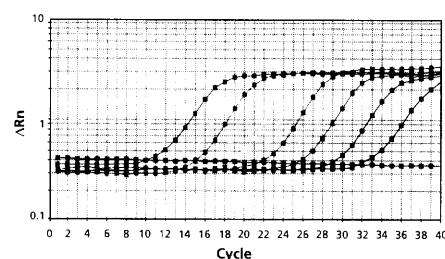
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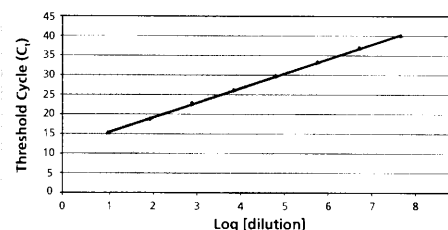
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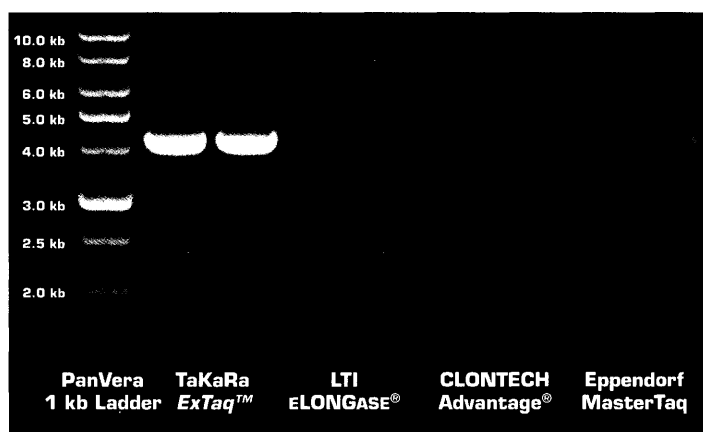
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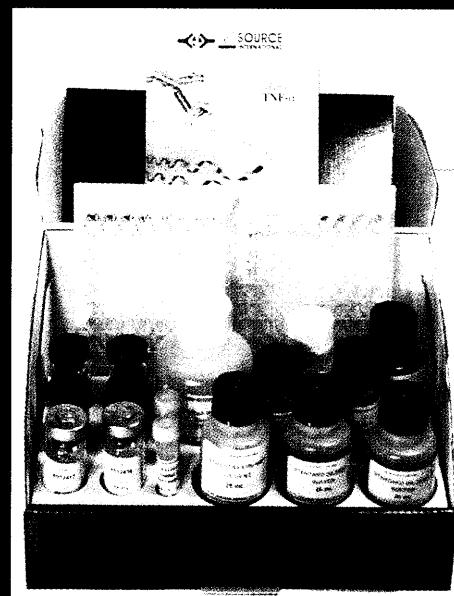
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 Memorial Sloan-Kettering Cancer Center
- 1990 Bachelor of Science, Department of Biochemistry, University of Pennsylvania

AWARDS AND HONORS

- 1990-present Research Fellowship from the Graduate School of Cornell University
- 1990 Magnus Cohn Leader
- 1987-1990 Dean's List
- 1988 John Danforth Leadership Award

PUBLICATIONS

1. John Doe, Gerson Hall, and Emily Research. *Complexes: Molecular Immunology* Vol. 63, No. 11/12, pp. 45-51, 1998
2. John Doe and Emily Research. *Identification of Immune System* *Journal of Immunology* Vol. 160, No. 1, pp. 1-10, 1998

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Russ Tuttle, Anthropology, University of Chicago
Robert Martin, Primatology, Anthropology, Tufts University
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Joe Wickett, Anthropology, American Museum of Natural History

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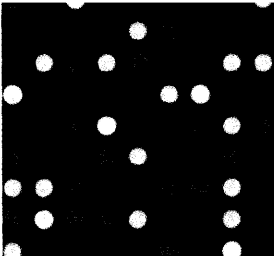
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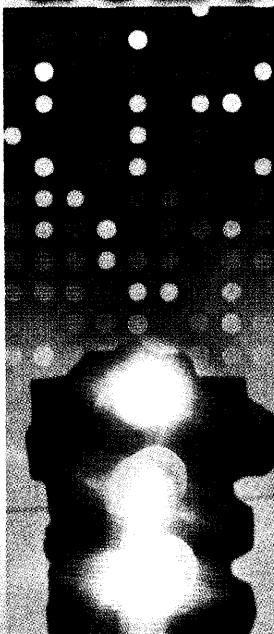
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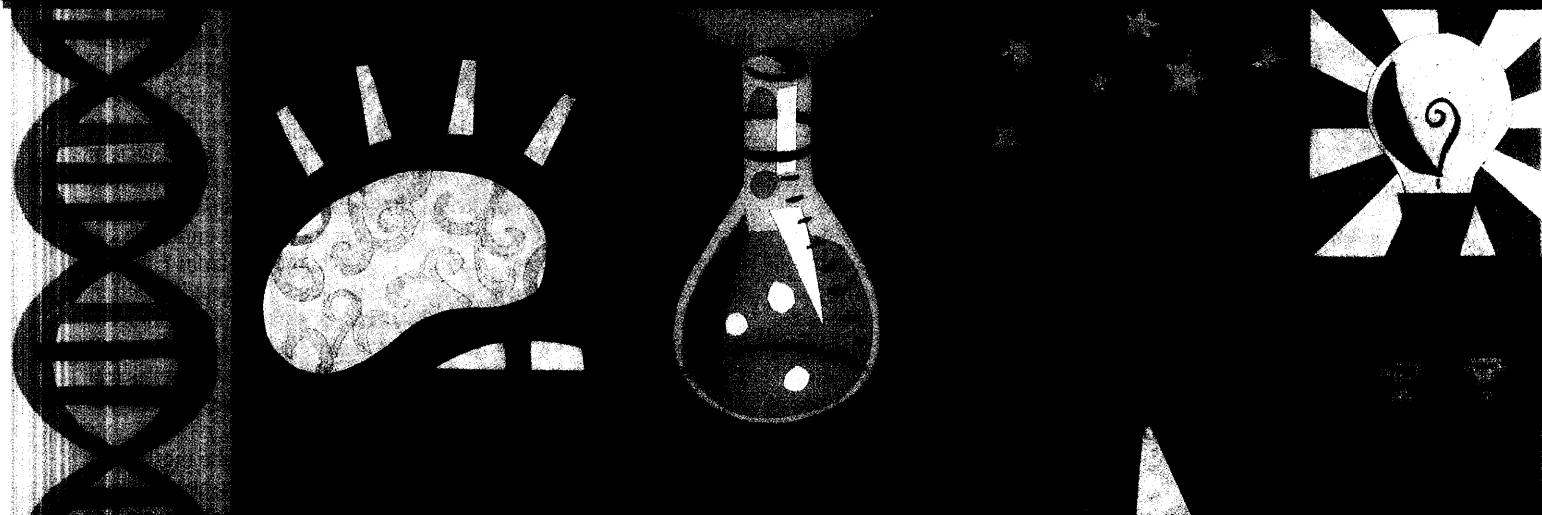
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