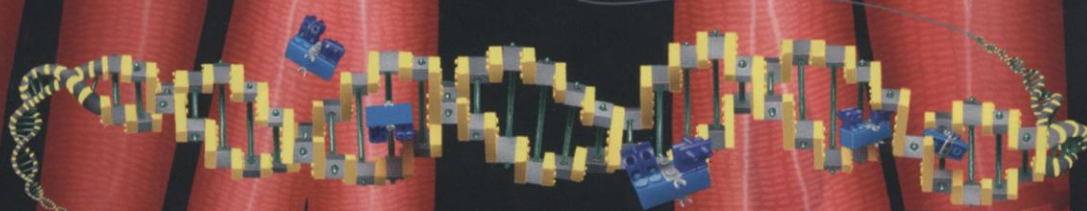


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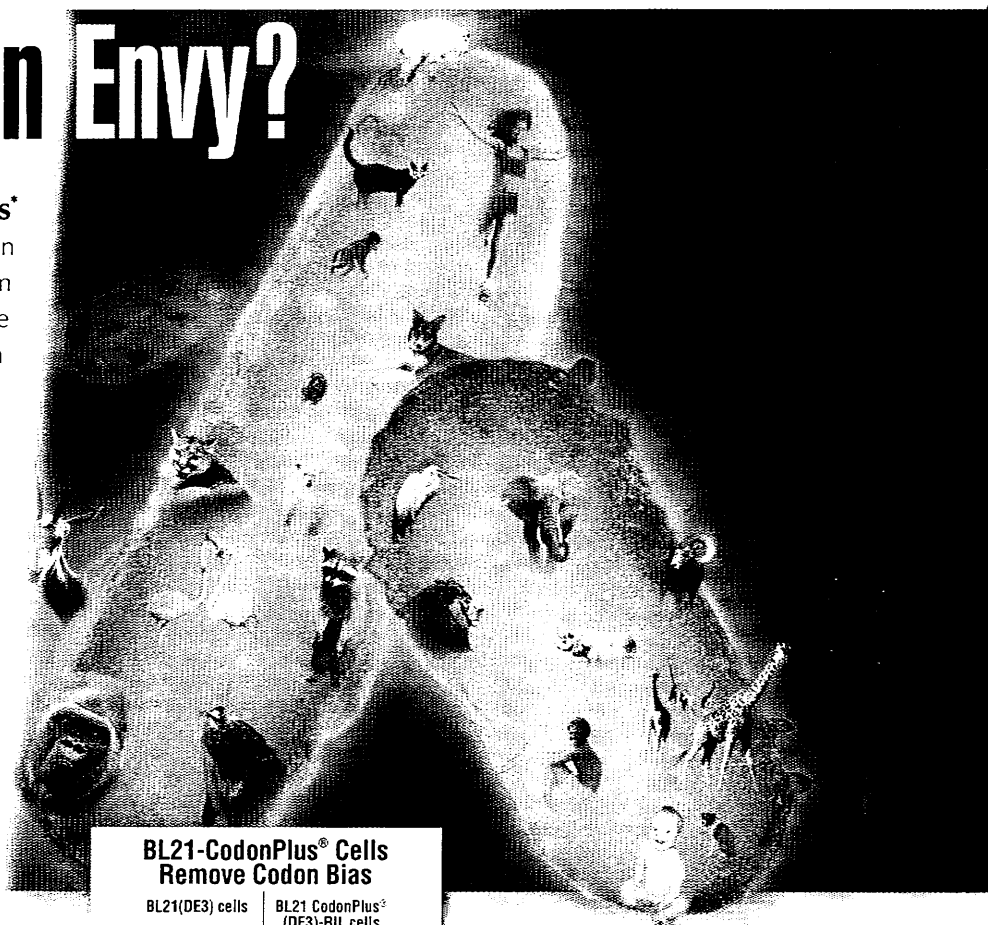
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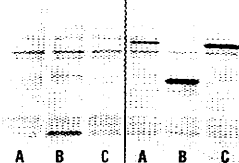
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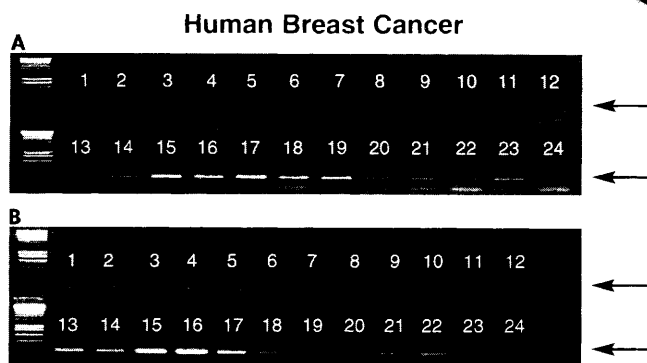
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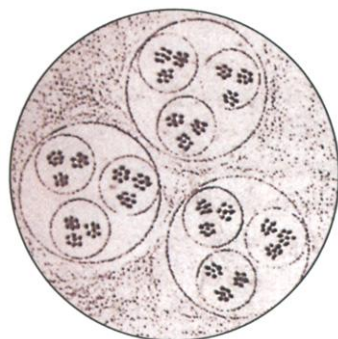
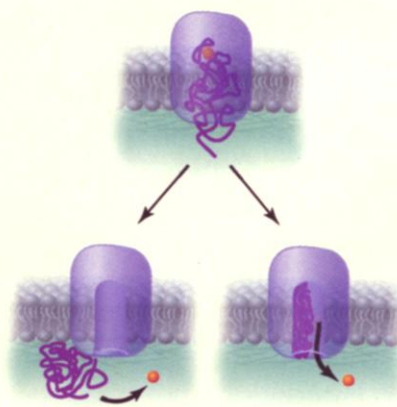
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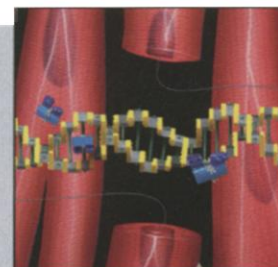
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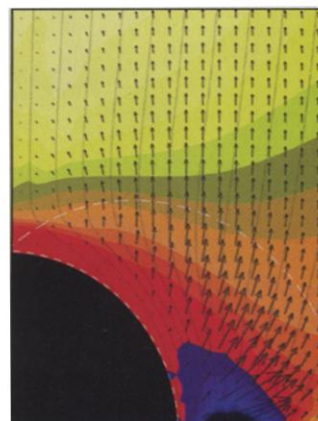
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COVER 1661

Lego bricks, known for their modularity, are an apt metaphor for the architecture and dynamics of biological processes from gene expression to tissue and organism function. The connections between components, how they are managed, and how they evolve are the keys to understanding biological complexity at various levels. The special section in this issue focuses on systems design and operation in biology. [Image: Cameron Slayden]



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Anatomy of projections in visual cortex

New on Science Express

Molecular basis of *Drosophila*'s antibacterial response



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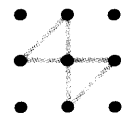
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Requirement for a Peptidoglycan Recognition Protein (PGRP) in Relish Activation and Antibacterial Immune Responses in *Drosophila*

K.-M. Choe, T. Werner, S. Stöven, D. Hultmark, K. V. Anderson

A pattern recognition receptor activates transcription of anti-microbial peptide genes in *Drosophila*.



Noble Gas-Actinide Compounds: Complexation of the CUO Molecule by Ar, Kr, and Xe Atoms in Noble Gas Matrices J. Li, B. E. Bursten, B. Liang, L. Andrews

Comparison of spectra for the linear CUO molecule in ices of the noble gases neon and argon reveals the unexpected formation of uranium-argon bonds.

Living with Lethal PIP3 Levels: Viability of Flies Lacking PTEN Restored by a PH Domain Mutation in Akt/PKB H. Stocker *et al.*

The protein kinase Akt is the only essential target of phosphatidylinositol (3,4,5) trisphosphate in flies.

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US: GrantsNet's March News K. Cottingham

Polar research funding, postdoctoral fellowships abroad, and the latest biomedical funding news, all in one place.

US: Authorship in Biomedical Research—Realities and Expectations M. Cho and M. McKee

Young scientists often find themselves in complicated negotiations over authorship. Here are some potential pitfalls, how to avoid them, and what to do if you can't.

Singapore: Inspiring Future Entrepreneurs J. Wong

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Using mathematical modeling to make testable predictions for T cell effector functions.

Perspective: Software for Signaling Networks, Electronic and Cellular L. Lok

Tools for modeling and analyzing cellular circuits.

Review: Ordered Just So—Lipid Rafts and Lymphocyte Function C. E. Sedwick and A. Altman

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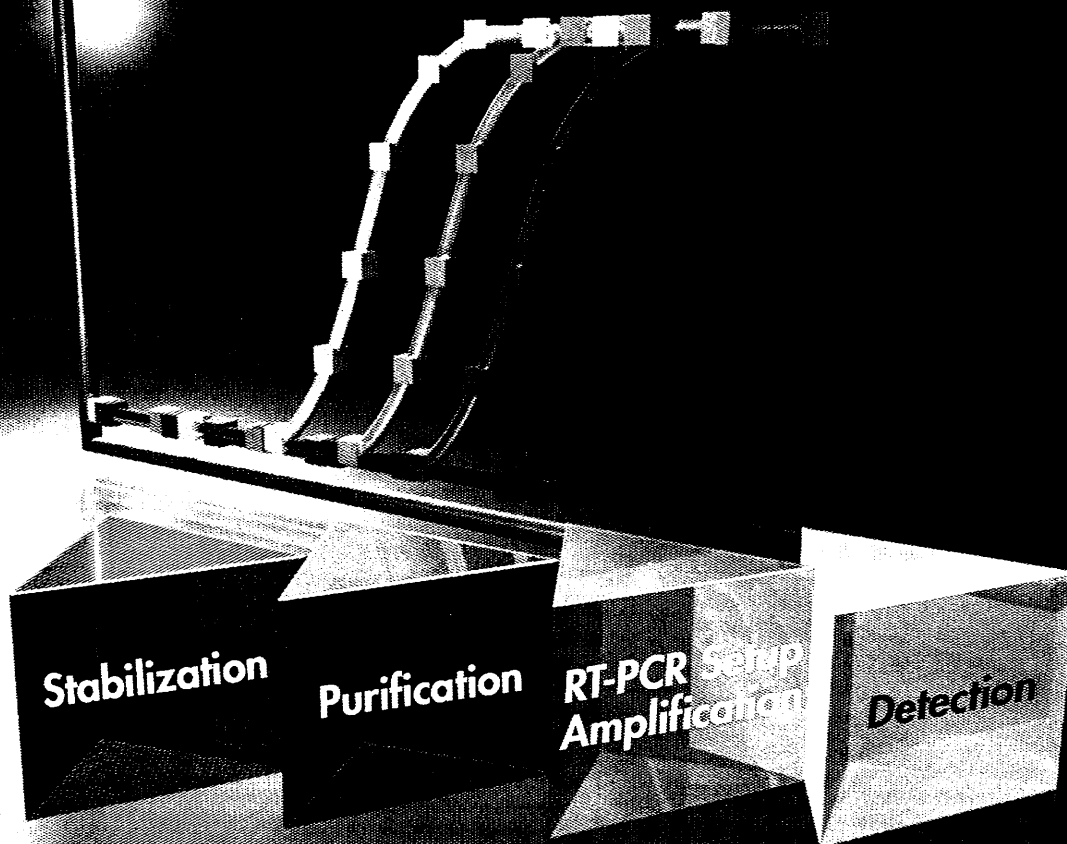
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THIS WEEK IN Science

edited by Phil Szuromi

A Polymer on the Mend

For a number of chemical reactions, the bonds that form can be broken and reformed through a thermally reversible process. Chen *et al.* (p. 1698) create a polymer with a network structure cross-linked by bonds formed through the Diels-Alder reaction. Fractures in the polymer can be fixed by a simple thermal treatment that does not require additional monomer and that can be repeated indefinitely.

Beating the Odds?

In birds and mammals, the sex of offspring is determined chromosomally and thus should produce nearly equal numbers of males and females. Evolutionary theory suggests that females might nevertheless adjust the sex ratio of their offspring according to prevailing environmental conditions. Puzzlingly, this ability is seen in some species but less so in others. West and Sheldon (p. 1685) used a meta-analytical technique to explore the constraints to adaptive sex ratio adjustment in birds and also in wasps, where the potential for sex ratio adjustment is much greater because the method of sex determination depends on whether eggs are fertilized. The mechanism of sex determination is not sufficient to explain all of the observed variation in sex ratio adaptation. An important factor is the ability of parents to predict their offsprings' environment. ✂

Cell Signals Show Their Where's

Two studies have used fluorescence resonance energy transfer (FRET) to find out how and where the molecular partners of cell signaling get together in cells. Phosphotyrosine phosphatases like PTP1B (protein tyrosine phosphatase-1B) oppose the signaling of activated receptor tyrosine kinases by dephosphorylating tyrosine residues. Haj *et al.* (p. 1708; see the Perspective by Gill) imaged a fluorescently tagged mutant of PTP1B and found that it interacted with epidermal- and platelet-derived growth factors in living mouse fibroblasts at the cytoplasmic surface of the endoplasmic reticulum. This interaction was maximal about 30 minutes after the receptors were stimulated and required endocytosis of receptors from the cell surface. Thus, internalization of receptors, which is required for some forms of signaling, also seems to target the receptor to a dephosphorylation compartment. In cardiac myocytes, the second messenger cyclic adenosine monophosphate (cAMP) somehow mediates distinct signals from different receptors, possibly through the spatial localization of these signals. Indeed, the primary target of cAMP, protein kinase

1691 Removing Spin in Quantum Magnets

In low-dimensional spin systems, interactions between nearest neighbors can result in large-scale magnetic ordering. What happens as magnetic atoms are exchanged for nonmagnetic ones? Several theoretical studies have still been waiting for an experimental test. Vajk *et al.* (p. 1691) can now modify the two-dimensional (2D) antiferromagnet, La_2CuO_4 , by replacing nearly half of the magnetic copper ions with nonmagnetic magnesium and zinc. The system develops from a connected antiferromagnet to a disconnected system that contains finite, but isolated, clusters.

And in Brevia ...

An analysis of mitochondrial DNA from the "Alice in Wonderland" dodo by Shapiro *et al.* (p. 1683) shows that the dodo's closest living relative is the Nicobar pigeon, and that their common ancestor dispersed across the Indian Ocean to the Mascarenes around the late Eocene.

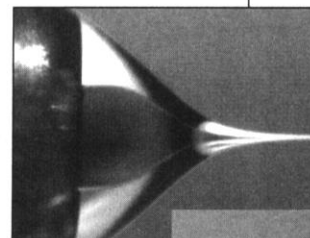
A, and the enzyme that produces cAMP, adenylyl cyclase, are both localized to the T tubules of myocytes that store Ca^{2+} required to stimulate contraction. Zaccolo and Pozzan (p. 1711) now report that PKA is activated in response to stimulation of β -adrenergic receptors in small microdomains around the T tubules. Diffusion of cAMP appears to be limited to a few micrometers by high activity of phosphodiesterases that degrade cAMP. Localization of PKA by A-kinase anchoring proteins (AKAPs) is required to allow activation.

Spinning Energy Out of a Black Hole

Relativistic jets of plasma have been associated with candidate black hole regions. These observations suggest that large amounts of energy can escape from black holes. One possible route is coupling to the rotation of a black hole—although black holes consume mass, they must still preserve its angular momentum and thus may rotate. Koide *et al.* (p. 1688; see the Perspective by Blandford) have simulated energy extraction from a rapidly spinning black hole with a large-scale magnetic field. In their simplified model, an Alfvén wave that is generated by rotational-frame dragging of space near the black hole transports energy outward along the magnetic field lines. This process reduces the energy that is fed into the black hole, which in turn reduces the rotation rate of the black hole and thus extracts energy. ✂

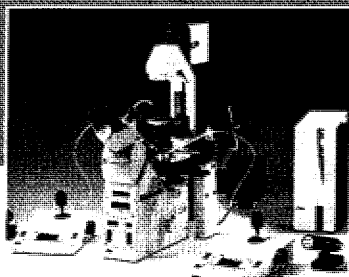
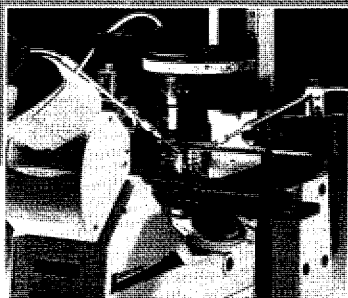
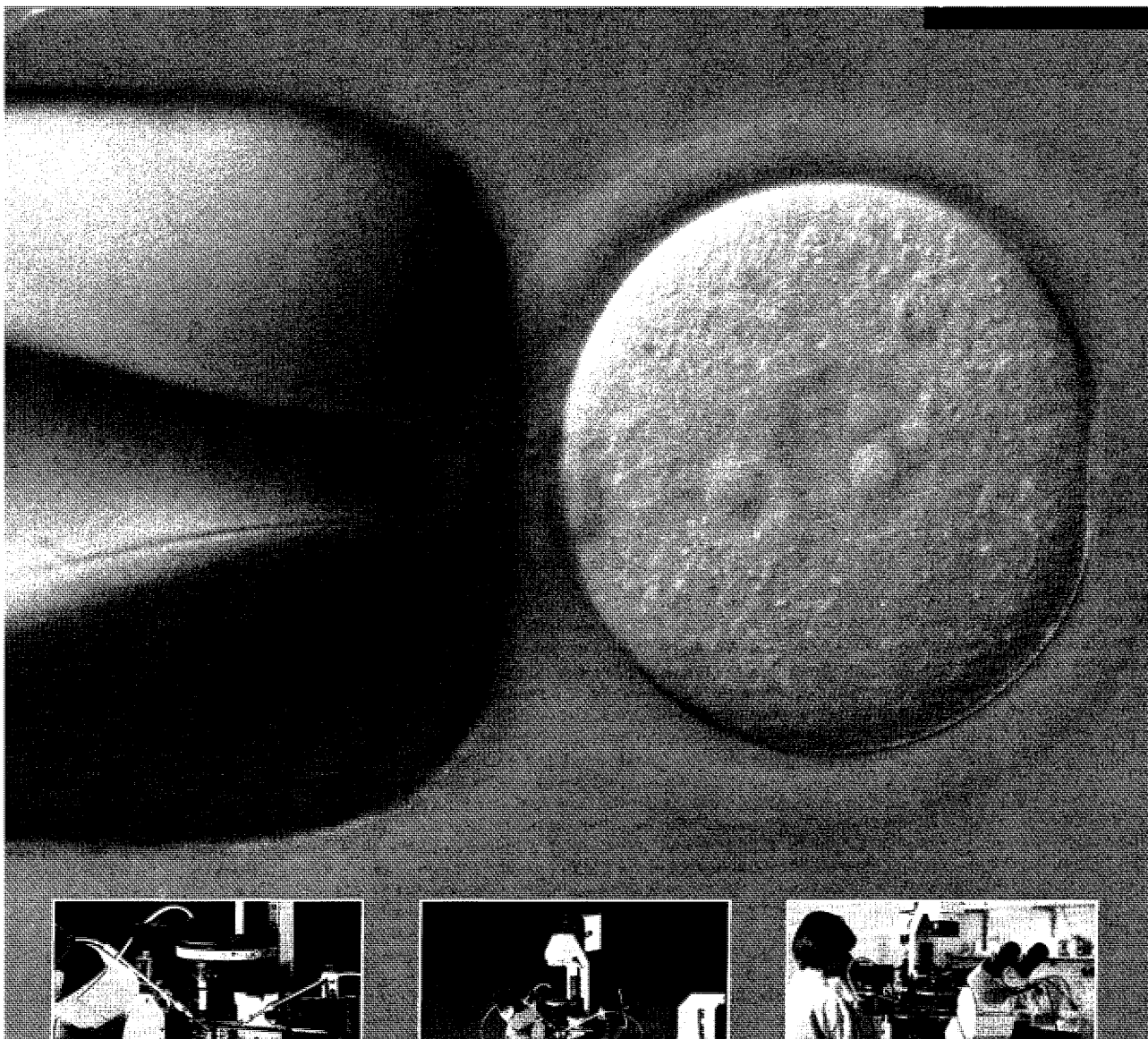
Coating a Water Droplet

Many techniques exist for the encapsulation of solid particles, but how do you coat a liquid with another liquid? In a process similar to the electrospraying of a single fluid, Loscertales *et al.* (p. 1695) generated a coaxial jet of two immiscible fluids. As charge was applied to the fluid jet, it was accelerated toward a grounded electrode. With the appropriate choice of flow rate and applied voltage, the jet broke up into a series of monodisperse droplets with sizes in the range from 10 to 0.15 micrometers. The outer fluid could be hardened through a photoreaction.



Molecular Iron Workers

In *Escherichia coli*, the outer membrane receptor FecA binds ferric citrate and transports it into the cytoplasm. Now Ferguson *et al.* (p. 1715; see the Perspective by Postle) have determined the



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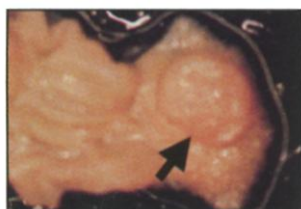
crystal structure of FecA with and without dinuclear ferric citrate at 2.0 and 2.5 angstroms, respectively. Ligand binding triggers changes in extracellular loops that close the entrance to the ligand-binding site. Allosteric transitions on the periplasmic end of the molecule likely transmit the signal to TonB, the inner membrane protein that drives transport of the substrate. The authors propose a four-stage mechanism for the energy-dependent transport of siderophores.

Misfolding Milestones in Protein Folding?

Nonnative protein conformations are of interest in understanding protein folding and because of their role in neurodegenerative diseases. Nuclear magnetic resonance (NMR) studies have shown that native-like hydrophobic clusters are retained in some proteins even under denaturing conditions. Klein-Seetharaman *et al.* (p. 1719; see the Perspective by Baldwin), using NMR and site-directed mutagenesis, show that nonnative interactions in lysozyme stabilize a native-like core comprising four hydrophobic clusters. All four clusters were disrupted when a tryptophan, located at the interface of the two structural domains of lysozyme and solvent-exposed in the native state, was mutated to glycine.

Finding Effectors

The identification of putative effector proteins that are injected into host cells by bacterial pathogens has been very difficult. Guttman *et al.* (p. 1722) used a combination of genetic screening followed by bioinformatic prediction to identify several dozen putative effectors from *Pseudomonas syringae*. The variety of effector proteins found—some of which have not been identified previously—suggests that pathogens use multiple independent molecular strategies to adapt to different hosts.



A Barrier to Colon Cancer?

The gastrointestinal (GI) tract is lined by a layer of mucus that acts as a physical barrier between the luminal contents and the intestinal epithelium. This mucus is comprised of highly glycosylated proteins called mucins whose precise roles in normal physiology and disease are poorly understood. Velcich *et al.* (p. 1726) make the surprising observation that mice deficient in Muc2, the

most abundant GI mucin, show an increased rate of intestinal epithelial cell growth and migration and spontaneously develop invasive tumors in the small intestine and rectum.

Redefining the Connections

The early processing stages of visual information from the eye to higher brain centers are anatomically well defined. A key component in this system is the pathway from visual areas V1 to V2. Using cytochrome oxidase staining in the macaque brain, Sincich and Horton (p. 1734) reevaluated this important connection and found that the central distinction in the parallel pathways is between patch columns and inter-patch columns rather than between magno- and parvocellular pathways. This result indicates that the nature of the parallel pathways may be in need of reformulation, and that both the dorsal and the ventral visual information processing streams receive combined form, color, and motion information.

How Placebos Work

A placebo, an inactive substance, can nevertheless substantially reduce the perception of pain. In a brain imaging study, Petrovic *et al.* (p. 1737; see the 8 February news story by Holden) investigated the mechanisms underlying this placebo analgesia effect. They compared placebo analgesia and opiate-induced analgesia and found significant overlap among brain regions associated with these two treatments, primarily within the anterior cingulate cortex and the brainstem. Furthermore, correlations in activity between these areas were observed in both analgesic conditions but not during pain itself. The anterior cingulate appears to mediate analgesic effects through cortical control of brainstem systems, and thus placebo manipulations may operate by engaging these systems in response to cognitive expectations or associations. **X**

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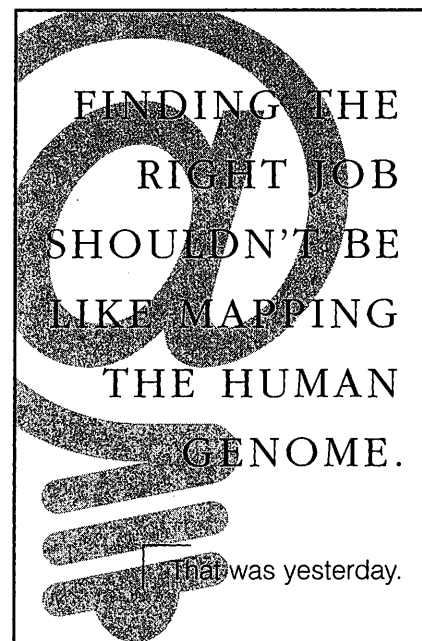
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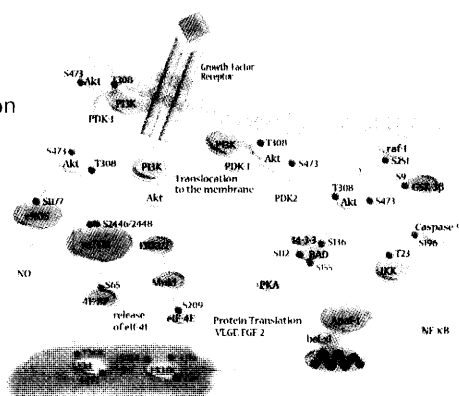
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¹ Morris, M. et al. (2008) *Nature Biotech.* 19: 1173-1176.
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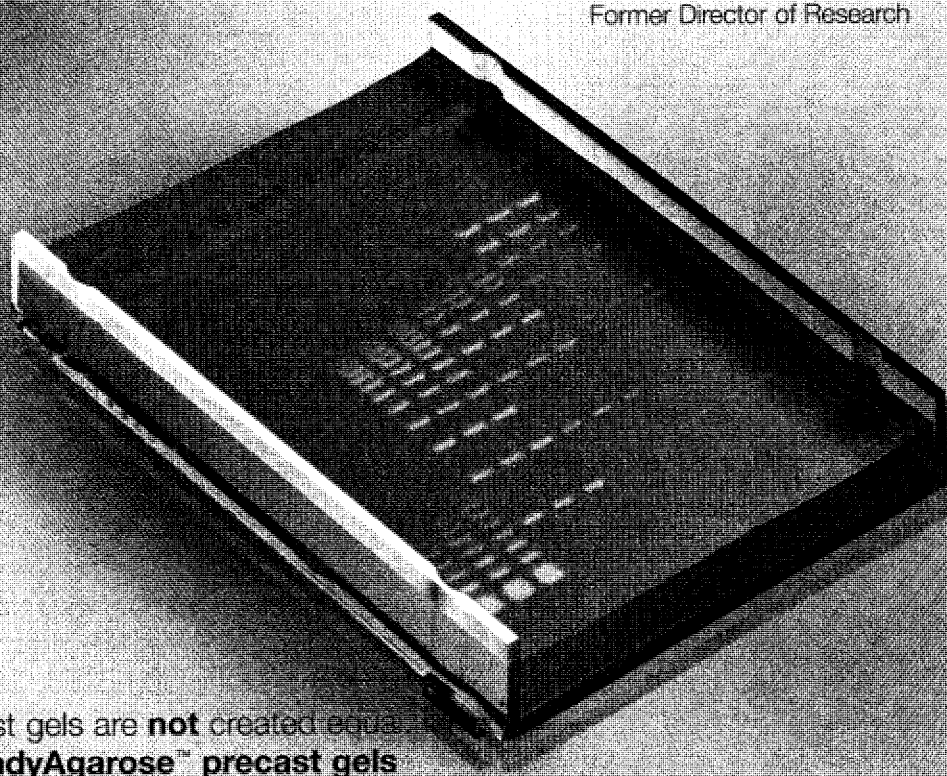
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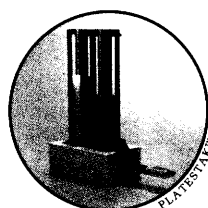
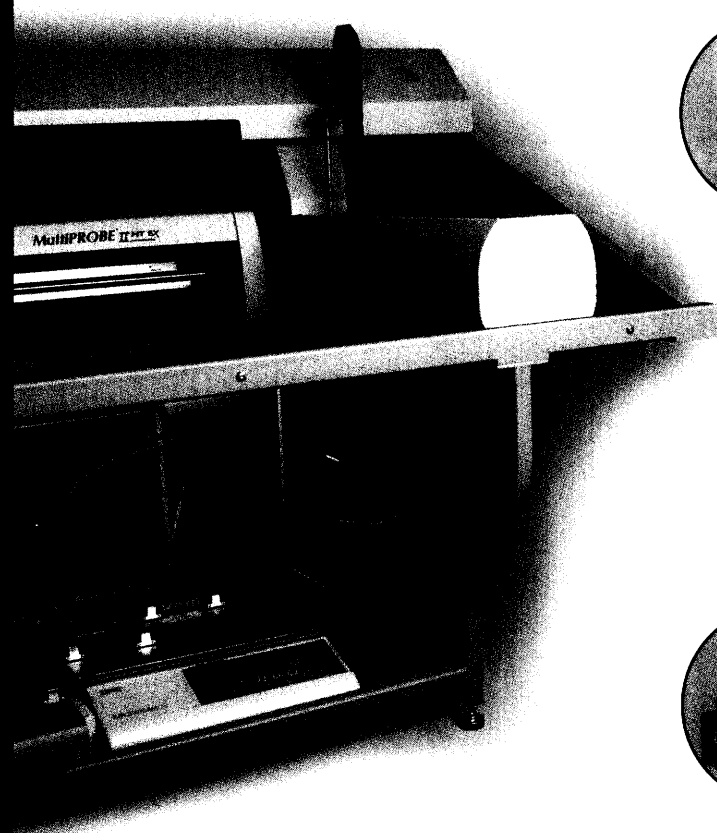
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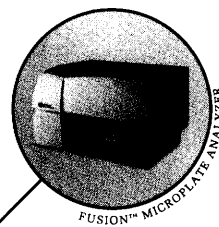
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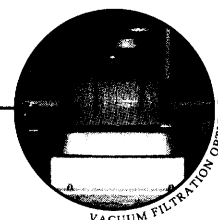
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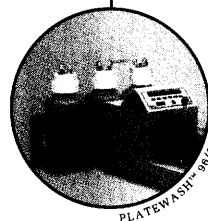


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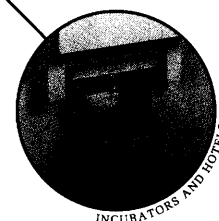


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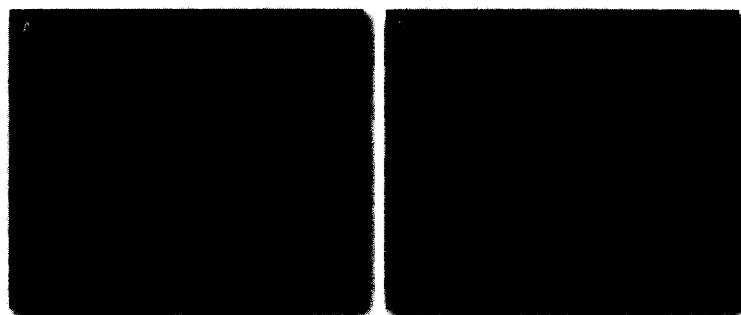


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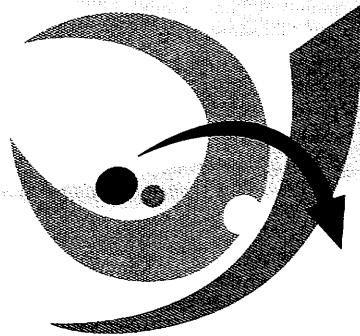
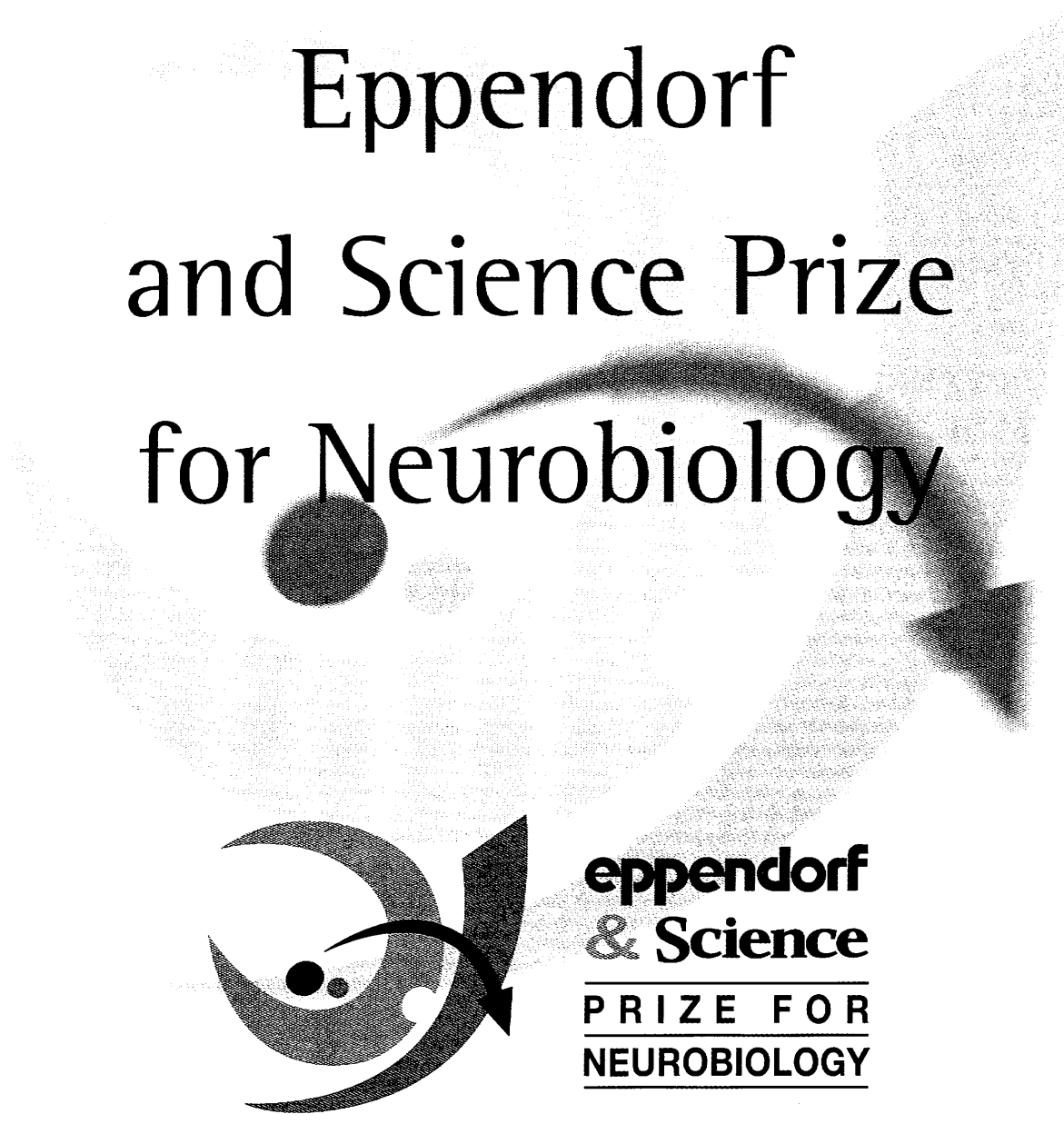
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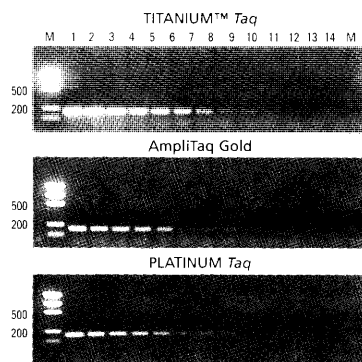
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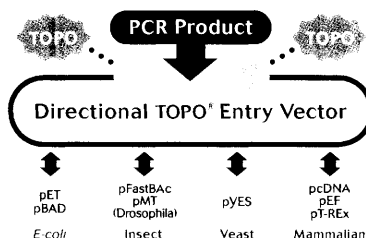


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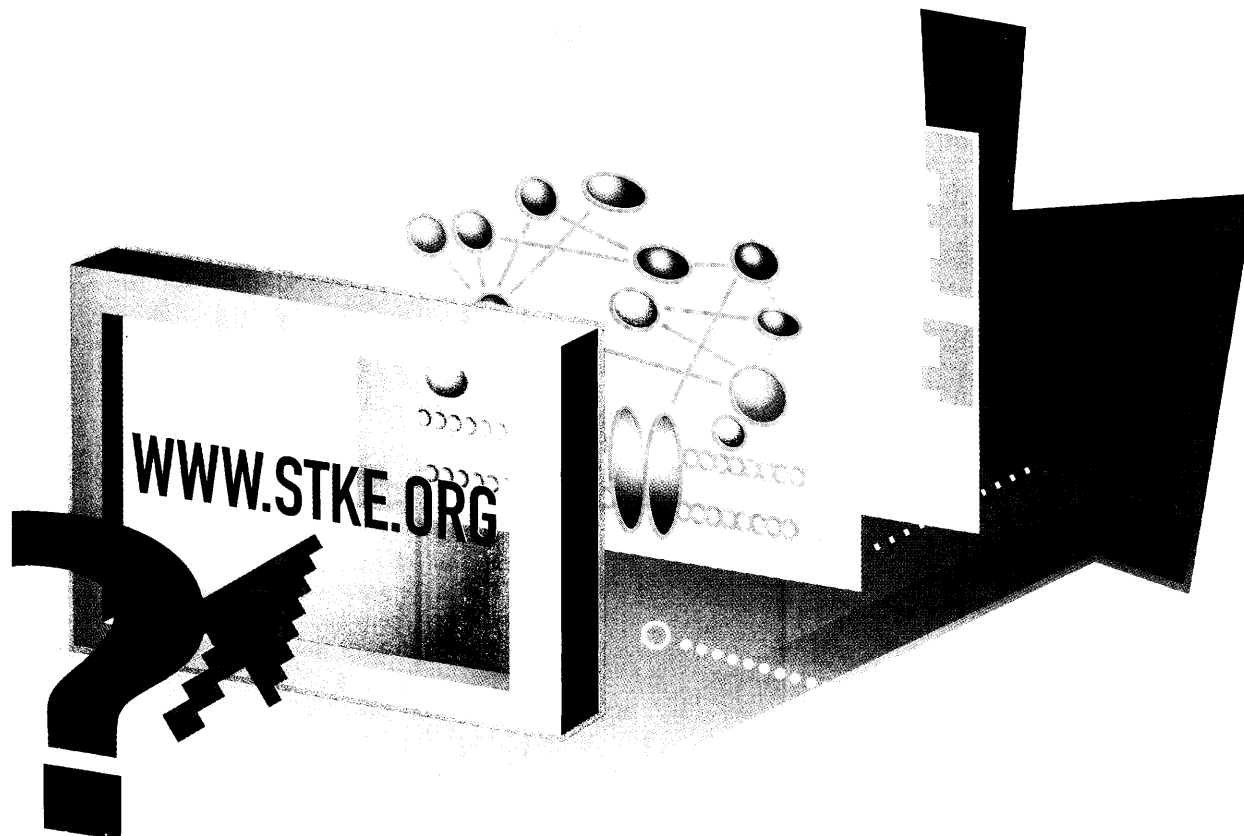
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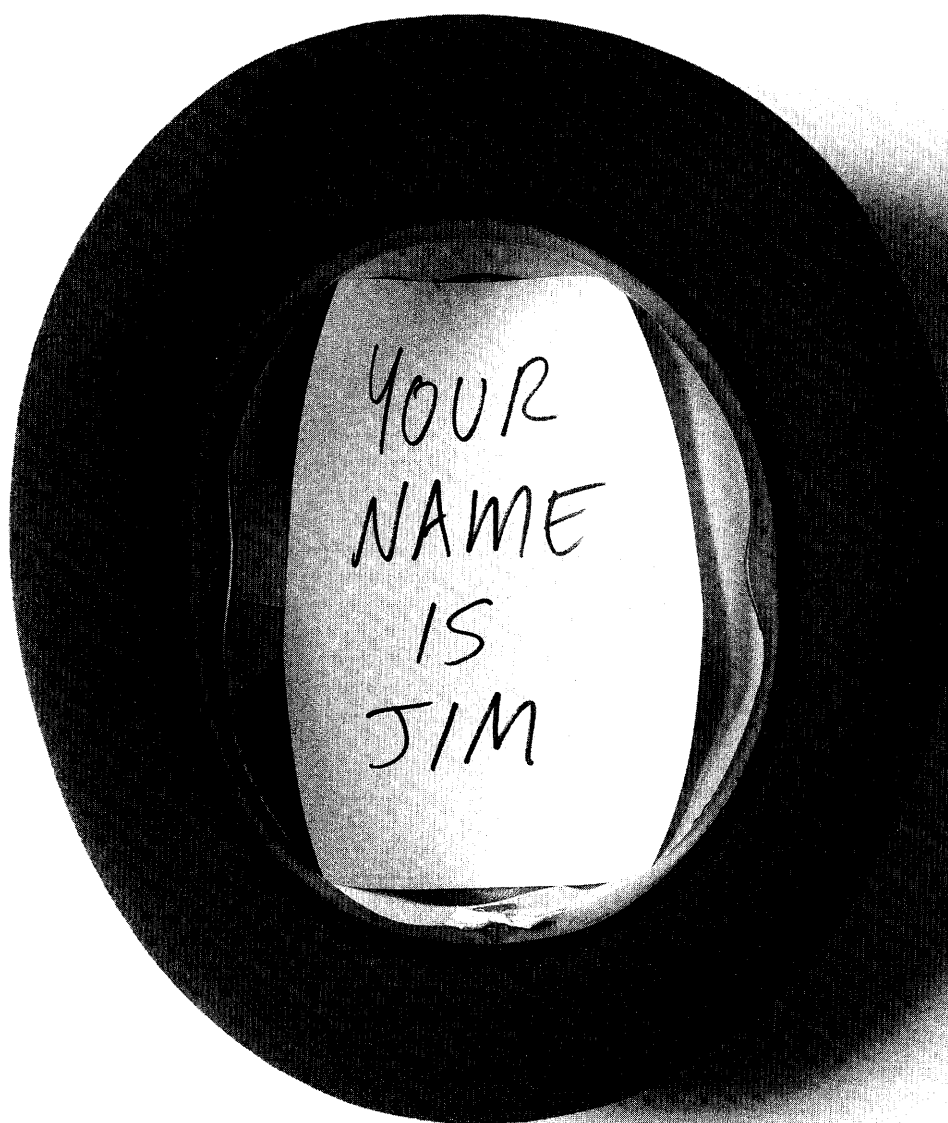


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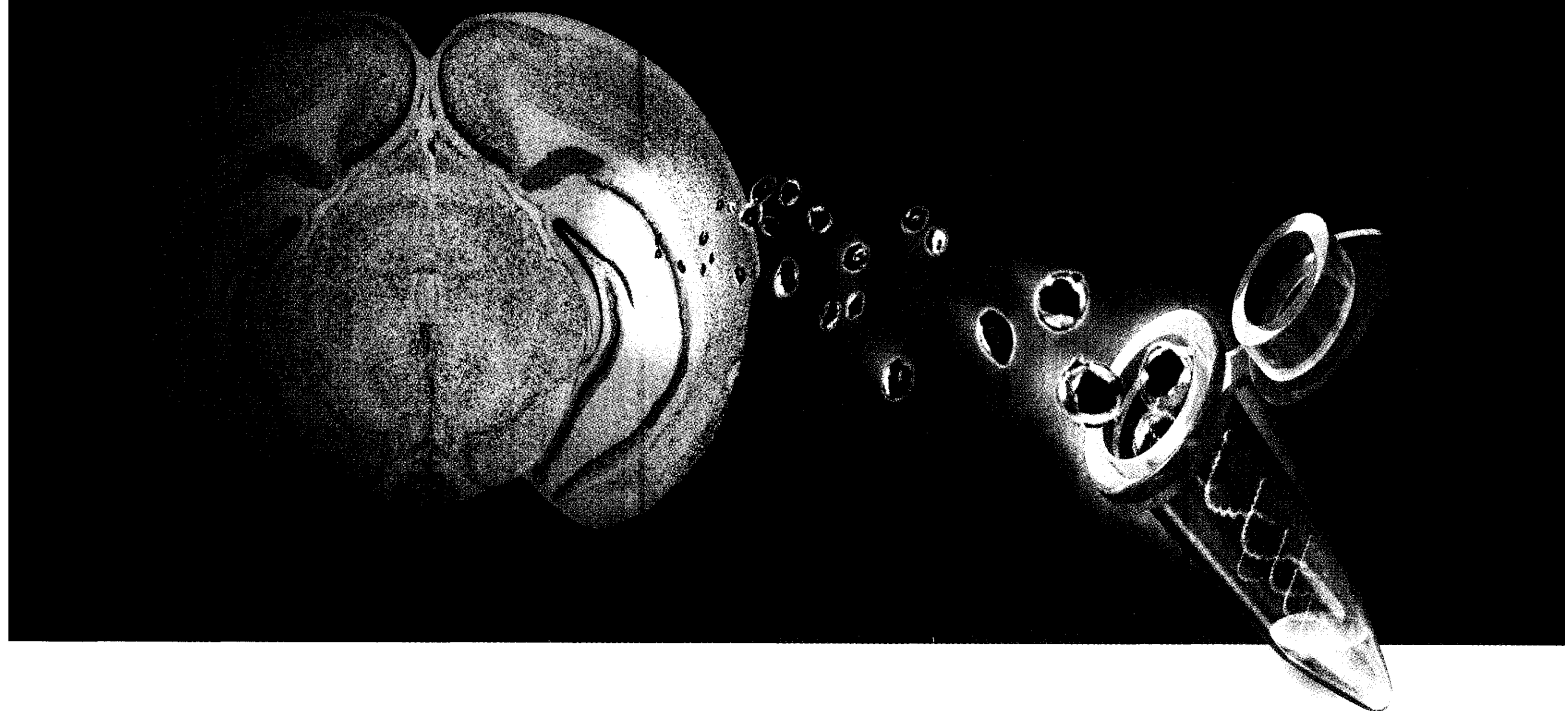
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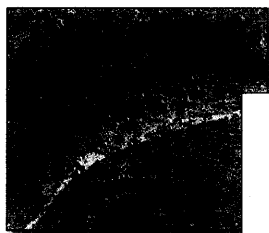
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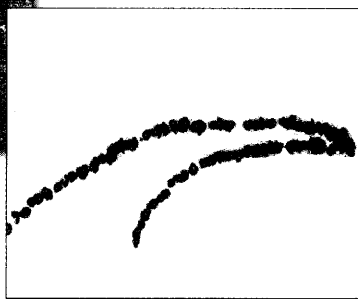


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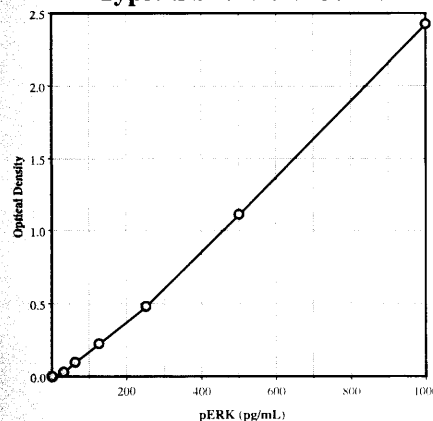
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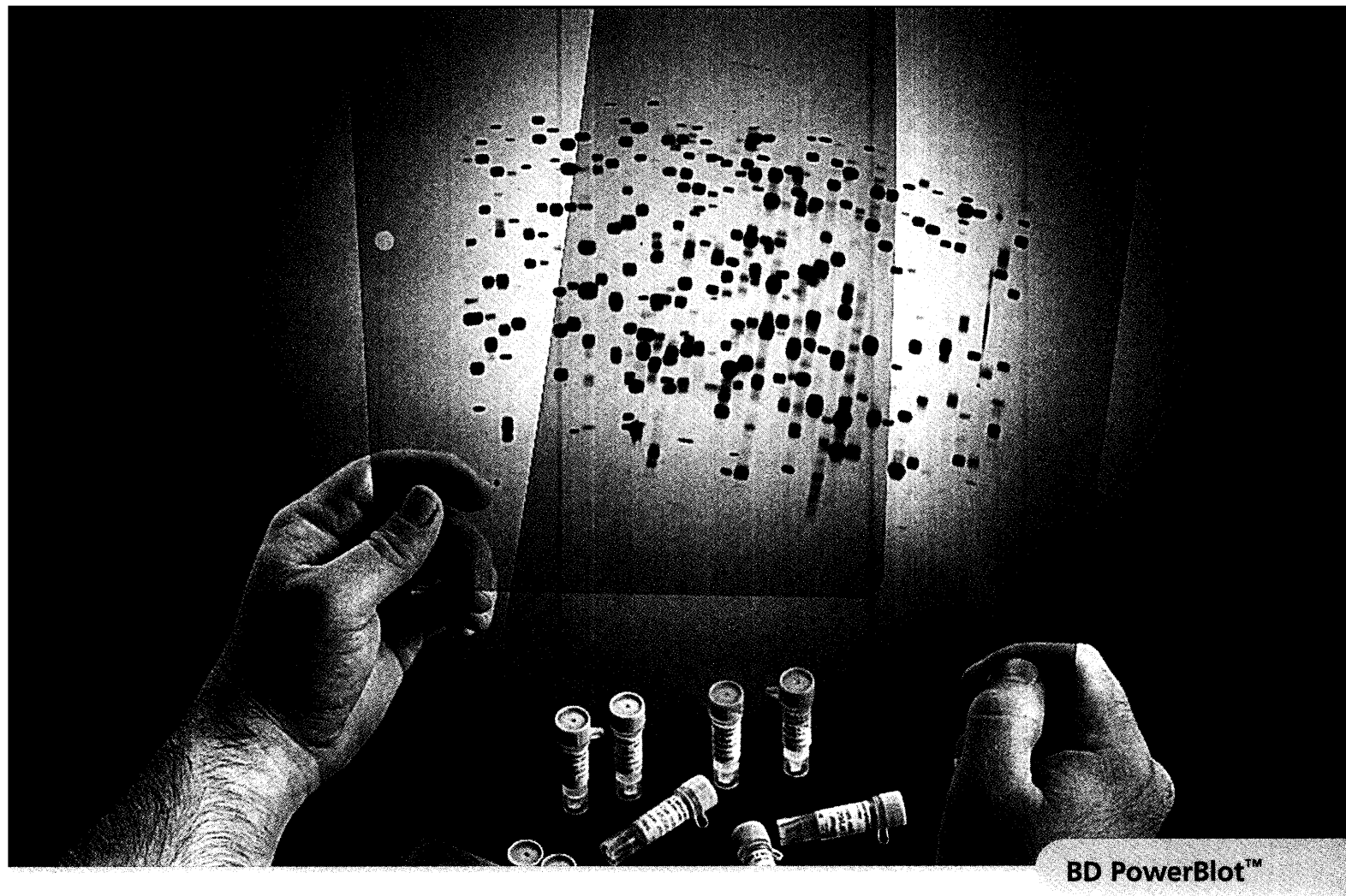


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Non-viral transfection of primary cells:

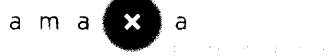
Impossible - you think?

e.g. 60% efficiency

Unbelievable?

in unstimulated T cells

At first that's what Oliver thought too:



Dr. Oliver Gresch, Scientific Product Specialist - joined amaxes in August 2001 "I tested the Nucleofector™* technology during my Ph.D. at the University of Cologne. Unlike any other non-viral transfection method, the Nucleofector™ technology achieves a direct transport of the DNA into the cell's nucleus. With optimized combinations of electrical parameters and cell-type specific solutions it works for a multitude of primary cells, even non-proliferating cells. This novel technology was so convincing that my decision was clear: I joined amaxes right after finishing my Ph.D."



Not yet convinced?

Well, call Oliver for further referrals

+49 (0)221 99199-400

or check our website

www.amaxes.com

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