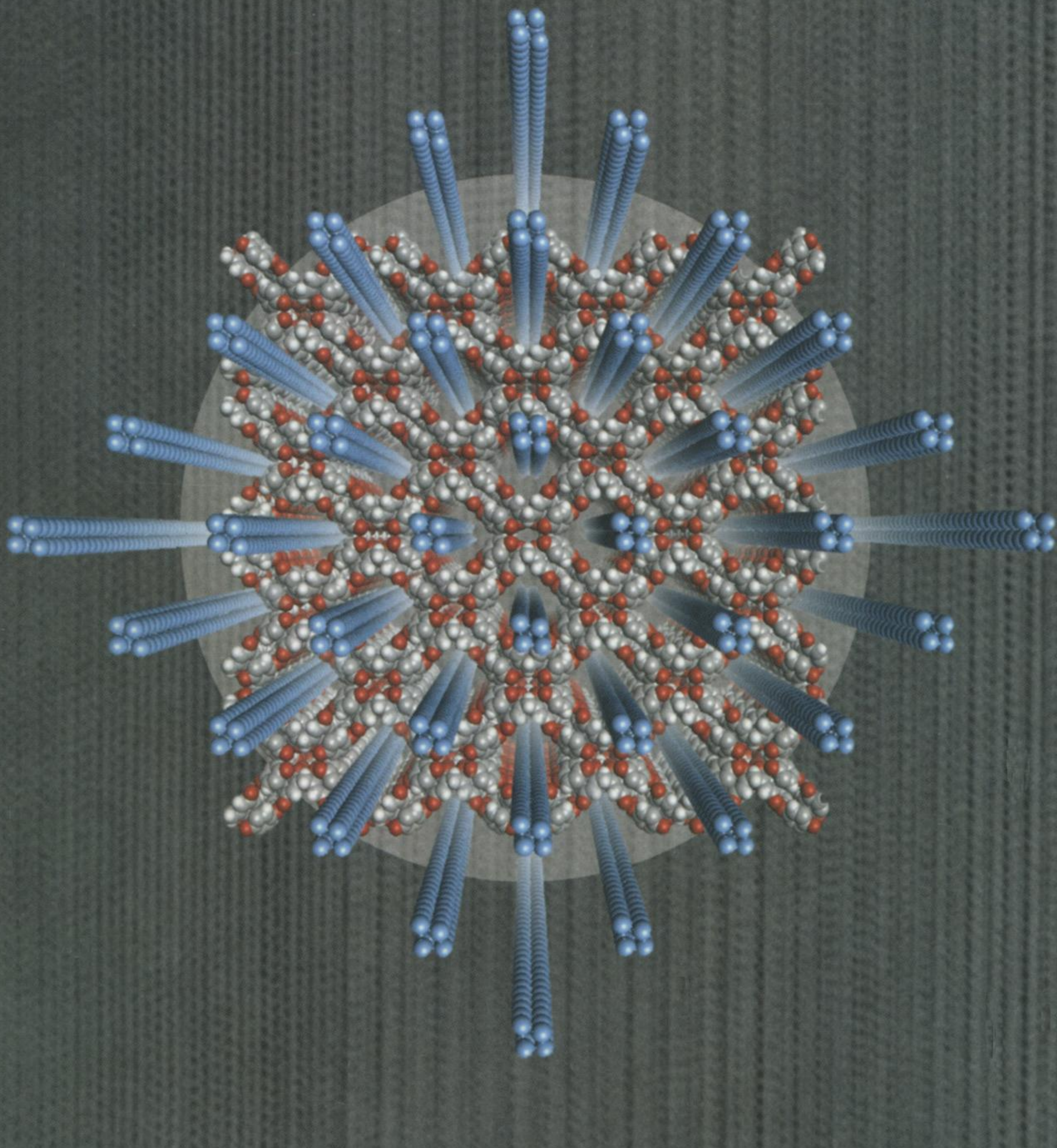
UNDERPAID BUT SATISFIED? U.S. LIFE SCIENCES SALARIES PAGE 395

12 October 2001

Science

Vol. 294 No. 5541
Pages 253–464 $9



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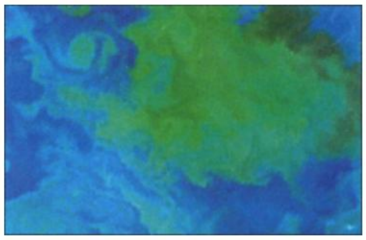

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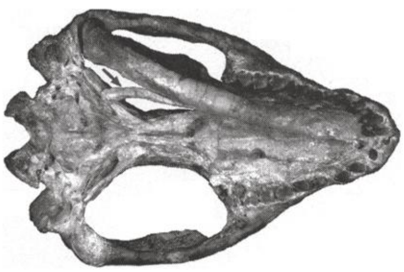

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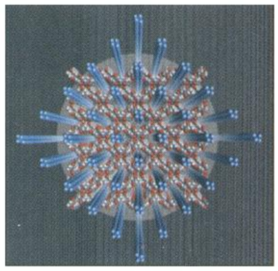

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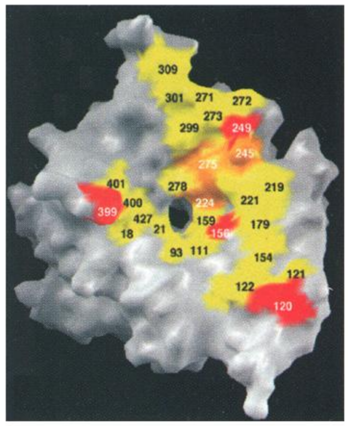
Single-crystalline silver nanowires (width, 0.4 nm) grown inside the pores of self-assembled calix[4]hydroquinone nanotubes. Because these nanowires are coherently oriented as three-dimensional arrays of ultrahigh density, they could be used as model systems to investigate one-dimensional phenomena and as connectors in nanodevices. [image: K. S. Kim]



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SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 2001 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): $115 ($64 allocated to subscription). Domestic institutional subscription (51 issues): $370; Foreign postage extra: Mexico, Caribbean (surface mail) $55; other countries (air assist delivery) $87. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. **Printed in the U.S.A.**

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CONTENT HIGHLIGHTS AS OF 12 OCTOBER 2001

science magazine — www.sciencemag.org

SCIENCE EXPRESS — www.sciencexpress.org

A Conserved Family of Prolyl-4-Hydroxylases That Modify HIF R. K. Bruick and S. L. McKnight

An evolutionarily conserved family of prolyl hydroxylases plays a key role in cellular oxygen sensing through modification of hypoxia-inducible factor.

A Phosphatase Associated with Metastasis of Colorectal Cancer S. Saha *et al.*

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Gene expression profiling reveals that a protein tyrosine phosphatase called PRL-3 may play an important role in the metastasis of human colorectal tumors to the liver.

Heterochromatin Is Required for Cohesion at Centromeres P. Bernard *et al.*

The heterochromatic nature of centromeres, and specifically the heterochromatin protein Swi6, allows association of Rad21-cohesin with the centromere, thus ensuring the correct segregation of sister chromatids.

TECHNICAL COMMENTS

Inverse Modeling of Atmospheric Carbon Dioxide Fluxes

Bousquet *et al.* (Reports, 17 November 2000, p. 1342) applied an inverse model to 20 years of atmospheric CO_2 observations to gain insight into the interannual variability of atmospheric CO_2 fluxes. Kaminski and Heimann point out that consistency with observed atmospheric CO_2 concentrations "is not sufficient in itself" for the model to be valid—a point that they emphasize by presenting an alternative flux field that achieves greater consistency with observations but that includes a large, clearly invalid CO_2 sink over Europe. Peylin *et al.* respond that their estimates were based not only on consistency between modeled and observed concentrations, but also on independent knowledge regarding the regional spatial structure of sources and sinks. They also discuss the general problem of finding the ideal spatial resolution for modeling large-scale atmospheric processes based on sparse data.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/294/5541/259a

SPECIAL FEATURE

Quarterly Author Index — www.sciencemag.org

science's next wave — www.nextwave.org

UK and Germany: The Eurodoc Exchange

Next Wave launches the Eurodoc Exchange—a place to share a vision for the future of research in Europe. In the coming weeks, we'll be hearing from Ph.D. students from across Europe, hosting an online discussion about career prospects and conditions, and developing solutions to put to Europe's policy-makers.

US: Postdoc Perspectives on the Salary Survey R. Weibl

Only on Next Wave can you find out exactly what the AAAS salary survey means for postdocs.

Canada: Heading South—Seeking a Brighter Future in New York City K. Borden

Moving her laboratory from Nova Scotia's Dalhousie University to Manhattan's Mount Sinai School of Medicine was, says the author, an incredibly difficult decision—but the choice boiled down to a promise for the future.

KNOWLEDGE ENVIRONMENTS

science's sage ke — www.sageke.org

Discussion: Analyzing DNA Arrays

Talk to the experts.

Viewpoint: Realizing Wisdom S. J. Olshansky

A student hits the stacks and wakes up to his teacher's insight.

science's stke — www.stke.org

Review: β-Adrenergic Signaling in the Heart: Dual Coupling of the β_2-Adrenergic Receptor to G_s and G_i Proteins R.-P. Xiao

Receptor coupling and pathway compartmentalization in the heart.

Review: Bridging with GAPs—Receptor Communication Through RGS Proteins K. M. Druey

RGS proteins connect G protein–coupled receptors to receptor tyrosine kinases, cell adhesion receptors, and ion channels.

Perspective: Is Dimerization of Chemokine Receptors Functionally Relevant? M. Thelen and M. Baggiolini

A critical analysis of the mechanisms underlying calcium signals initiated by chemokine receptors.

Connections Map: $G\alpha_i$ and $G\beta\gamma$ Canonical Pathways R. Iyengar and D. Aaronson

Filling in G protein signaling.

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THIS WEEK IN Science

edited by Phil Szuromi

Messages in Moondust

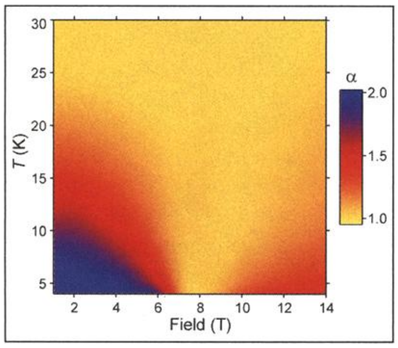
The surface of the Moon, brought back by the Apollo missions, is a useful tracer of solar system processes as divergent as solar convection and the formation of the Moon. Nishiizumi and Caffee (p. 352) have quantified a beryllium-10 excess in Apollo-17 lunar soils that they attribute to low-energy solar wind ions rather than to higher energy galactic or solar cosmic rays. The inferred flux rate indicates that beryllium-10 is directly ejected in the solar wind without any mixing in the deeper convective zones of the Sun. The Moon probably formed in a giant impact between the proto-Earth and a Mars-sized bolide that hit the Earth. Analysis of the oxygen isotopic concentrations of Apollo lunar soils by Wiechert *et al.* (p. 342) indicate that the oxygen isotopes are homogeneous and similar to terrestrial measurements. Thus, the proto-Earth and the smaller, hypothetical bolide were likely composed of similar materials formed at about the same distance from the Sun.

348 Silver Liners

Nanoscale materials can show interesting properties, but not all of them show the strength and stability of carbon nanotubes. For example, small metal structures can be quickly destroyed by oxidation, but clever tricks in chemistry and templating methods can improve their stability. Building on recent synthesis work in which calix[4]hydroquinone nanotubes were fabricated, Hong *et al.* (p. 348; see the cover) have trapped silver ions within these tubes to form 0.4-nanometer-wide nanowires. These tube-supported wires show long-term stability in air and aqueous environments. Produced in three-dimensional arrays of support tubes, these wires may have potential as model systems for studying confinement phenomenon or as connectors in nanodevices.

Magnetic Field–Induced Quantum Criticality

Quantum criticality, where a phase transition can be induced in the limit of zero temperature by application of external parameter (such as pressure, electric fields, or chemical substitution) has proven fruitful ground for experimental and theoretical investigation of correlated systems. However, the parameters used to tune these systems can create problems of their own, such as restricting the dimensionality of the system or introducing disorder that may mask some of the more interesting properties. Grigera *et al.* (p. 329; see the Perspective by Aeppli and Soh) present magneto-transport data on the ruthenate $Sr_3Ru_3O_7$ that reveal the existence of a well-defined, magnetically tuned quantum critical point. A closer examination of the temperature dependence of this transition reveals behavior that is not readily explained by the current understanding of quantum criticality.



CREDIT: GRIGERA *ET AL.*

Splitting a Discontinuity

Seismic data has delineated two globally distributed velocity discontinuities in Earth's mantle at depths of 410 and 660 kilometers (km), as well as a third discontinuity at 520 km that is not well defined and not globally distributed. Deuss and Woodhouse (p. 354; see the Perspective by Vidale) have now delineated a splitting of the 520-km discontinuity into velocity jumps at 500- and 560-km depths. They attribute the velocity discontinuity to a transformation of garnet to perovskite. The differences in the depth of the discontinuity appear to be related to small temperature or compositional variations that could be used to help constrain the rheology of the mid-mantle.

Mammalian Middle Ear

The middle ear of mammals may have evolved by transferring bones from the jaw to the middle ear, but there has been no fossil evidence to support this hypothesis. Wang *et al.* (p. 357) have found a well-preserved Meckel's cartilage in two Cretaceous mammals from China. The Meckel's cartilage connected the dentary and the ear and probably served as the middle ear in these two mammals. The morphology of the two skulls suggest that the dentary in mammals enlarged over evolutionary time to enhance mastication while the postdentary unit decreased to enhance hearing. Eventually, these features separated to create two ear ossicles in the braincase separated completely from the jaw.

Feeling the Earth's Magnetic Field

The use of Earth's magnetic field for orientation by vertebrates is the subject of two reports (see the news story by Brown). After hatching in Florida, young loggerhead sea turtles migrate within the North Atlantic gyre surrounding the Sargasso Sea. Lohmann *et al.* (p. 364) investigated the orientation of hatchling loggerheads in different magnetic fields corresponding to three different geographical positions at the periphery of the gyre. The young turtles orient in the different fields in ways that help to keep them within the gyre, which suggests that the young turtles are genetically programmed to the local geomagnetic field. The sensory and neural basis of magnetic field orientation has been determined in a mammal by Němec *et al.* (p. 366). Neurons in the superior colliculus of the Zambian mole rat, which leads an almost entirely subterranean existence, can be selectively activated by magnetic field stimuli.

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Integrins are large, heterodimeric ($\alpha\beta$) transmembrane proteins that bind to many extracellular components as well as to other cell adhesion proteins. They are important in normal cellular processes such as attachment, migration, and proliferation and are

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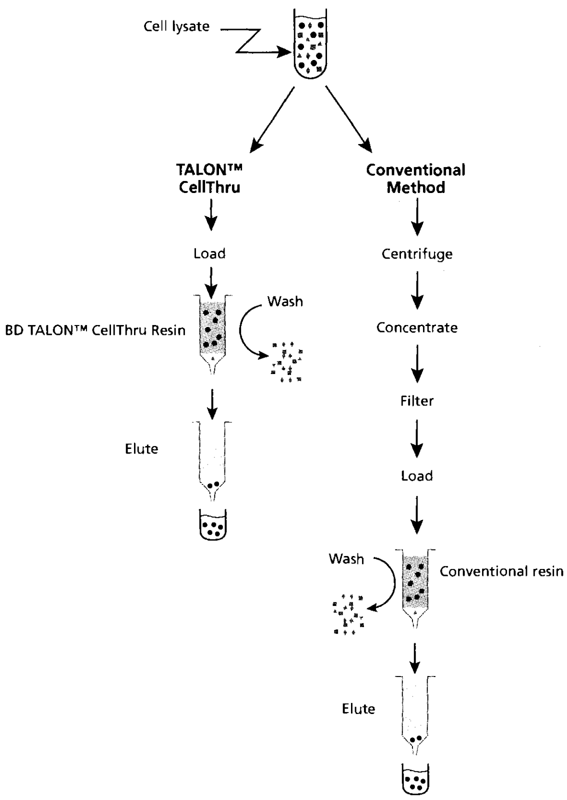
Illustration inspired by the art of Morris Louis (1912–1962).



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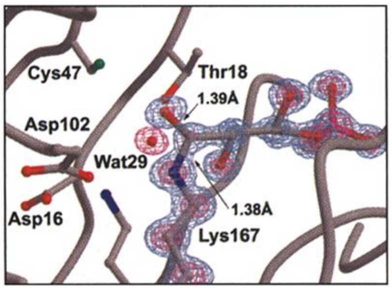
also implicated in pathological states such as neoplasia and metastasis. Xiong *et al.* (p. 339; see the Perspective by Humphries and Mould and the 7 September news story by Couzin) present the crystal structure of the extracellular regions of the complex of αV and β3. There are 12 domains, of which the most interesting are the amino-terminal propeller from the α chain and the A domain from the β chain. This pair of domains forms an interface with similarity to that between the α and β subunits of guanine nucleotide binding, or G proteins, and also contains the binding site for the Arg-Gly-Asp tripeptide motif present in many integrin ligands, such as fibronectin.

Getting First Dibs on Calcium

Calcium ions (Ca^{2+}) that enter a cell through L-type voltage-activated channels (LTCs) are linked to expression of certain genes involved in key neuronal functions, whereas Ca^{2+} entering the cell by other means can exert different effects. Dolmetsch *et al.* (p. 333; see the Perspective by Ikeda) use a clever strategy to explore this perplexing aspect of specificity in cell signaling. They first engineered an LTC that is resistant to a channel inhibitor and then expressed and analyzed it in cultured primary neurons that were treated with the inhibitor to eliminate endogenous channel function. A calmodulin-binding region of the LTC is essential for Ca^{2+}-induced activation of the transcription factors CREB and MEF-2. Thus, the Ca^{2+} entering though LTCs is apparently sensed by calmodulin molecules already positioned at the mouth of the channel. This activation of calmodulin is required for sustained activation of the p42 and p44 mitogen-activated protein kinases, which in turn convey the signal on into the nucleus.

Creating Carbon-Carbon Bonds



Class I aldolases catalyze the formation of carbon-carbon bonds and are therefore of interest as biocatalysts for stereospecific organic synthesis. Heine *et al.* (p. 369) have used cryocrystallography to determine structures at 1.1 angstrom resolution for two covalent intermediates of the type I aldolase, D-2-deoxyribose-5-phosphate aldolase (DERA), the carbinolamine and the Schiff base. Using the atomic-resolution structural information together with site-directed mutagenesis and nuclear magnetic resonance data, the authors propose a detailed mechanism that delineates all of the essential catalytic residues. They find that a water molecule in the active site mediates proton transfer during catalysis.

Glycolipids and the Bacterial Cell Wall

Vancomycin is sometimes the only antibiotic available for combating infections caused by specific Gram-positive bacteria, and the rise of strains resistant to vancomycin is becoming a major public health concern. From an analysis of the effect of glycolipid derivatives of vancomycin on *Escherichia coli*, Eggert *et al.* (p. 361) have found that the mechanism by which these derivatives killed bacteria does not appear to be the same as that used by the parent compound. These results suggest possible modifications of vancomycin that might extend its utility.

Regulating Protein Kinase B

Protein kinase B (PKB) has proven to be a key regulatory element in growth factor signaling, cell survival, and transformation to a cancerous phenotype. Maira *et al.* (p. 374) screened for proteins that physically interacted with PKB and identified a human protein, which they call carboxyl-terminal modulator protein (CTMP), that binds to PKB at the plasma membrane and inhibits activation of the kinase. Inhibition of CTMP expression enhanced activation of PKB, whereas cells expressing a viral homolog of PKB became transformed and proliferated abnormally, and could form tumors in vivo. However, clones of such cells stably expressing CTMP grew more slowly and either failed to form tumors in vivo, or formed tumors that grew more slowly. Thus, CTMP appears to be an important regulator of PKB, an enzyme with critical roles from insulin signaling to protection of cells from apoptosis.

CREDIT: HEINE *ET AL.*

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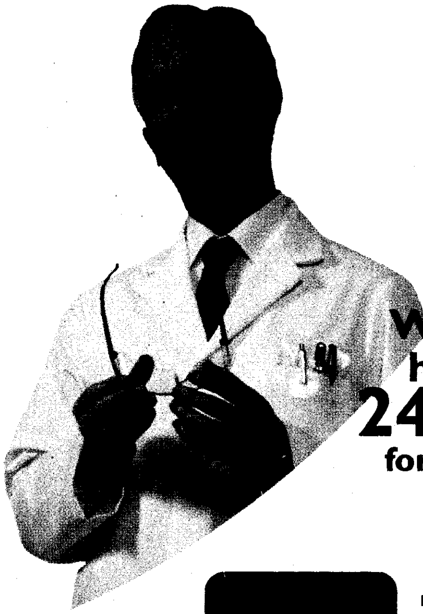

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FIG. 1 Cells are not fixed

Actin filament labeling of human fibroblast (HS68) cells using anti-actin antibody delivered by CHARIOT. (65% transfection efficiency)

FIG. 2 Cells are fixed

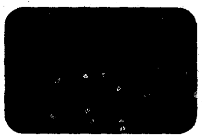

FIG. 3 CHARIOT delivery of a 10 kDa protein, labeled with lucifer yellow at the C-terminus, to the nucleus of human fibroblast (HS68) cells. Cells are not fixed. (70% transfection efficiency after 30 min. incubation)

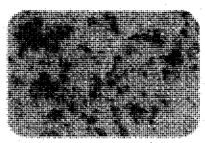

FIG. 4 CHARIOT delivery of a 119 kDa β-galactosidase protein into COS cells. Cells are fixed and stained 2 hours post-transfection. (60% transfection efficiency)

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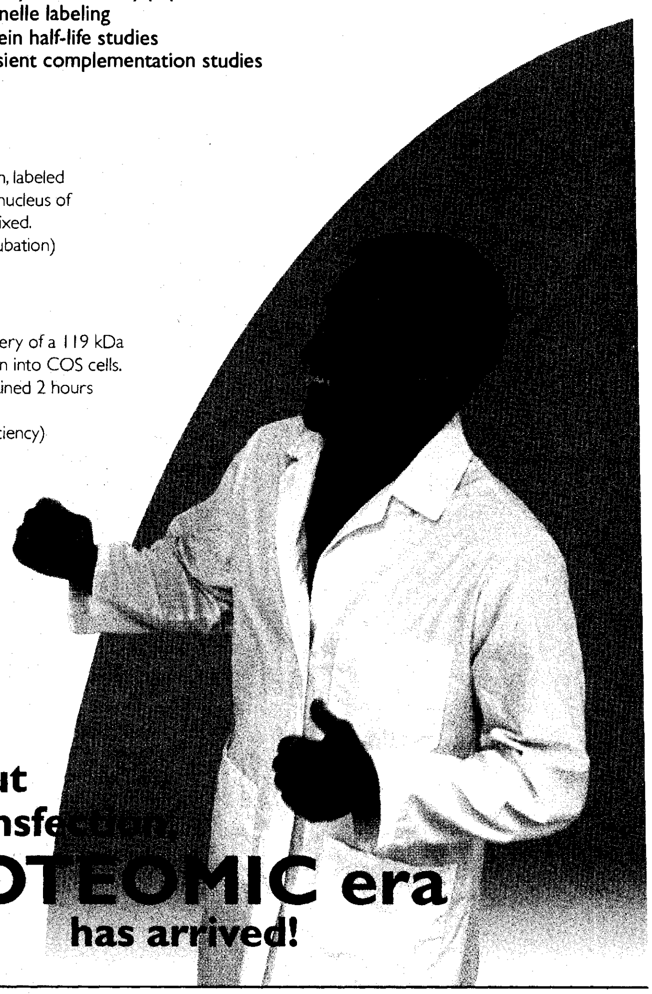

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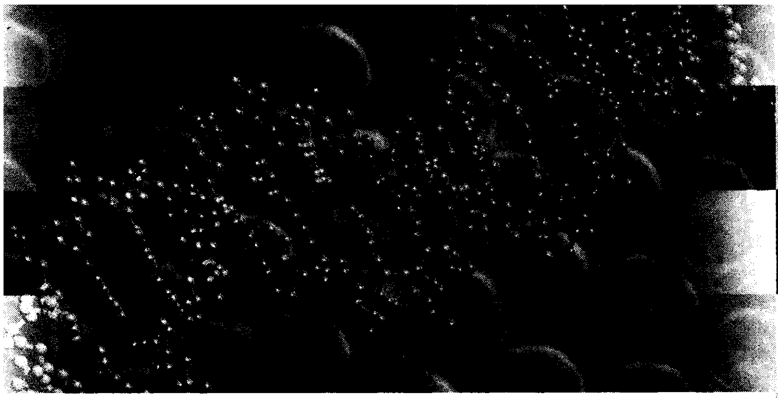

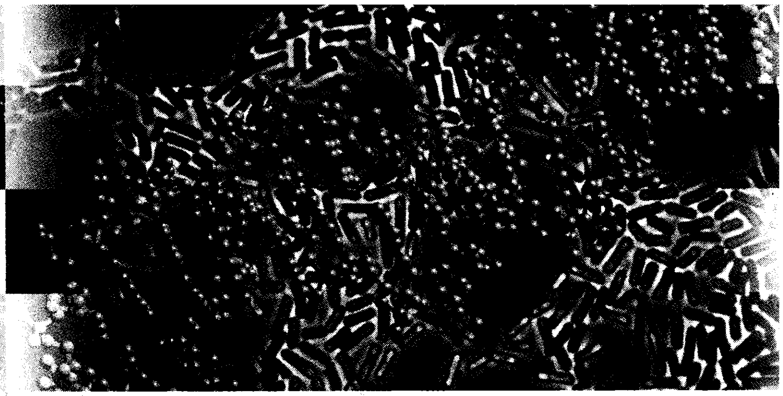

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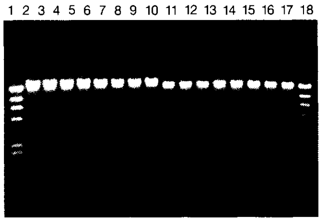

- Yields obtained using the Eppendorf Perfect gDNA Blood Kit and from a competing product. 200 µl fresh human whole blood, 5 µl eluate volume applied.

Lanes 1 and 18:	λ *Hind* III Marker
Lanes 2 to 9:	Eppendorf gDNA Blood Kit
Lanes 10 to 17:	Competing kit

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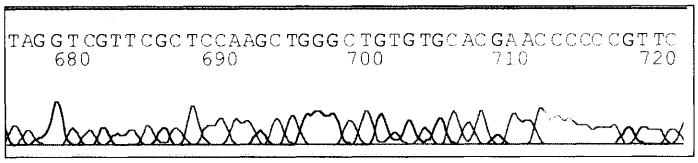

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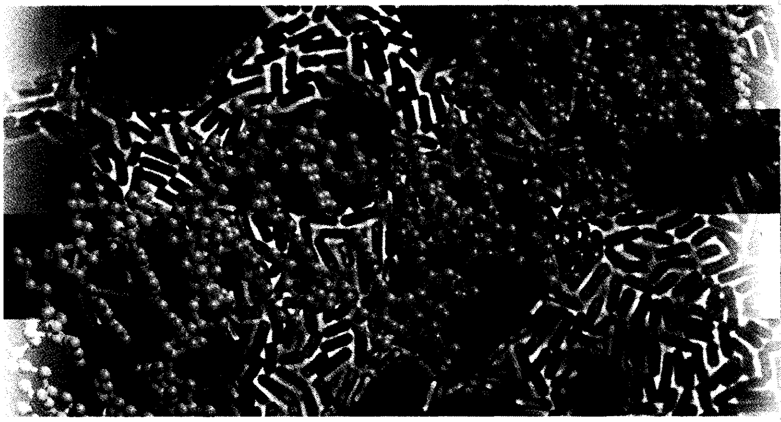

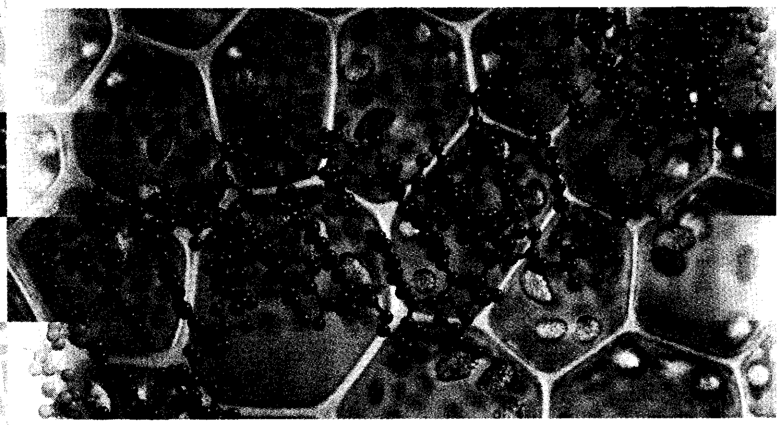

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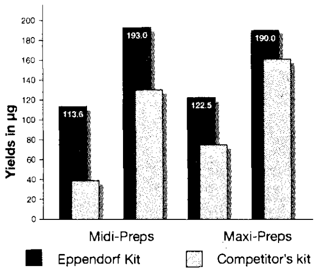

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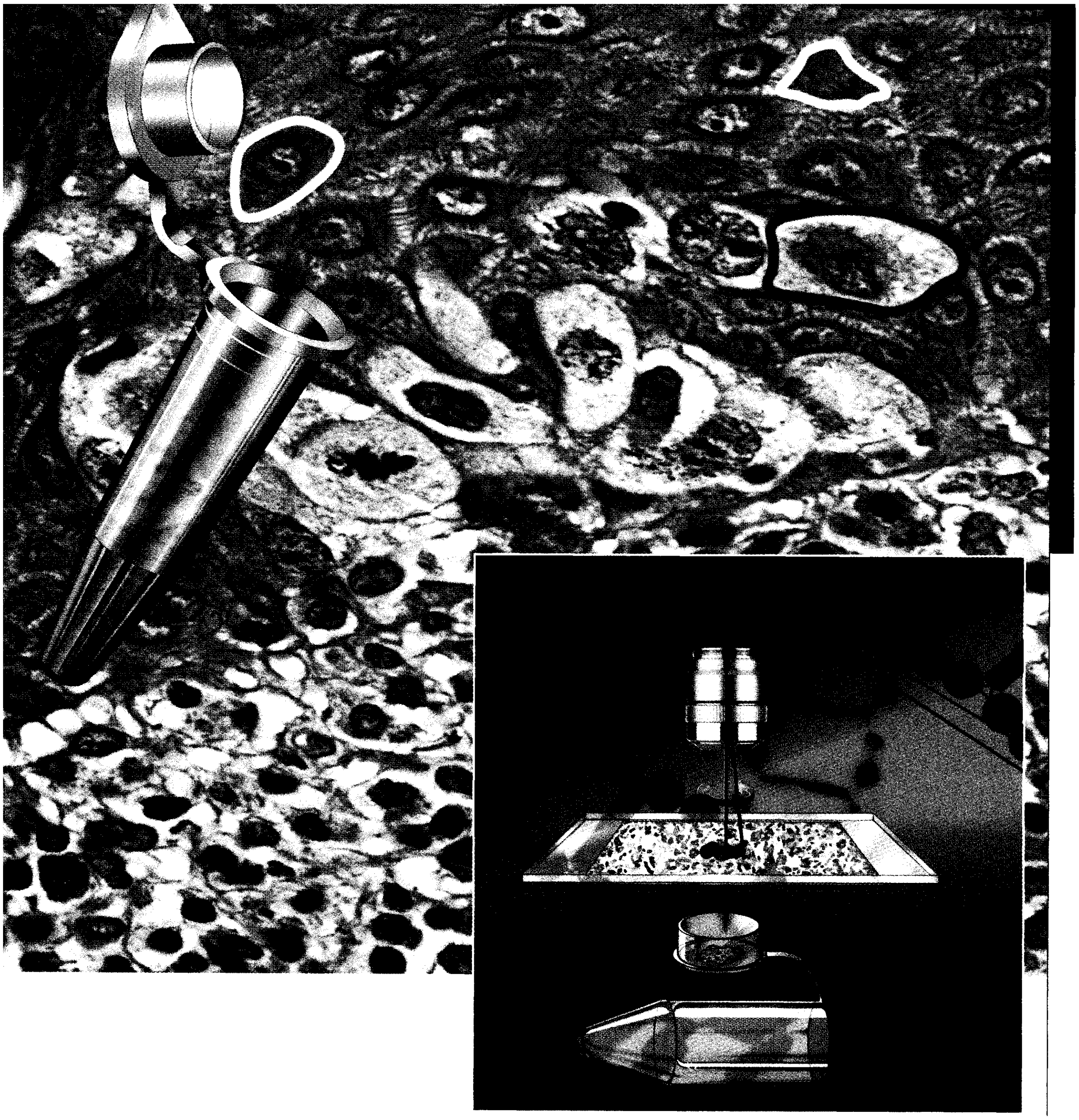

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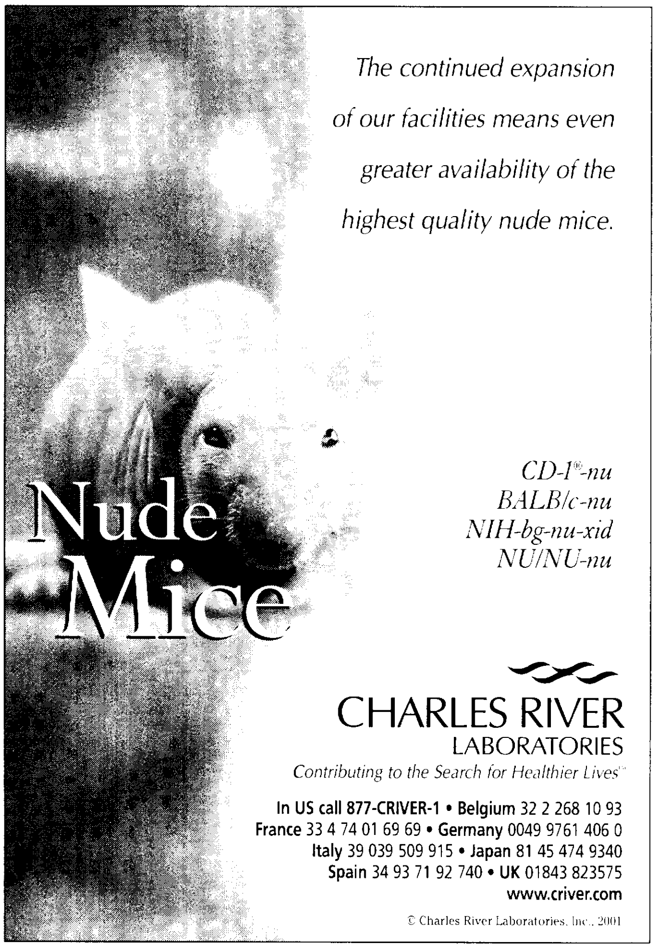
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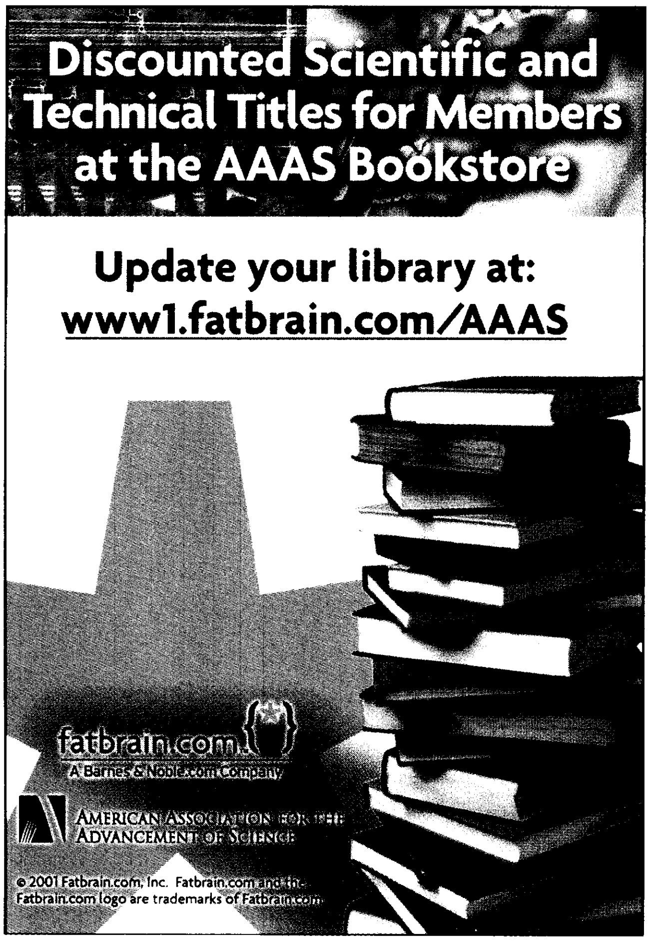
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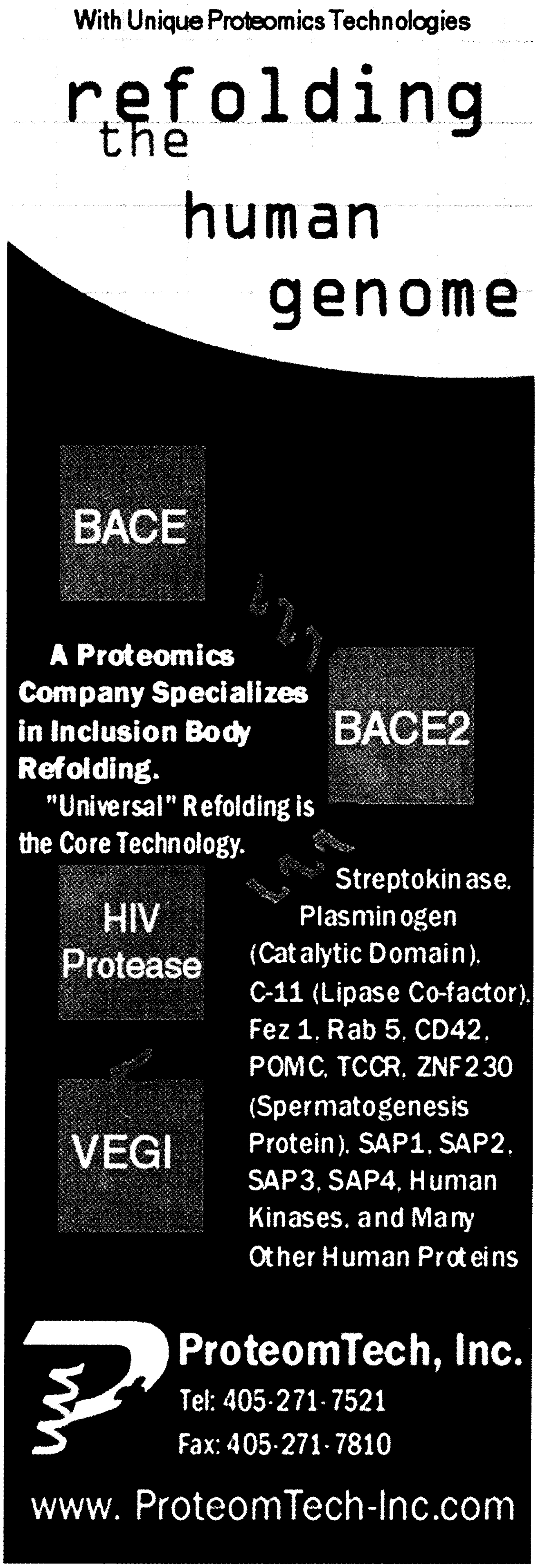
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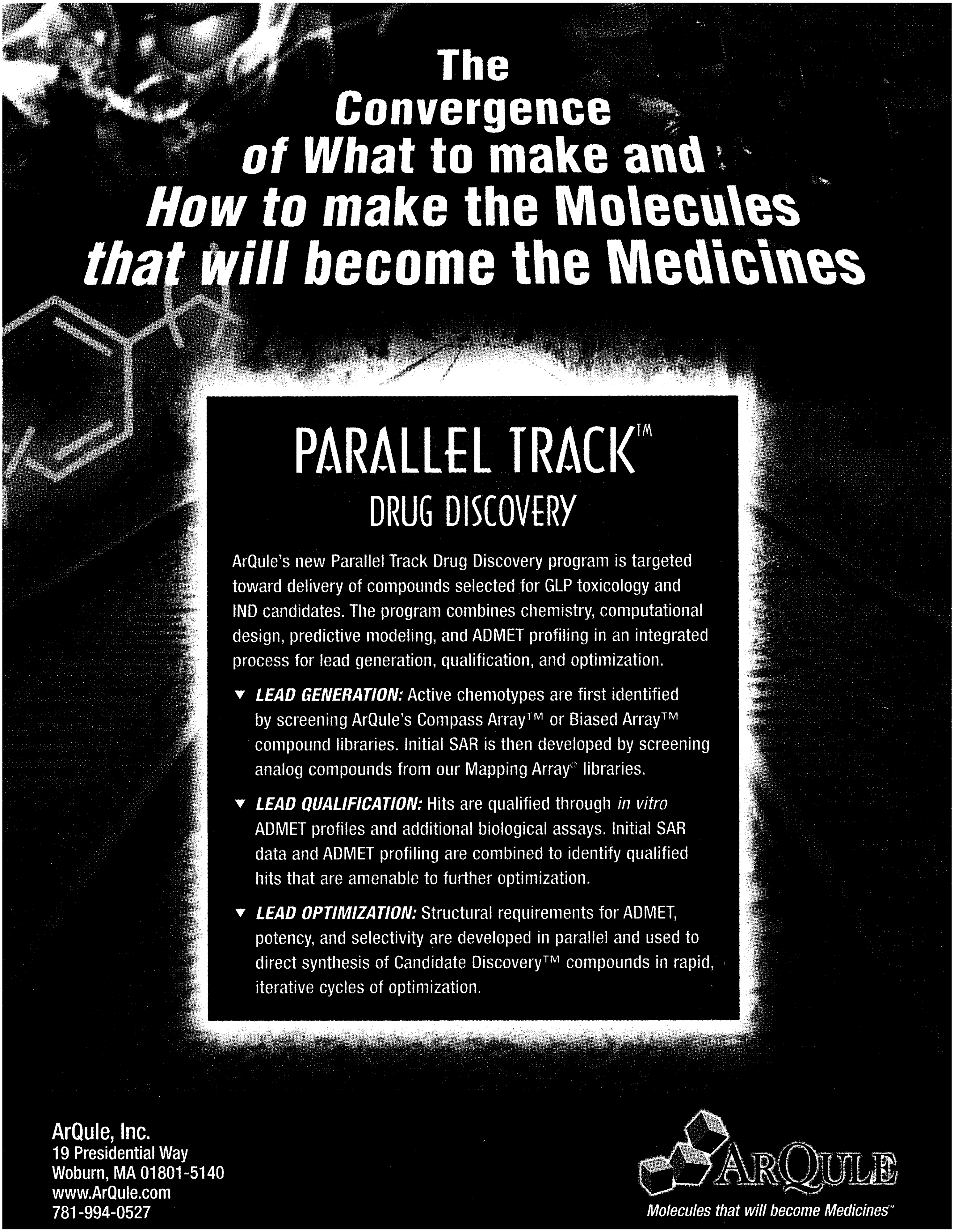

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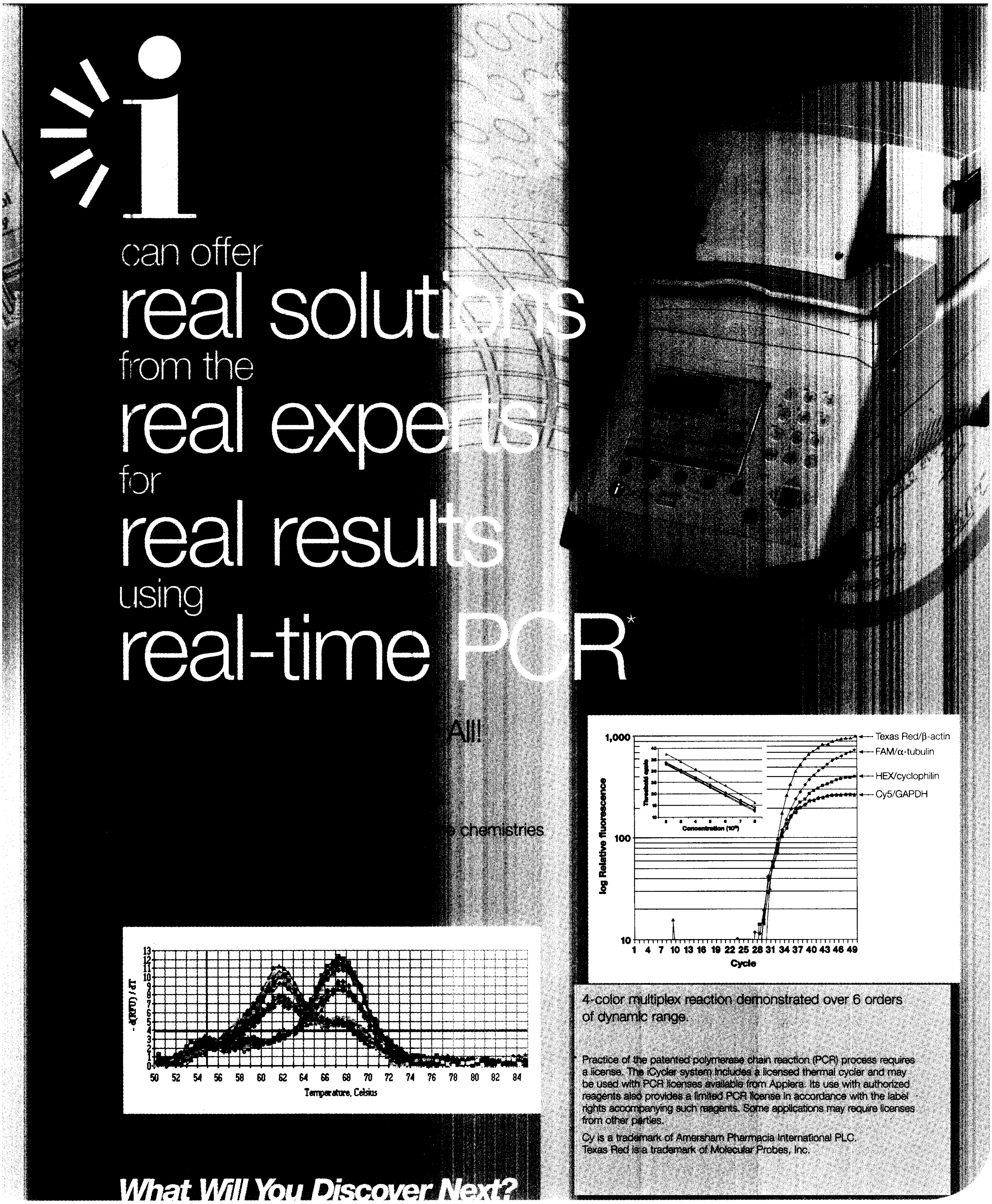
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