21 January 2000

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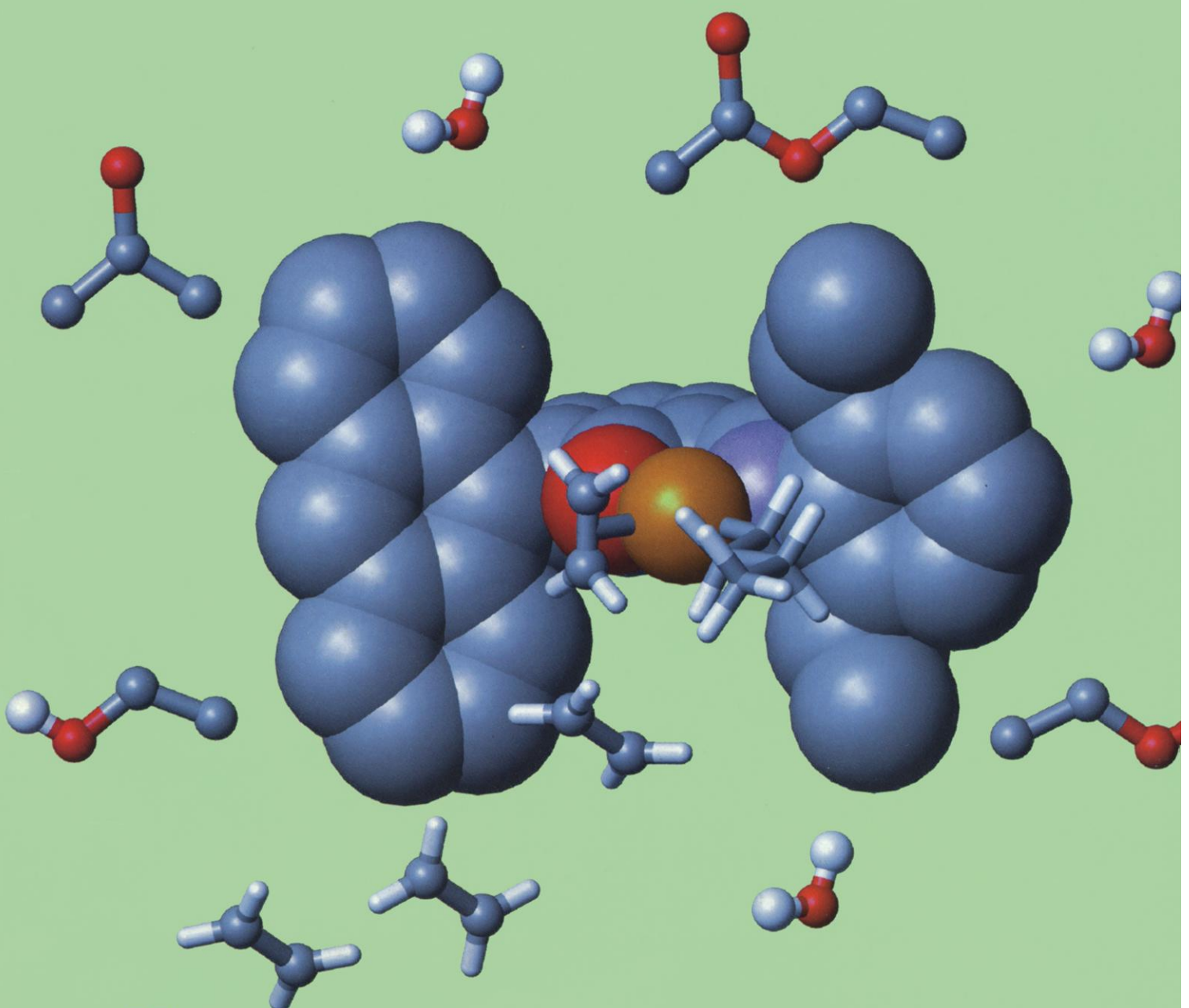

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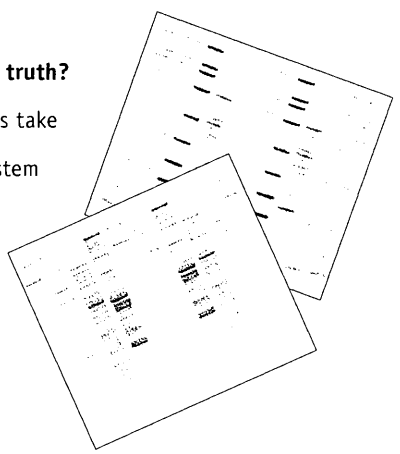

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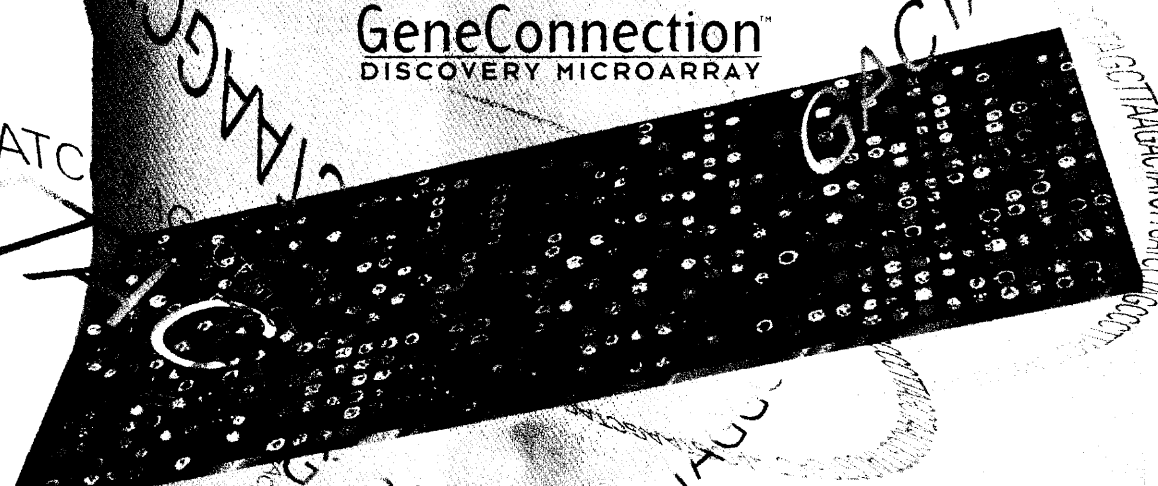

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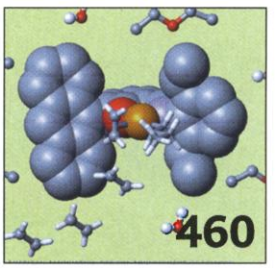
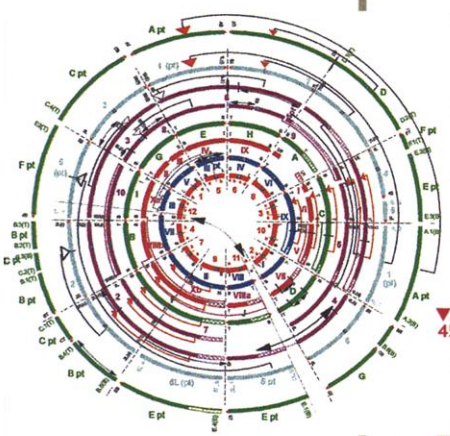


COVER Model of a neutral single-component nickel complex that polymerizes ethylene in the presence of organic functional groups that are detrimental to conventional systems. The high activity and efficiency of this neutral catalyst complex were realized through modular ligand modification. The ligand [attached through the nitrogen (purple) and oxygen (red) atoms] surrounds the metal center (orange), preventing side reactions and decomposition. [Image: T. R. Younkin, J. I. Henderson, O. A. Scherman]



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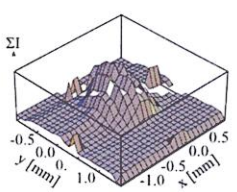

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Imaging molecular alignment

DEPARTMENTS

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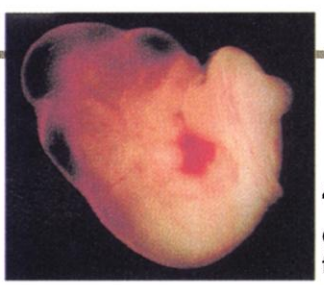
Maternal care



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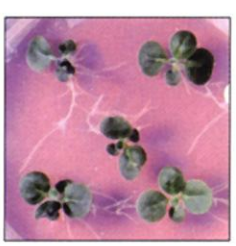

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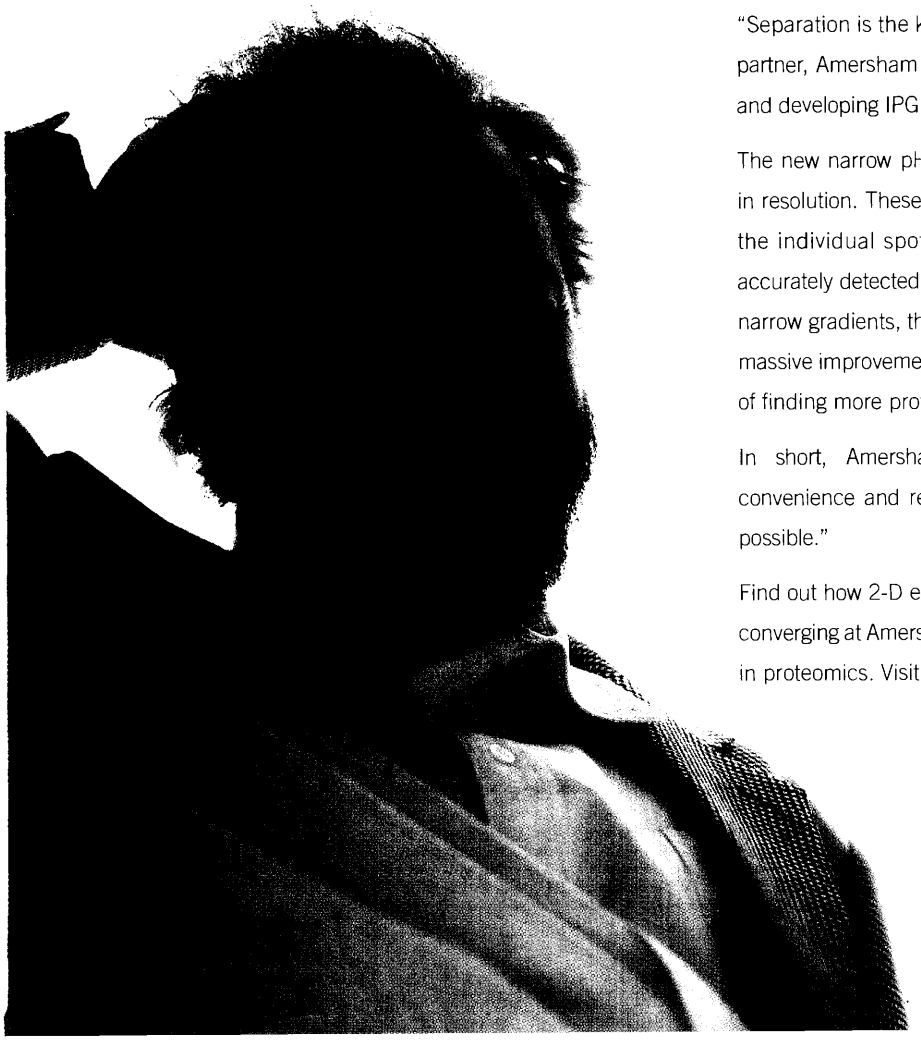

Dr. Hanno Langen, head of the proteomics group at Hoffmann-LaRoche genetics department.

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THE BIG (WOBBLY) TOP

True polar wander is thought to result from a shift of Earth's spin axis related to a major change in the distribution of mass in the mantle. In most cases, shifting paths of paleomagnetic poles are called apparent polar wander because the shifting is related to plate motions and not changes in the orientation of the axis. Sager and Koppers (p. 455; see the news story by Kerr) have found evidence for a true polar wander event in polar paths calculated for the Pacific plate in the Late Cretaceous. They suggest that about 84 million years ago Earth's rotation axis shifted at a rate of 3° to 10° per million years. This large and rapid shift is correlated in time with major plate reorganizations and a magnetic field reversal, and it may have been caused by a complete overturn of the mantle.

ROBUST POLYETHYLENE CATALYSTS

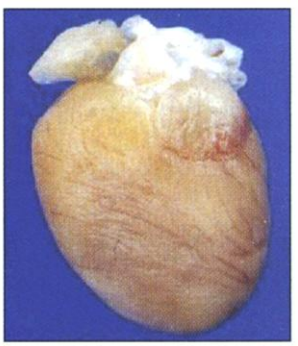
Polyolefins represent the bulk of all commercial polymers made each year, but both the traditional catalysts for Ziegler-Natta polymerization and the newer cationic metallocene catalysts are readily deactivated if "heteroatoms" such as oxygen, nitrogen, or sulfur are present or if even traces of impurities are present in the starting materials. These requirements greatly limit the incorporation of monomers with functional groups that could modify the polymer's properties. Neutral nickel catalysts, while more tolerant of functional groups, usually produce shorter oligomers. Younkin *et al.* (p. 460; see the cover and the Perspective by Jacobson and Breinbauer) now report that nickel salicylaldimine complexes form high molecular weight, linear polyethylene. These catalysts require no co-catalysts, remained active after air or water exposure, and could tolerate the presence of ethers, ketones, and esters.

GUIDING THE LIGHT

Optical circuitry requires a method for directing light just as electronics requires wires. Silica-based optical waveguides formed on a substrate via a sol-gel process and patterned by soft-lithographic techniques exhibit amplified stimulated emission (ASE, a kind of mirrorless lasing) and have the potential for incorporation into such integrated optical circuits. So far, the intensity needed for ASE has been rather high. Yang *et al.* (p. 465) show that the threshold intensity can be decreased by an order of magnitude by using mesoporous silica doped with rhodamine 6G dye. The combination of these patterned waveguides showing ASE may provide a route for one-step processing of microlaser arrays and integrated optical circuits.

A STUNNING PHENOTYPE

Myocardial stunning is a common form of heart damage that occurs when blood flow to the heart is temporarily stopped and then re-established. Murphy *et al.* (p. 488) show that a proteolytic fragment of the myofilament



protein troponin I (TnI) has a causal role in pathogenesis. Transgenic mice expressing this fragment in the heart developed the characteristic features of stunned myocardium. In addition, myocardial biopsies from coronary artery bypass patients were found to contain TnI proteolytic fragments. These results indicate that aberrant processing of contractile proteins can cause heart failure.

A COMPACT DATABASE

Quantum mechanical approaches to information storage can speed up the retrieval of specific items from a database because, unlike ordinary data bits, extra information can be encoded in the quantum bits ("qubits") as the phase difference between the two states that represent 0 and 1. For example, Grover has recently shown theoretically that a single operation on all of the items in a quantum register should be able to retrieve an entry in which the state of one qubit is "flipped." Ahn *et al.* (p. 463; see the Perspective by Knight) have stored information in N Rydberg states (N, either 6 or 8) in a beam of cesium atoms. They show that they can prepare the single-flip states and read them out with single laser pulses.

NOT YOUR USUAL MAGNETIC RESONANCE

Magnetic resonance is normally induced with magnetic fields and radio frequency pulses, but in semiconductors optical pumping or detection of magnetic resonance has been achieved. Kikkawa and Awschalom (p. 473) now report on the creation and detection of magnetic resonance in gallium arsenide through an all-optical route. Circularly polarized light created electron spins that interacted with nuclear spins through hyperfine interactions. Optical pumping induced local magnetic fields up to 0.4 Tesla in a period of 250 seconds, which is a relatively long time scale for electronic processes and more typical of nuclear spin polarization. Resonant depolarization was observed that corresponded to gallium-69 but was also observed at a frequency that did not correspond to any nuclear moment present in the sample, which suggests that the phenomena observed may be more complex.

HISTONE ACETYLATION AND V(D)J RECOMBINATION

In thymocytes, recombination of the V(D)J gene segments of the T cell receptor (TCR) is developmentally regulated. What signals this developmental change? It appears that chromatin structure plays a role in changing the accessibility of recombination signal sequences to the recombinase, but the identity of the particular chomatin modification that functions in this case has been unknown. McMurry and Krangel (p. 495; see the Perspective by Schissel) examined a transgenic human V(D)J recombination reporter construct and an endogenous mouse TCR α/δ locus, and they show that acetylation of histone H3 provides this chromatin modification. Regions displaying H3 hyperacetylation corresponded with those displaying accessibility to recombinase. Thus, histone acetylation is linked to V(D)J recombination.

TREATING ROTAVIRUS INFECTIONS

Although rotavirus-induced diarrhea kills nearly 1 million children each year in developing countries, the mechanism of pathogenesis has not been clear. Lundgren *et al.* (p. 491; see the news story by Winkelgren) have evidence that the enteric nervous system is responsible for changes in the intestinal secretory response (potential differences across the epithelium and fluid transport) that results from rotavirus infection. They test-

CONTINUED ON PAGE 391

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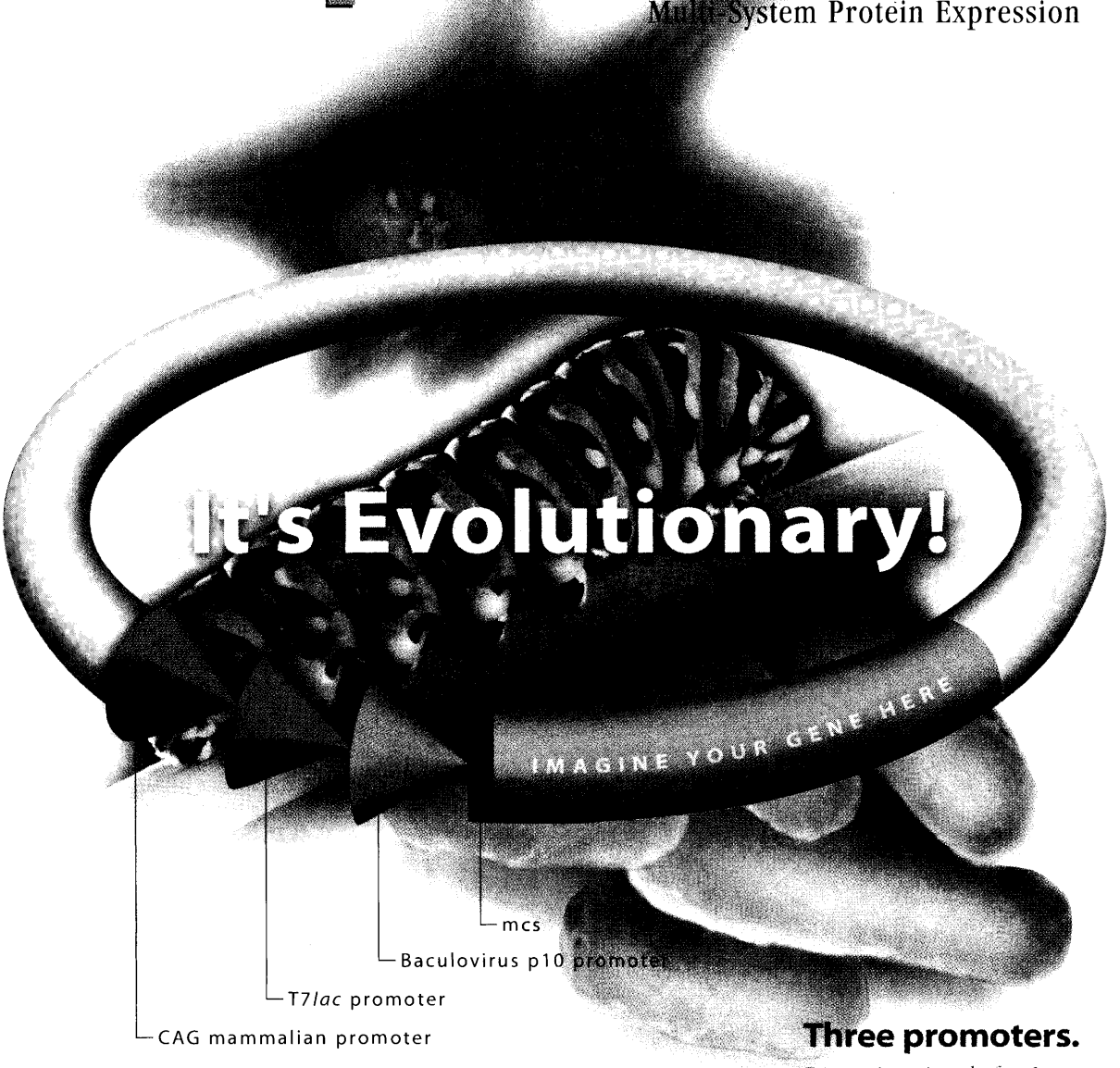

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 389

ed drugs known to act specifically on the nervous system and found that the local anesthetic lidocaine could decrease diarrhea in live baby mice if they were treated after infection.

PAYING FOR TOO MUCH COMPLEMENT

A developing embryo is at the mercy of the natural and specific immune systems of the mother. Because the complement system is designed to lyse cells and to alert phagocytes to the presence of intruders, it may well be that the system needs to be regulated closely so that the embryo can survive. Lack of regulation of the complement system in humans can lead to chronic inflammatory conditions. Xu *et al.* (p. 498; see the news story by Hagmann) report that the loss of the Crry protein, a major complement inhibitor in the mouse, leads to complete inability of embryos to survive to birth caused by spontaneous complement activation and the subsequent inflammatory infiltration. Regulation of complement is thus critical for prevention of the destruction of embryos in the maternal environment.

MOONLIGHTING ENZYMES

The existence of a one-to-one correspondence of specific amino acid "charging" activity to aminoacyl transfer RNA (tRNA) synthetase enzyme (which is responsible for aminoacylating a respective tRNA molecule) has been thought to be an essential element of accurate protein synthesis. However, the complete genome sequences of two thermophilic methanogenic archaea failed to identify genes for cysteinyl-tRNA synthetase. Stathopoulos *et al.* (p. 479; see the Perspective by Yarus) now show that, in *Methanbacterium thermoautotrophicum* and *M. jannaschii*, proline aminoacyl tRNA synthetase is endowed with dual functionality during protein synthesis in which the enzyme can specifically charge the tRNAs for proline and cysteine with their respective amino acids.

FIGHTING STOMACH ACID

The bacteria *Helicobacter pylori* (associated with gastritis, ulcers, and stomach cancer) has had to adapt to the acidity of the stomach, which acts as a defense against many pathogens. It survives low pH from gastric acids by using a urease to produce ammonia. The activity of urease depends on UreI, which Weeks *et al.* (p. 482) show is a proton-gated urea channel that lets urea into the cell at low pH for generation of ammonia.

BEATING THE HEAT (AND THE COLD)

Many plant varieties can adapt to colder or warmer climes. By limiting expression of a desaturase enzyme through antisense technology, Murakami *et al.* (p. 476; see the Perspective by Sharkey) have demonstrated that the ability of the tobacco plant to tolerate higher growing temperatures is limited by their trienoic fatty acid content. The effect is particular to the fatty acids of the chloroplast membranes. Trienoic fatty acids, already correlated with cold-tolerant plants, may alter critical membrane characteristics.

TECHNICAL COMMENT SUMMARIES

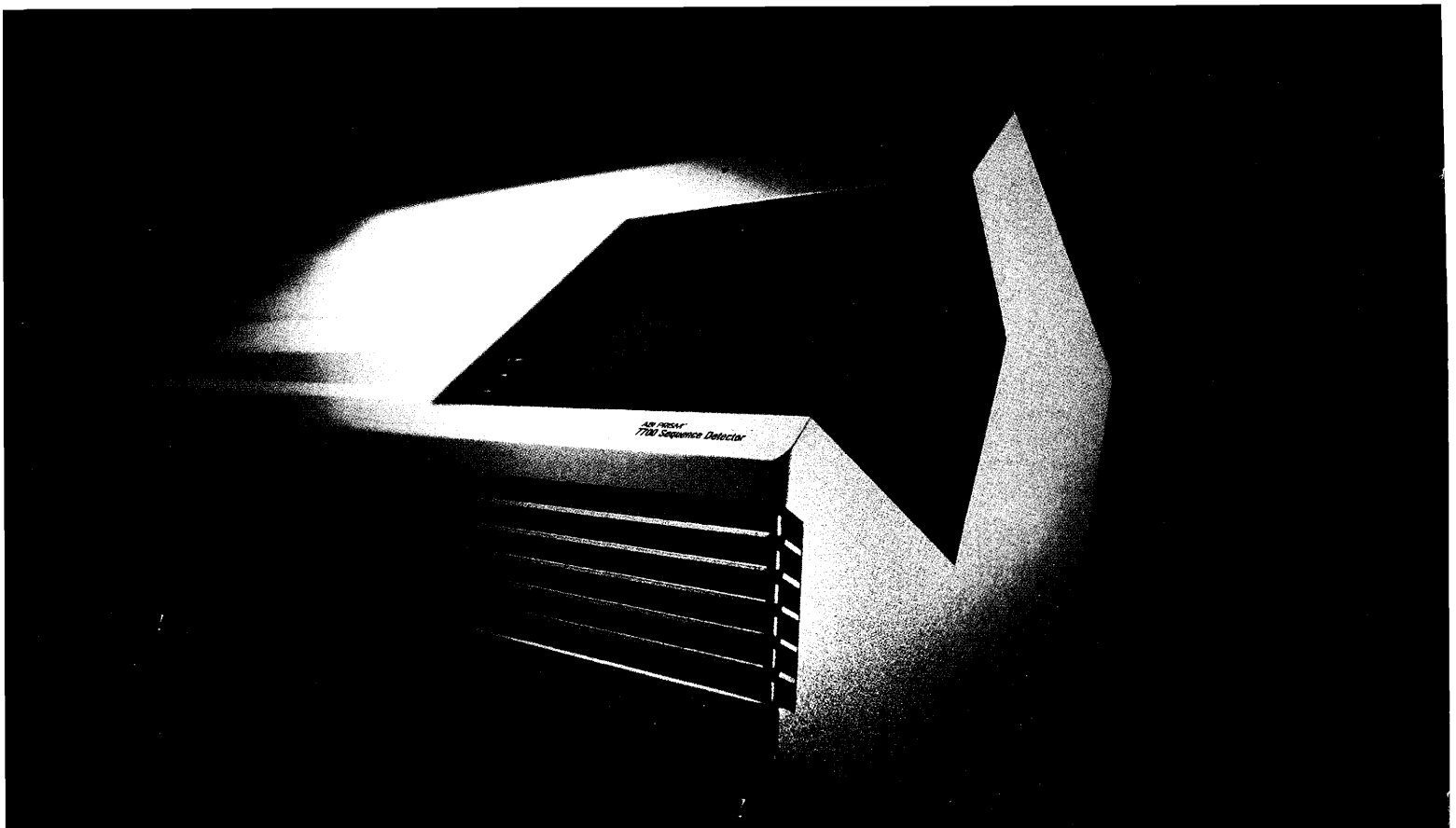
Activation and Inhibition of the *Staphylococcus agr* System

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full//287/5452/391a

Balaban *et al.* (Reports, 17 Apr., p. 438) showed results which suggested that immunization with RNAIII activating protein (RAP) can inhibit *Staphylococcus aureus* infection in mice and that treatment with a RAP-derived linear heptapeptide can likewise suppress infection. Both the RAP antibodies and the peptide presumably inhibit activation of virulence genes at the *agr* locus, the encoding locus of RNAIII; however, Balaban *et al.* found that RAP purified from an *agr*-null *S. aureus* strain was equally protective relative to RAP purified from wild-type *S. aureus*. This result implied that RAP is independent of *agr*.

Novick *et al.* comment that they were unable to produce *agr*-activating supernatants from *agr*-null strains of *S. aureus*, despite repeated attempts, and conclude that *agr* activation or inhibition activity is more likely tied to autoinducing peptides than to RAP or its derived peptide.

In response, Balaban *et al.* attribute the different results to different purification procedures used by Novick *et al.* (which, Balaban *et al.* suggest, may not have taken adequate account of RAP's sensitivity to boiling), and reiterate their view that RAP uses a different signal transduction pathway to regulate RNAIII synthesis.



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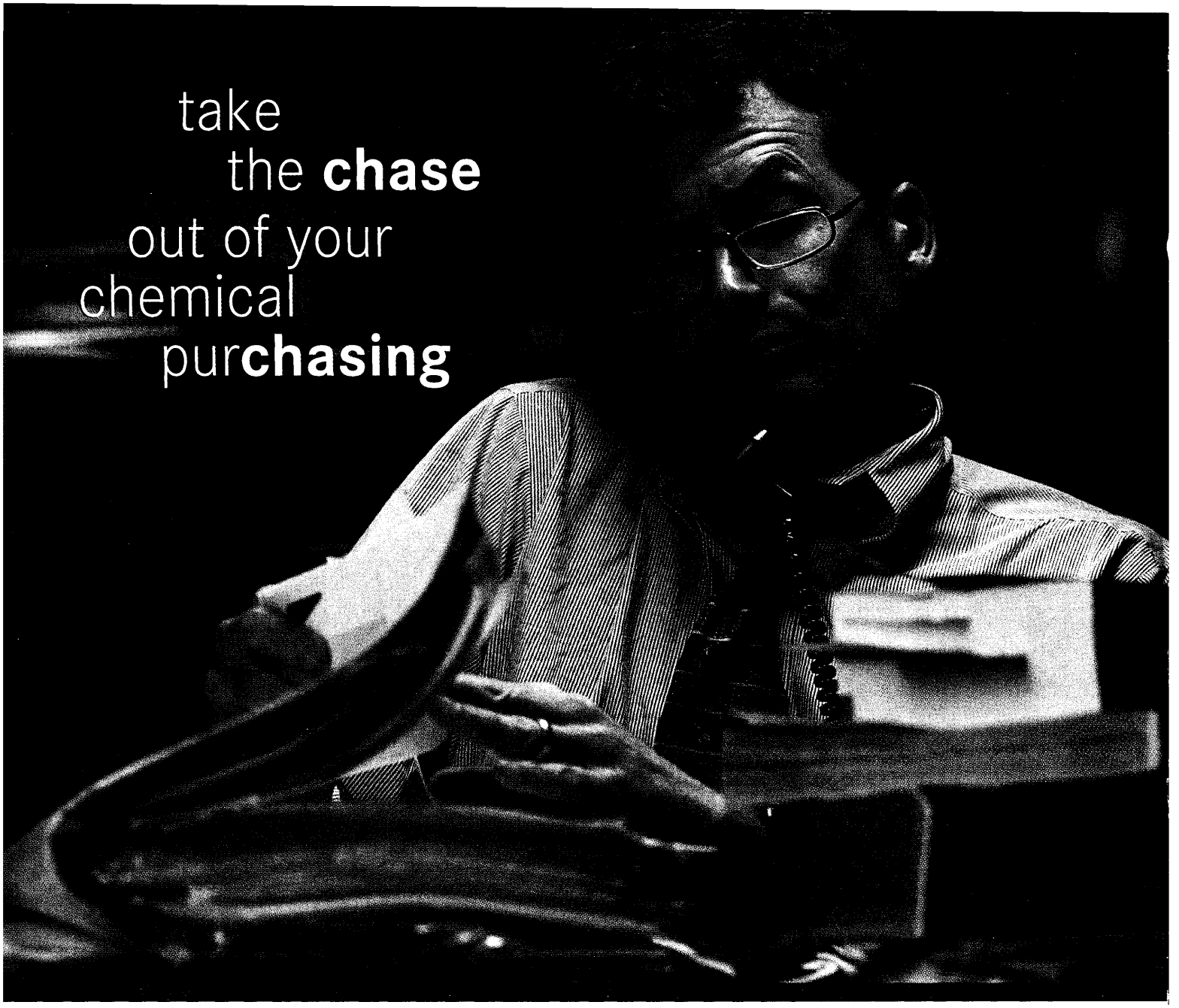

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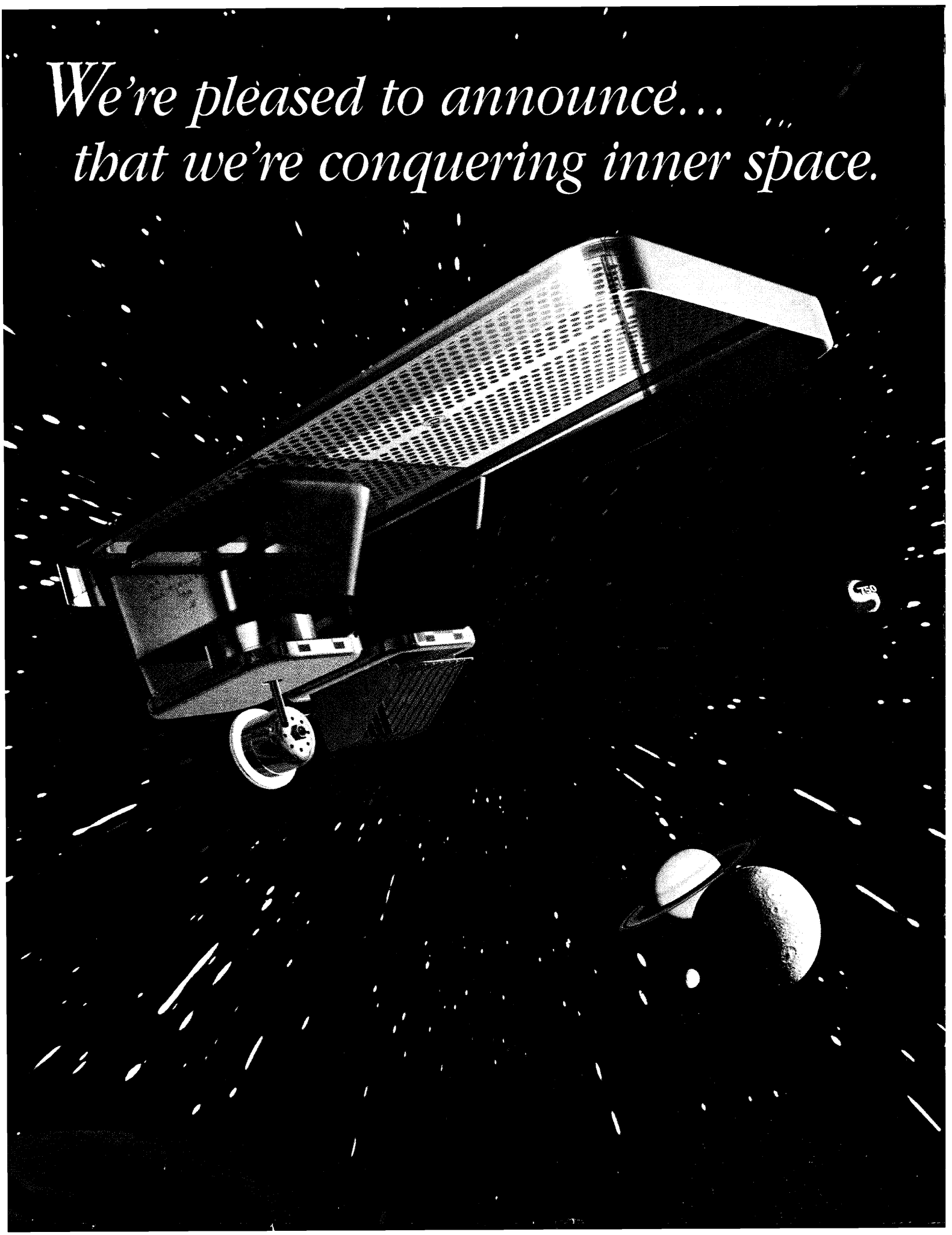

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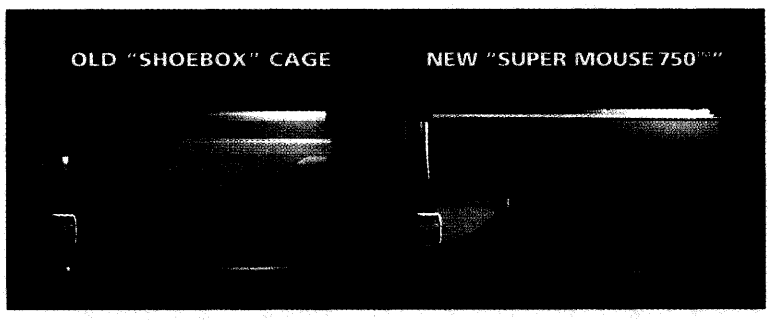

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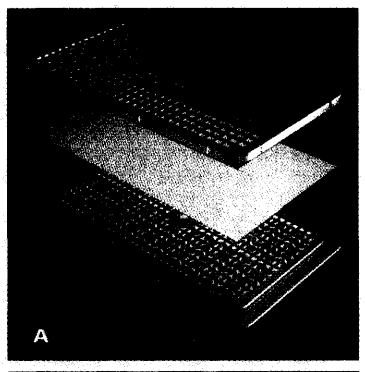

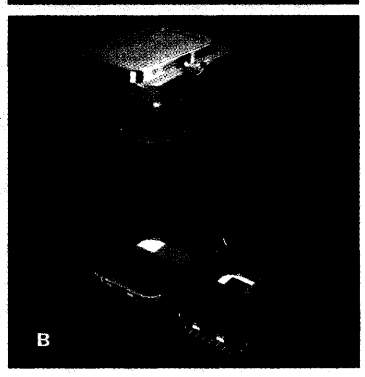

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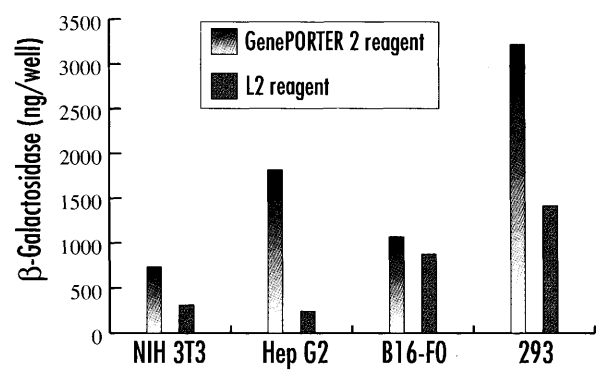

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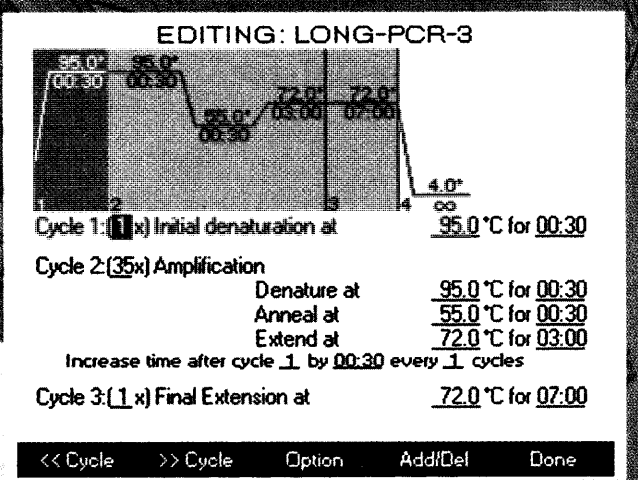

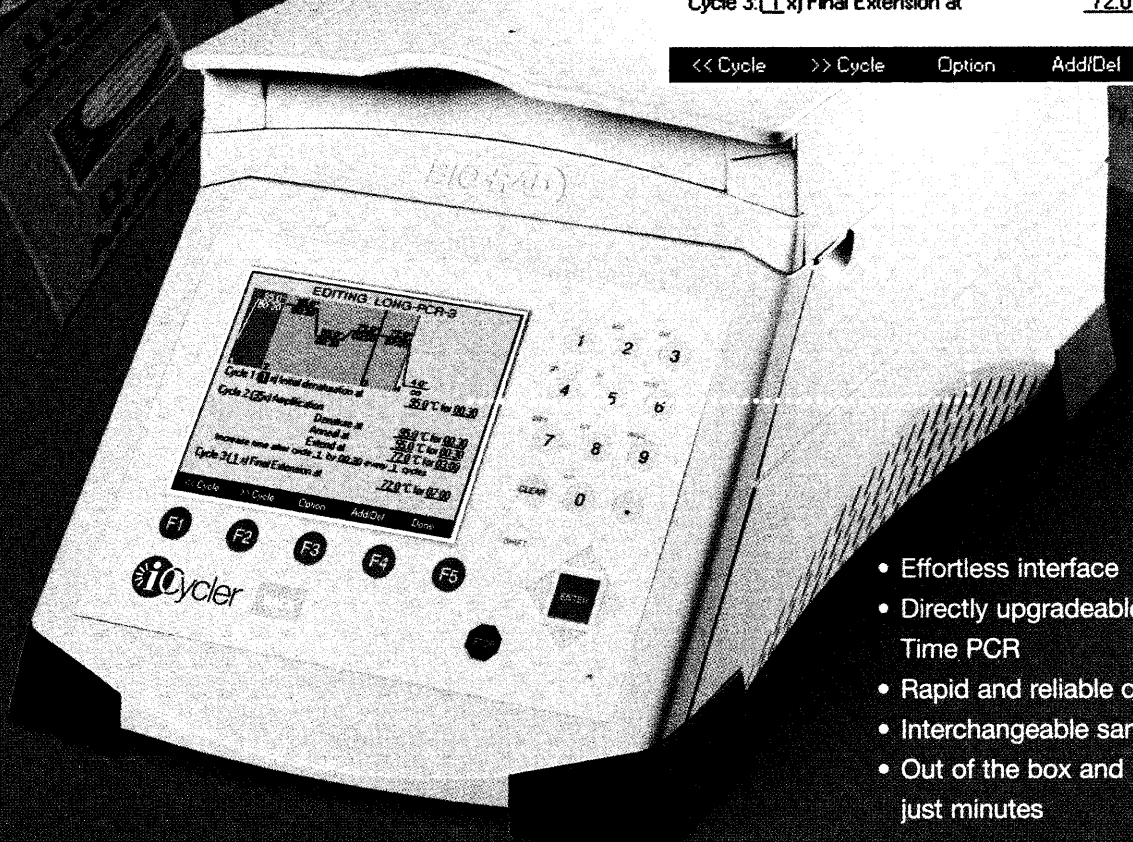

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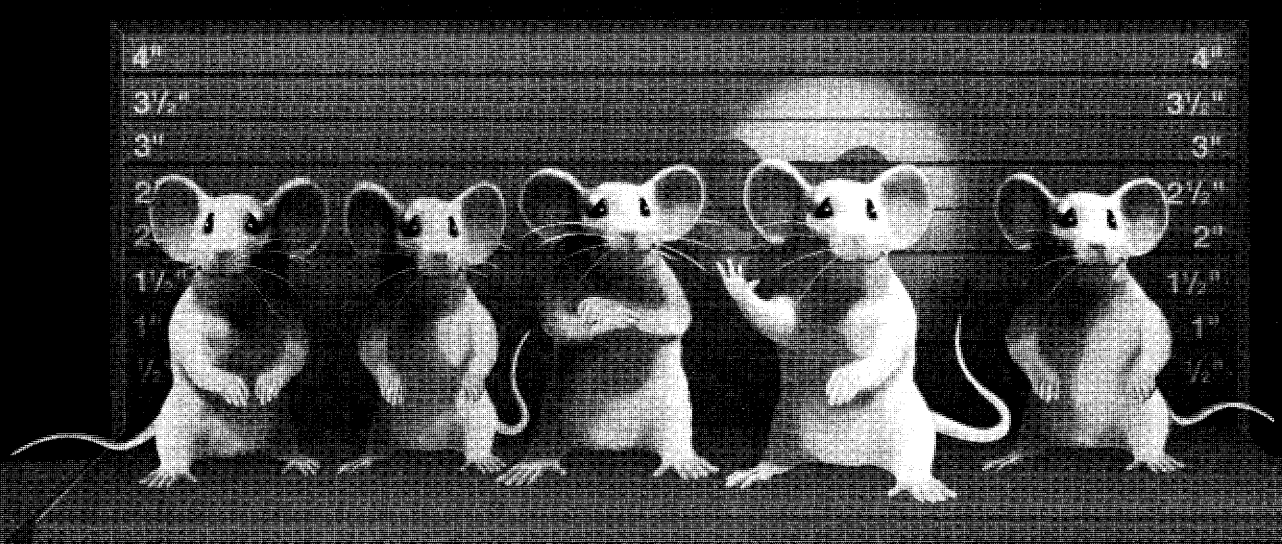

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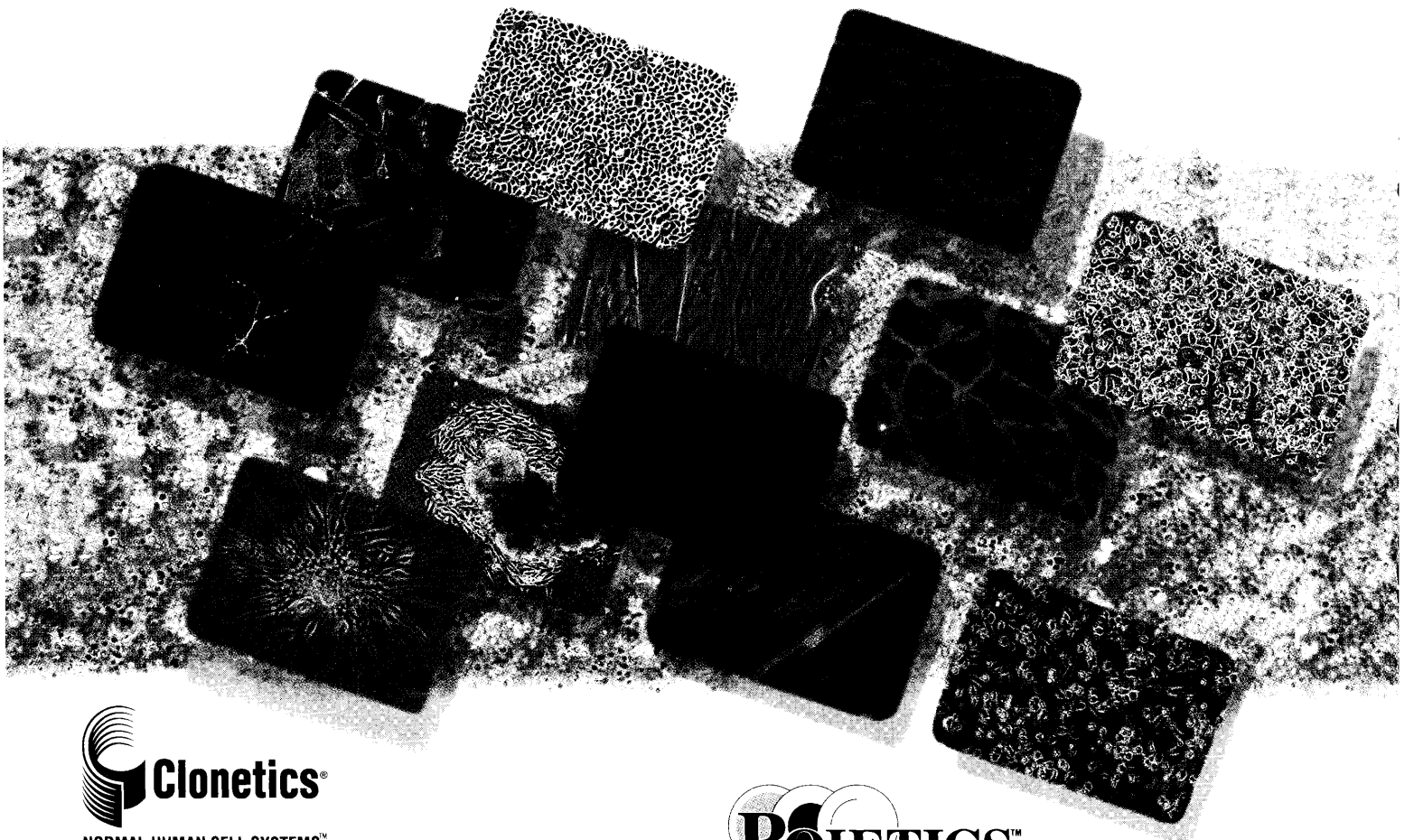

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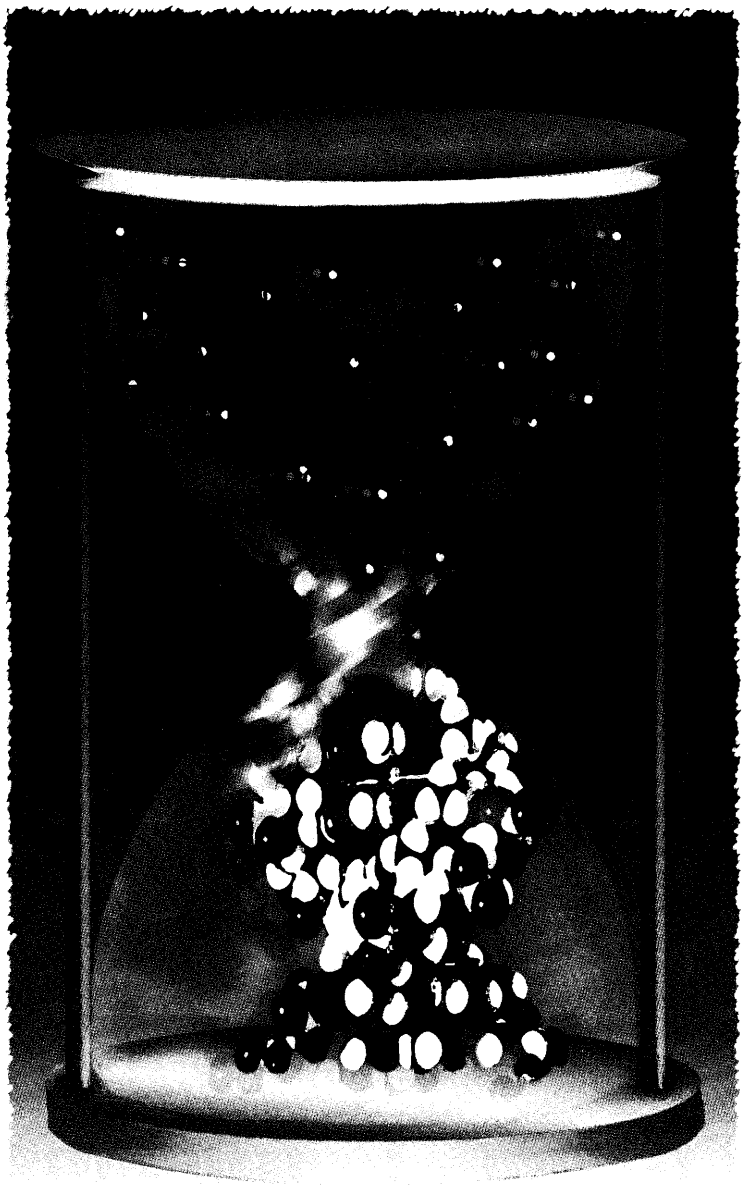

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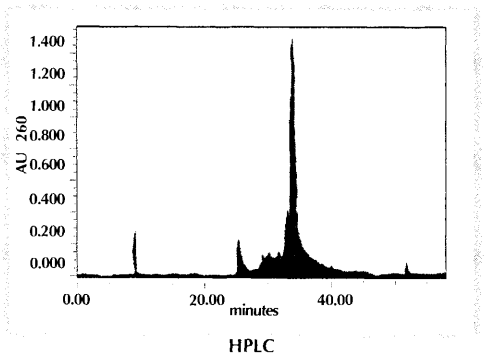

HPLC

Figure 2

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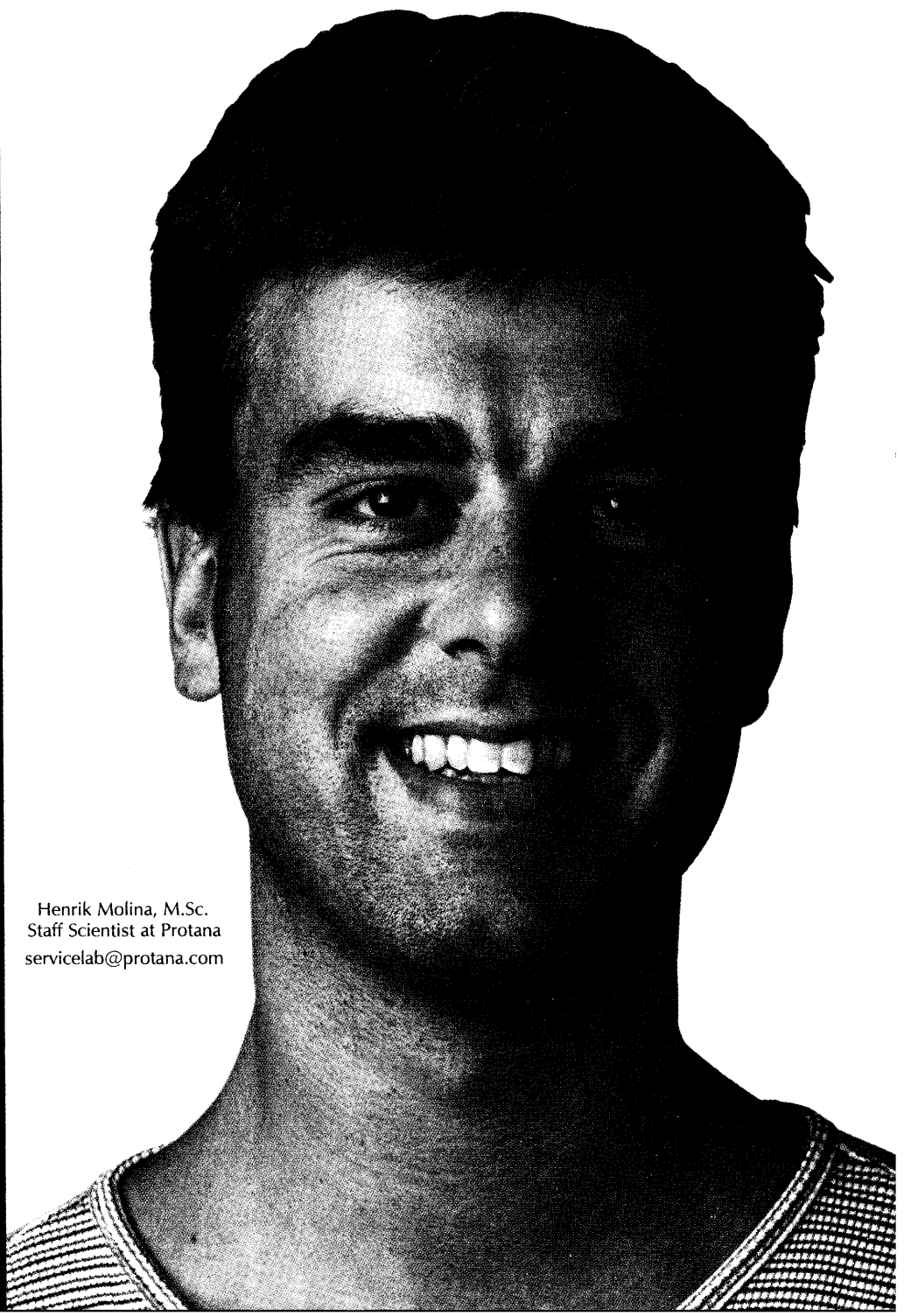

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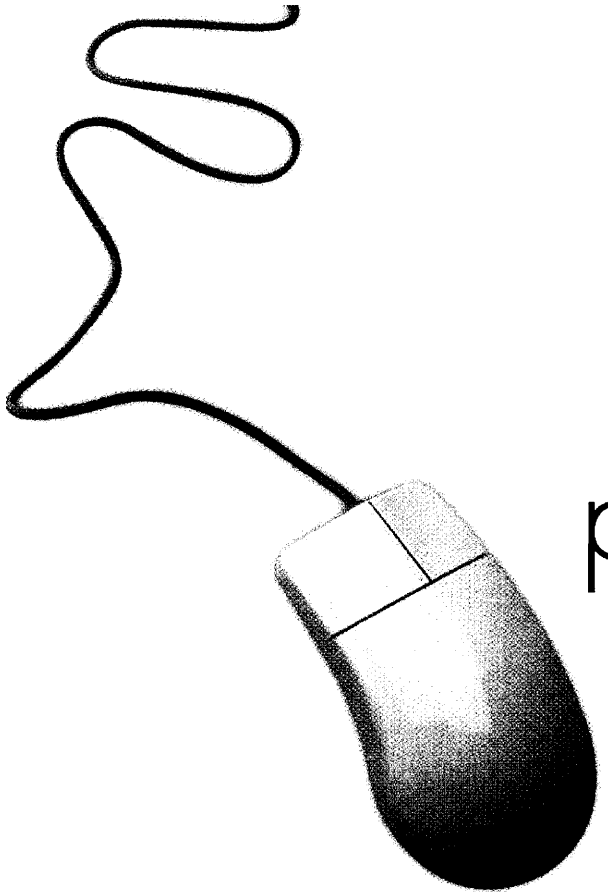

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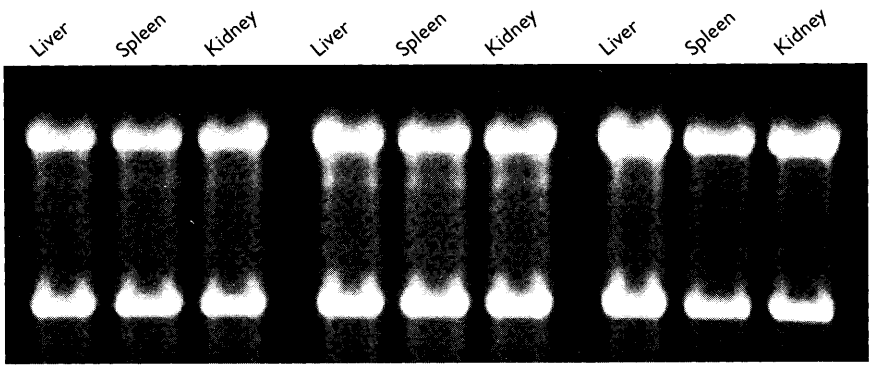

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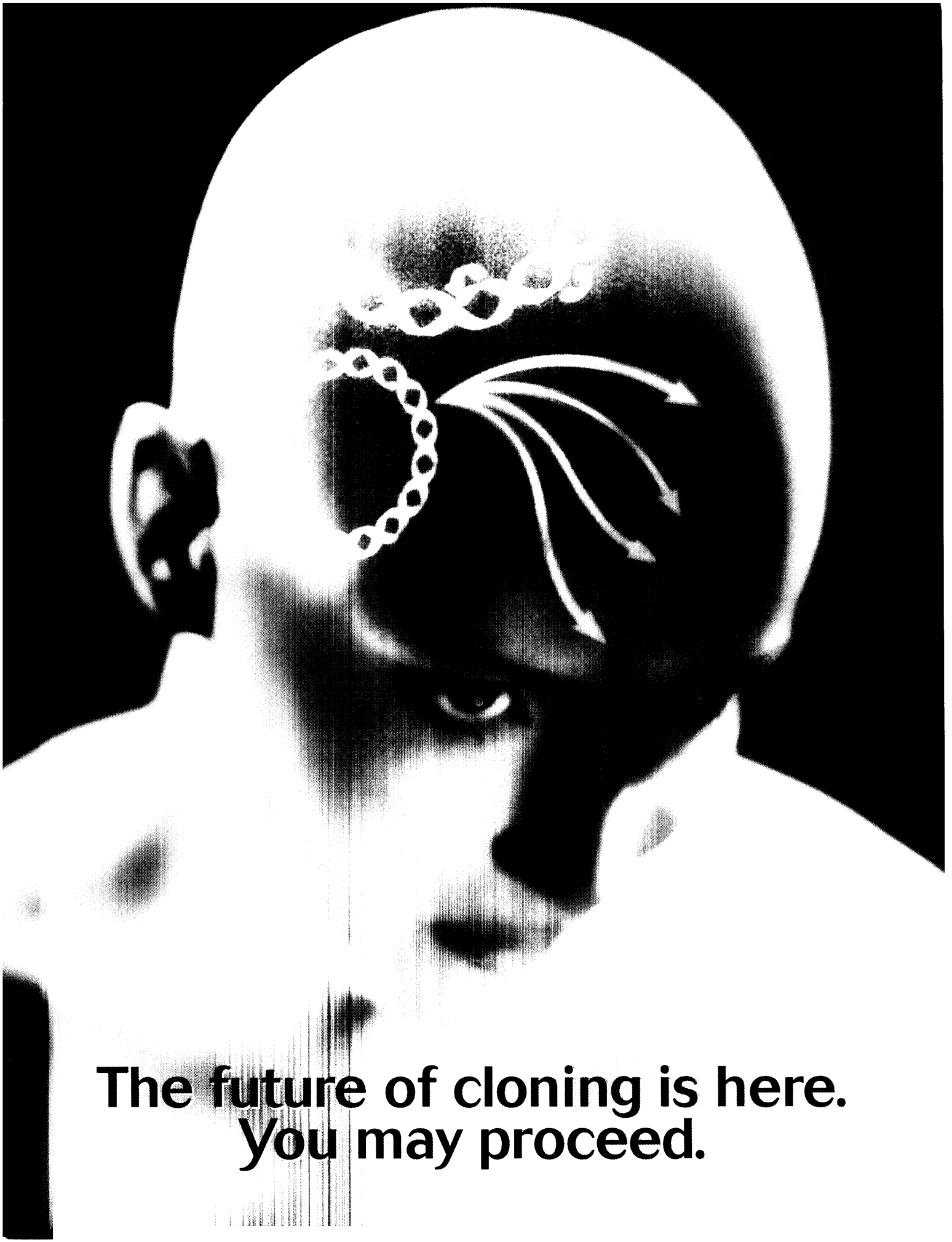

The future of cloning is here.
You may proceed.

The Echo™ Cloning System. Rapidly Clone Your Gene into Multiple Expression Vectors—Without Subcloning.

Cloning to Analysis—Fast. In the future, there will be a fast, efficient way to get from gene cloning to gene analysis without subcloning. Guess what? The future is here and it's the Echo™ Cloning System. Now you can clone your gene into as many expression vectors as you choose and:

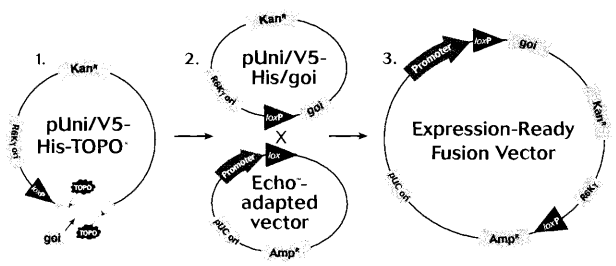
- *Save hours by eliminating repetitive cloning and sequencing*
- *Get the expression results you need by testing expression in multiple systems*
- *Experience flexibility by easily Echo™-adapting your favorite expression vector for use in the system*

The Key to the Future. The key to the Echo™ Cloning System is the donor vector pUni/V5-His-TOPO®. In minutes you can create a universal donor construct that contains your gene of interest. pUni/V5-His-TOPO® incorporates Invitrogen's patented TOPO® Cloning technologies to allow simple, 5-minute, bench-top cloning of your *Taq*-amplified PCR product. With TOPO® cloning you:

- *Save time–there's no need for post-PCR modifications*
- *Save money–extra primer sequences are not required*
- *Get great results–≥95% cloning efficiency*

Unlock the Power. Now you're ready to unlock the power of the Echo™ Cloning System. With your donor vector construct, you can recombine or "Echo" your gene into an unlimited number of expression vectors.

Figure 1 Rapid Cloning of the Gene of Interest Using the Echo™ Cloning System



1. PCR amplify and TOPO® Clone your gene of interest (goi).
2. Incubate pUni/V5-His containing your goi with an Echo™-adapted expression vector in the presence of Cre recombinase.
3. Your recombinant vector is ready for expression.

In the Future, There's No Subcloning. With your donor construct and an Echo™-adapted expression vector in hand, an expression-ready plasmid is just minutes away. Echo™-adapted expression vectors contain a *lox* site for directional, Cre recombinase-mediated recombination (Figure 1). Vectors are currently available for expression and characterization in a broad range of the most advanced bacterial, yeast, insect, and mammalian systems (Table 1). Without ever subcloning, your gene is ready for expression.

Table 1 Echo™-Adapted Expression Vectors

	Echo™-Adapted Vector	Advantage
E. coli	pBAD/Thio-E	Tightly-regulated expression
	pCR® T7-E	High-level, inducible expression
YEAST	pYES2.1-E	High-level, regulated expression in *Saccharomyces cerevisiae*
	pYC2-E	Regulated expression in *S. cerevisiae* from a low-copy number plasmid
INSECT	pIB-E	Stable expression with the InsectSelect™ System
	pBlueBac4.5-E	High-level expression with the MaxBac® Baculovirus Expression System
MAMMALIAN	pcDNA3.1-E	Strong, constitutive expression
	pcDNA4/HisMax-E	QBI SP163-enhanced expression from the CMV promoter
	pIND-E	Tightly-regulated expression in the Ecdysone-Inducible Mammalian Expression System
	pcDNA4/TO-E	High-level induced expression in the T-REx™ System

Think About the Future. The Echo™ Cloning System is the future of cloning. No more time-consuming subcloning strategies or restriction digests. No more repetitive cloning. Clone your gene in five minutes, recombine it into as many expression vectors as you want, and get the expression results you need. The next time you need to clone a gene into an expression vector, stop and think about the future. Then call Invitrogen.

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1600 Faraday Avenue • Carlsbad, California 92008 • Tel: 1-800-955-6288 • Fax: 760-603-7201 • Email: tech_service@invitrogen.com • www.invitrogen.com

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P.O. Box 2312
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