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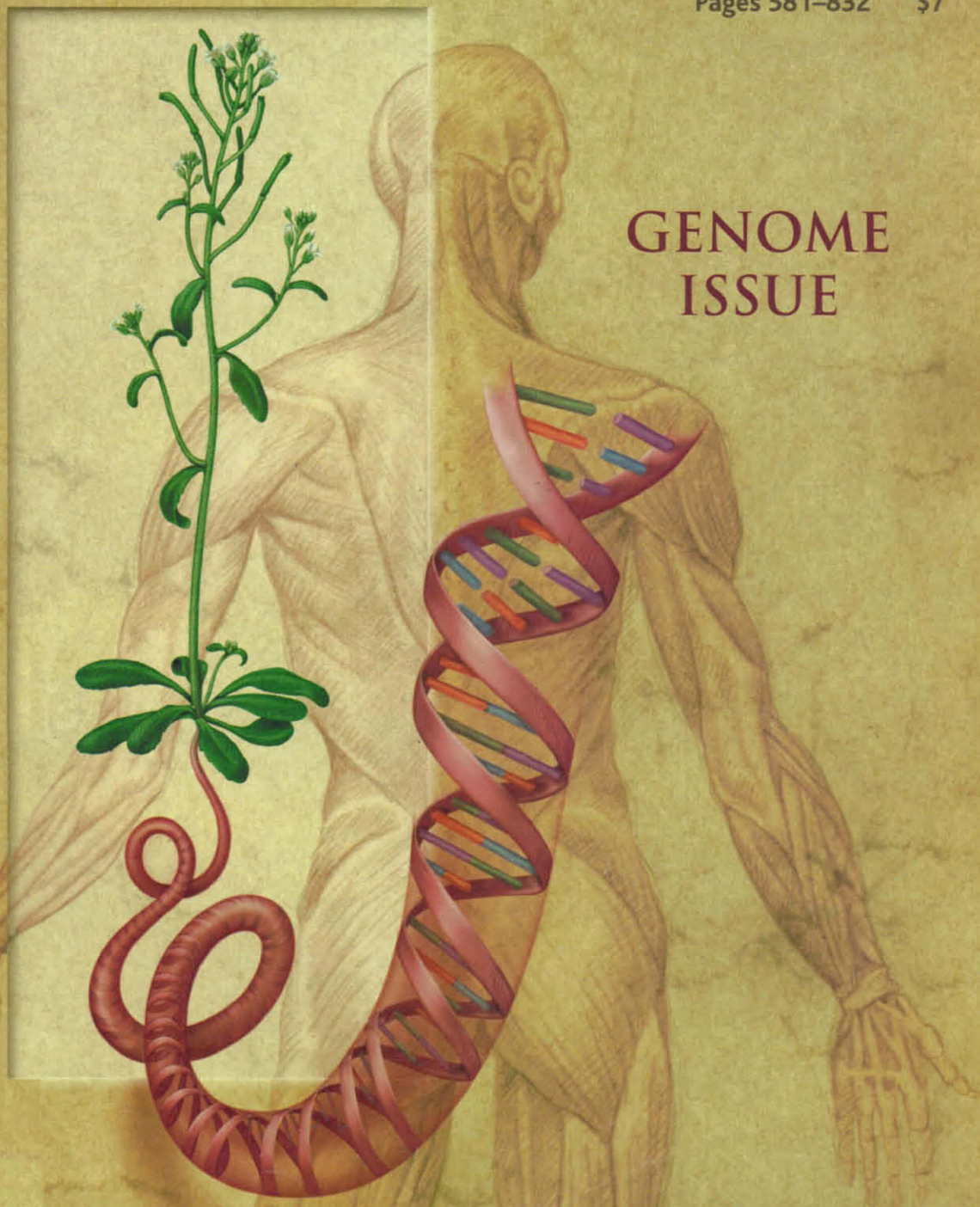

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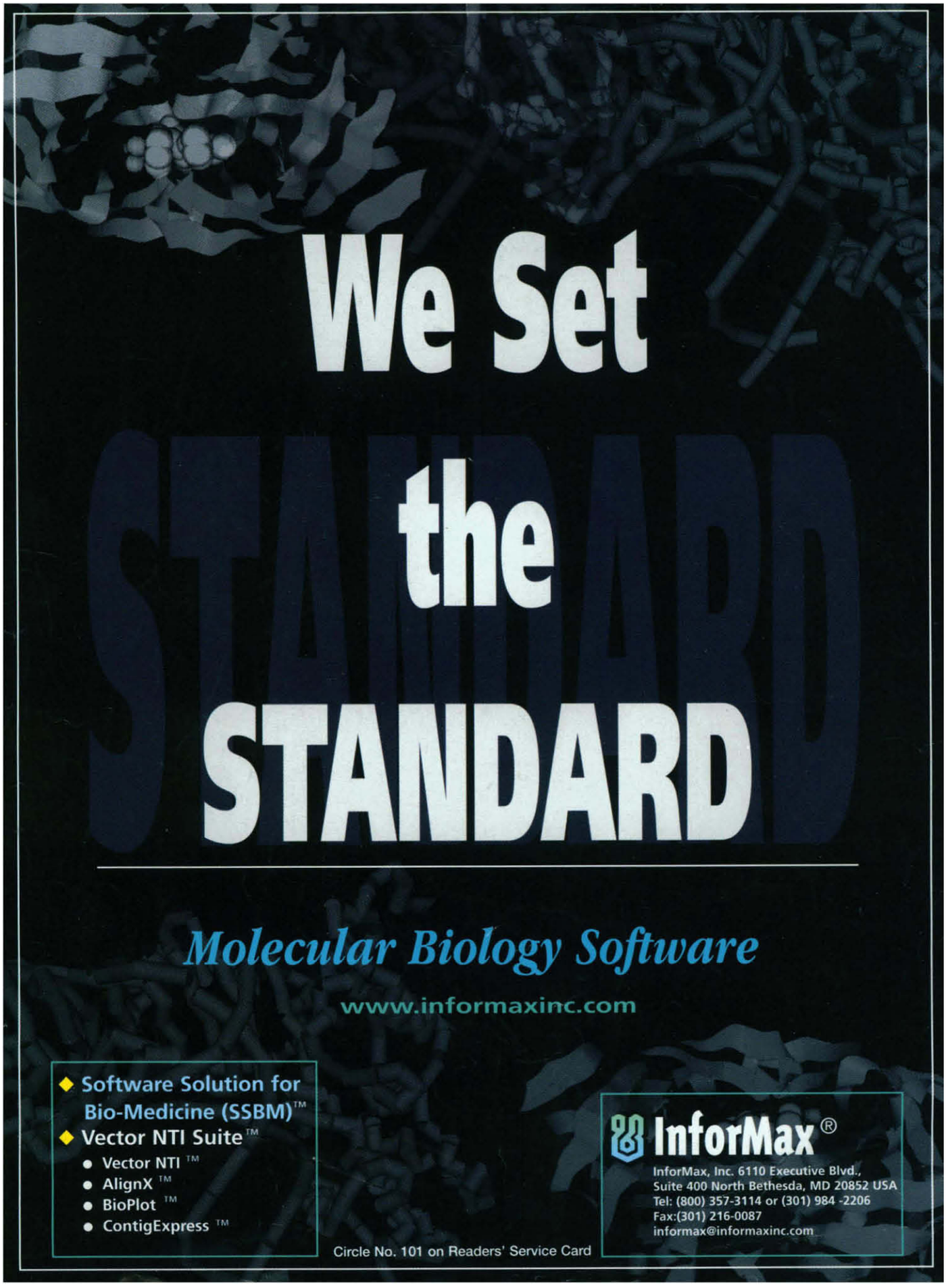
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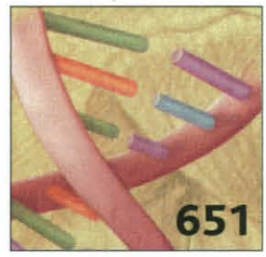

Cover The cover illustrates both the diversity and commonality in living organisms that genome analysis is revealing. The special section (beginning on p. 651) and several related items in this issue highlight progress and look at the future in understanding and using genomic information from a variety of organisms. This year's chart describes advances in the analysis of the genome of the flowering plant *Arabidopis thaliana*. [Illustration: Katherine Sutliff]

NEWS

RESEARCH

See related News story on p. 608, Editorial on p. 625, Perspective on p. 638, Research Article on p. 699, and Reports on pp. 744 and 754.

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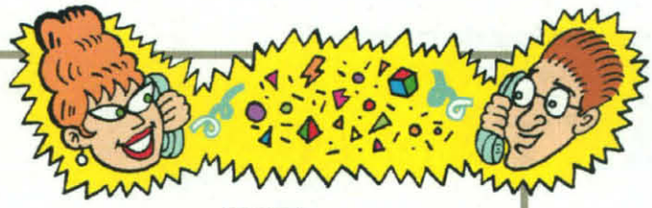

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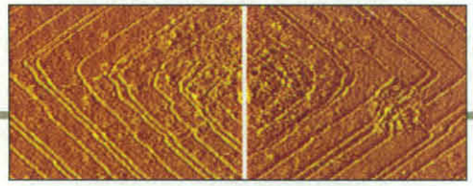
From Pasadena to Albuquerque by light beam



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Stepped growth of calcite straightened out

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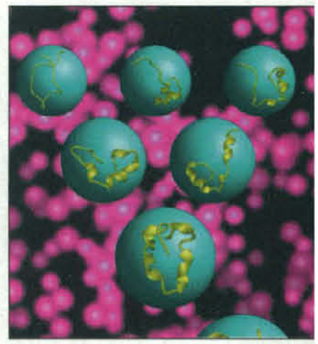

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When a microsecond is a long time

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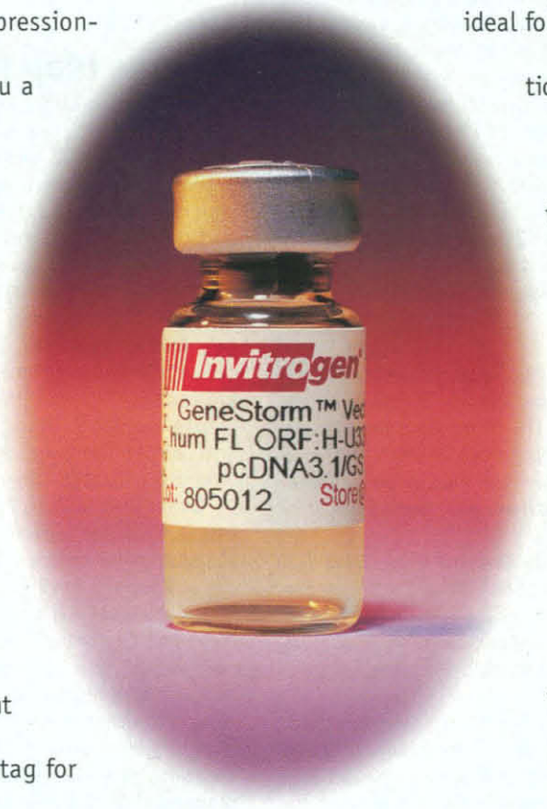

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TRULY TELEPORTED

Quantum states can be correlated at a distance. This effect, called entanglement, is one of the fundamental ways in which the quantum realm differs from the classical. Furusawa *et al.* (p. 706; see the Perspective by Caves) report that continuous quantum variables, in this case the amplitude and phase of an optical field, can be teleported (sent by classical channels) between a sending and receiving station. The signal enters and leaves the sending and receiving stations independently through a third system and is not destroyed in the measurement process. Without entanglement, the fidelity of transmission did not exceed 50%; with the use of entangled states, the authors achieve a fidelity of 58%.

CORE-MANTLE BOUNDARY ANOMALIES

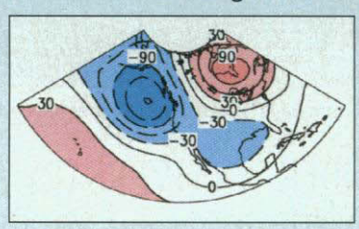
Some mixing occurs between the iron-rich liquid outer core and the silicate-rich solid lower mantle in the 1000-kilometer region (called the D" region) above the core-mantle boundary (CMB), but it has been difficult to distinguish whether the D" region is a distinctive layer or just isolated regions of anomalous material. Bréger and Romanowicz (p. 718) measured the differences in travel times of different seismic shear waves through the D" region below the central Pacific Ocean. They then perturbed the velocity structure in a model of the D" region to account for the experimental data. Their refined model shows a slow velocity zone associated with the Hawaiian hot spot plume source at the CMB and a fast velocity zone associated with chemical heterogeneity, which indicates that the D" region is not a well-defined layer but is heterogeneous.

ADDING WATER TO TEMPERATURE RECORDS

Much of our information on temperatures during glacial times comes from analysis of oxygen isotope records, but interpretations are complicated because the records typically reflect both the effects of temperature and the change in the composition of the oceans and precipitation as a result of storage of water in large ice sheets. Beyerle *et al.* (p. 731) present both a test of the relation between oxygen isotopes and temperatures and a paleoclimate record from underneath a glacier-covered region by examining groundwater changes in an aquifer in Switzerland. Groundwater moves slowly through the aquifer, and older waters record information from when they last equilibrated with the atmosphere. Combined use of noble gases dissolved in the groundwater and oxygen isotope analyses shows that glacial-age temperatures were about 5 Celsius degrees cooler in the region than they are today.

LIMITS ON CLIMATE PREDICTABILITY?

The weather of the next few days can be predicted with reasonable accuracy, but long-term climate prediction has been thought to be almost impossible because even very small changes in the initial conditions given to models can grow exponentially after a short time. Imperfect observation quality and coverage, therefore, preclude prediction beyond 5 to 15 days. However, as the recent successful El Niño prediction shows, there are exceptions to this rule, and these exceptions extend at least to some extent beyond the tropical Pacific to higher latitudes, such as the North Pacific and North America. Shukla (p. 728) uses climate modeling case studies to demonstrate the predictability of these climatic features and to discuss some of the underlying reasons, in particular the role of sea-surface temperatures in reducing the influence of atmospheric variability on climate.



BIOMINERALIZATION CLOSE-UP

Many factors affect the growth of biominerals such as calcite ($CaCO_3$), including surface steps and the presence of organic compounds. Teng *et al.* (p. 724) used atomic force microscopy to quantify the thermodynamic and kinetic controls on the growth of calcite from solution. The experiments confirm the Gibbs-Thomson connection,which relates the growth of a crystal face along a step to the oversaturation of the solution. Addition of aspartic acid greatly changed the step morphology and free energy of the system.

GROWING QUANTUM DOT CRYSTALS

Quantum dots, nanoscale structures that confine electrons, can form spontaneously on a surface if certain materials are deposited on an appropriate substrate; their size and shape will depend on the lattice mismatch between the two compounds. Springholz *et al.* (p. 734) show that if successive layers of PbSe quantum dots in a matrix of $Pb_{1-x}Eu_xTe$ layers are deposited, the particles begin to align vertically as well as in the plane of deposition and form a three-dimensional quantum dot crystal. Such crystals may be of interest for optoelectronic nanodevices.

PROTEIN FOLDING OVER MILLISECONDS AND MONTHS

Detailed simulations of protein folding are computationally intensive and are normally performed for periods corresponding to nanoseconds, but proteins typically fold on microsecond time scales. Duan and Kollman (p. 740; see the Perspective by Berendsen) have performed a millisecond simulation of a 36-residue protein starting from a fully denatured structure. The protein forms intermediate structures, one of which has a lifetime greater than 100 nanoseconds and resembles the fully folded structure. Despite the use of parallel processing, the simulation still required about 4 months of central processing unit time on Cray supercomputers.

COMPLEXITIES OF SPORE FORMATION

In yeast, sporulation is a key process for reproduction that produces haploid germ cells. Because the complete genomic sequence of *Saccharomyces cerevisiae* is now available, Chu *et al.* (p. 699) were able to use DNA microarray technology to increase by an order of magnitude the number of genes associated with the sporulation process. Studies of the expression patterns and of consensus sequences in mutant and wild-type cells allowed previously unsuspected associations to be made between genes and regulatory factors.

STALKING SOMATOSTATIN AGONISTS

Generation of nonpeptide compounds that activate receptors that normally bind peptide hormones has proven to be difficult, although the utility of such compounds for study of the biological roles of such receptors and for the development of therapeutic drugs has long been recognized. Rohrer

CONTINUED ON PAGE 591

THE MJ RESEARCH NOTEBOOK

Volume VIII...No. 4 *A Bulletin of Technological Advance in Molecular Biology* *Autumn 1998*

A Fundamental Physical Phenomenon

Discovered in 1834, the Peltier Effect Is Still Not Fully Understood

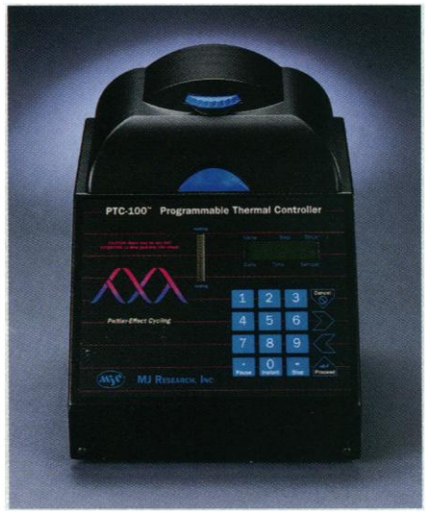
Jean Peltier was a watchmaker from Baie de Somme, France, who "retired" to Paris at the age of 31 after his wife inherited a small fortune. His avocations were the study of electricity and meteorology, as well as the development of new language akin to Esperanto to facilitate the uniting of Europe.

Jean Peltier
1785 - 1845
(artist's rendering)

But it is his 1834 publication in the *Annales de chemie* (56) 371-86 for which we know him today. Peltier was one of the first to realize that current and voltage are separate entities. He discovered that if a current was passed through a bimetallic junction, one side became hot and the other side became cold. If the polarity was reversed, so the hot and cold sides reversed. This, quite simply, is the Peltier effect.

This phenomenon remained largely a laboratory curiosity until the 1930's, when the Russian physicist A.F. Ioffe managed to build a working Peltier heat pump using semiconductors rather than metals. Other investigators followed Ioffe's pioneering work, including the physicists Clarence Zener and Paul Grey. Many scientists of the 1950's thought that Peltier heat pumps would largely supplant mechanical refrigeration, but they were never able to get the Peltier pumps to operate at the efficiency or scale needed for general application.

To this day, the exact nature of the Peltier effect is not fully understood. The current hope for improved efficiency lies in "quantum wells" of laminated crystals, which are much researched.



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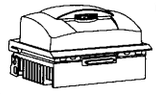
PELTIER CYCLERS BEST CHOICE FOR DNA REACTIONS

INTRODUCED BY MJ IN 1988, NOW ADOPTED BY OTHERS

WATERTOWN, Mass. — Since the development of DNA amplification technologies in the late 1980's, life scientists have increasingly become consumers of thermal cycling equipment. Thermal cyclers are critical devices in driving PCR* and cycle sequencing reactions, and many technologies have been introduced over time. One technology—Peltier effect instrumentation—has truly come to dominate.

MJ Research started this trend with the introduction of the PTC-100 thermal cycler in 1988. This pioneering design featured two bidirectional Peltier heat pumps mounted to the base of its aluminum sample block. The electronic Peltier pumps allowed for greater thermal precision than with any other thermal cycler available at the time (±0.5°C), an extended thermal range (0°-100°C), as well as the highest capacity of any instrument of the era (it was the first cycler to fit 96-well plates).



PTC-200/225 block w/Peltier Pump

Most other brands of the eighties used mechanical refrigeration or were heat-only devices with active thermal control in one direction only. These technologies usually suffered from poor uniformity or erratic control, and they have largely been abandoned today. Instead, virtually all cycler manufacturers now offer Peltier instrumentation.

But MJ always had the technological lead. Since the PTC-100, three major new lines have been introduced, and all four lines remain in manufacture today. The flagship DNA Engine & Tetrad cyclers feature interchangeable blocks, have the ability to work with robots, and fit virtually any type of vessel. They offer a precision of control unparalleled in the industry, which is perhaps the most outstanding feature of MJ cyclers.

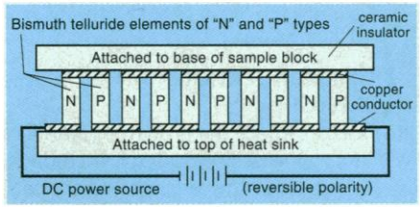
PTC-225 Tetrad™

Growing Crystals of Bismuth Telluride

MJ Makes Its Own High-Performance Heat Pumps

In 1988, there were several US and European manufacturers of Peltier heat pumps, but none made pumps designed for thermal cycling. Rather, they were designed for chilling only, so MJ had to develop new technology.

Substantial work was done to modify geometries, improve the materials, and develop a "suspension" that could handle rapid expansion and contraction. At first, these pumps were made in collaboration with other companies, but for the past several years, MJ has made all its modules itself. It was simply impossible to implement all the potential improvements without total control over the production process.



Typical thermal-cycling Peltier heat pump

Thus MJ literally starts with raw bismuth and tellurium metals that are mixed and converted in special furnaces into "P" and "N" semiconductor crystals. The crystals are precisely cut and treated, then carefully assembled into Peltier heat pumps. The pumps are thoroughly tested, then installed in thermal cyclers. The result is a heat pump that can withstand the stresses of thermal cycling thousands of times longer than best pre-1988 Peltier technology.

* PCR is covered by patents owned by Hoffmann-La Roche, Inc. & F. Hoffmann-La Roche Ltd. Users should obtain license to perform the reaction.

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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 589

et al. (p. 737) identified nonpeptide agonists of high affinity that are specific for particular subtypes of the somatostatin receptor. (Somatostatin participates in control of release of other hormones from the pituitary and pancreas, and analogs have application in treatment of cancer and other cell proliferation disorders.) They screened combinatorial libraries constructed to mimic interactions determined by modeling known peptide agonists. The new compounds were used to probe the biological roles of two of the five distinct somatostatin receptor subtypes.

COMBATING CHOLESTEROL

Individuals with abetalipoproteinemia have extremely low levels of plasma lipoproteins. This disorder is caused by an inherited deficiency in microsomal triglyceride transfer protein (MTP), a molecule required for assembly and secretion of lipoprotein particles. Wetterau *et al.* (p. 751) postulated that inhibitors of MTP might have therapeutic potential as cholesterol-lowering drugs. In a high-throughput screen of chemical compounds, they isolated an orally active MTP inhibitor that lowered plasma lipoprotein levels in several animal models, including a rabbit model of hyperlipidemia that is resistant to existing drugs. MTP inhibitors may open up a new avenue for treatment of humans who are at risk for atherosclerosis because of high cholesterol levels.

ANCIENT AEROBATICS

Some of the oldest (paleozoic) dragonfly-like insects have "smart" structures on their wings. Wootton *et al.* (p. 749; see the news story by Vogel) show that these ancient insects had devices analogous to those seen in modern dragonflies that deform the wing in response to aerodynamic loading. Despite the analogies, the two types of structures are not homologs—in one case (the triangle-subtriangle complex) they are effectively built the opposite way around, thus providing a vivid illustration of adaption arriving at the same functional solution through different morphological routes.

DON'T COUNT THEM OUT

Can monkeys count? Brannon and Terrace (p. 746; see the Perspective by Carey) trained two monkeys to use a touch-sensitive screen to order images on the basis of how many items were present. The monkeys would first touch the image containing one item (a geometric shape of varying color and size on a background of varying color, or even a piece of clip art), then the image containing two items, and so forth up to four items. When presented with pairs of images each containing between five and nine items, the monkeys could select the image with more items.

SURPRISES IN *CHLAMYDIA*

Chlamydia are bacterial pathogens that can cause disease in the eye and the genital tract. In reporting the sequence of the complete genome, Stephens *et al.* (p. 754; see the Perspective by Hatch) have found genes that no one thought *Chlamydia* had and did not find genes that were thought to be essential for all bacteria. They have also found candidate proteins that could be responsible for the virulence of the organism.

SECRETED WEAPON OF TB

Three million people die each year of tuberculosis (TB), an infectious disease caused by certain strains of mycobacteria. In the host cell, these bacteria replicate in special intracellular compartments called phagosomes and are thought to escape destruction therein by secreting proteins that remodel the phagosomes. Berthet *et al.* (p. 759) show that a secreted mycobacterial protein called ERP (exported repetitive protein), which is found only in strains that cause TB and leprosy, is present in phagosomes and is essential for intracellular replication.

TECHNICAL COMMENT SUMMARIES

Cellulose Biosynthesis in *Arabidopsis*

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5389/591a

T. Arioli *et al.* performed a "molecular analysis of cellulose biosynthesis in *Arabidopsis*" (wall cress plant) with the use of an "*rsw1* mutant [gene with a] temperature-sensitive allele [that] is changed in one amino acid" (Reports, 30 Jan., p. 717).

R. H. Atalla comments that the results, while "an important contribution," do not rule out "two alternative interpretations of the soluble β-1,4–linked glucan" that accumulates in the presence of the mutant *rsw1* gene. He states that "careful permethylation analyses ... will be important to the full development of the implications of the observations made by Arioli *et al.*"

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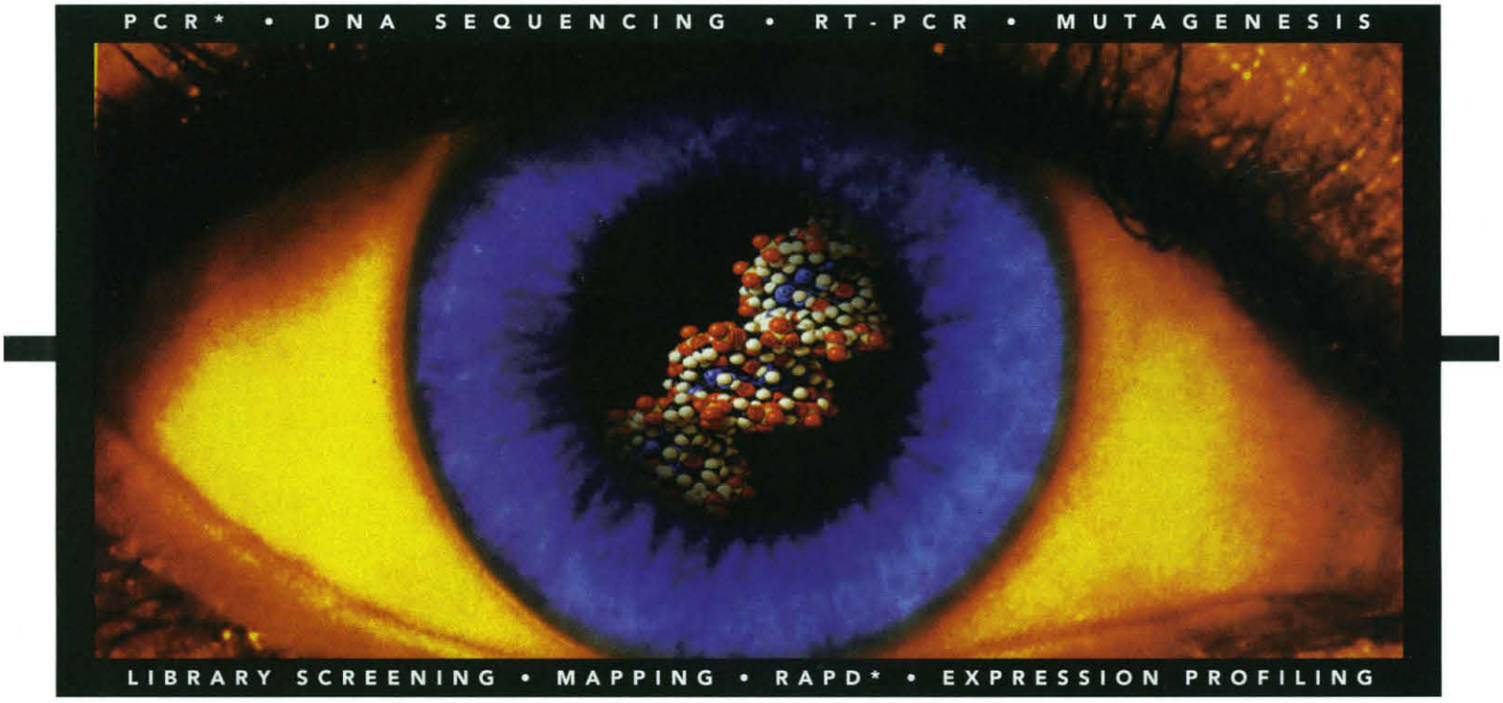

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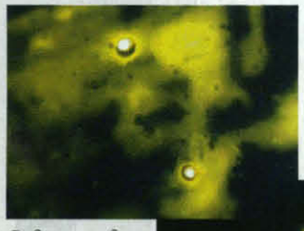

Before transfer, fluorescent image

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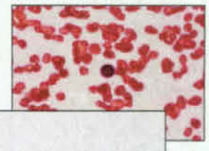
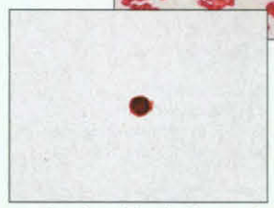
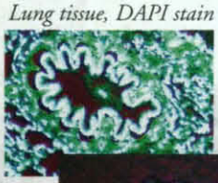




Single white blood cell transfer

Lung tissue, DAPI stain



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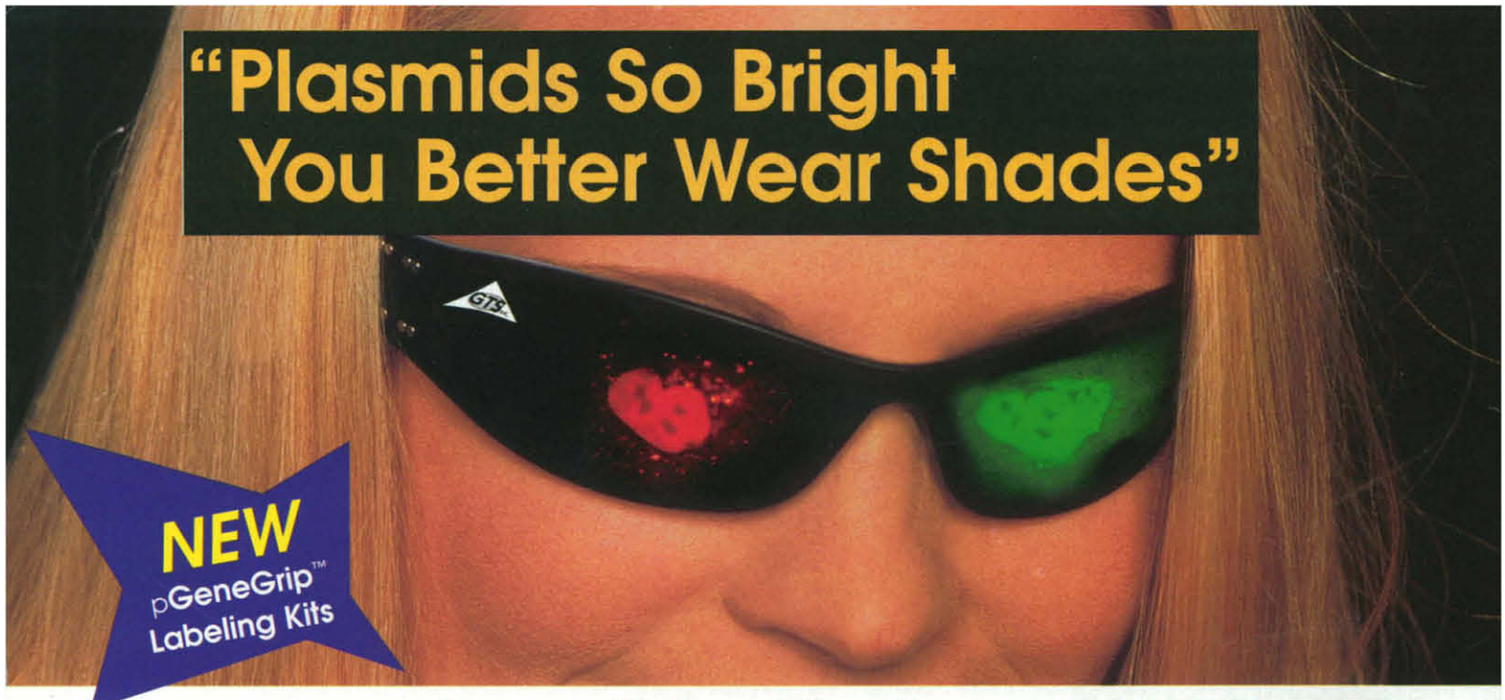

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	100 ug	G102015		100 ug	G102005
Fluorescein/CAT	25 ug	G102020	Biotin/Blank Vector	25 ug	G103000
	100 ug	G102025		100 ug	G103005
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	100 ug	G102055			
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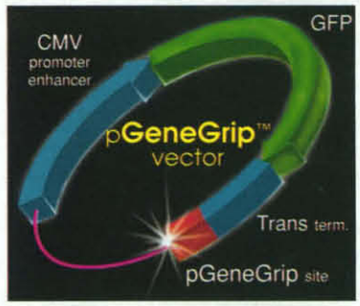

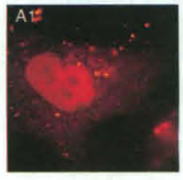

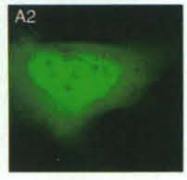

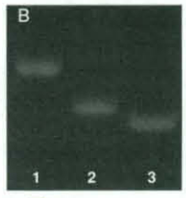

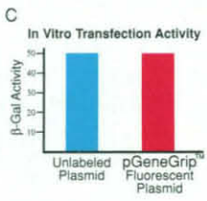

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A. Fibroblasts transfected with pGeneGrip™ Rhodamine/GFP vector:
1. Rhodamine labeled DNA
2. GFP expression

B. Electrophoresis of pGeneGrip™ Rhodamine labeled fluorescent vector Lanes: 1. β-gal, 2. GFP, 3. Blank

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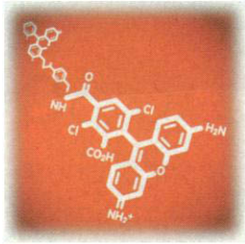

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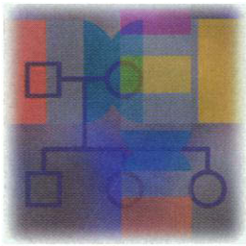

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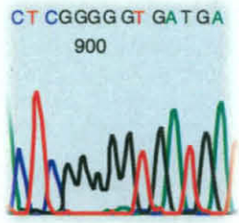

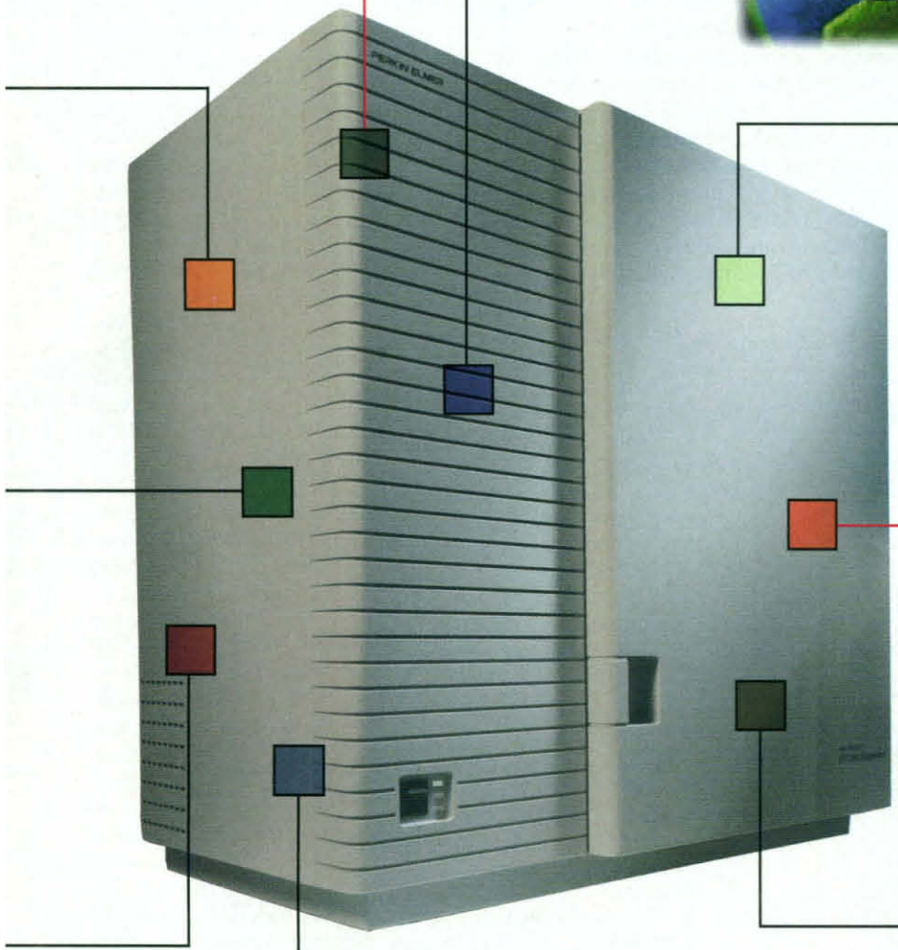

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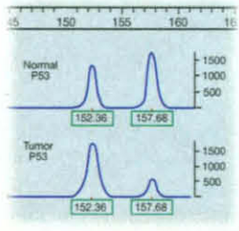

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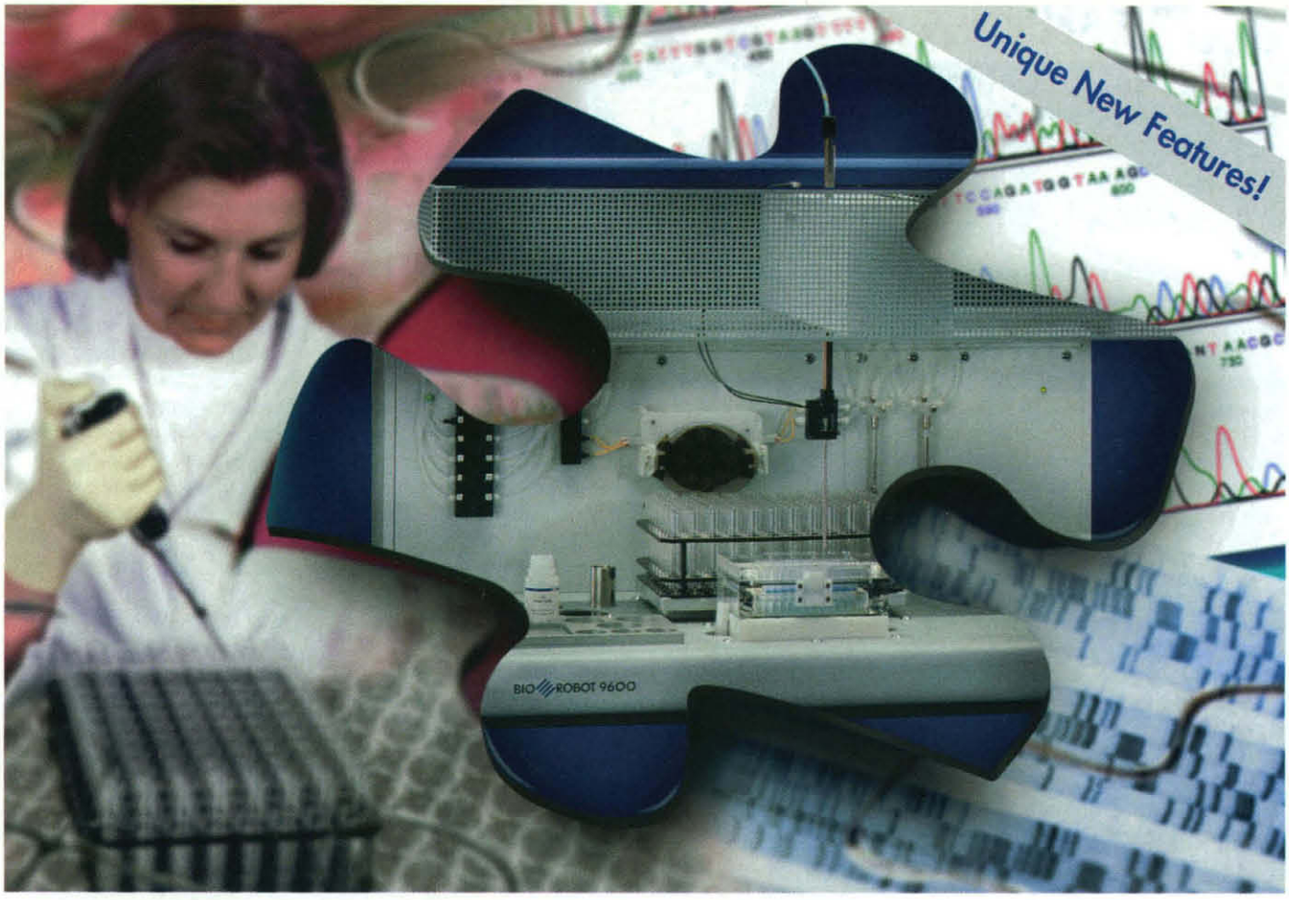

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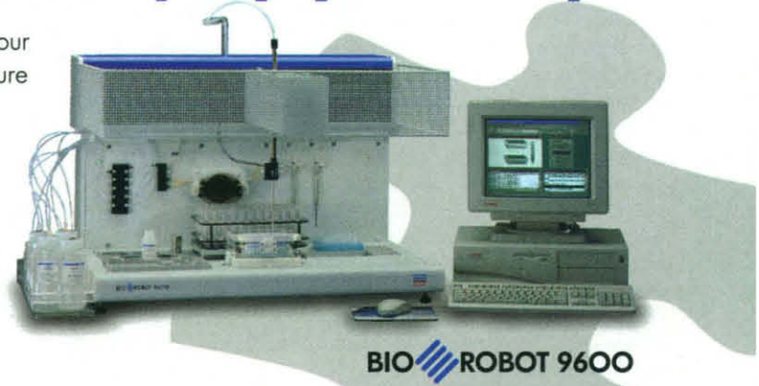

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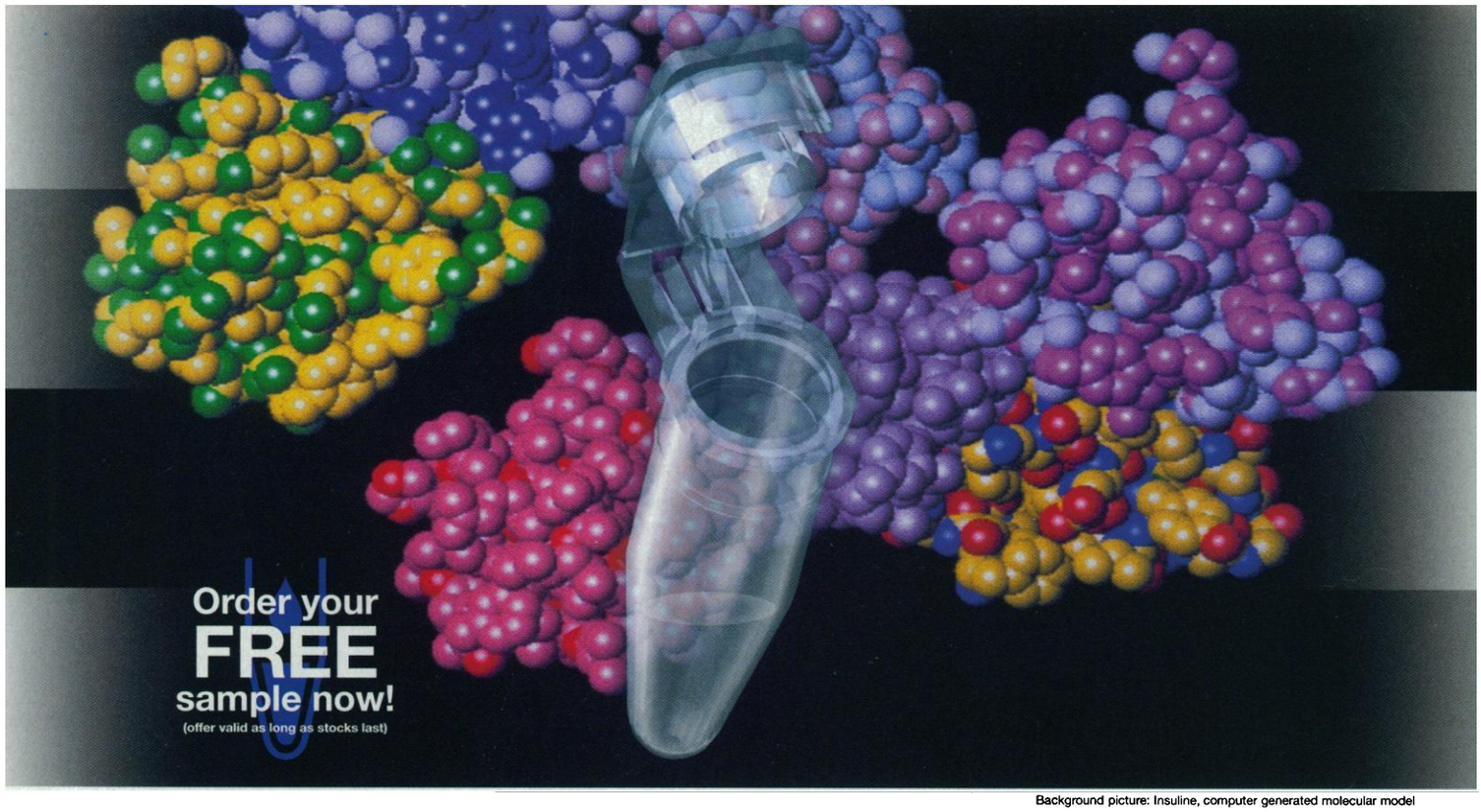

Background picture: Insuline, computer generated molecular model

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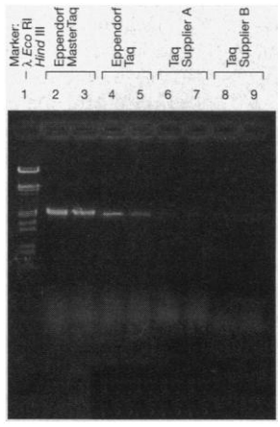
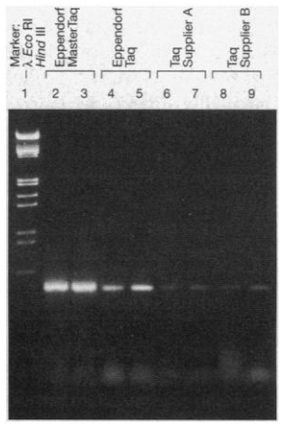


● **Fig.1: Amplification of a SSU rRNA gene from total genomic algae DNA**
PCR was performed from genomic algae using different Taq DNA Polymerases. Equal volumes of the PCR reactions were analyzed by gel electrophoresis.



● **Fig. 2: Amplification of a GAPDH specific DNA fragment from genomic blood DNA**
PCR was performed from human genomic blood with different Taq DNA Polymerases. Equal volumes of the PCR reactions were analyzed by gel electrophoresis.

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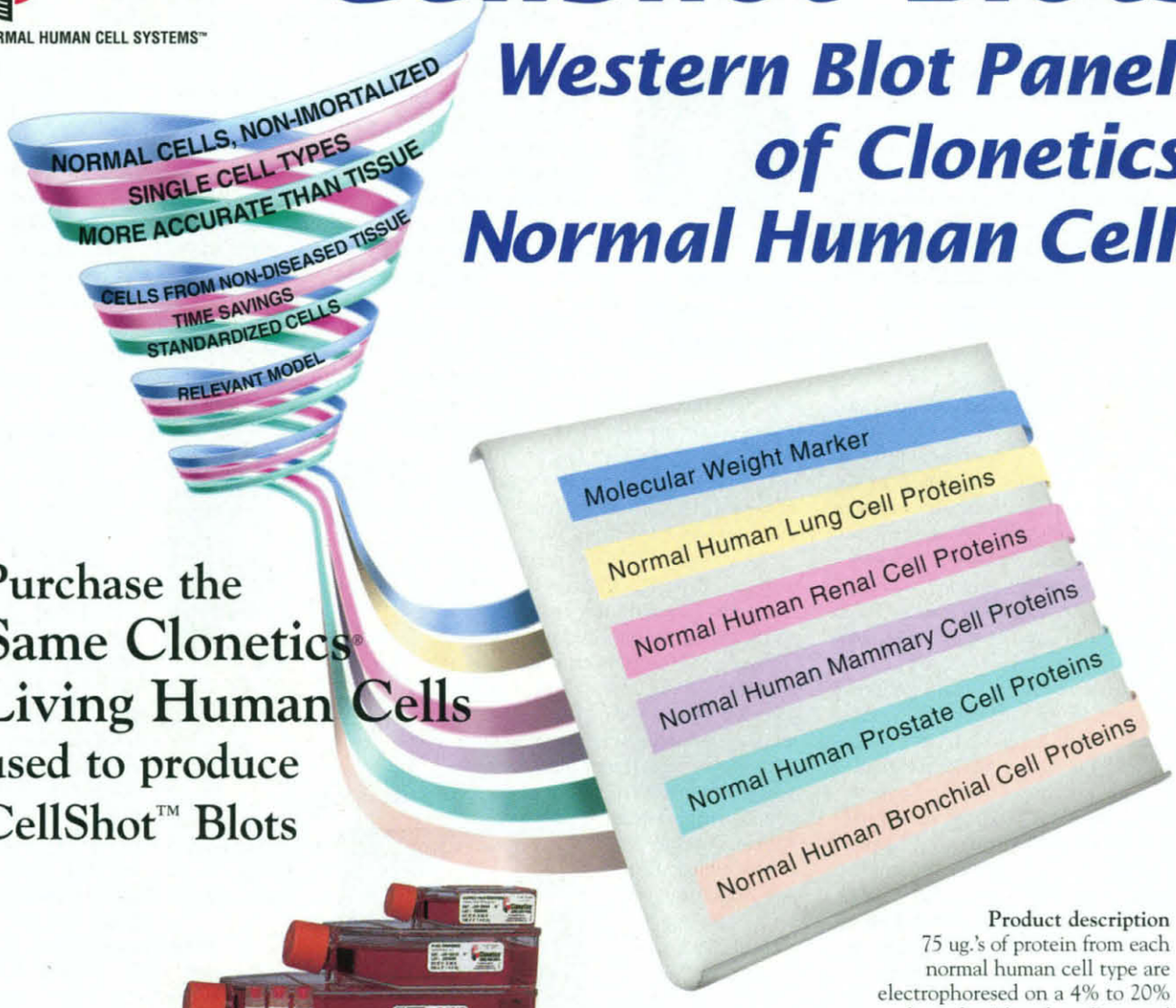

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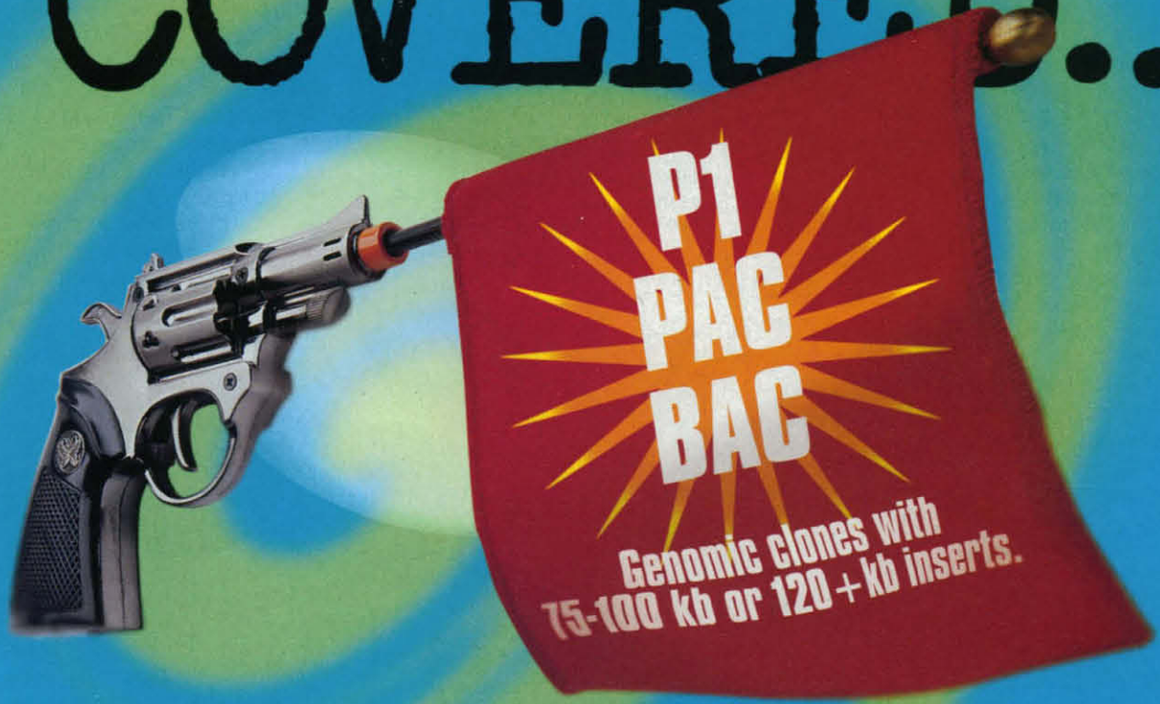

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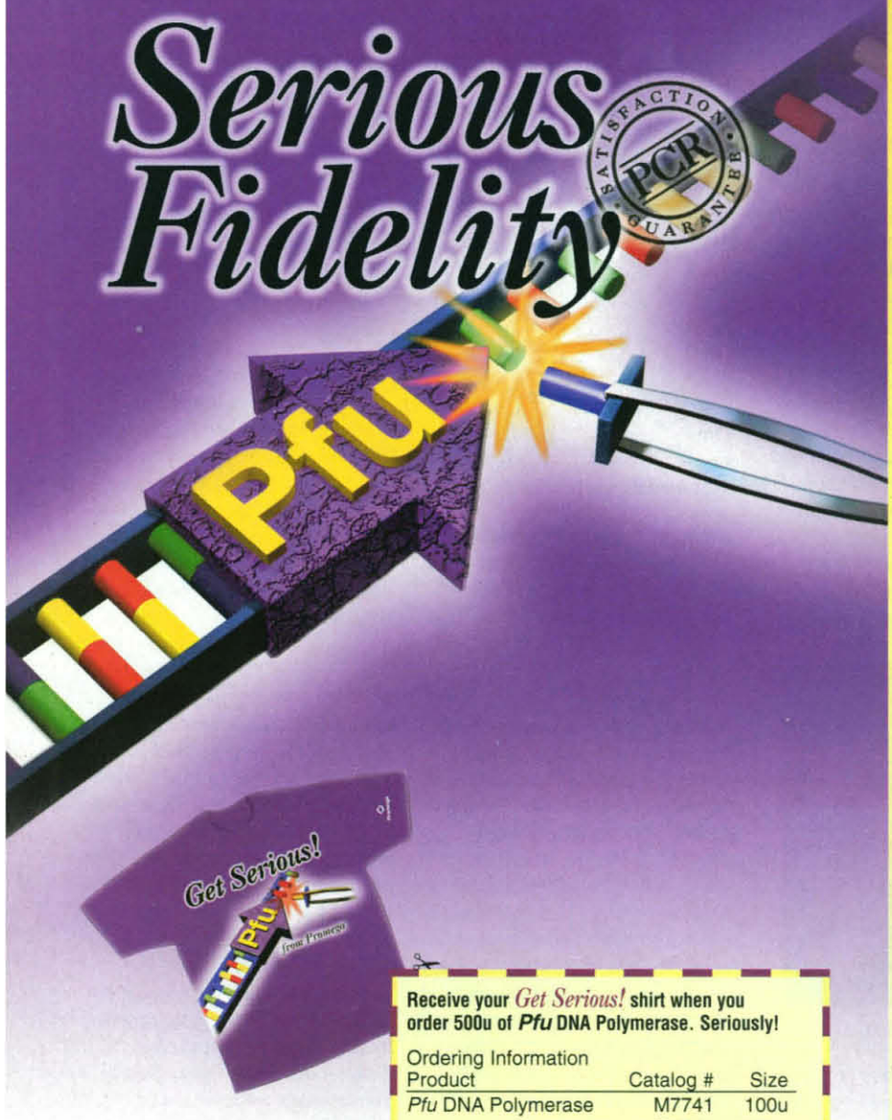

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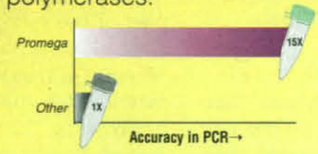

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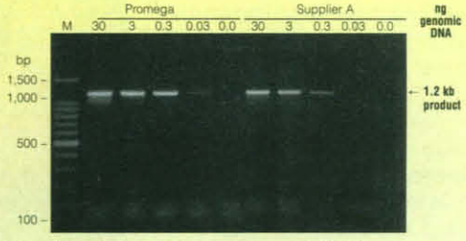

Comparison of amplification performance of native *Pfu* DNA Polymerase between Promega and another supplier.

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References

1. Cline, J., Braman, J.C. and Hogrefe, H.H. (1996) *Nucl. Acids Res.* **24**, 3546.
2. Andre, P. *et al.* (1997) *Genome Res.* **7**, 843.
3. Slater, M. *et al.* (1998) *Promega Notes* **68**, 7.

†Accuracy is defined as the average number of nucleotides the polymerase incorporates before making an error.

*The PCR process is covered by patents issued and applicable in certain countries. Promega does not encourage or support the unauthorized or unlicensed use of the PCR process. Use of this product is recommended for persons that either have a license to perform PCR or are not required to obtain a license

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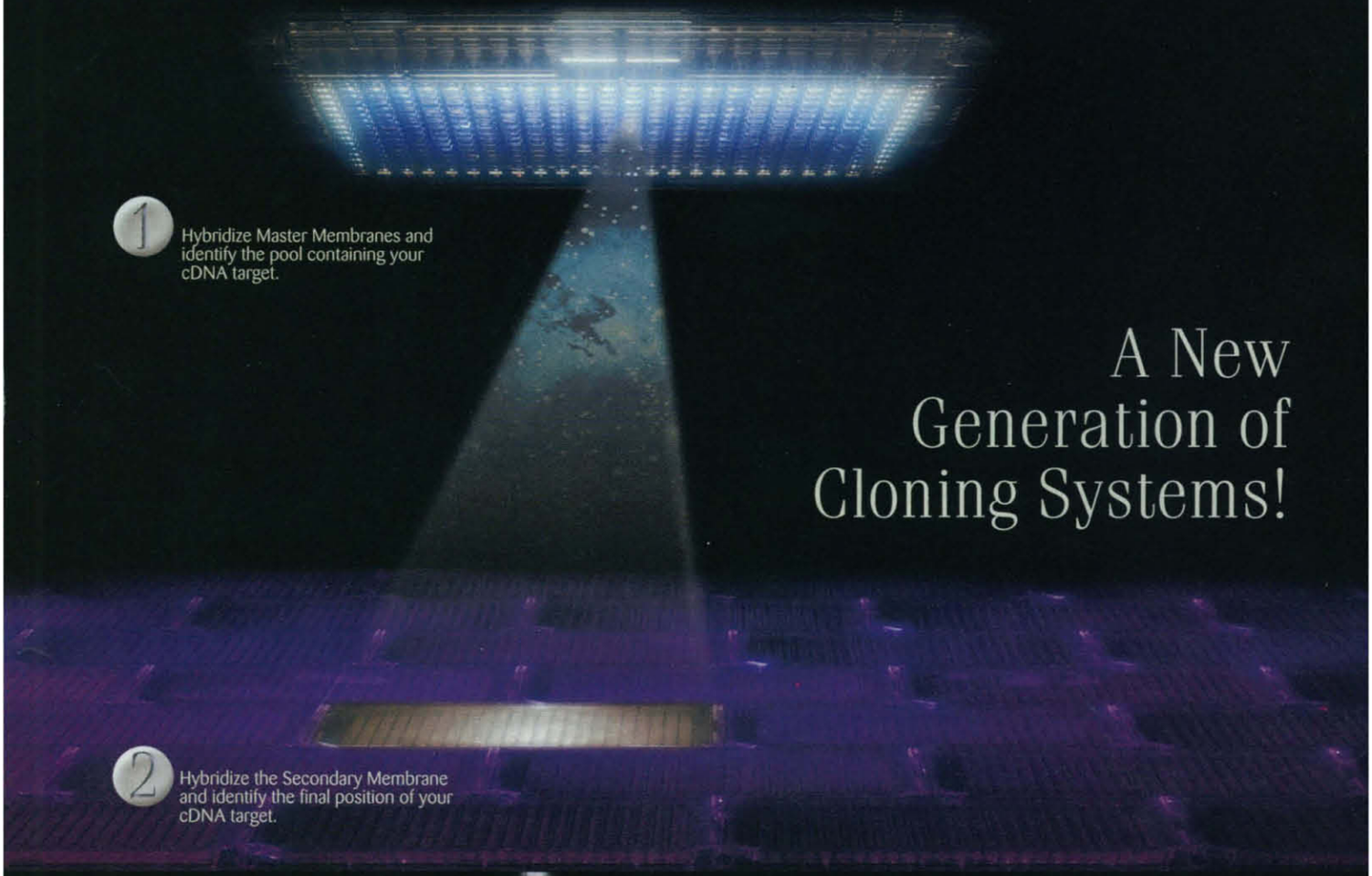

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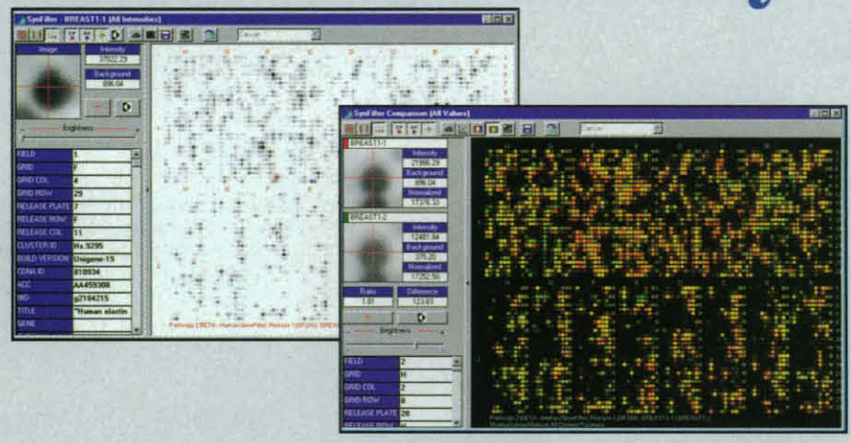

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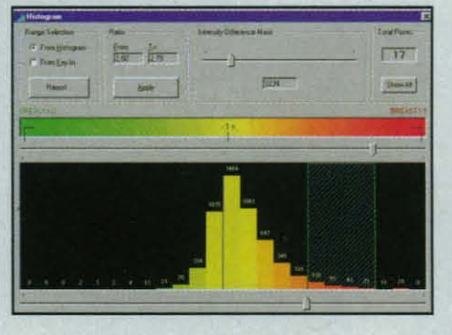

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2. http://www.ncbi.nlm.nih.gov/UniGene/index.html

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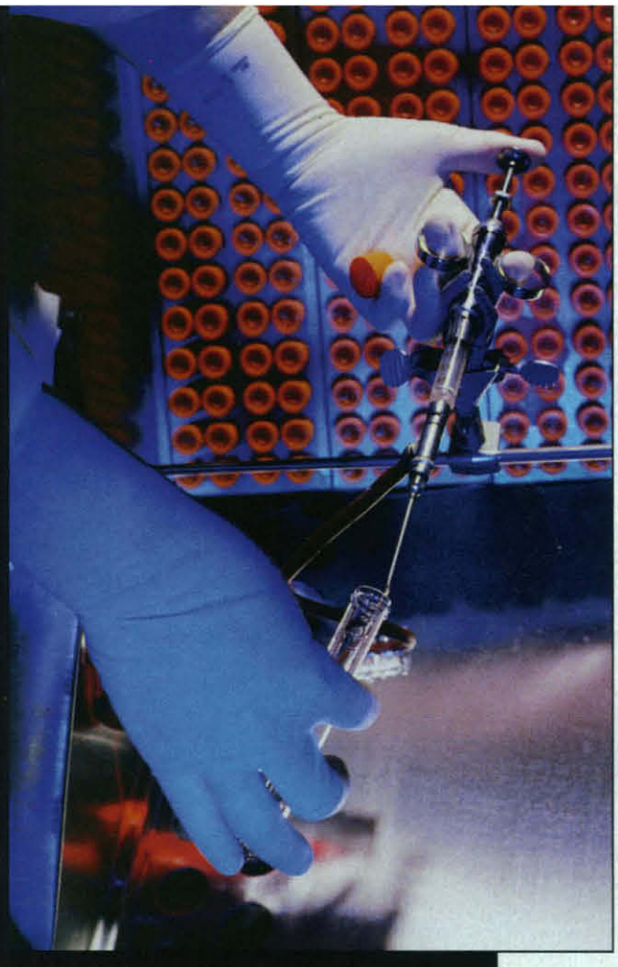

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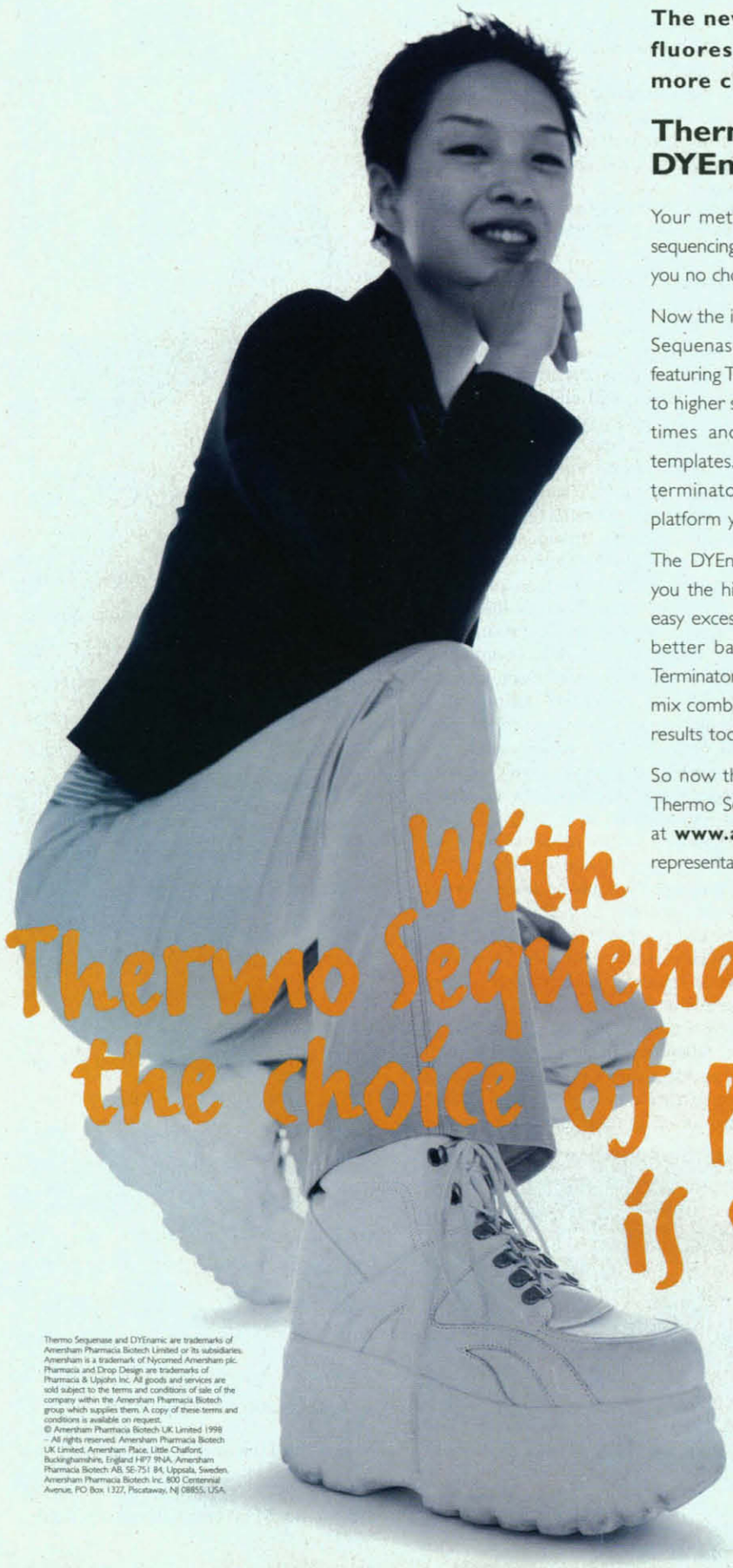

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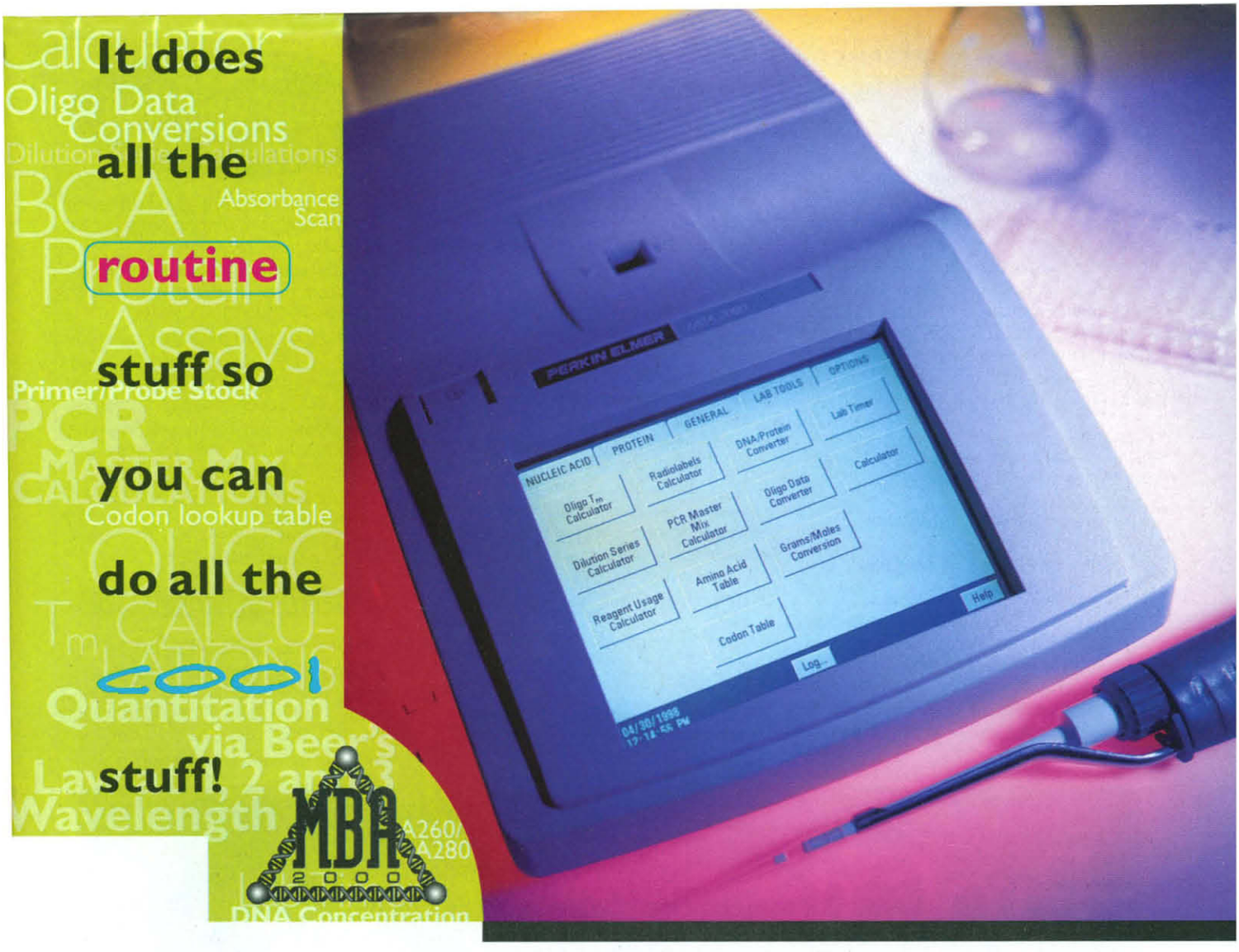

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DHGP

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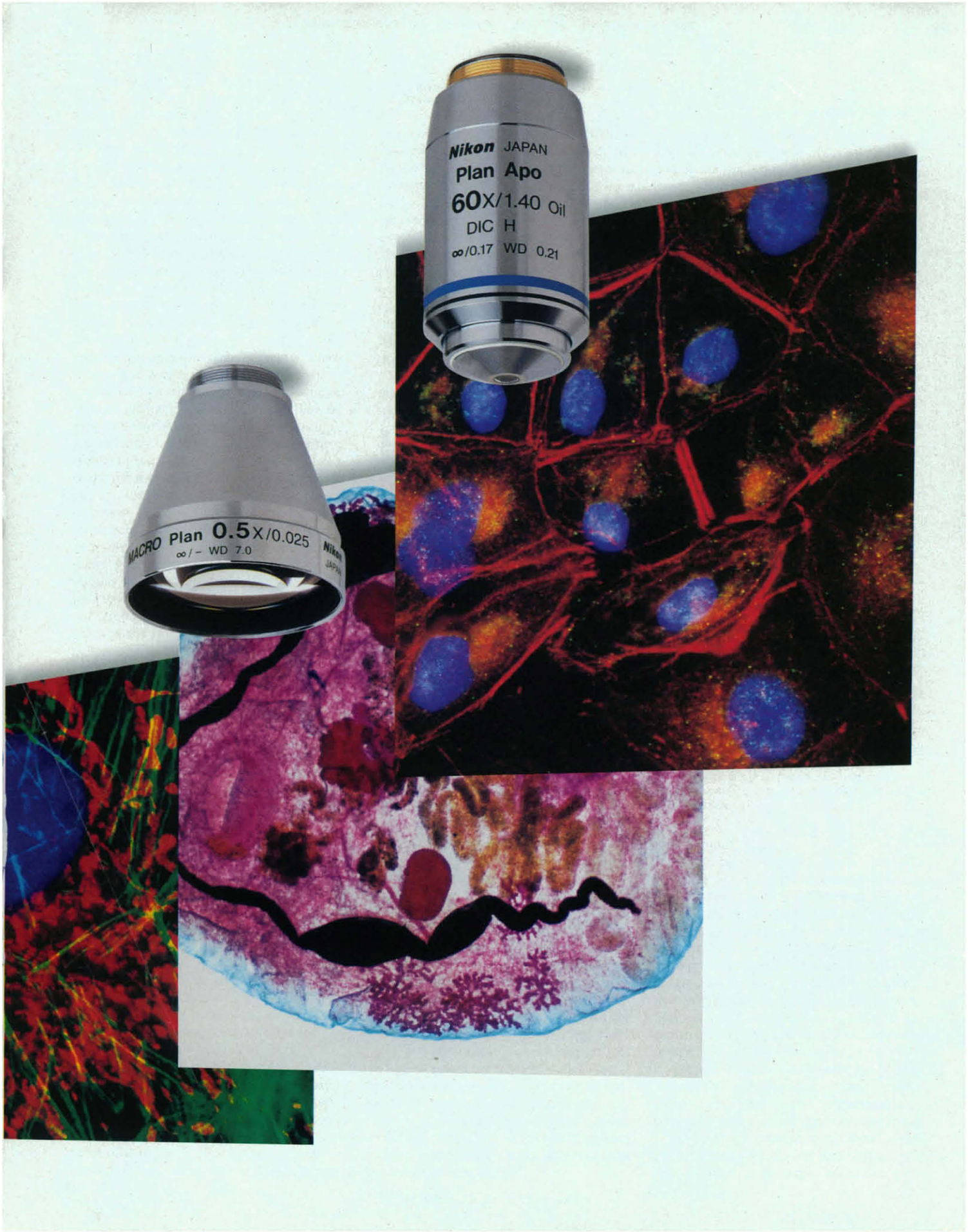
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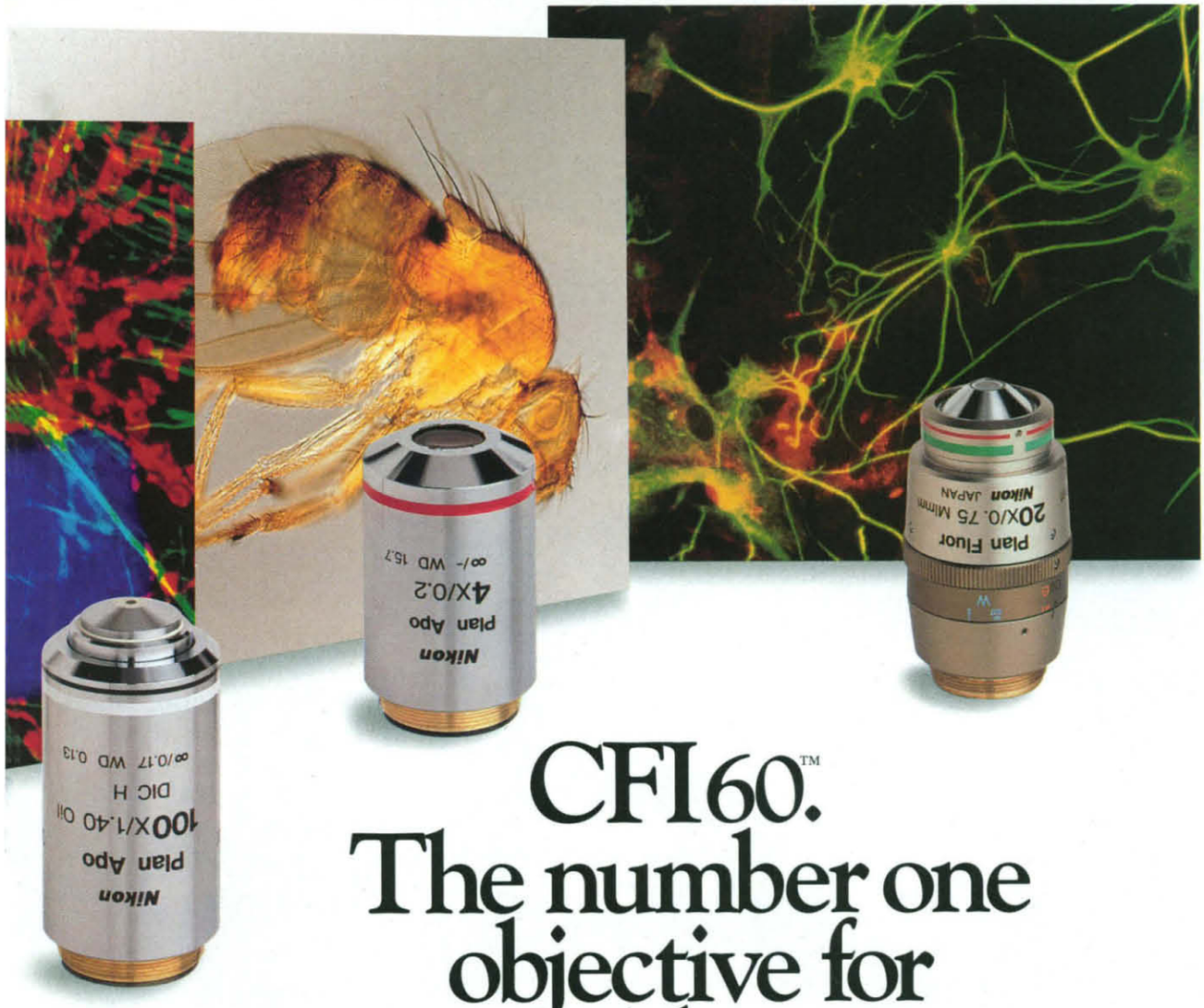

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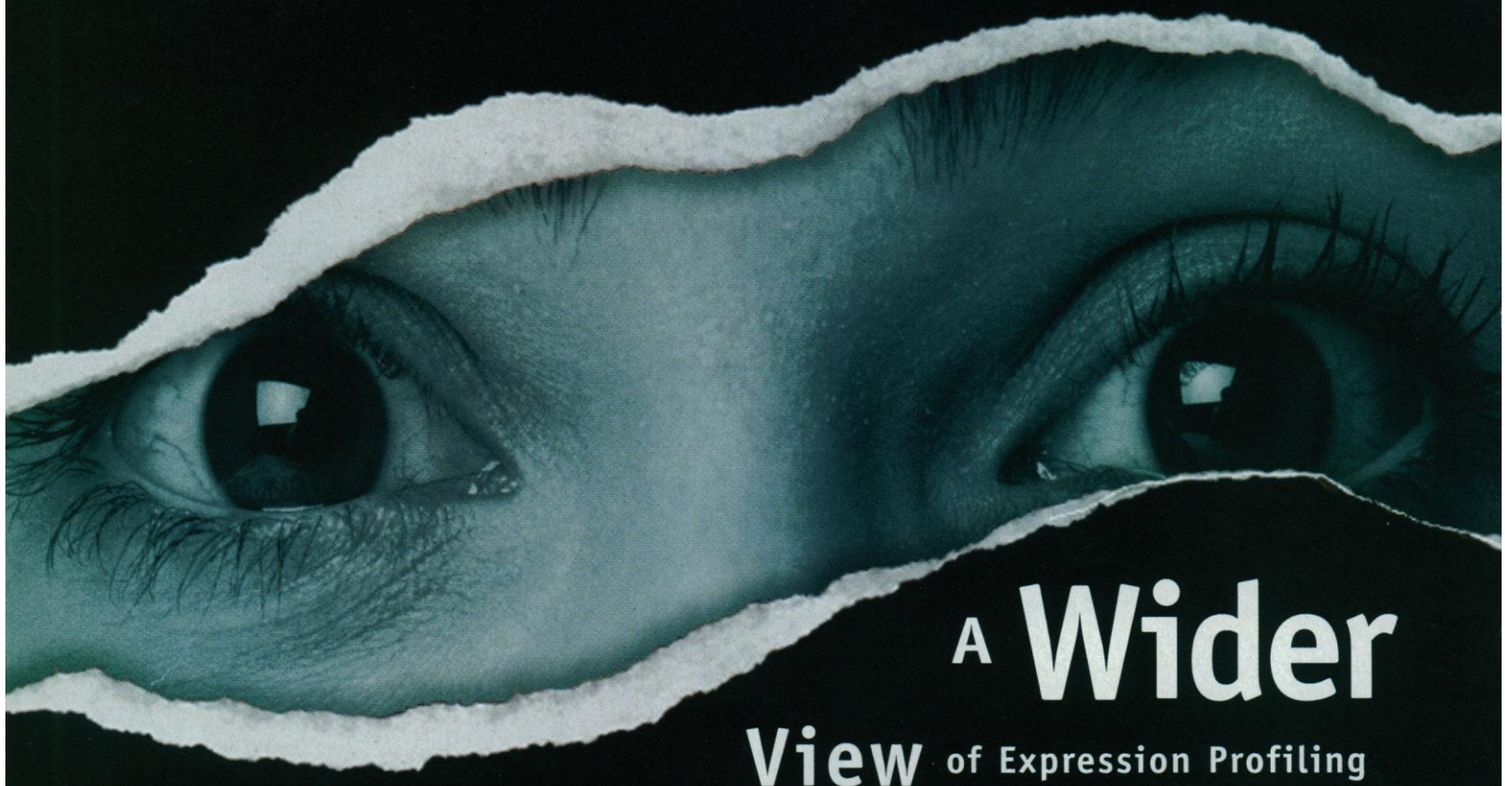

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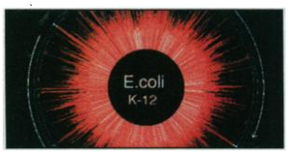

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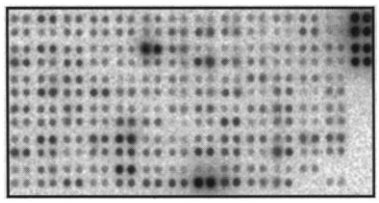

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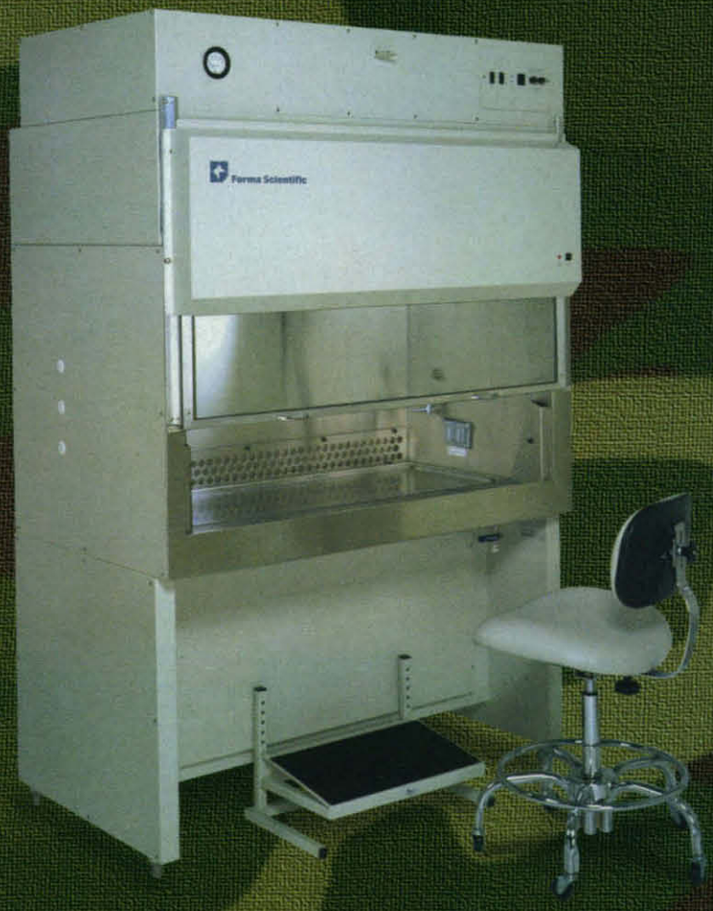

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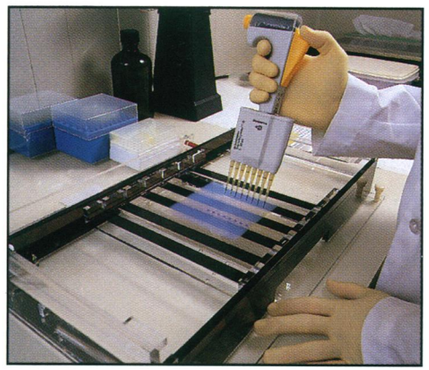

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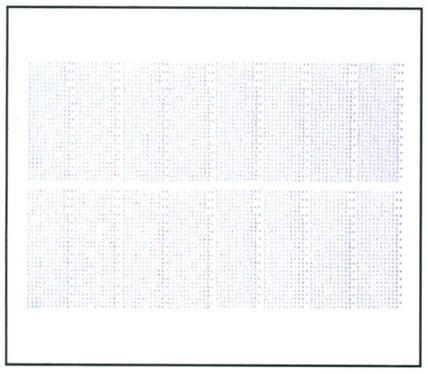
The medium resolution Stanford G3[1] panel and the high resolution Stanford TNG panel were created at the Stanford Human Genome Center. A server for the chromosome localization of markers using the G3 panel is available at **http://www-shgc.stanford.edu**. A limited server for chromosome localization of markers for the Stanford TNG panel is found at **http://www-shgc.stanford.edu/RH/TNGindex.html**.

The low resolution GENEBRIDGE 4[2] panel is a subset of the 199 clone panel developed in a collaboration between the labs of Peter Goodfellow and Jean Weissenbach. Chromosome localization of markers may be performed by accessing the server at **http://www-genome.wi.mit.edu**.

Additional panels offered by Research Genetics include mouse, baboon, zebrafish, rat and canine. All of these panels originated in Peter Goodfellow's lab at Cambridge University. The panels are all formatted to fit into a 96-well format and all have retention rates averaging 25-30%

Ref: 1. Stewart, E. et al (1997) *Genome Research 7* 422-433.
2. Gyapay, G. et al (1996) *Human Molecular Genetics 5* 339-346.



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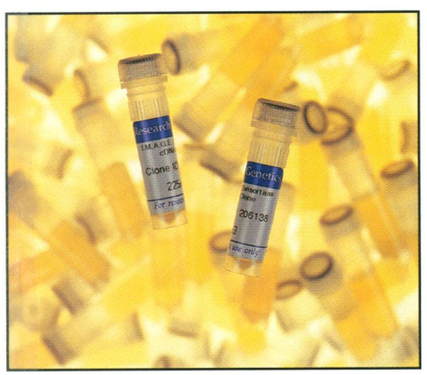

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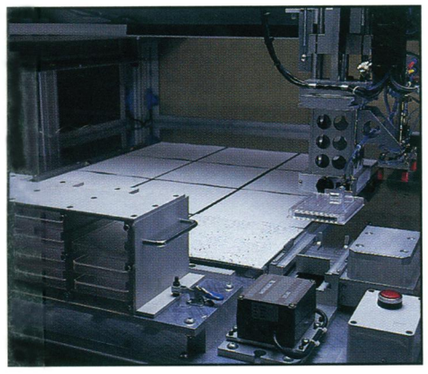

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Science

Arabidopsis thaliana

GENOME MAPS 9

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and Pamela J. Hines

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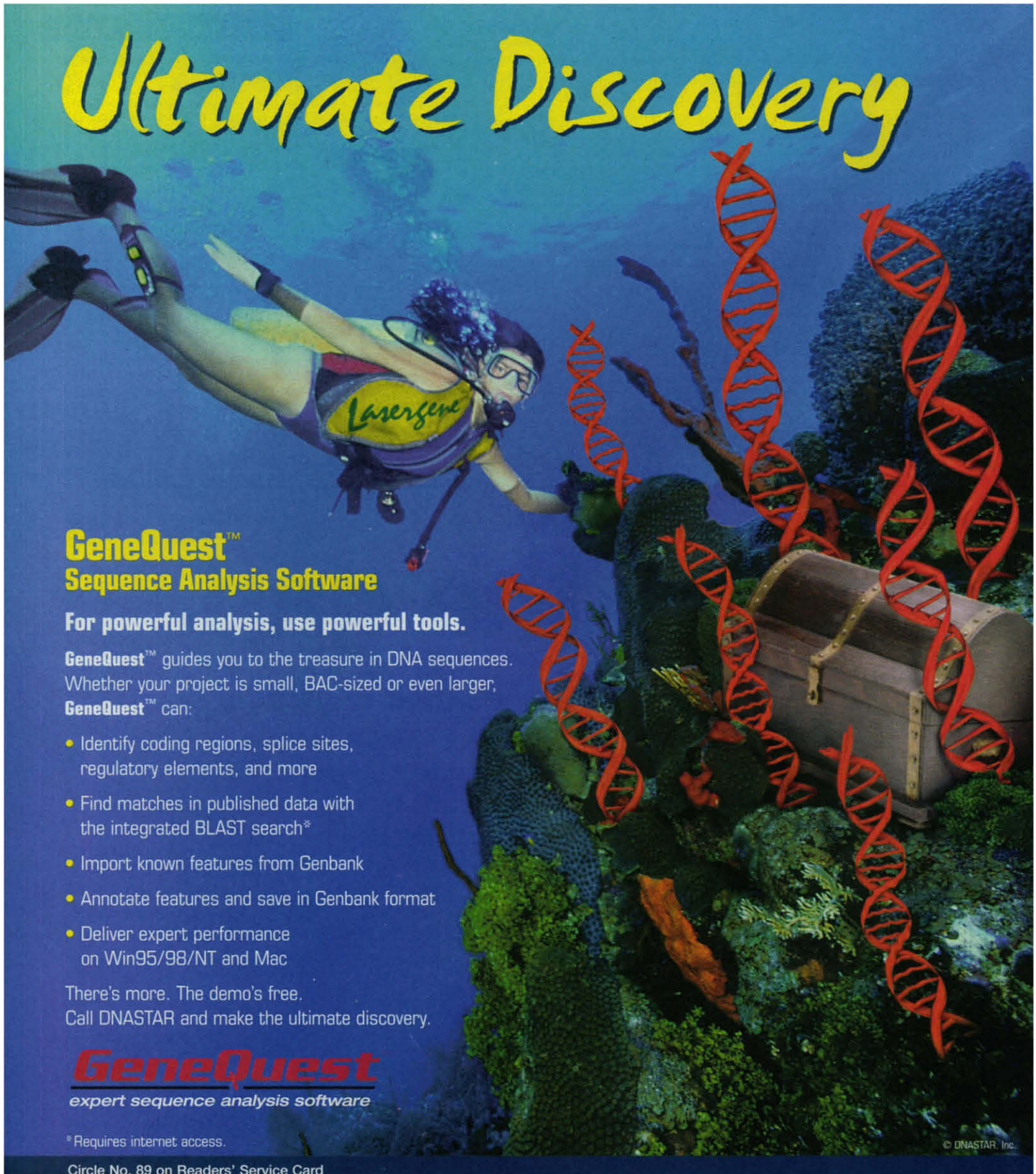

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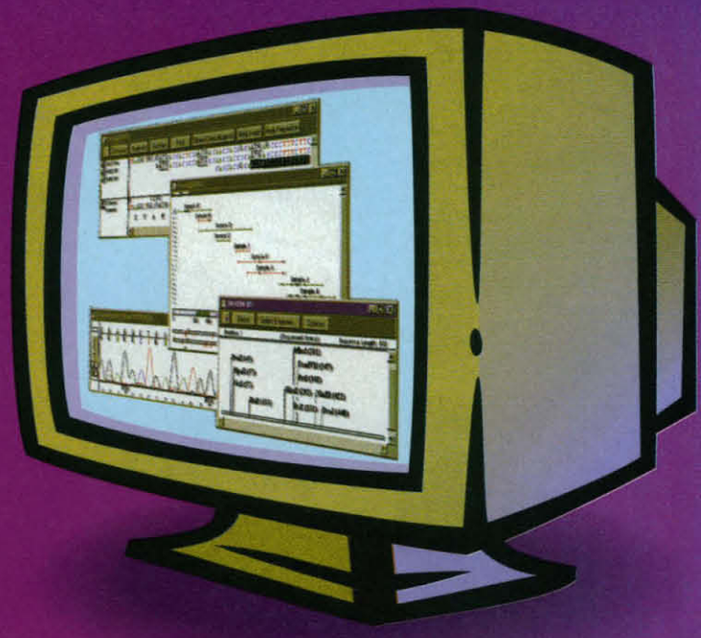

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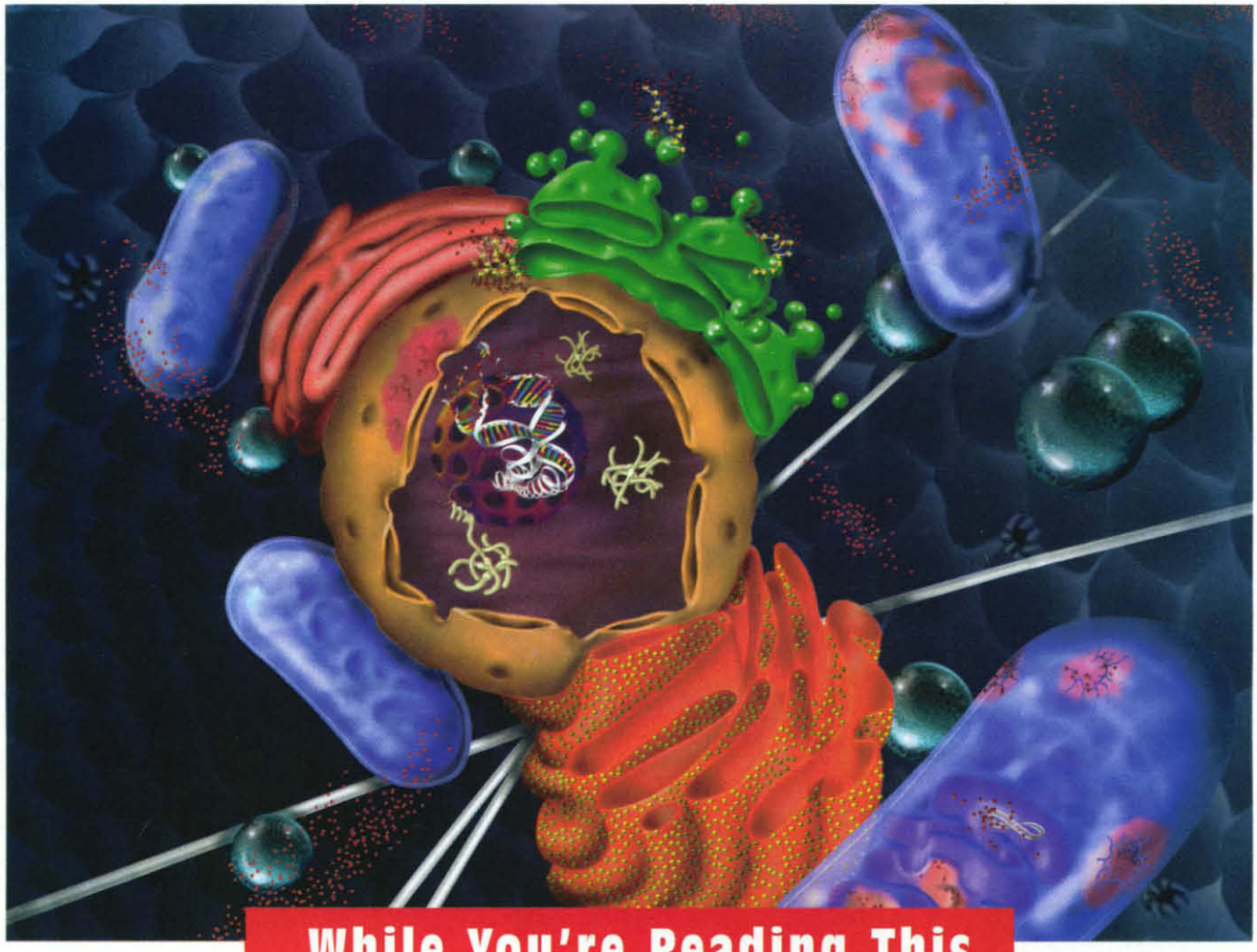

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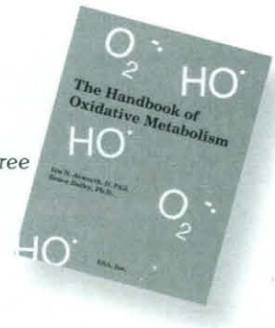

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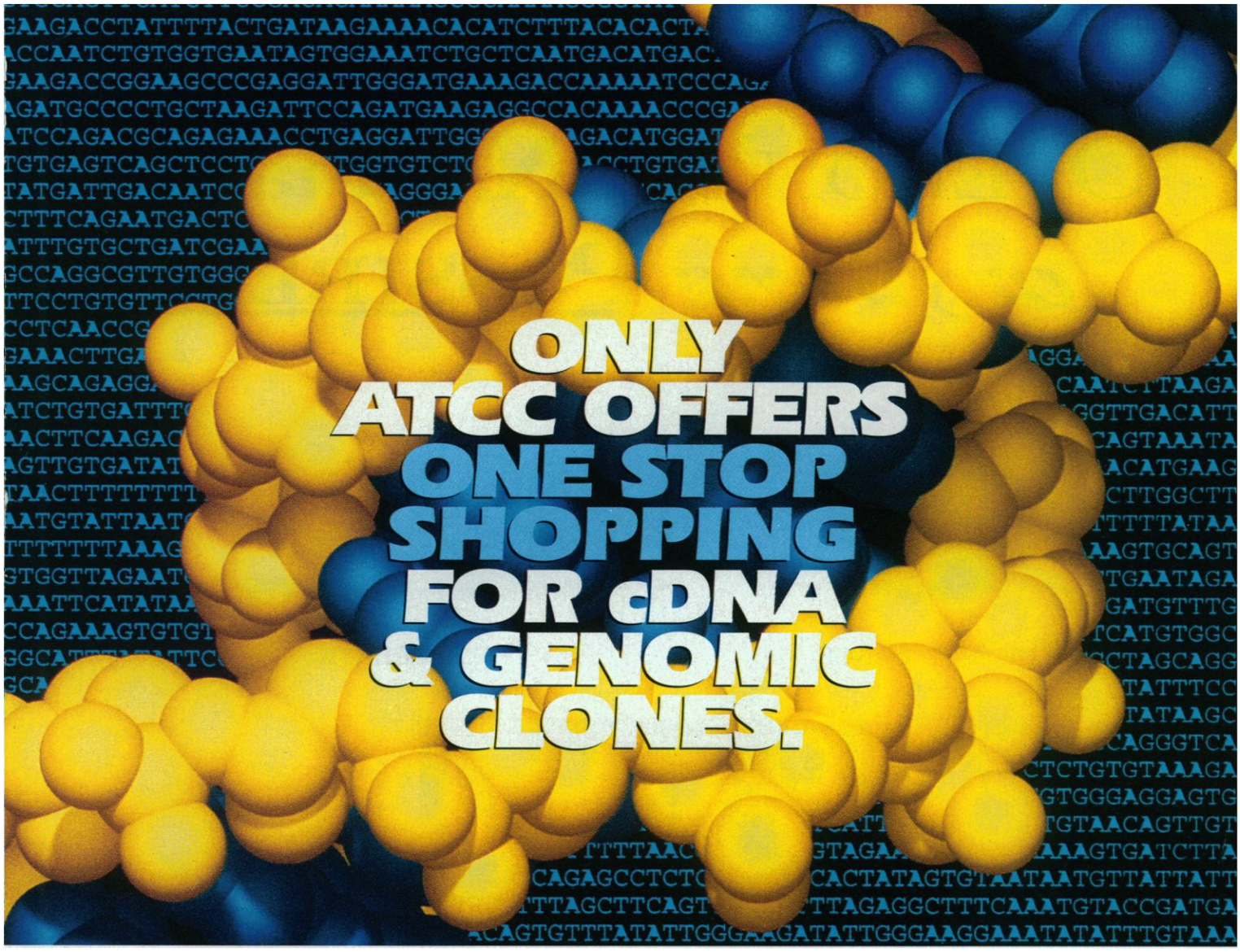

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** Lennon, G., Auffray, C., Polymeropoulos, M., Soares, M.B. 1996. The I.M.A.G.E. Consortium: An Integrated Molecular Analysis of Genomes and their Expression. Genomics 33, 151-152.*

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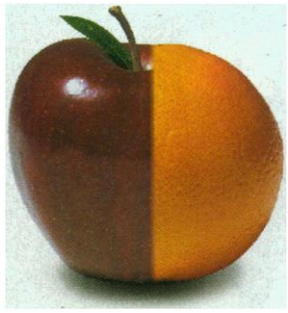

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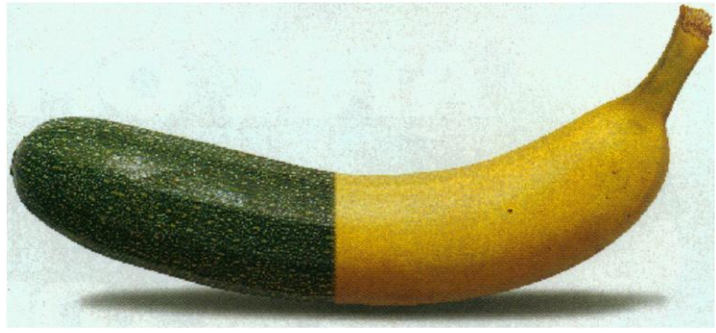

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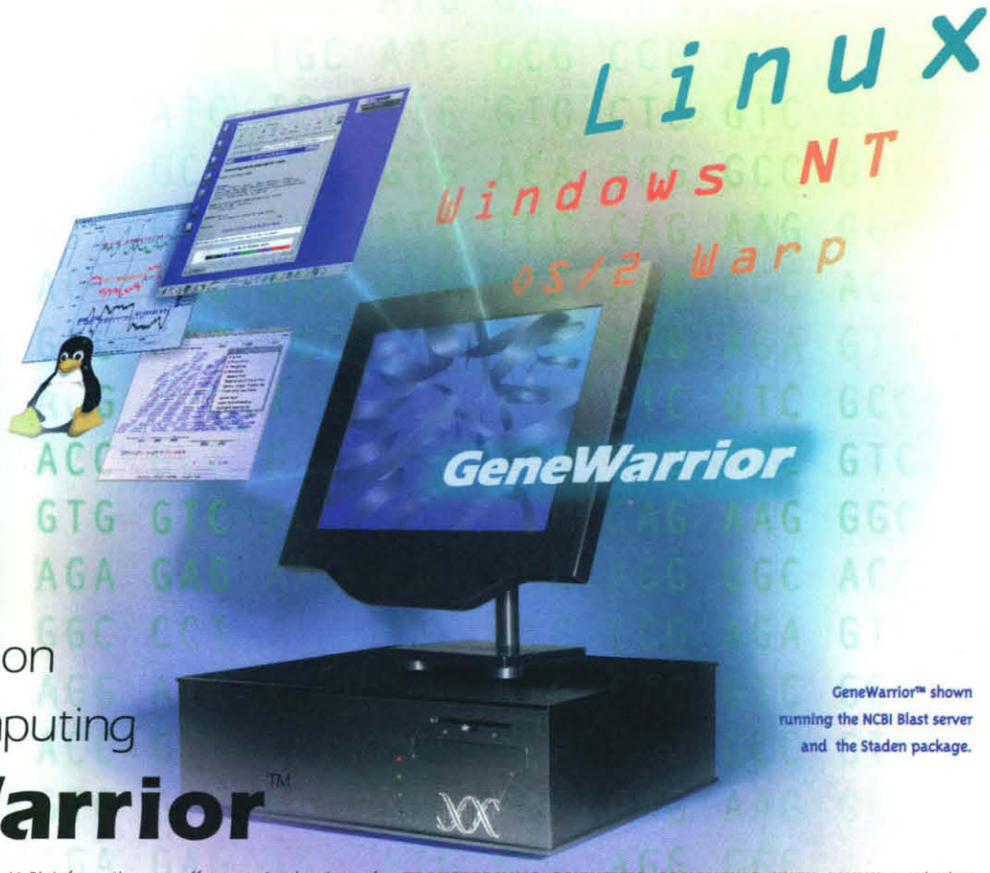
Charles Darwin, "On the Origin of Species" (1859)



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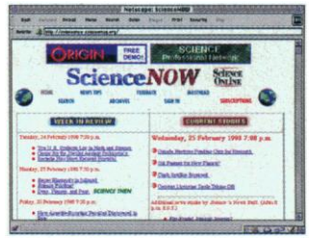

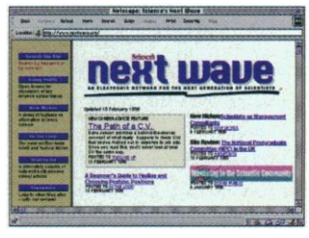

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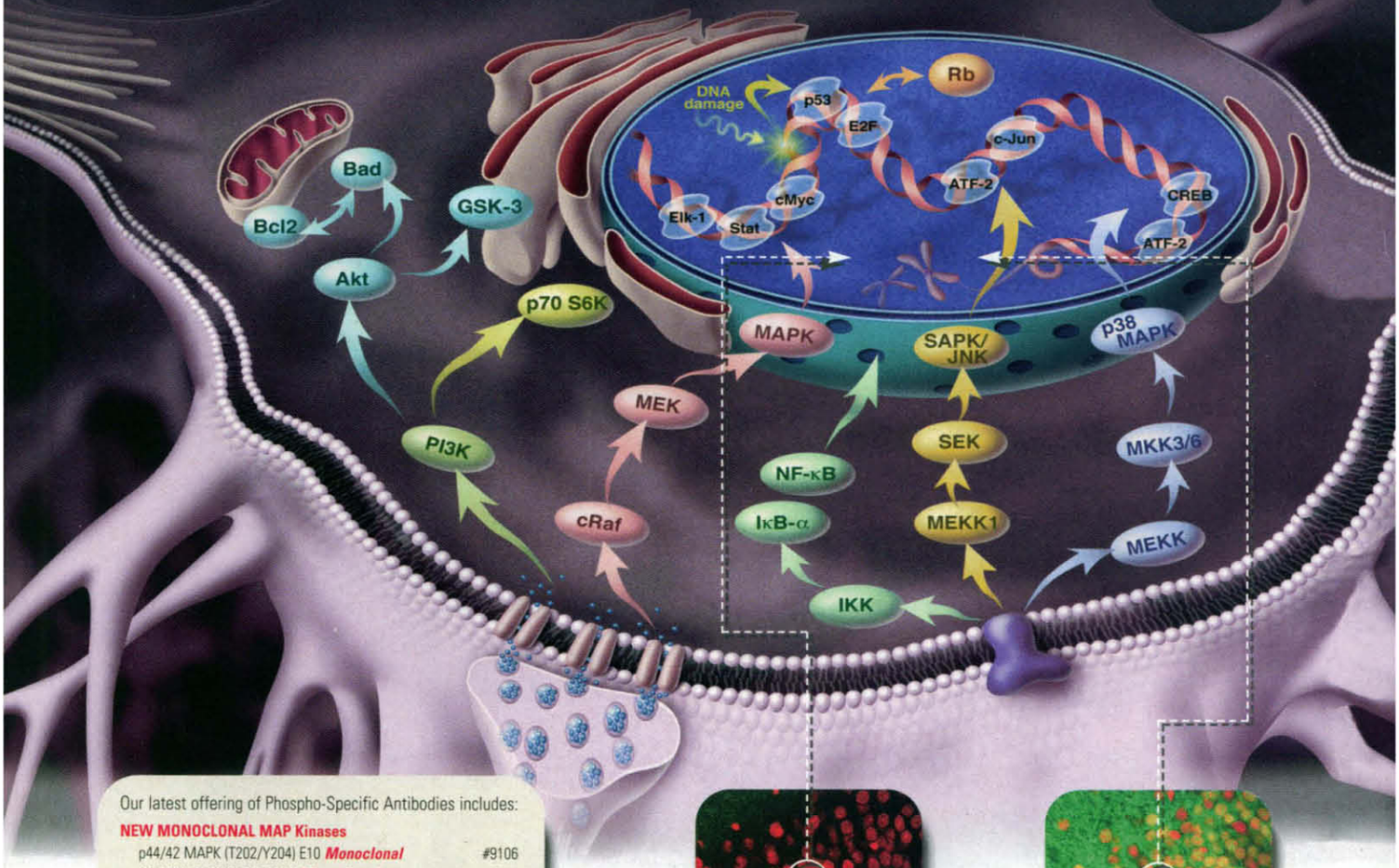

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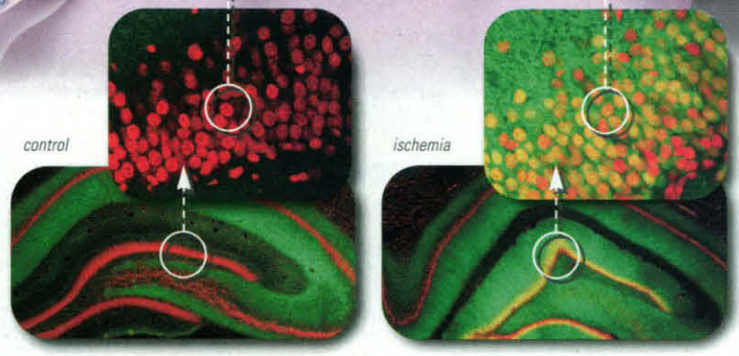

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Confocal images of immunostaining with Phospho-p44/42 MAP Kinase E10 Monoclonal Ab (green) and propidium iodide (red) in rat hippocampus from tissue sections of control and 15 minute transient cerebral ischemia followed by 30 minutes of reperfusion. Photo shows high resolution dentate gyrus (top) and low resolution hippocampus (bottom). Yellow represents overlay of red and green. (Provided by Dr. Bingren Hu, UCSD).

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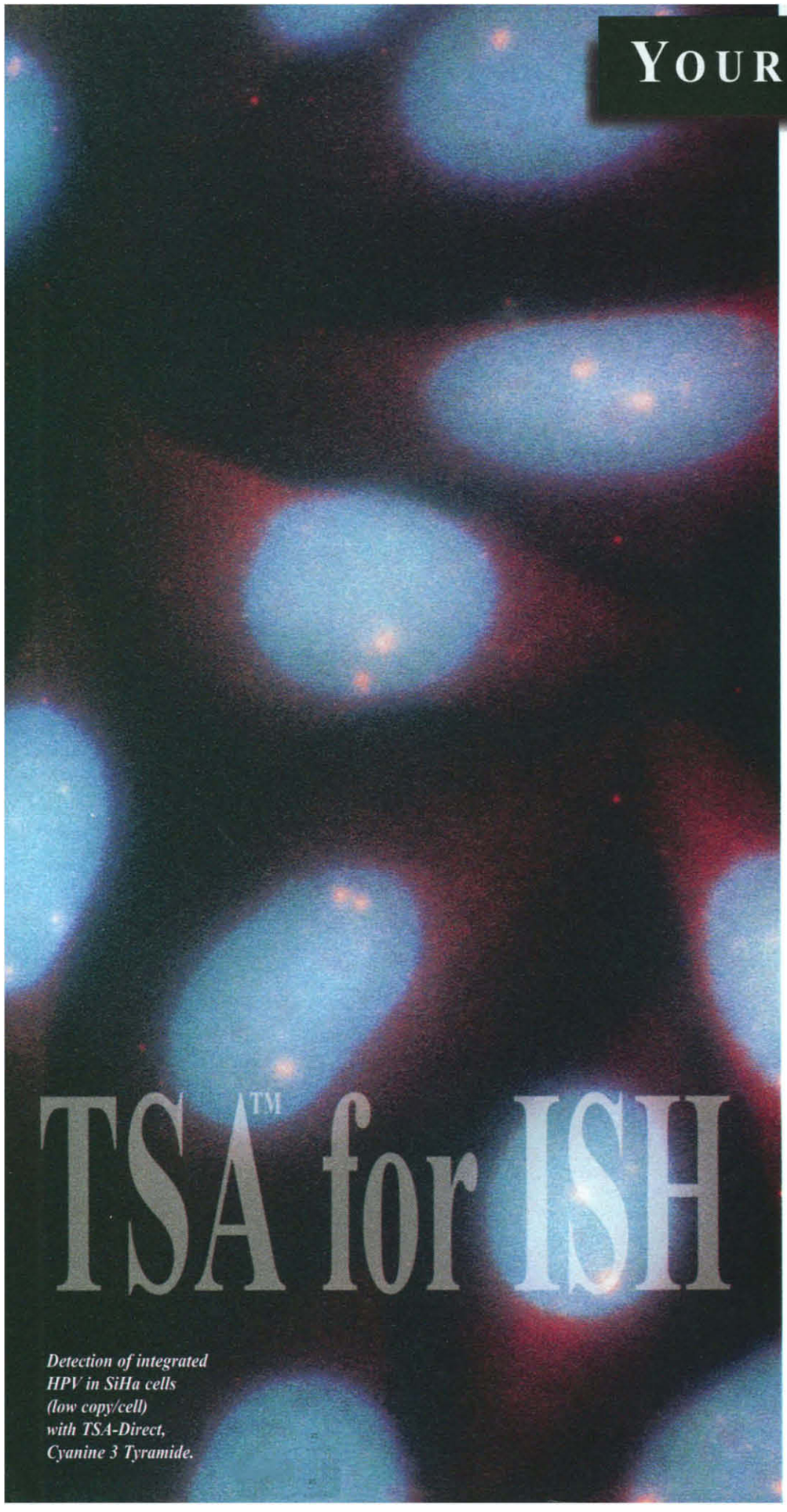

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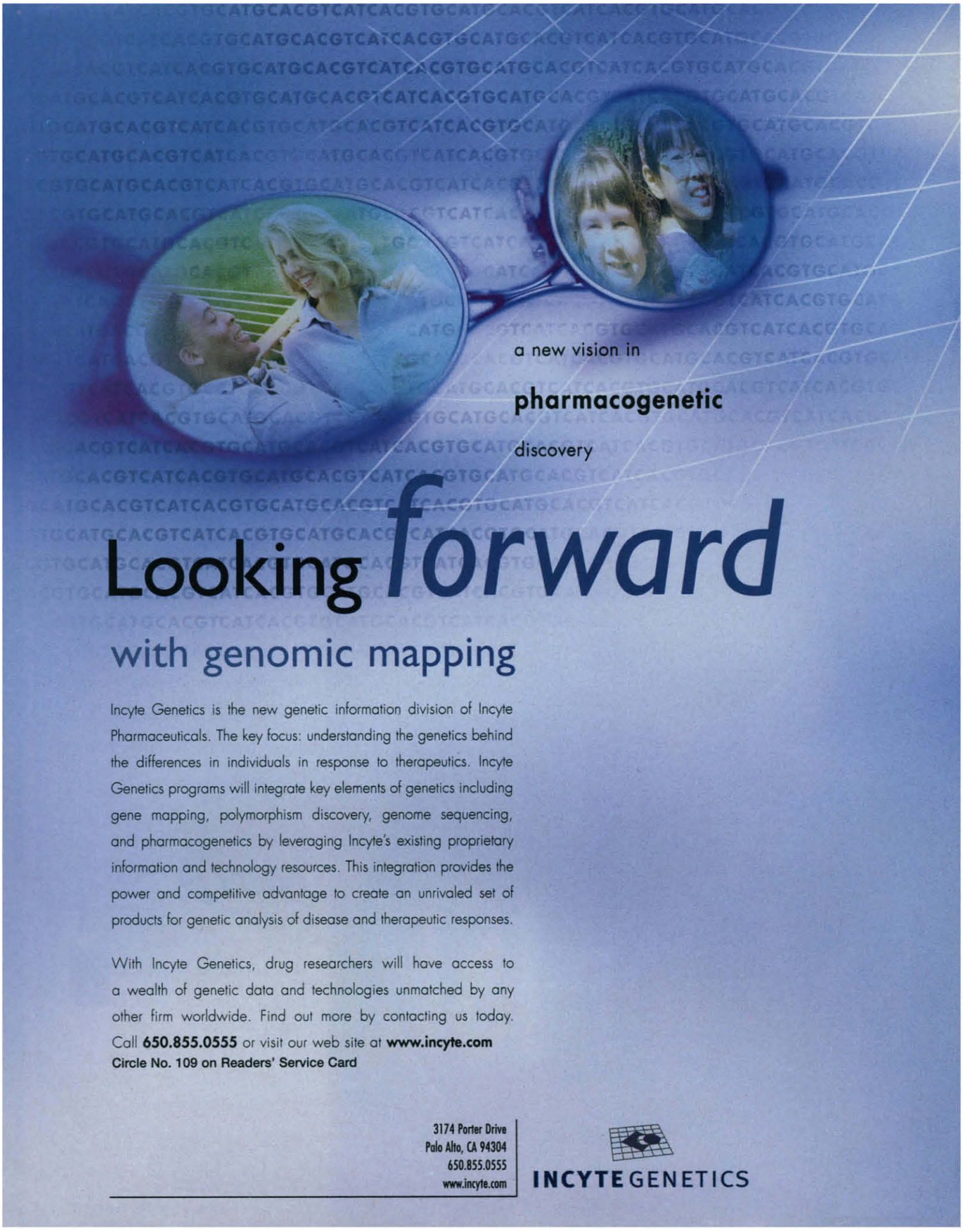

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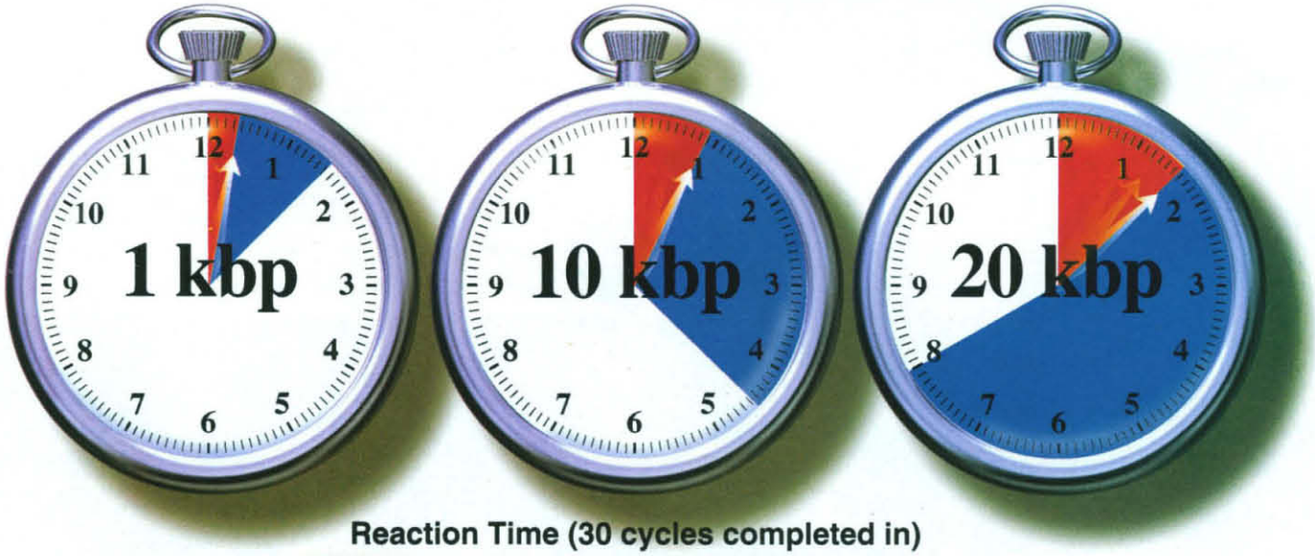

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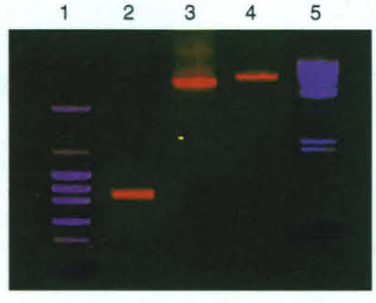

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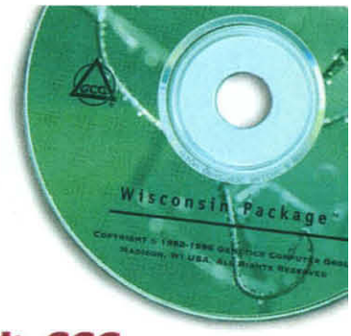

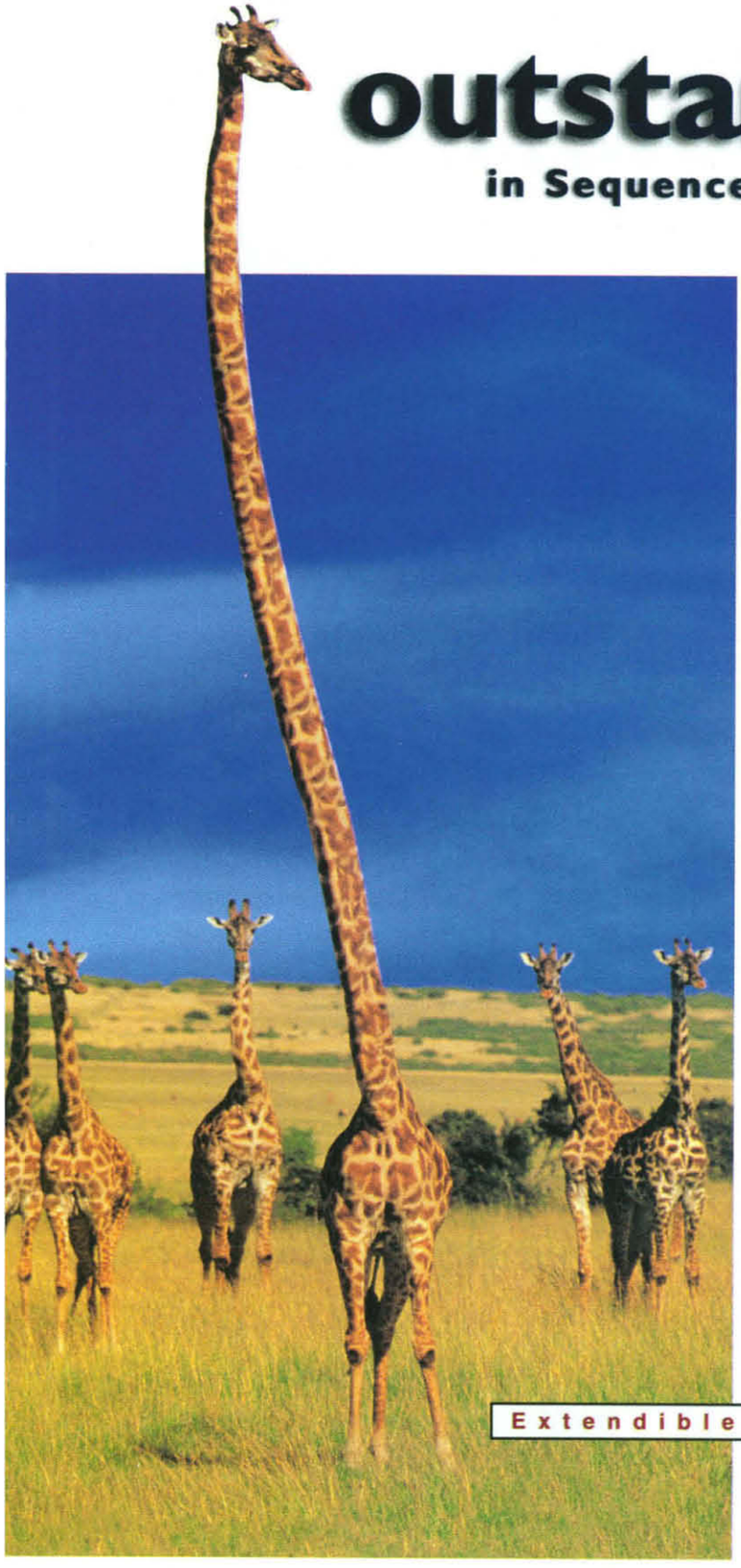

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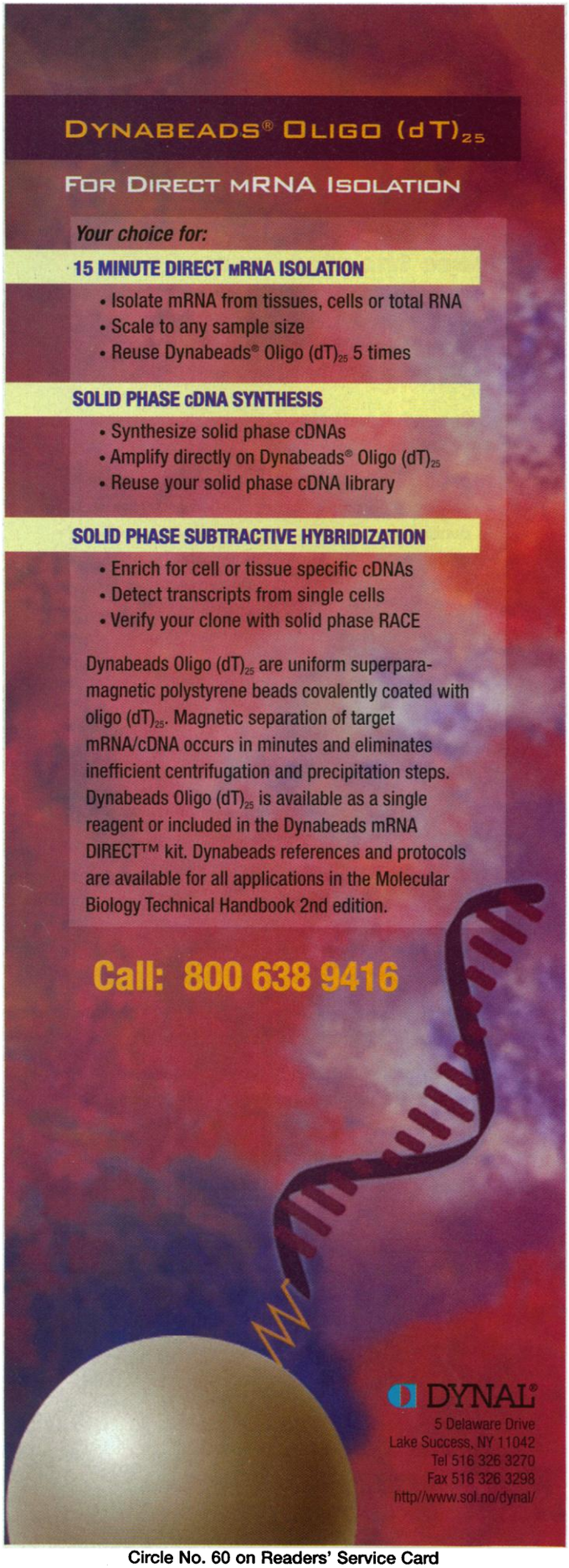

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