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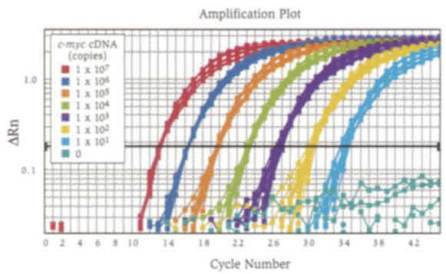

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Science

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New cancer drugs, new challenges

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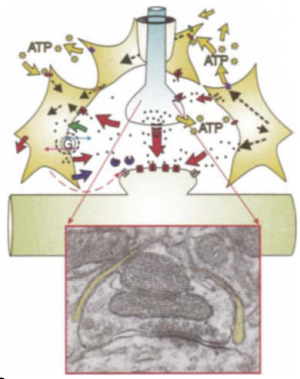
NEWS FOCUS

SCIENCE'S COMPASS



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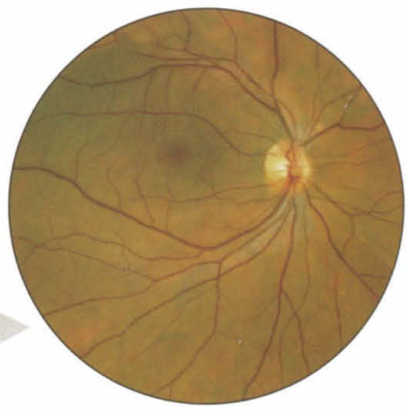

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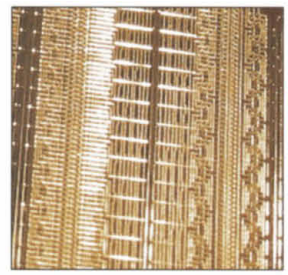
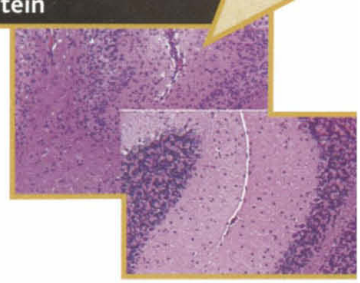


COVER 580

A microfluidic chip, fabricated from silicone elastomer, that contains 2056 integrated microvalves in an area of one square inch. The chip is analogous to an electronic comparator and is an example of microfluidic large-scale integration. The complex plumbing in the chip allows 512 chambers to be mixed pairwise, with individual addressing and recovery of the results. [Photo: S. Maerkl]

589
Kilimanjaro ice spire

New on *Science* Express Neurotoxicity of cytosolic prion protein



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CONTENT HIGHLIGHTS AS OF 18 OCTOBER 2002

science magazine www.sciencemag.org

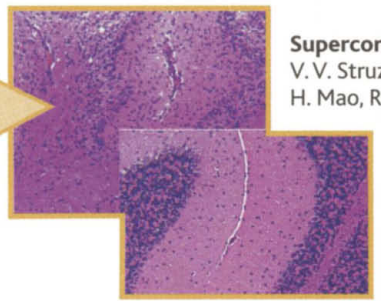
SCIENCE EXPRESS www.sciencexpress.org

Neurotoxicity and Neurodegeneration When PrP Accumulates in the Cytosol J. Ma, R. Wollmann, S. Lindquist

Mice expressing a cytosolic isoform of the prion protein develop profound neurological problems.

Conversion of PrP to a Self-Perpetuating PrP^{Sc}-like Conformation in the Cytosol J. Ma and S. Lindquist

Under certain circumstances, accumulation of prion protein in the cytosol leads to spontaneous generation of the self-perpetuating, misfolded scrapie isoform.



Superconductivity in Dense Lithium V. V. Struzhkin, M. I. Eremets, W. Gan, H. Mao, R. J. Hemley

Inducing a superconducting phase in lithium by applying pressure at low temperature reveals that it is not a simple metal.

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career resources for scientists

SINGAPORE: Scientists in Venture Capital T. Yugarani

Some Singaporean scientists find their niche in V.C.

UK: Creating and Exploiting Intellectual Property—My Job as a Manager A. Bach

A first-hand account with an insider's tips for breaking into the IP job market.

NETHERLANDS: Time to Reconsider S. Löhner

A Ph.D. student leader offers her solutions to some burning issues.

CANADA: Tenure Review—The Long and the Short of It L. McKarney

The contentious debate over the appropriate length of faculty probationary periods heats up again...

US: Biotech Job Market Hype—Reading the Media Spin D. Jensen

Our *Tooling Up* columnist tells the real story about how to open doors to biotech careers.

US: A Career Development Plan for Postdocs L. Haak

A FASEB blueprint offers professional development guidance for postdocs and their PIs.

KNOWLEDGE ENVIRONMENTS

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science of aging knowledge environment

PERSPECTIVE: Mitochondrial Abnormalities and Oxidative Imbalance in Neurodegenerative Disease O. Ogawa, X. Zhu, G. Perry, M. A. Smith

Coenzyme Q_{10} delays disease progression in Parkinson's patients.

NOTEWORTHY THIS WEEK: Losing Their Grip R. J. Davenport

Old immune cells let transgressors slip away.

NOTEWORTHY THIS WEEK: All Fat Is Not Created Equal M. Beckman

Stomach surplus hinders rodents' ability to use glucose.

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signal transduction knowledge environment

PERSPECTIVE: Will the Real LHC II Kinase Please Step Forward? J. F. Allen and H. L. Race

How electron flow through the chloroplast photosystems is regulated by the wavelength of light.

PERSPECTIVE: Semaphorins—Green Light for Redox Signaling? A. Ventura and P. G. Pelicci

MICAL may be a monooxygenase involved in mediating growth cone signaling.

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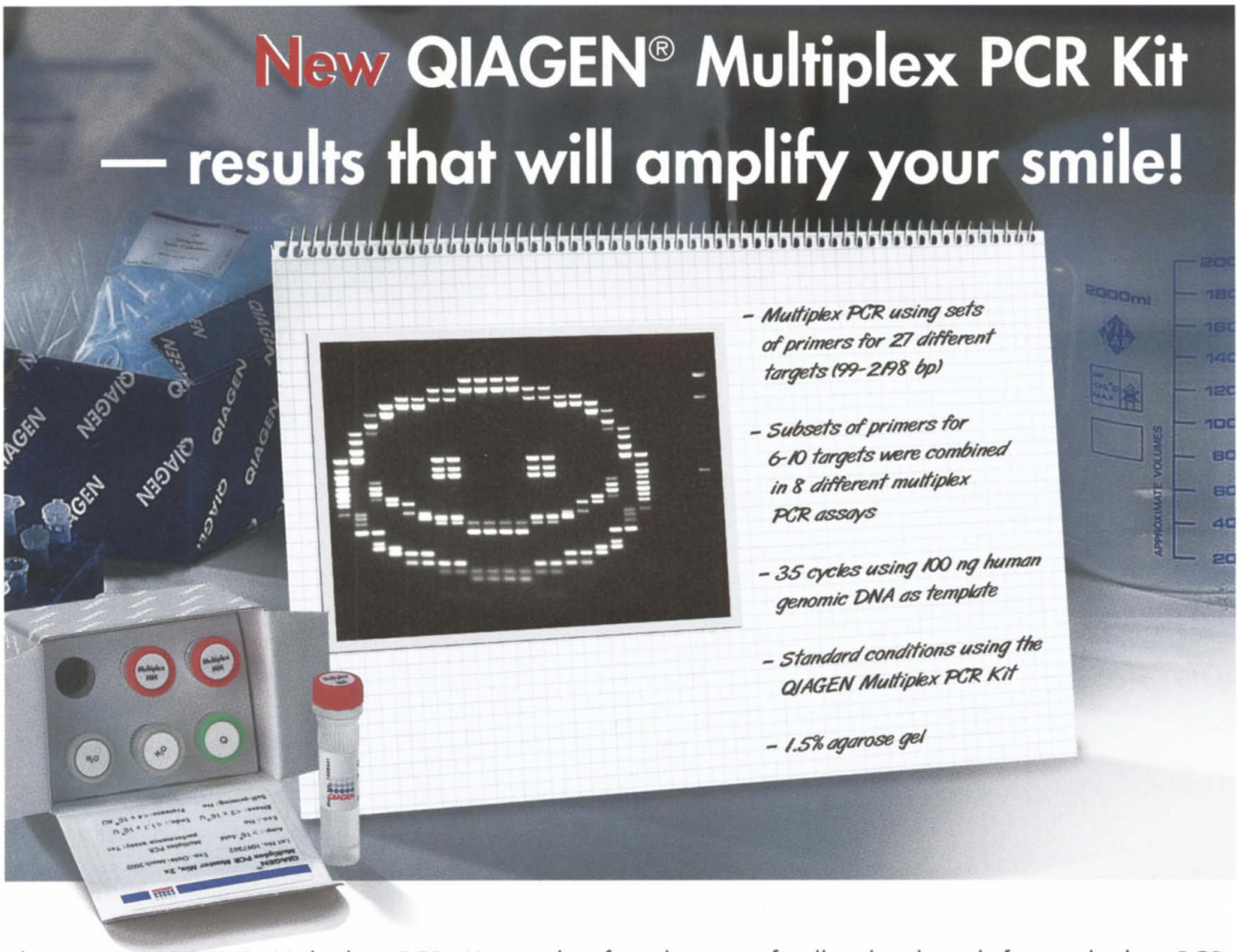

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THIS WEEK IN Science

edited by Phil Szuromi

Flow-Through Integrated Circuits

In an electronic integrated circuit, all of the necessary components are fabricated onto a single semiconductor, which eliminates the need for manual assembly of the individual transistors, capacitors, and resistors. Thorsen *et al.* (p. 580; see the cover) have now fabricated an analog in a microfluidics system with a set of individually addressable microvalves. Such a system can act as a fluidic random-access memory and can also be used as a series of microreactors in which each reactor can be individually controlled.

593 Satellite Disk Drives

The Galilean satellites Io, Europa, Ganymede, and Callisto accreted in the disk of debris developed during the formation of Jupiter. Io, Europa, and Ganymede are currently synchronized in their orbital patterns, which indicates that initially random orbits have migrated into a stable system. Peale and Lee (p. 593) show that the orbital patterns were stabilized by disk-satellite interactions. Thus, the orbital patterns are primordial and do not require unusual tidal torques from Jupiter.

And in Brevia ...

The stable carbon isotopic composition of a stalagmite from Belize determined by Frappier *et al.* (p. 565) displays a strong correlation to the El Niño–Southern Oscillation, which suggests that the surrounding ecosystem may be acting as a climate signal amplifier.

Peering into the Vortex Core

The existence of magnetic vortex cores was predicted almost 40 years ago, but they have only recently been observed experimentally. However, the rather low spatial resolution of the magnetic surface probes could not resolve the spin structure within the vortex core. Wachowiak *et al.* (p. 577; see the Perspective by Miltat and Thiaville), using a spin-polarized scanning tunneling microscope, now provide such details. They verify the long-standing predictions that the width of the core is dependent on the stray field from the out-of-plane magnetization and can be increased or reduced by the application of a magnetic field parallel or antiparallel to the core magnetization, respectively.

African Ice

Ice core records are generally associated with high latitudes, but low-latitude glaciers are now providing glimpses into climate in those regions for which we have poorer records of recent climate. One such place is tropical east Africa. Thompson *et al.* (p. 589; see the Perspective by Gasse and the news story by Krajick) report results from cores drilled in the ice fields on the top of Mount Kilimanjaro, Kenya. They analyzed the oxygen isotopic composition, dust content, and major ion abundance of six cores, the oldest of which extends back to approximately 12,000 years before present, to create a high-resolution record of the Holocene climate in this region.

We're JAMMing

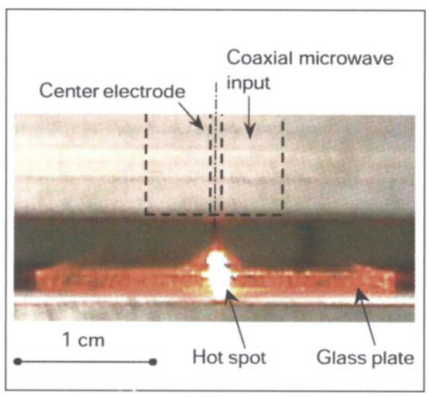
A protein motif, termed JAMM, has been identified that appears to be responsible for encoding a metallo-isopeptidase activity important in cleaving either ubiquitin or ubiquitin-like Nedd8 moieties from proteins (see the Perspective by Hochstrasser). Cope *et al.* (p. 608) show that in the COP9 signalosome, the JAMM motif acts to deneddylate substrates, such as those that are important in eye development. Verma *et al.* (p. 611) show that in the proteasome lid subcomplex, the JAMM motif is important in cleaving ubiquitin from a variety of substrates, and that inactivation of the JAMM motif is lethal in yeast.

Model Grasslands

The soil biota provides many services, including soil fertility, bioremediation, control of soil structure, and habitat for vertebrates. Information on how disturbances, such as land degradation, erosion, and elevated CO_2, affect the soil community and the ecosystem processes they control is important for global sustainability. However, investigating these relations has been a challenge, given the complexity of soil habitat and its biodiversity and the density and abundance of soil-dwelling organisms. Bradford *et al.* (p. 615) manipulated biodiversity by changing the size of the organisms introduced into soil microcosms and found marked responses in the short term in plant community composition and other variables. Strikingly, there was no change in two major ecosystem parameters generally measured for aboveground (and global) ecology—total ecosystem carbon balance and net primary production.

Hot Spot

Microwave radiation, long used for heating and drying, can now be used for drilling nonconductive materials such as ceramics, glass, concrete, and silicates. Jerby *et al.* (p. 587; see the news story by Sincell) describe the design and operation of a drill that focuses the radiation, creating a localized hot spot at the subsurface below the drill tip. As many materials better absorb microwave radiation as the temperature increases, a runaway reaction occurs at the drill tip, which can be slowly pushed through the molten material. The drill has the advantage that it is both quiet and creates little mess, and may fill a niche where conventional mechanical drills or laser drills are not ideal.



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CONTINUED ON PAGE 493

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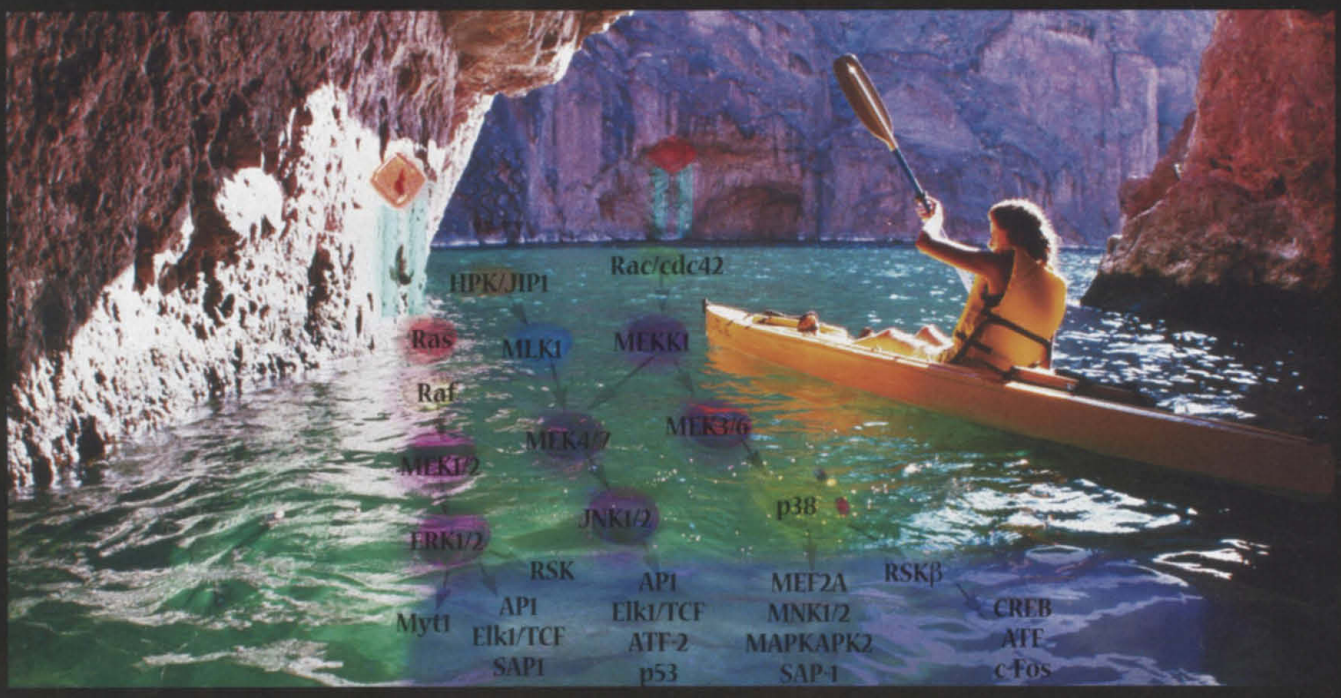

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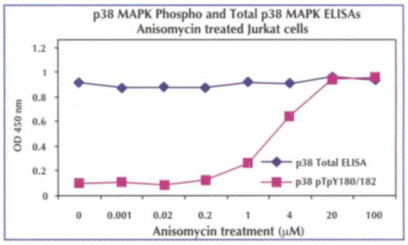
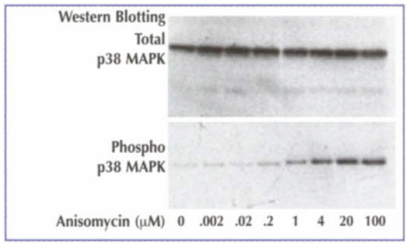


Solid Results



Cell lysates from Jurkat cells treated with various concentrations of anisomycin were tested with Total p38 MAPK ELISA (Cat.#KHO0061), phospho p38 MAPK ELISA (Cat.#KHO0071) and Western blotting. The data show excellent correlation between ELISA and Western blotting.

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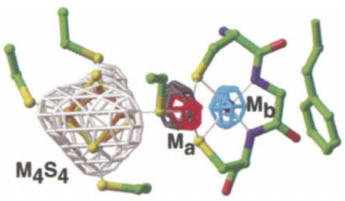
Biosilica Via Highly Phosphorylated Peptides

The cell walls of diatoms—unicellular algae that are the greatest primary producers of the ocean—are made from intricately patterned biosilica. Highly modified peptides called silaffins, which have been extracted from diatom biosilica, can precipitate nanometer-scale silica spheres under appropriate conditions. Kröger *et al.* (p. 584; see the Perspective by Wetherbee) now show that extraction under milder conditions preserves the native silaffins, which are highly phosphorylated. The native silaffins form a composite with silica that is likely to play a key role in the in vivo formation of biosilica by diatoms.



A Copper Surprise in CO Reduction

Acetogenic bacteria can use carbon dioxide (CO_2) as their sole carbon source. Key to this ability is the bifunctional enzyme, carbon monoxide dehydrogenase/acetyl coenzyme A synthase (CODH/ACS). In the CODH subunit, CO_2 is reduced to CO, while in the ACS subunit the CO is combined with a methyl group and coenzyme A (CoA) to form acetyl-CoA. Doukov *et al.* (p. 567; see the Perspective by Peters) have solved the structure of CODH/ACS from *Moorella thermoacetica* at 2.2 angstroms (Å). Focusing on the metal cluster where acetyl-CoA is assembled (C-cluster), they find an $[Fe_4S_4]$ cubane bridged to not to just a Ni atom but to a Cu-Ni binuclear site. The presence of Cu in CODH/ACS enzymes has not been reported previously, and, based on the binuclear center, the authors propose a binuclear catalytic mechanism. A long channel (138 Å) provides a passage for CO and prevents it from being released into solution.

Developing in the Shadows

Visual inputs from right and left eye are segregated in the brain's visual cortex into ocular dominance columns. Although evidence suggests that ocular dominance columns form only in response to neuronal activity, other results have also suggested that they may form in response to intrinsic developmental cues. Now, taking advantage of a naturally occurring imbalance in visual inputs, Adams and Horton (p. 572) show that asymmetric visual deprivation is a normal part of development and that formation of ocular dominance columns is affected. The blood vessels that course over the retina shade each eye's retina in unique patterns. In the brain of the squirrel monkey, representations of these visual asymmetries are reflected in the ocular dominance columns. Compared with macaques and humans, the squirrel monkey's general ocular dominance columns are rather smaller and less well delineated. This difference may account for why the asymmetries of visual input caused by retinal blood vessels have a more apparent affect on the organization of the squirrel monkey's visual cortex.

Discerning the Cause of the Pause

The written word is readily identified by the blank spaces surrounding it. How do we learn to identify where one spoken word ends and the next begins? A previous study of infants has suggested that words can be identified by taking a low probability transition between syllables as a word break; that is, two syllables that rarely occur in order are more likely to be the end of one word and the start of the next. Another previous study suggests that infants can generalize from experience with a structured set of syllables and segment unfamiliar syllables into the same word structure. Peña *et al.* (p. 604; see the Perspective by Seidenberg *et al.*) have examined both kinds of pattern recognition in adults and found that generalization can be induced by a subliminal gap of 25 milliseconds between words, but that increased exposure to a continuous stream of syllables does not result in learning.

The Signature of Stem Cells

Are there genes that characterize various sets of stem cells? Ivanova *et al.* (p. 601) and Ramalho-Santos *et al.* (p. 597) used transcriptional profiling of mammalian embryonic and adult stem cells to identify genes that are common among hematopoietic stem cells, embryonic stem cells, and neural stem cells. These subsets of genes may provide stem cells with the ability to self-renew, to generate differentiated cells, or to do both, and hence represent, according to the authors, "stemness" or a "stem cell molecular signature."

CREDIT: DOUKOV *ET AL.*

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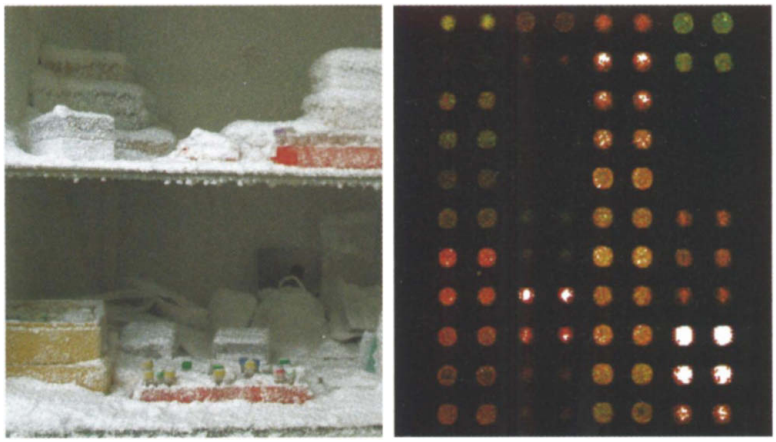

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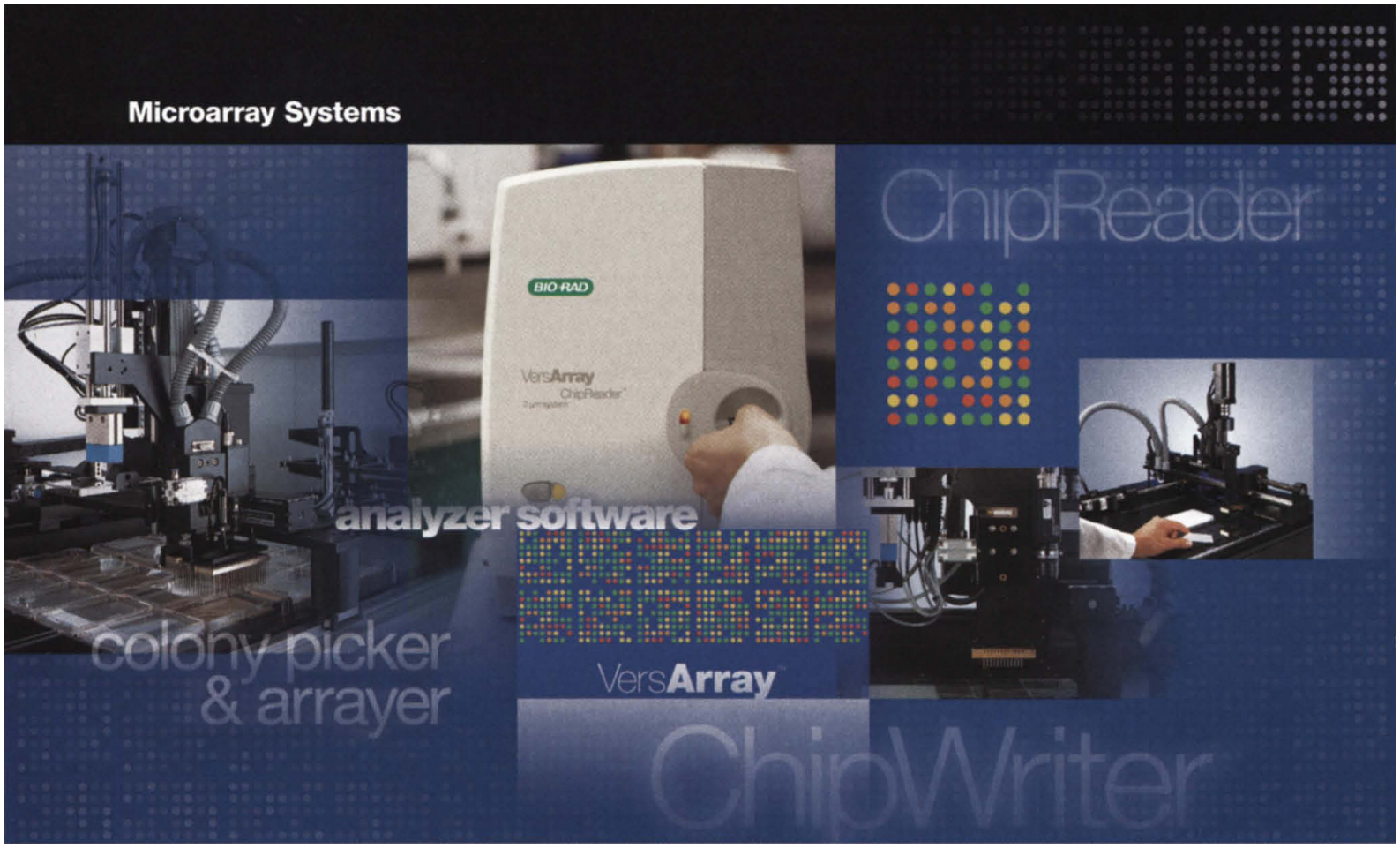

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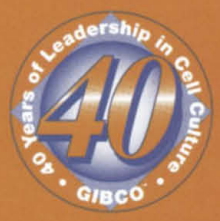

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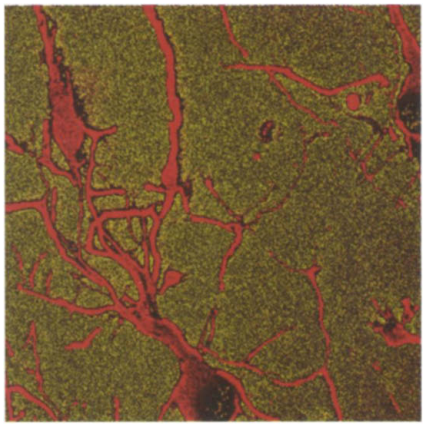

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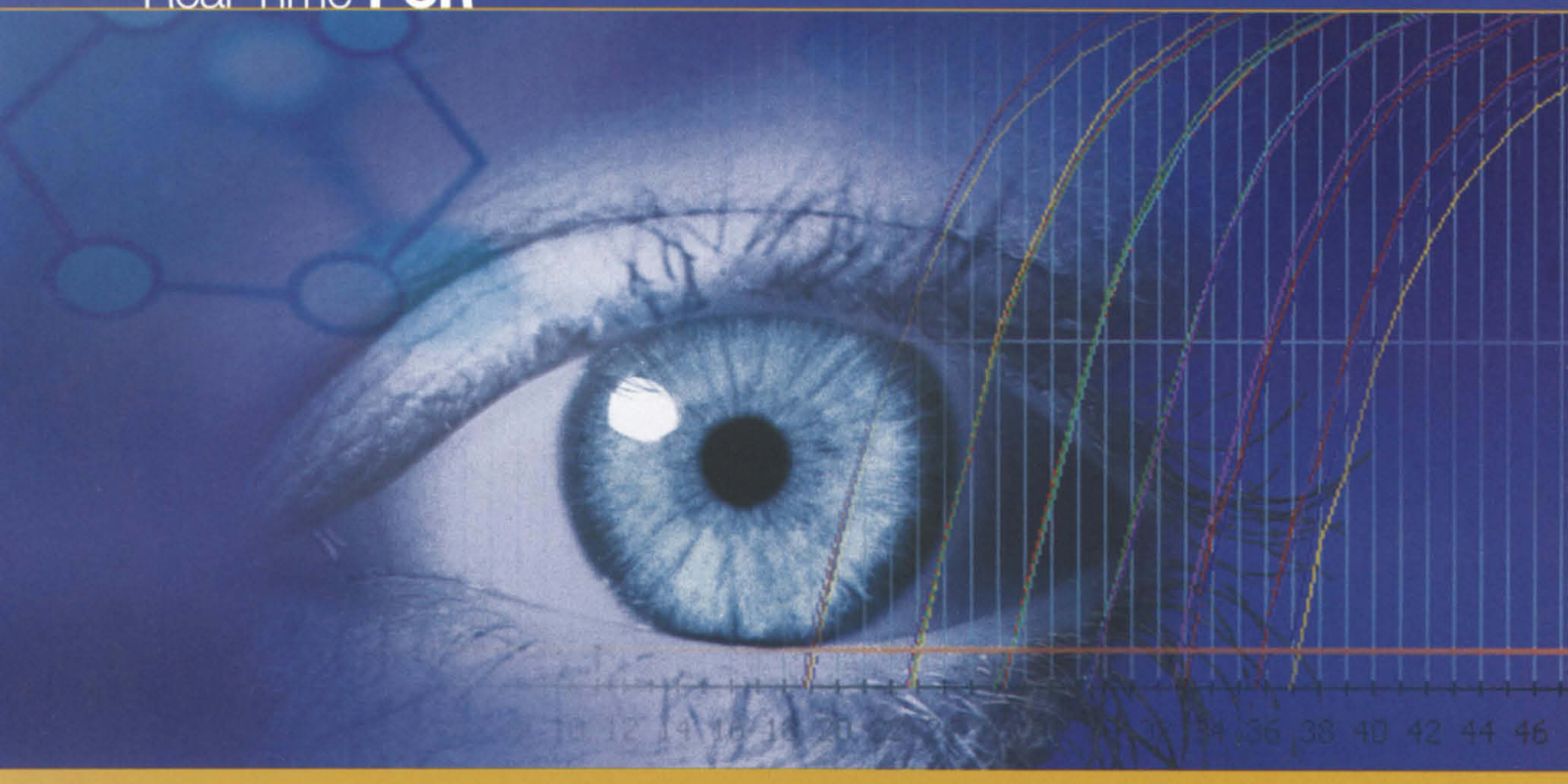

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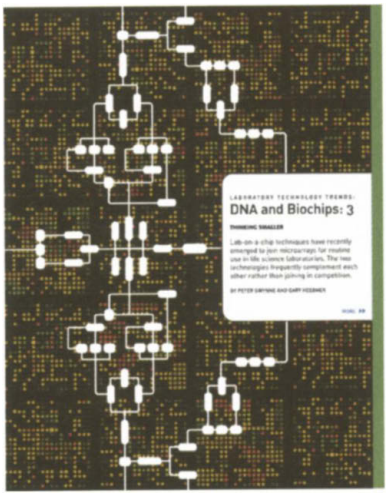

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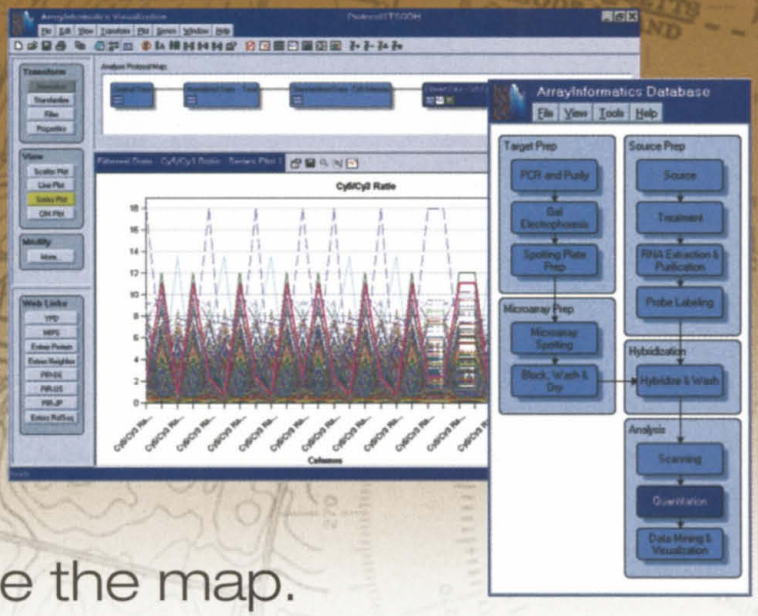

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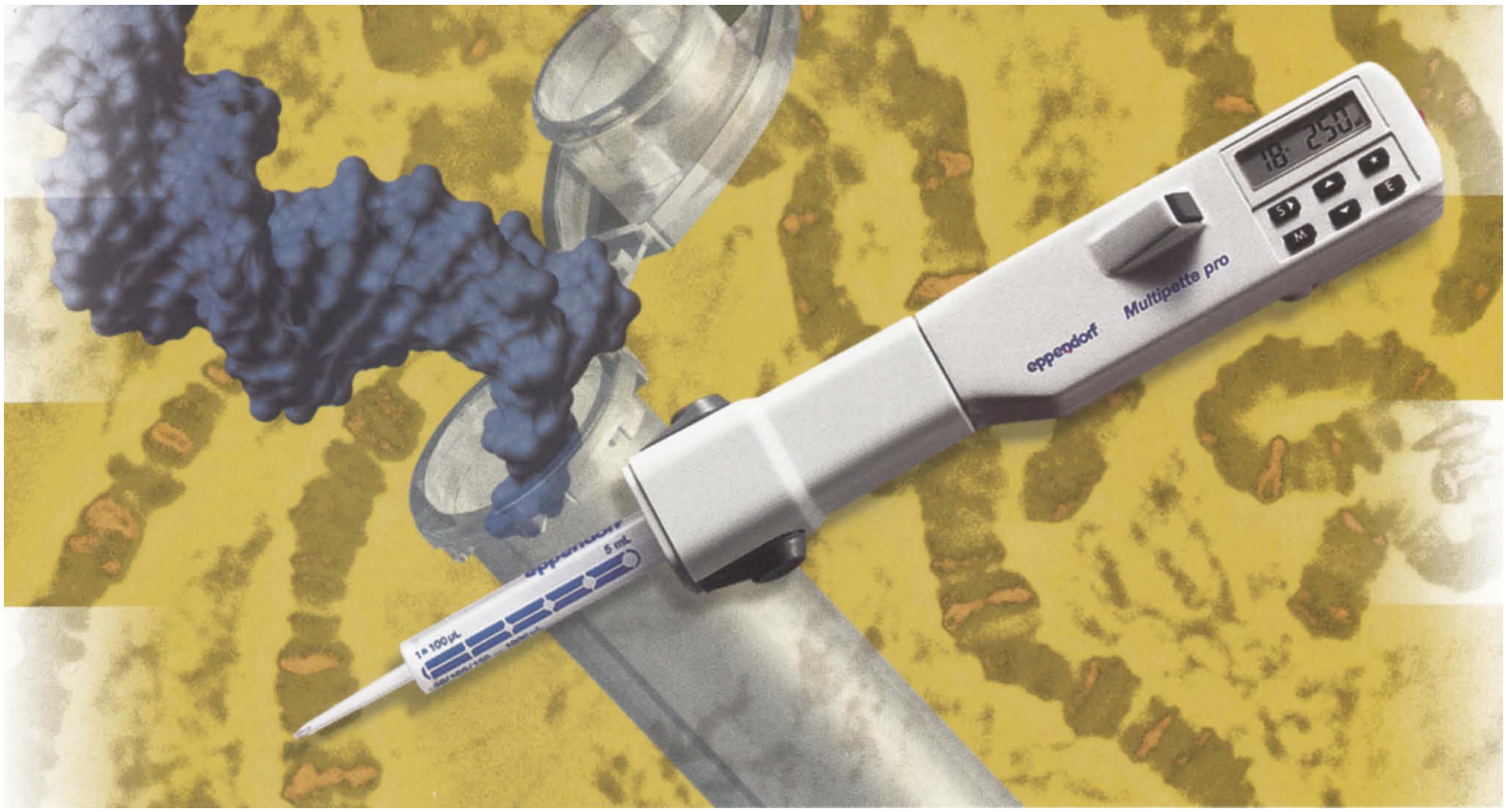

Synergy!

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Multipette® pro and Eppendorf® PCR MasterMix: an unbeatable intelligent team for reproducible experiments in the PCR field.

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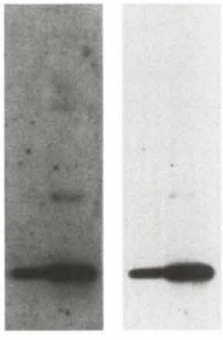

High background, shading, overexposed bands and speckling are problems inherent to film exposure. High background and shading can be caused by overexposure, poor blocking buffer, or inappropriate enzyme-labeled probe or antibody concentration. Overexposed bands are a common occurrence when the enzyme-labeled probe or antibody concentration used is too high, or if the film was exposed for too long. Speckling and shading occur when enzyme conjugates form complexes and precipitate on the blot. Erase-It™ Background Eliminator can correct all these problems without the need to re-expose your blot to film or re-do the experiment, allowing you to visualize your data within minutes. The Erase-It™ Solution can be used with newly exposed films or exposed films that have been stored for years. In addition, the Erase-It™ Kit can be used with any brand of film.

Highlights:

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- Fast, easy background elimination from overexposed, speckled or shaded films
- Works with any X-ray film, new or old
- No need for time-consuming re-exposures to find the optimal image
- No need to re-optimize assay reagents to obtain the optimal image

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Product #	Description	Pkg. Size
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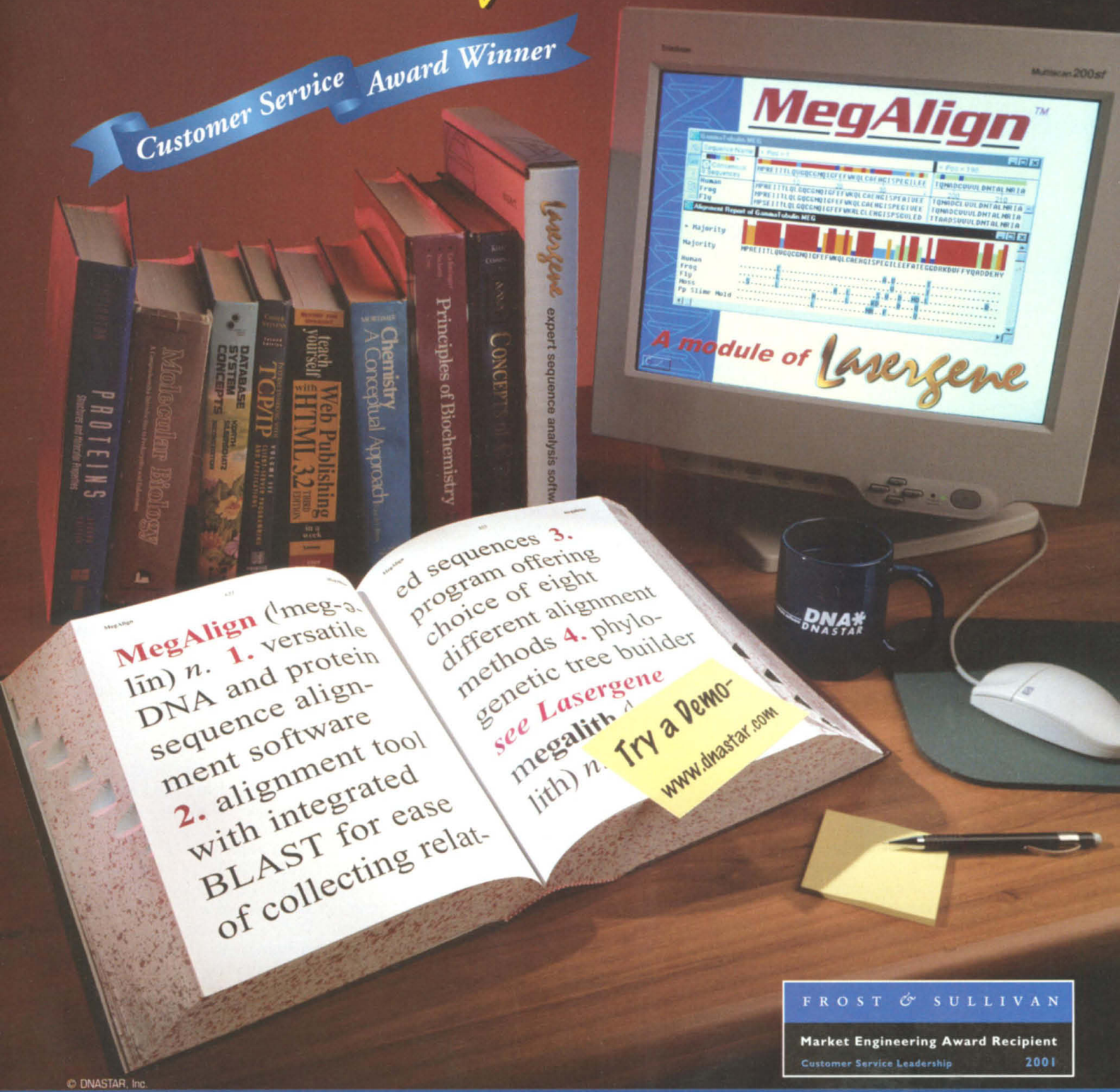
Defining Sequence Alignment



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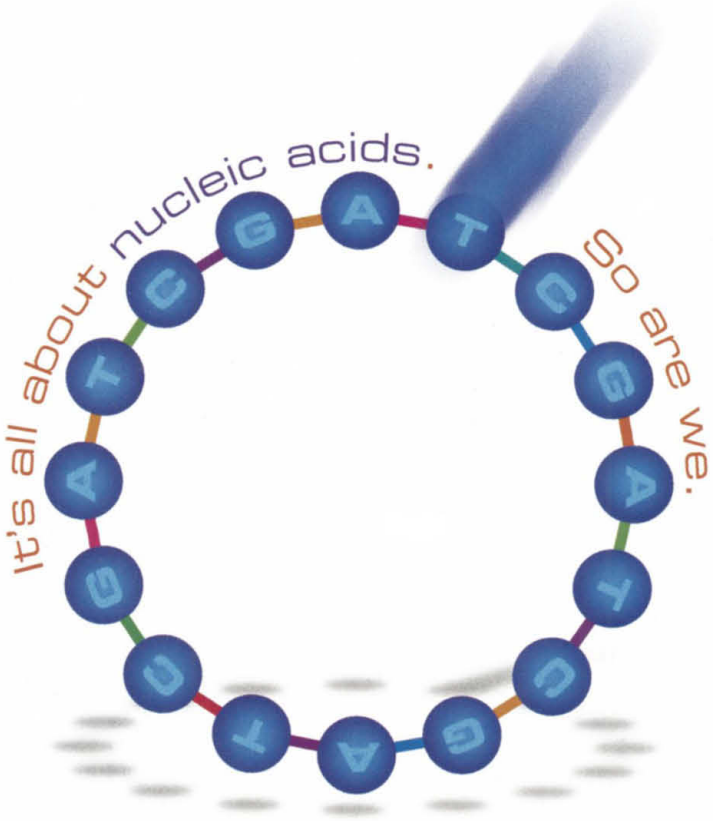

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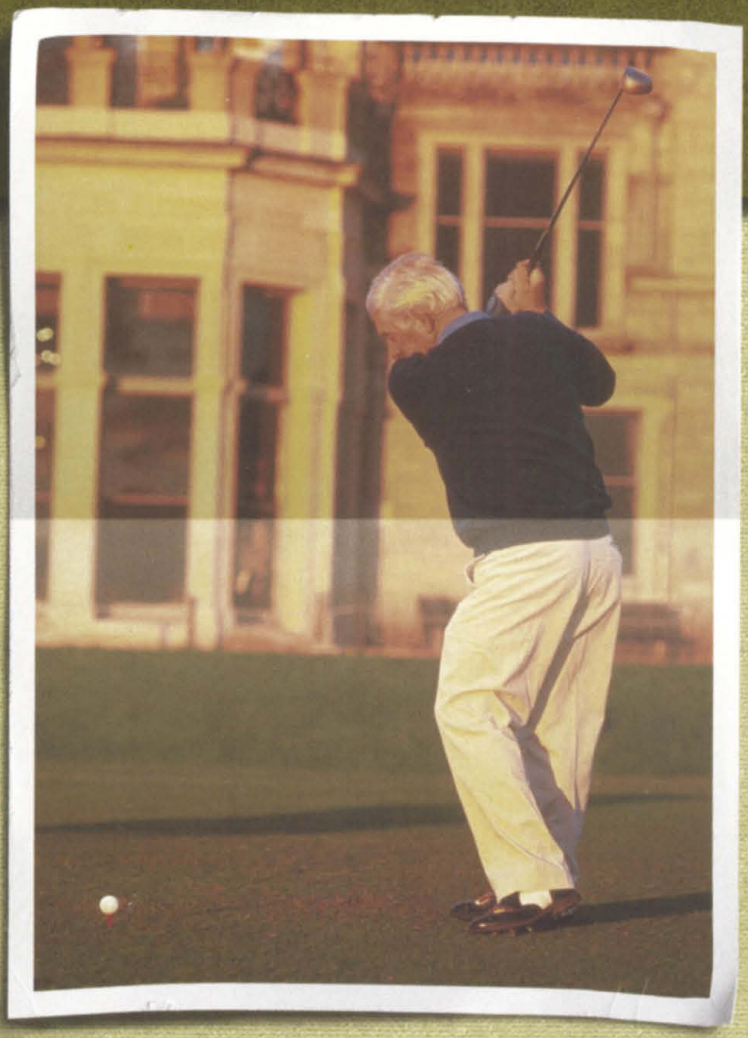
THE ONLY THING YOU WANT TO KNOW ABOUT SCOTLAND IS HOW COMPANIES LIKE AGILENT, SUN MICROSYSTEMS AND IBM VALUE OUR HIGHLY SKILLED AND EXPERIENCED WORKFORCE.

RIGHT. SO ABOUT ST. ANDREWS THEN.



The Royal & Ancient Golf Club was founded at St. Andrews in 1754 and governs the rules of golf everywhere in the world except the USA.

The original "Old Course," or Home of Golf, consisted of 22 holes. It was later reduced to 18, initiating the current standard.

King James II of Scotland banned golfing in 1457 because he thought it was distracting young men from their archery practice.

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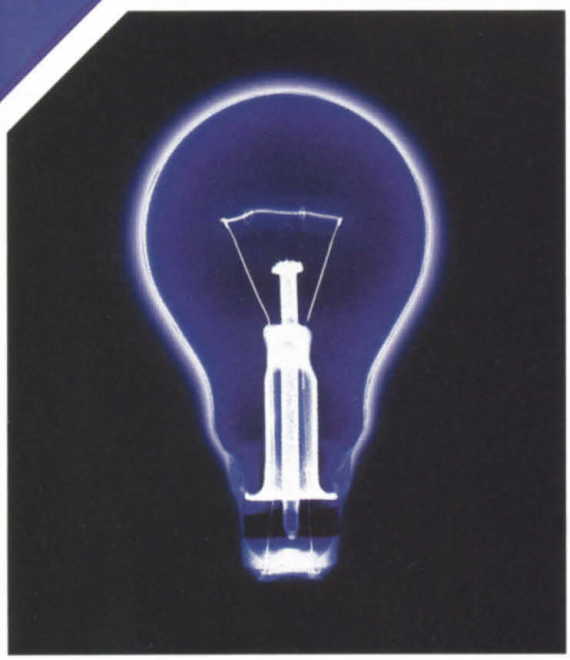
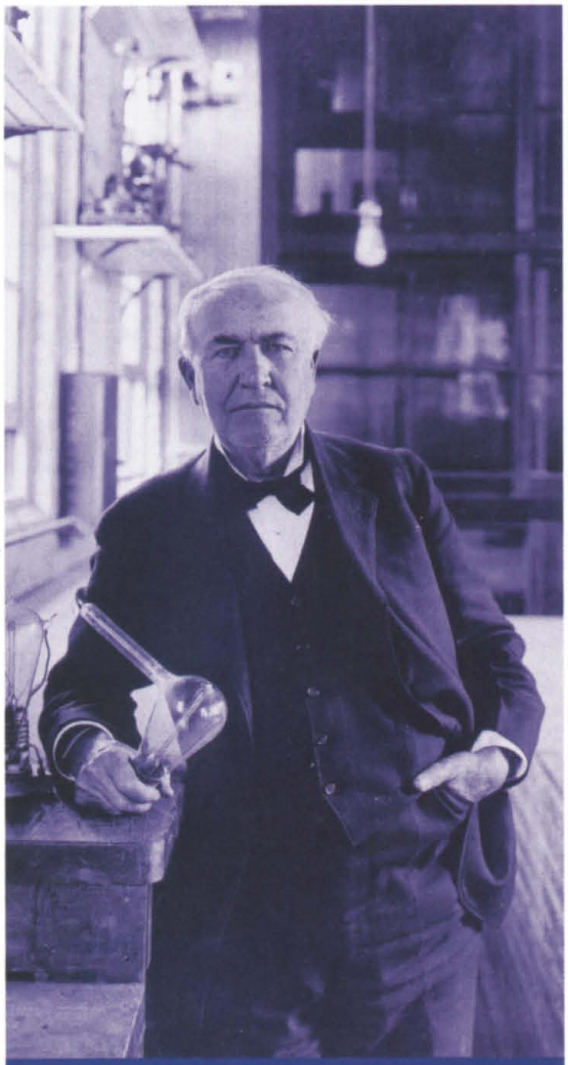


In 1880

ANOTHER LIGHT BULB WENT ON.



Thomas Alva Edison with the Edison effect bulb, c.1918

In 1879, Thomas Alva Edison invented the first practical light bulb. And in 1880, he had another bright idea: to found a journal called *Science*, in order to advance scientific discovery.

Today, AAAS publishes *Science*, one of the world's most widely cited science journals, for more than 146,000 members and weekly subscribers. AAAS members join us at the frontier of knowledge with the latest scientific reports, seminal research, and breaking news—while also supporting improved science education, sound science policy, and international cooperation.

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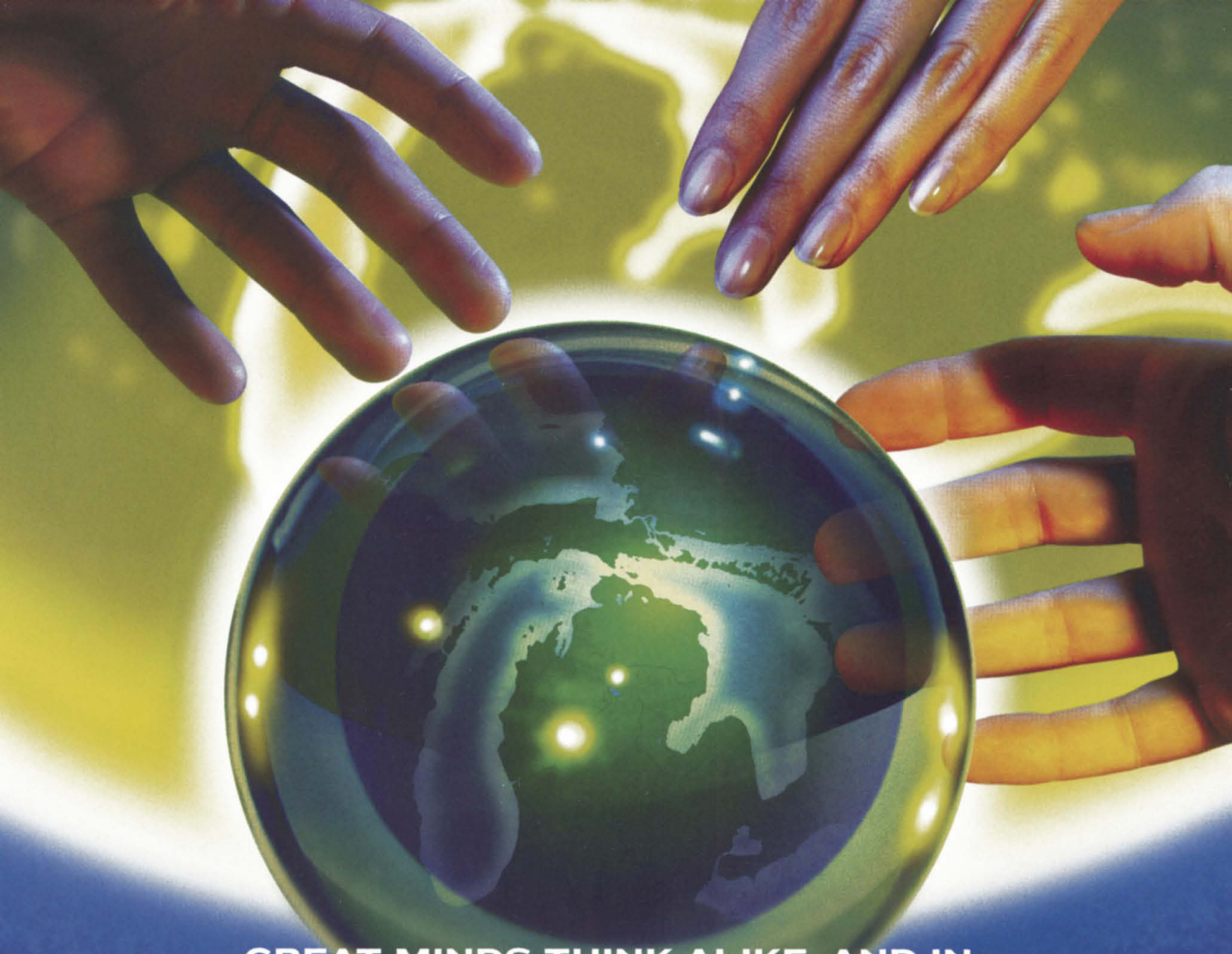

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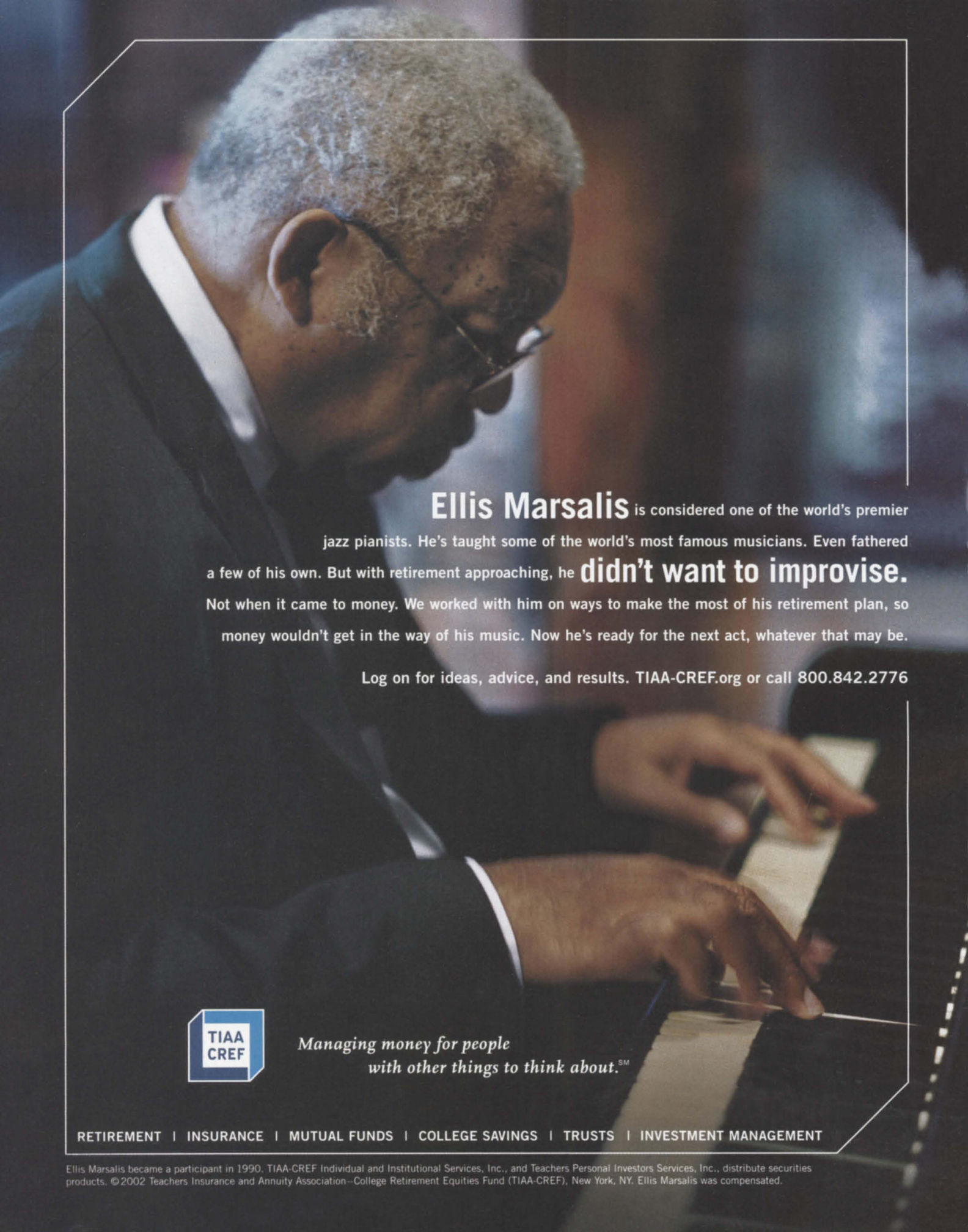

Ellis Marsalis became a participant in 1990. TIAA-CREF Individual and Institutional Services, Inc., and Teachers Personal Investors Services, Inc., distribute securities products. Ellis Marsalis was compensated.

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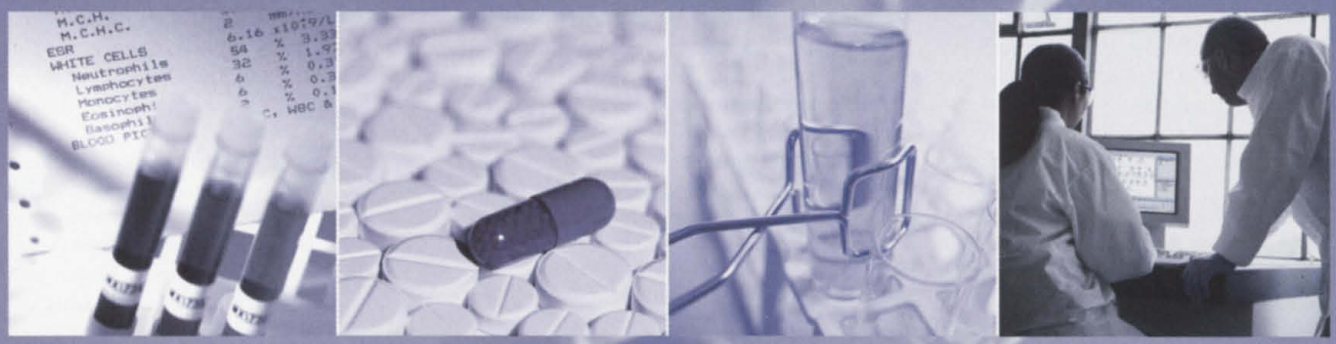

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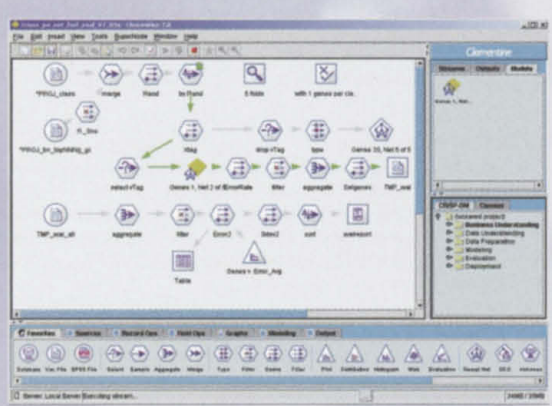

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