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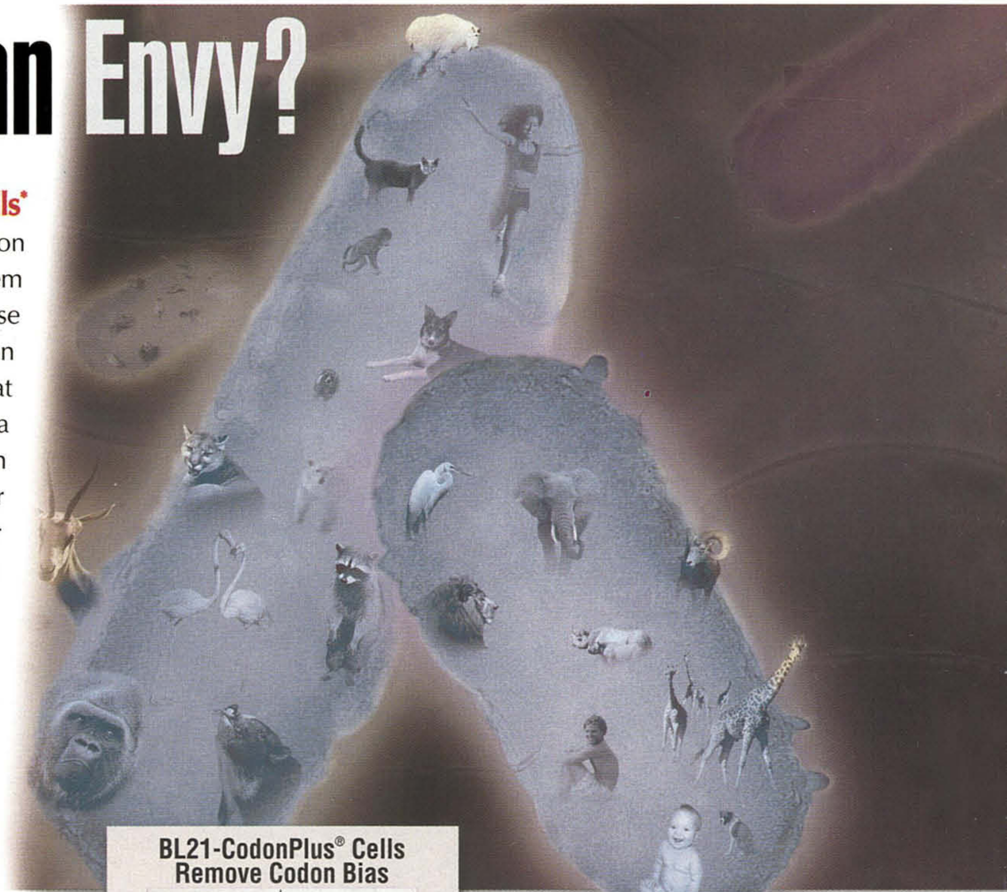

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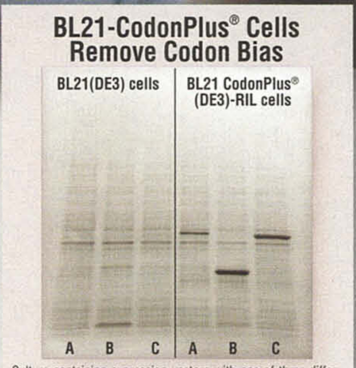

Culture containing expression vectors with one of three different proteins (A, B, or C) were induced at mid-log growth with IPTG. Cell lysates were separated by SDS-PAGE and visualized with Coomassie blue staining.

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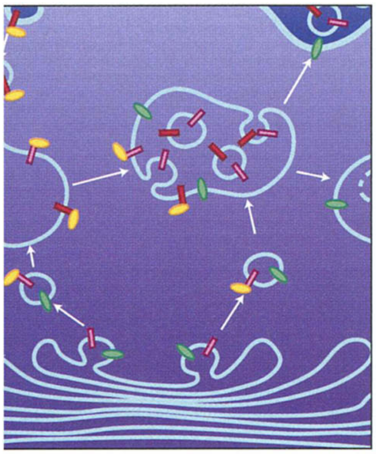
NEWS



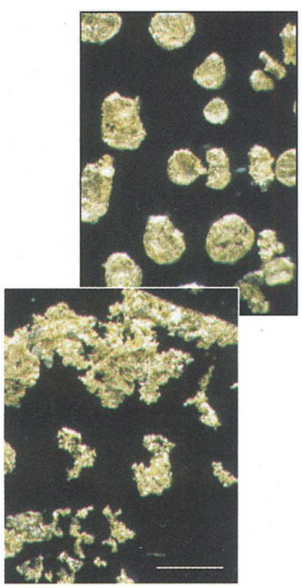
1792
Cellular supermolecule

NEWS OF THE WEEK

NEWS FOCUS

1797
GM fish and the environment

SCIENCE'S COMPASS



1815
Two types of gold

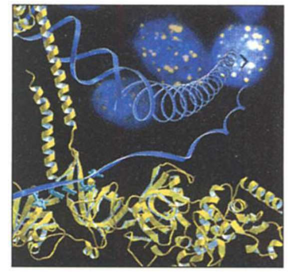
1807 LETTERS

POLICY FORUM

BOOKS *ET AL.*

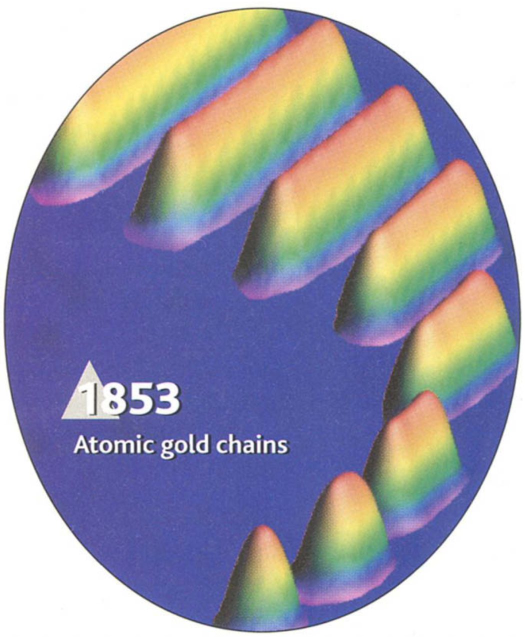
PERSPECTIVES

REVIEW

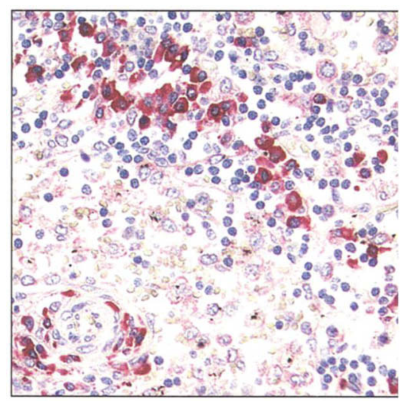


COVER 1837

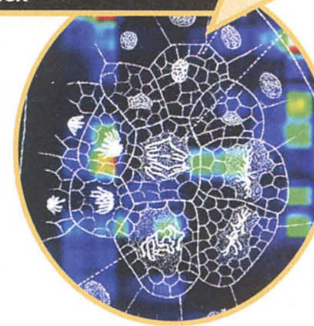
The crystal structure of BRCA2, a protein defective in hereditary breast cancer, reveals domains similar to those found in proteins that bind to DNA. The ability to bind DNA, confirmed by the structure of a BRCA2-DNA (cyan bases) complex, implicates BRCA2 in binding the DNA substrates (blue ribbons) involved in homologous recombination–mediated DNA repair. [Image: H. Yang *et al.*]



1867
Depressive dendritic cells



New on *Science* Express Stem cell (Stammzelle) flashback



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CONTENT HIGHLIGHTS AS OF 13 SEPTEMBER 2002

science magazine   www.sciencemag.org

SCIENCE EXPRESS   www.sciencexpress.org

Separable Roles for rent1/hUpf1 in Altered Splicing and Decay of Nonsense Transcripts J. T. Mendell, C. M. J. ap Rhys, H. C. Dietz

Nonsense-mediated decay and alternative splicing of mRNAs containing premature termination codons are functionally separable processes.

A Stem Cell Molecular Signature N. B. Ivanova *et al.*

"Stemness": Transcriptional Profiling of Embryonic and Adult Stem Cells M. Ramalho-Santos, S. Yoon, Y. Matsuzaki, R. C. Mulligan, D. A. Melton

Gene expression profiles for mammalian hematopoietic, neural, and embryonic stem cell populations identify their "molecular signatures."

TECHNICAL COMMENTS

Humped Pattern of Diversity: Fact or Artifact?

Molino and Sabatier (Reports, 23 Nov. 2001, p. 1702) examined tree diversity in tropical rain forests and found evidence to support the hypothesis that intermediate levels of disturbance—gaps in the canopy caused by dead and fallen trees—produce maximum species richness. Arim and Barbosa comment that "the humped pattern of species diversity in a gradient of disturbance is a methodological artifact" and that expected species richness with different proportions of individuals from any two species groups will result in a humped distribution. In a response, Molino and Sabatier agree with Arim and Barbosa's analysis but maintain that it does not explain their observed disturbance-diversity relation—and they present data showing that "low and high disturbance levels allow dominance of few species, whereas intermediate disturbances increase both the number of niches and species evenness."

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/297/5588/1763a

science's next wave   www.nextwave.org

career resources for scientists

SINGAPORE: Regional News Bytes J. Wong

Snippets of sci-tech and job market news from around the Asia-Pacific region.

UK: Tailored Advice E. Pain

Our new CareerDoctor, Sara Shinton, will answer readers' questions about job hunting and career changing in the UK.

EUROPE: Reduce, Refine, Replace M. Balls

Changing EU regulations impel research into alternatives to animal experiments—and raise new career opportunities.

GERMANY: University Spin-Offs—What Works? S. Blackley

A recent conference examined the nuts and bolts of university entrepreneurship.

CANADA: Attracting and Retaining Women Engineers L. McKarney

Although more women have been enrolling in Canada's engineering programs, their presence in the workforce still lags.

US: Project Management and Discovery R. Austin

Conventional project management methodologies, says a Harvard management theorist, work best when there is not much genuine discovery going on.

KNOWLEDGE ENVIRONMENTS

science's sage ke   www.sageke.org

science of aging knowledge environment

NOTEWORTHY THIS WEEK: NO-Aspirin, No Atherosclerosis R. J. Davenport

Souped-up painkiller fights blood vessel plaques.

NOTEWORTHY THIS WEEK: Outfoxing Insulin Resistance M. Leslie

Researchers nab the gene that adjusts response to a sugar-regulating hormone.

science's stke   www.stke.org

signal transduction knowledge environment

EDITORIAL GUIDE: New Concepts—Updated Reviews N. R. Gough and L. B. Ray

Unveiling a new tool for navigating the rapidly advancing field of cellular signaling.

UPDATED REVIEW: Nuclear Lipid Signaling R. F. Irvine

A new version of the review discussing the phospholipase C and phospholipid signaling cycle in the nucleus.

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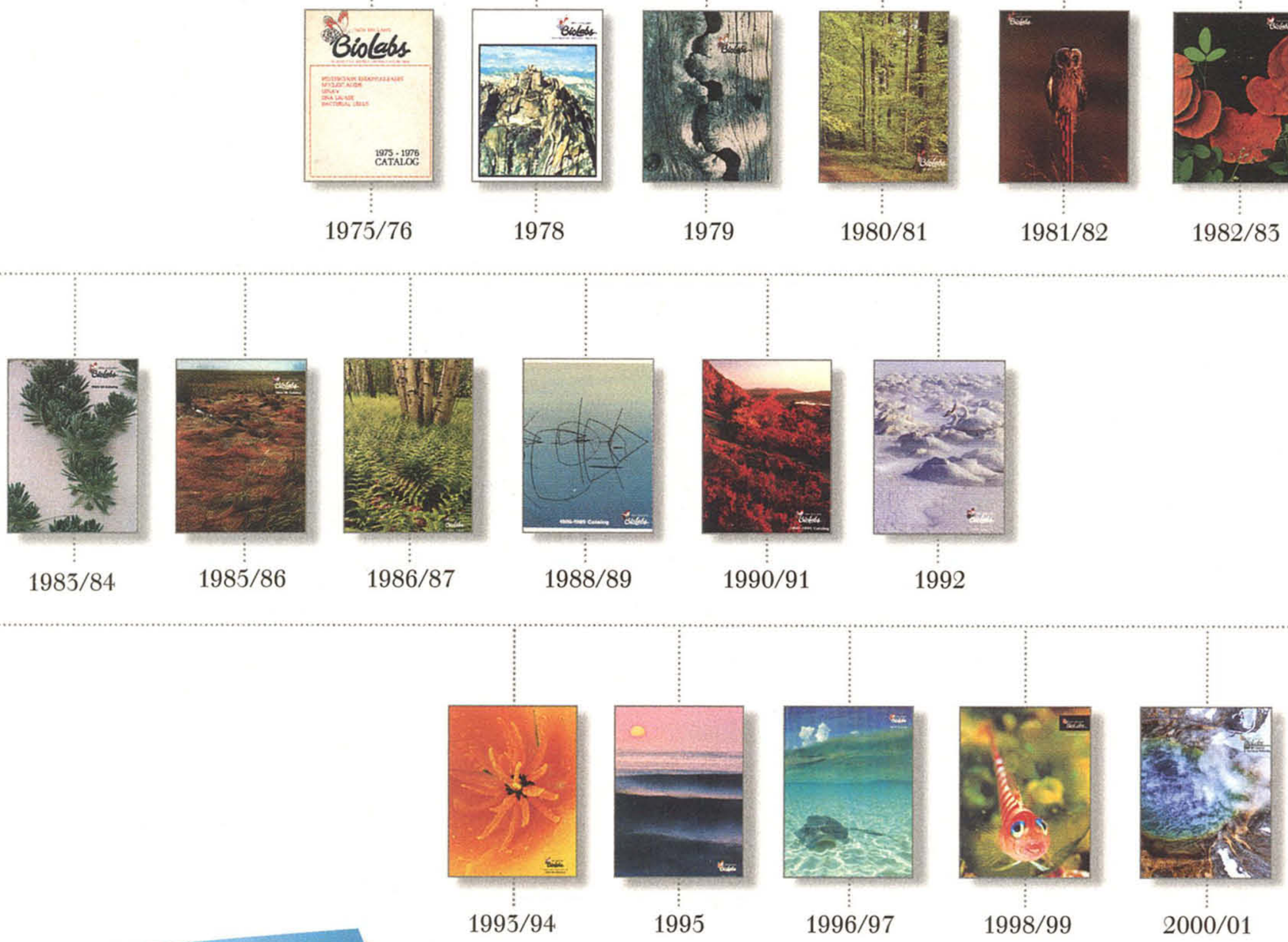

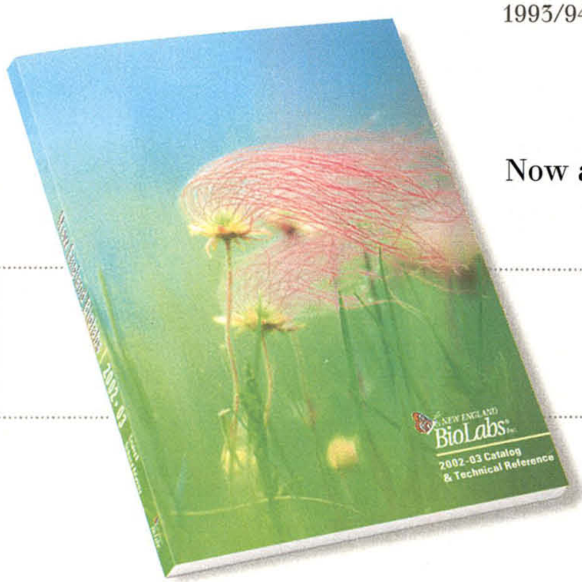

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THIS WEEK IN Science

edited by Phil Szuromi

Ultrafine Gold Chains

How do the electronic properties of a metal atom change when clusters of different sizes and geometry are formed? Nilius *et al.* (p. 1853) used scanning tunneling microscopy (STM) to build gold chains with defined numbers of atoms on a nickel-aluminum alloy surface. They then used the STM to perform scanning tunneling spectroscopy on these structures. Conductivity spectra taken at 30 points along a 20-atom chain show how the one-dimensional band structure develops. ✗

1858

Reducing Stress in California

The buildup of stress and strain between and within fault zones is poorly understood but important for assessing seismic hazards. Fialko *et al.* (p. 1858) measured small surface displacements on nearby fault zones related to the 1999 magnitude 7.1 Hector Mine earthquake in southern California. They model the displacements as an elastic response to the large event and find that the fault zones are compliant in the shallow crust.

The Buffer Zone

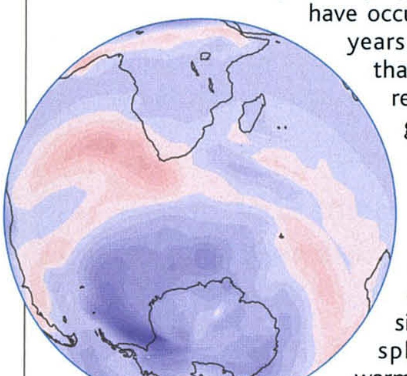
Diatoms are a type of photosynthetic marine plankton that form siliceous skeletons and thus have an absolute metabolic requirement for silicon. Because diatoms often are the dominant phytoplankton in regions of high productivity where abundant nutrients are available, it has been hypothesized that the precipitation of silica must somehow provide a competitive advantage. Milligan and Morel (p. 1848) suggest that this function may be to act a buffer, thereby increasing the activity of extracellular carbonic anhydrase, the enzyme which catalyzes the slow reaction from dissolved bicarbonate to the CO_2 used for photosynthesis.

Not So Fast

The unusual strength of hydrogen bonds accounts for many of the exceptional properties of liquid water. Mitsui *et al.* (p. 1850) investigated how the properties of small water clusters change when grown on a platinum surface. Dimers, trimers, and tetramers were much more mobile than the monomer. The mobility decreased again when the cluster contained five or more molecules. The results indicate that the hydrogen bonds are particularly strong in the small water clusters, and the misfit between their structure and that of the underlying substrate enhances their mobility. Larger clusters form a stable hexagonal honeycomb structure that is commensurate with the underlying surface.

An Overly Simple Seesaw

A popular paradigm for understanding global oceanic heat budgets is that of a "bipolar seesaw," wherein a heat gain in one hemisphere is balanced by a loss in the other. This concept has been invoked to explain the apparently alternating periods of hemispherically opposed heating and cooling that have occurred during the past 100,000 years of the last glacial cycle and that are recorded in temperature records from high latitudes. Morgan *et al.* (p. 1862; see the Perspective by Stocker) present a new ice core record of air temperatures from coastal Antarctica which shows that a simple bipolar seesaw is an oversimplification. Their analysis reveals that Southern Hemisphere cooling preceded the warming that began in the Northern Hemisphere about 14,500 years ago. Thus, the temperature changes observed in Antarctica cannot be caused only by abrupt changes in North Atlantic thermohaline circulation and must reflect a more complex partitioning of heat between the poles.



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Old Gold Deposits

Gold deposits in the Kaapvaal Craton of South Africa represent about 40% of the gold production on Earth, yet the origin of this large concentration remains controversial. Kirk *et al.* (p. 1856; see the Perspective by Frimmel) used the rhenium-osmium isotopic system to derive an age of formation for the gold and pyrite aggregates. The gold and pyrite is older than the conglomerate rock that hosts them. Thus, the gold was derived from detritus from older source rocks and not hydrothermal in origin. The age of the gold mineralization coincides with the age of stabilization of the Kaapvaal craton (about 3 billion years ago) and indicates that the gold was probably derived from hot and fertile mantle sources.

Controlling Chromatin Through RNA Interference

The link between RNA and the epigenetic regulation of gene expression are well known from studies of X-chromosome dosage compensation, where the noncoding RNAs Xist and Tsix play a critical role in silencing genes on the X-chromosome. RNA interference (RNAi) also silences gene expression at the posttranscriptional level by destroying cognate RNAs and is thought to defend the genome against invasion of "foreign" nucleic acids. Volpe *et al.* (p. 1833; see the Perspective by Allshire) now show that the RNAi machinery regulates the formation of centromeric heterochromatin in fission yeast. At least one component of the RNAi machinery, Rdp1, is bound to centromeric sequences. RNA transcripts identified as originating from these centromeric repeats are the likely targets of RNAi. Consistent with this result, Reinhart and Bartel (p. 1831) have isolated a series of small RNAs derived from these transcripts that are very likely the predicted siRNAs generated by RNAi. ✗

On the Mend

The breast cancer susceptibility gene *BRCA2* is necessary for the repair of double-stranded DNA breaks through homologous recombination, in which the intact member of a chromosome pair is used as a template to mend the damaged partner. Yang *et al.* (p. 1837; see

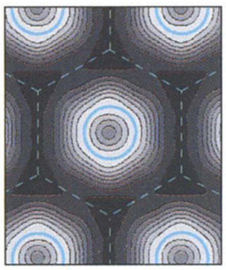
✗ Published online in *Science* Express

CONTINUED ON PAGE 1767

the cover and the Perspective by Wilson and Elledge) present the structure of the carboxyl-terminal domain of BRCA2 in complex with a second protein DSS1 and with single-stranded DNA. The binding of BRCA2 directly to DNA may enable it to serve as a scaffold for assembling the components that undertake the restoration of chromosome integrity.

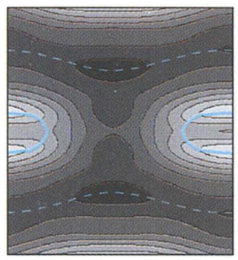
Ribosome Regulation by Protein Products

The leader peptide regulation of the *Escherichia coli* tryptophanase operon, *tnaC*, has a stop codon at position 25 that yields a 24 residue peptide in the absence of inducer. However, in the presence of tryptophan, the leader peptide stays attached to the stalled ribosome as a peptidyl tRNA and termination is blocked. By altering codons and spacing between codons in the leader peptide, Gong and Yanofsky (p. 1864; see the Perspective by Sachs and Geballe) show that the sequence of the nascent peptide can regulate the translating ribosome, perhaps by creating a ribosome binding site for free tryptophan. Hence, peptides are not only products of translation but they can also control ribosome movement during translation.



Caught in the Act

The process of membrane fusion is key to many cellular events in membrane trafficking, virus entry, and cell division. However, the mechanism of fusion itself, and a detailed structural understanding of how two lipid bilayers can fuse in a nonleaky fashion, have been difficult to nail down. Yang *et al.* (p. 1877; see the Perspective by Gruner) have now visualized a structure that seems to represent a lipid bilayer fusion intermediate consisting of a kind of stalk structure formed by the opposed lipid monolayers.



Dendritic Cells Show Self-Control

Dendritic cells (DCs) are increasingly being recognized for their ability to shut down some types of immune response and for contributing to the state of immune tolerance. Elucidation of putative tolerogenic DC subsets is under way, although the mechanisms by which these cells might modulate immunity have yet to be established. Munn *et al.* (p. 1867) now describe a subset of human DCs that can inhibit T cell responses, at least in vitro, to alloantigens through the catabolism of tryptophan by the enzyme indoleamine 2,3-dioxygenase (IDO). It is known that IDO can prevent antigen-specific responses of T cells in vivo, as well as in vitro. The present demonstration that a subset of human DCs can inhibit T cell responses via IDO in vitro makes it plausible that these cells might use the same mechanism in vivo. Whether DCs actually regulate immune responses to self-antigens, transplants, and tumors by this mechanism remains to be established.

Type-Setting Methylation Marks in Chromatin

Histone methylation, which is involved in the formation of heterochromatin, can also control DNA methylation and hence gene expression. The role of chromatin-remodeling factors in this pathway has been ill-defined, although it is known that the SWI/SNF-like protein DDM1 in *Arabidopsis* is required for the DNA methylation of centromeric and heterochromatic repeats. Gendrel *et al.* (p. 1871) analyze the methylation state of histone H3 and show that DDM1 is required for the maintenance of H3 methylation patterns in interstitial heterochromatin, but is not required to maintain the overall level of histone methylation. The authors speculate that DDM1 functions to "type-set" these epigenetic methylation marks.

Light-Activated Fluorescence

In order to study a cohort of proteins in a living cell, Patterson *et al.* (p. 1873) developed a fluorescent tagging method that can be photoactivated. Proteins were engineered to express a variant of green fluorescent protein that has low fluorescence until specifically photoactivated under a microscope. The dynamics of nuclear transport and lysosomal membrane exchange in living cells are described.

CREDIT: YANG *ET AL.*

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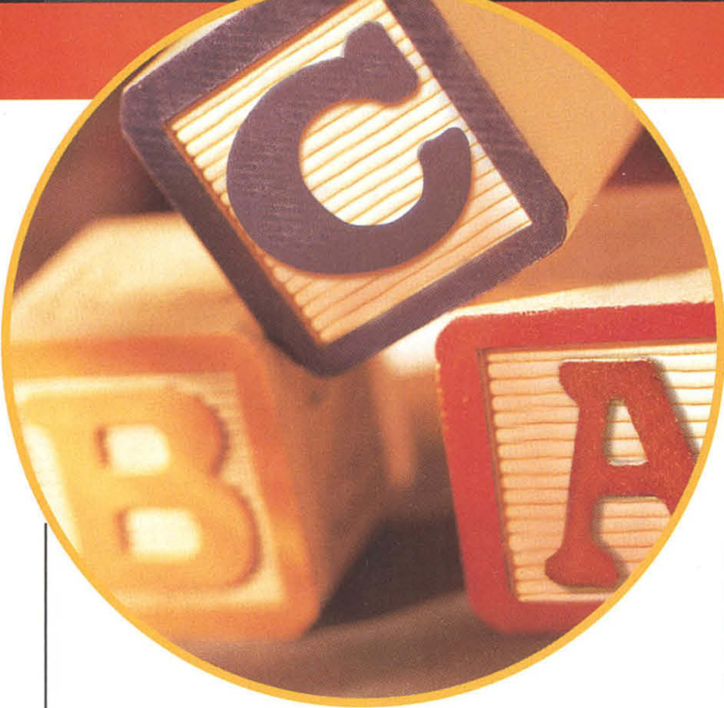

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1. Smith, P.K., *et al.* (1985). Measurement of protein using bicinchoninic acid. *Anal. Biochem.* **150**, 76-85.

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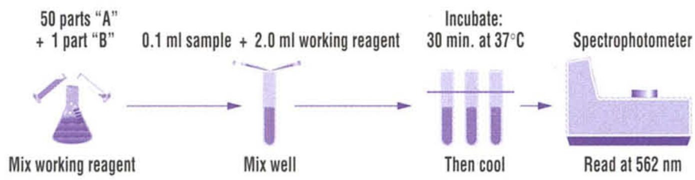

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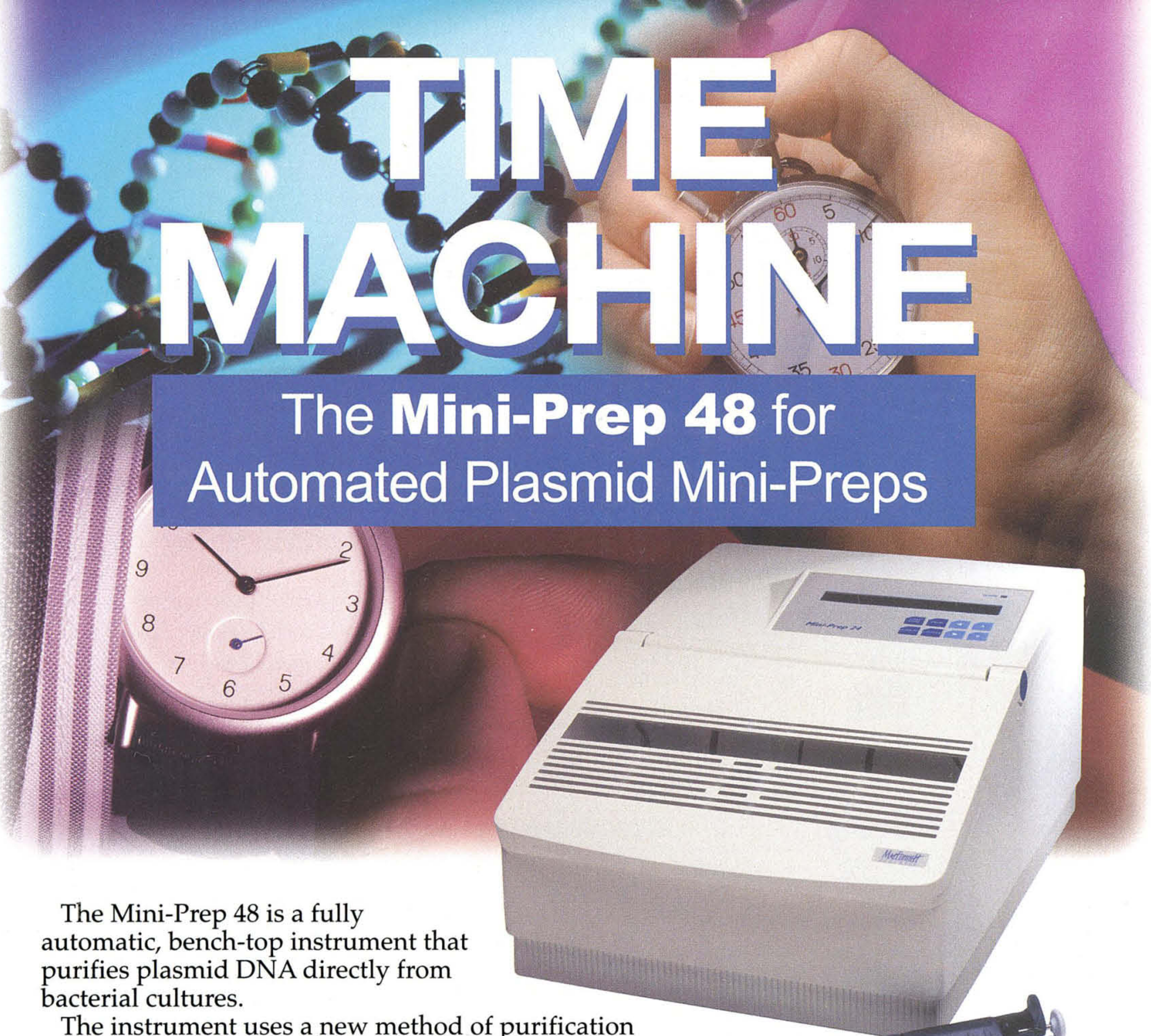

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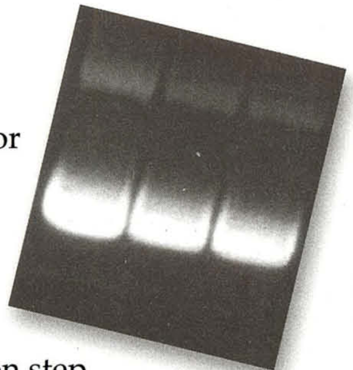

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Look for it on page 1886.

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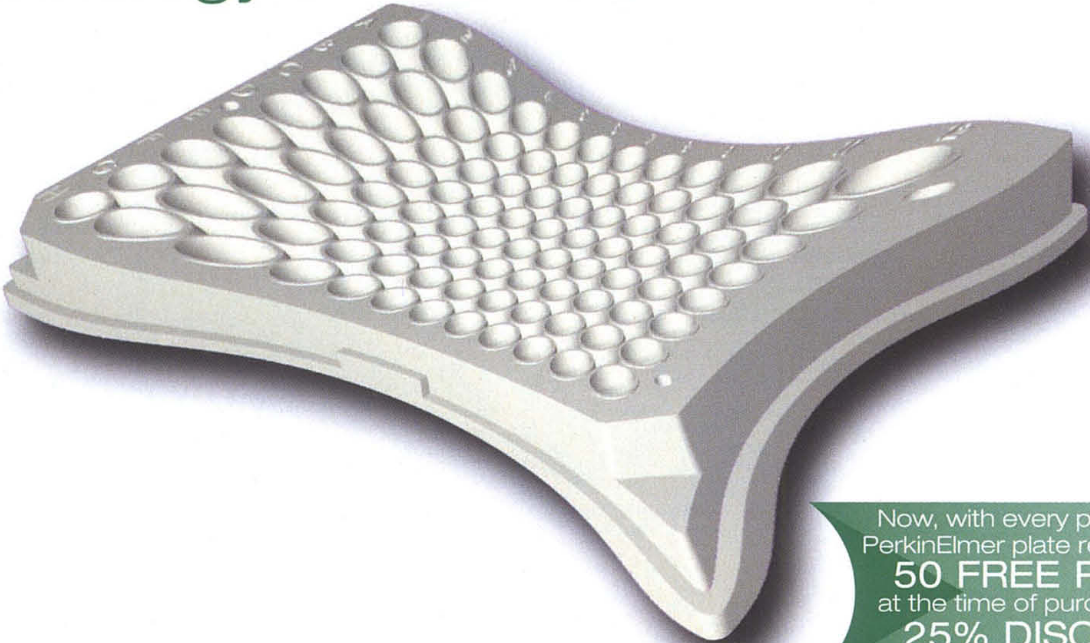

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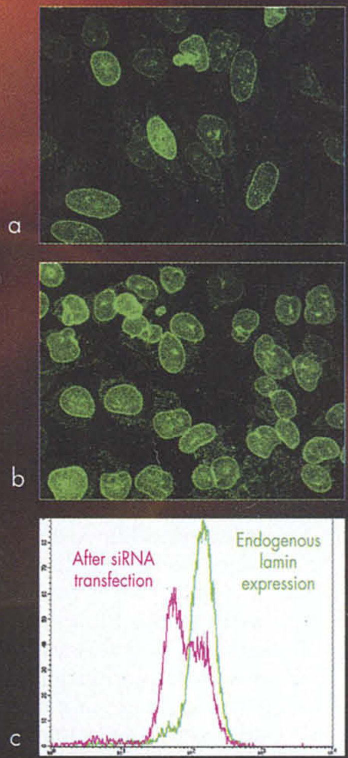

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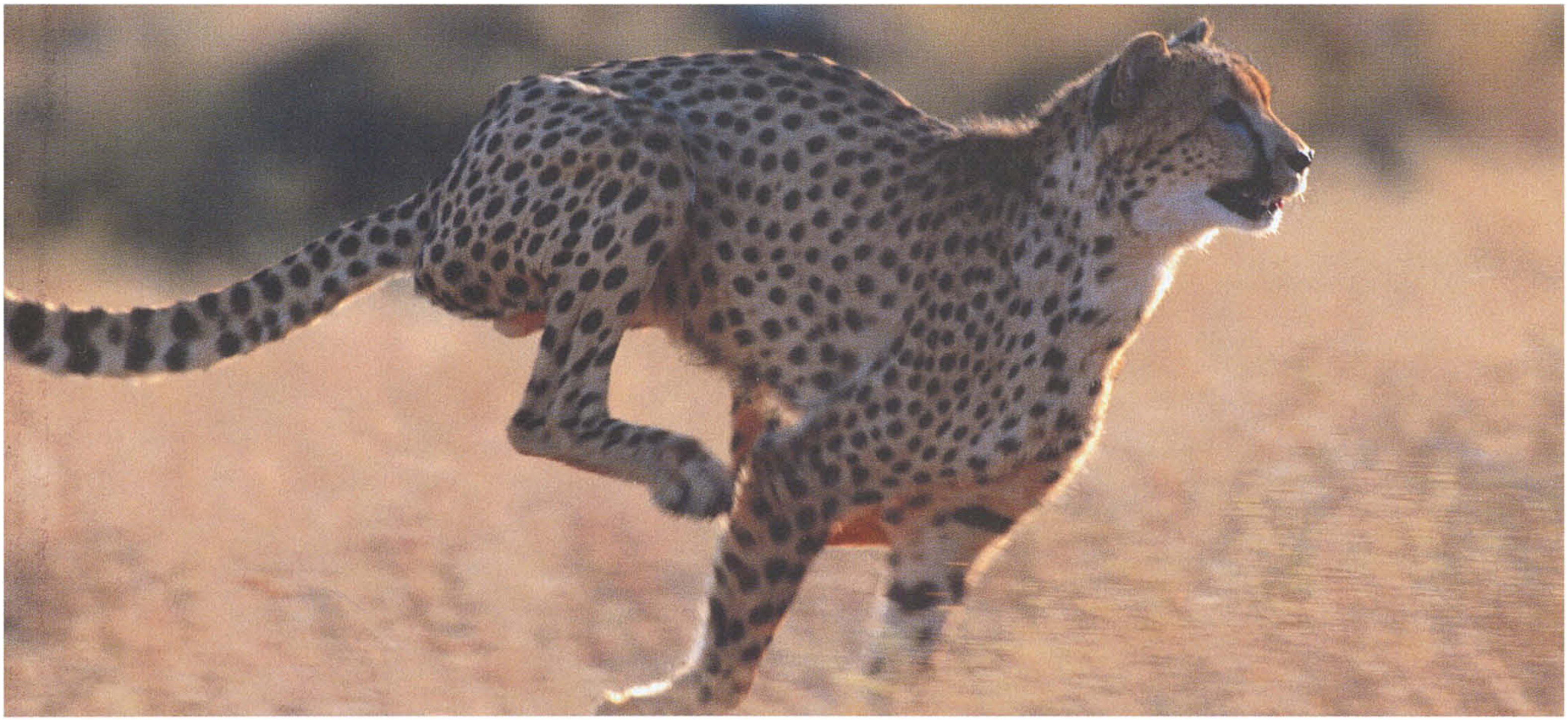

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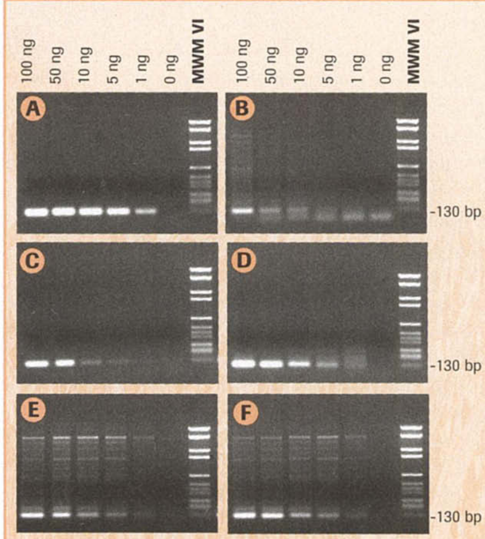

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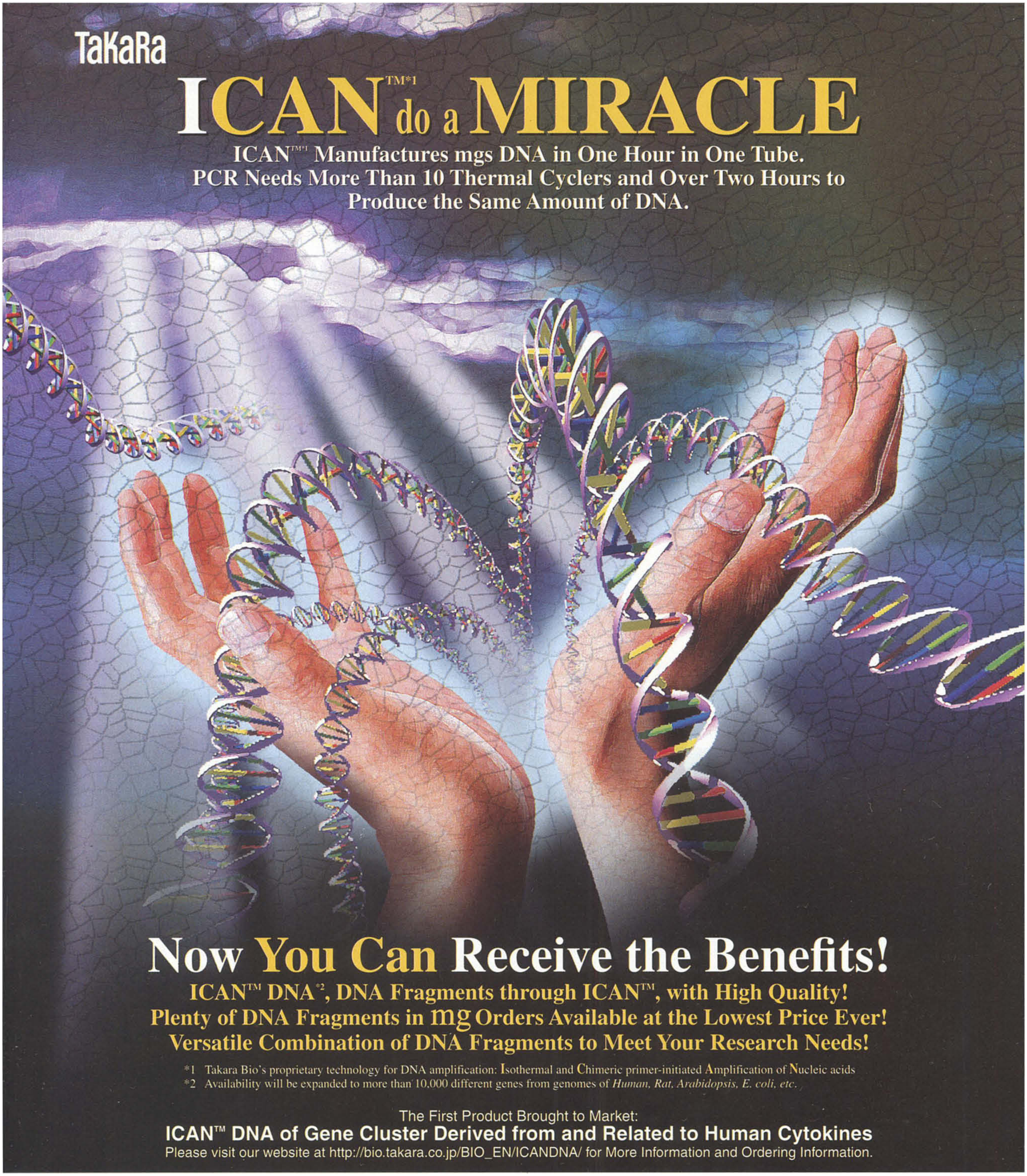

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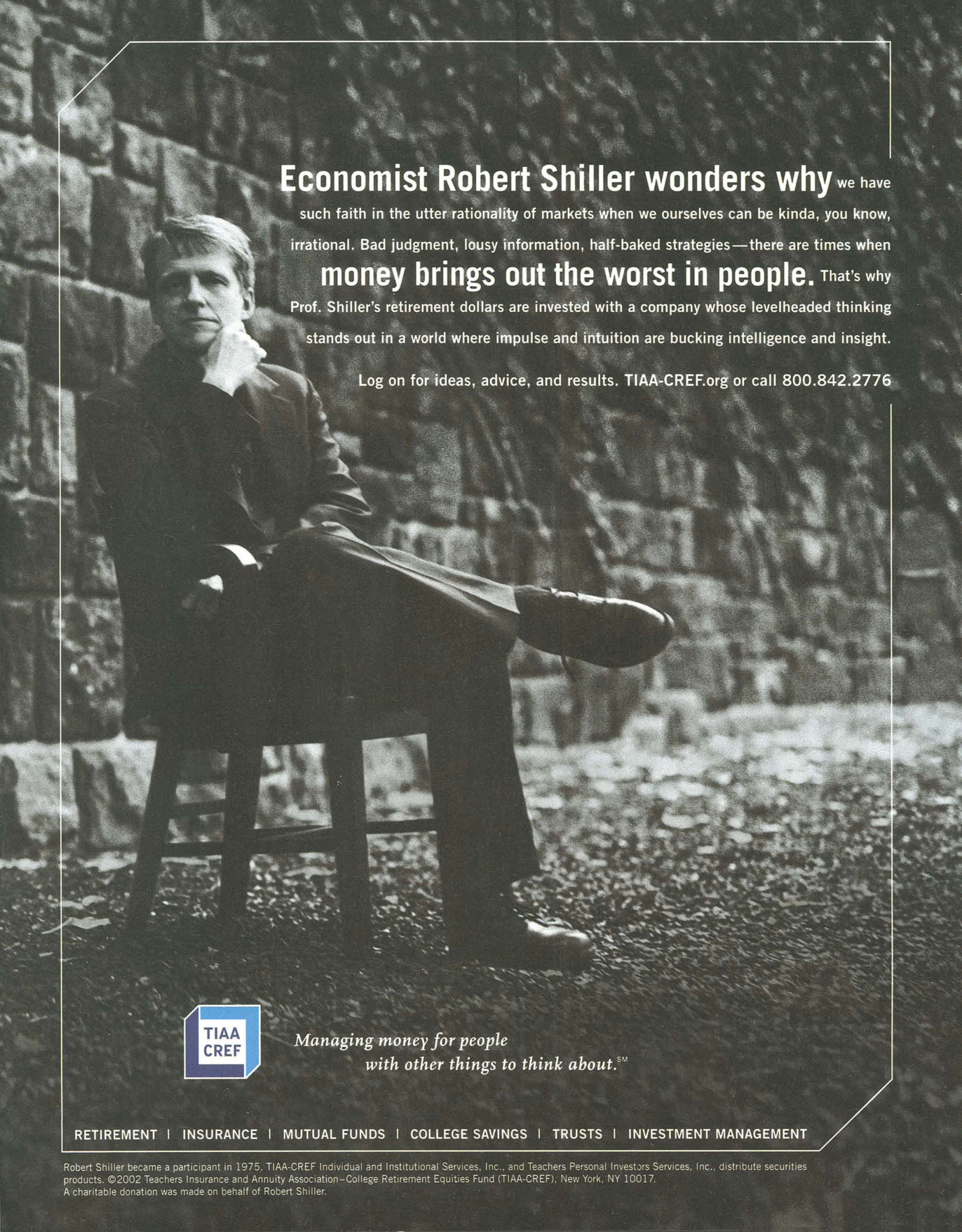
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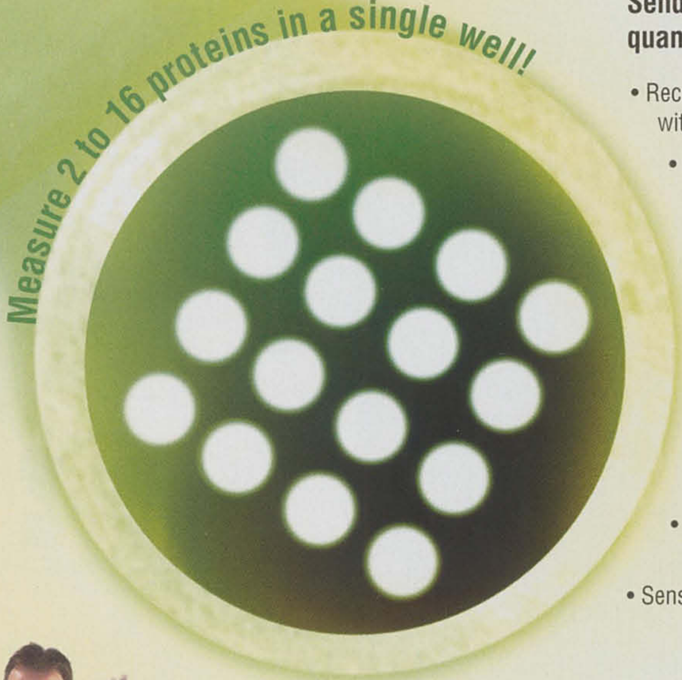

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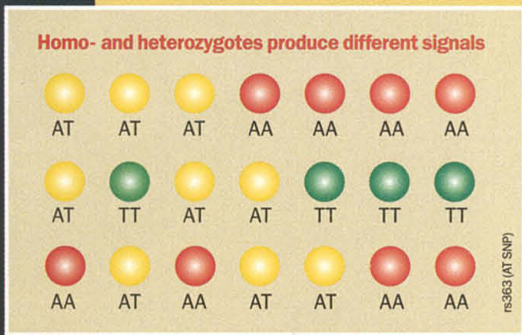

What's more, Serologicals' **Amplifluor™ SNPs Genotyping System** is compatible with high-throughput screening techniques and is usable on virtually any endpoint or real-time detection instrument.

Visit **www.serologicals.com/snps** or call us for detailed information.

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Reference

1. Myakishev MV, Khripin Y, Hu S, Hamer DH, "High-Throughput SNP Genotyping by Allele-Specific PCR with Universal Energy-Transfer Labeled Primers", *Genome Res.* 2001;11(1)163-169.

Amplifluor is covered under U.S. patents #5,866,336, 6,090,552, 6,117,986. The Polymerase Chain Reaction is covered by patents owned by Roche Molecular Systems, Inc. and F. Hoffman-La Roche Ltd. Purchase of a Serologicals PCR related product does not convey a license to use the PCR process covered by these patents. Purchasers of these products must obtain a license to use the PCR process before performing PCR.

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