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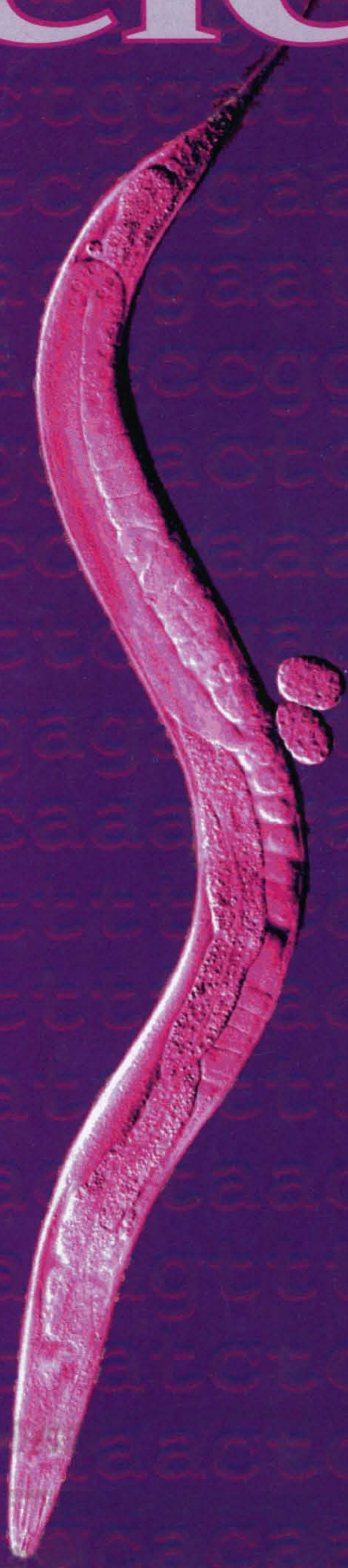
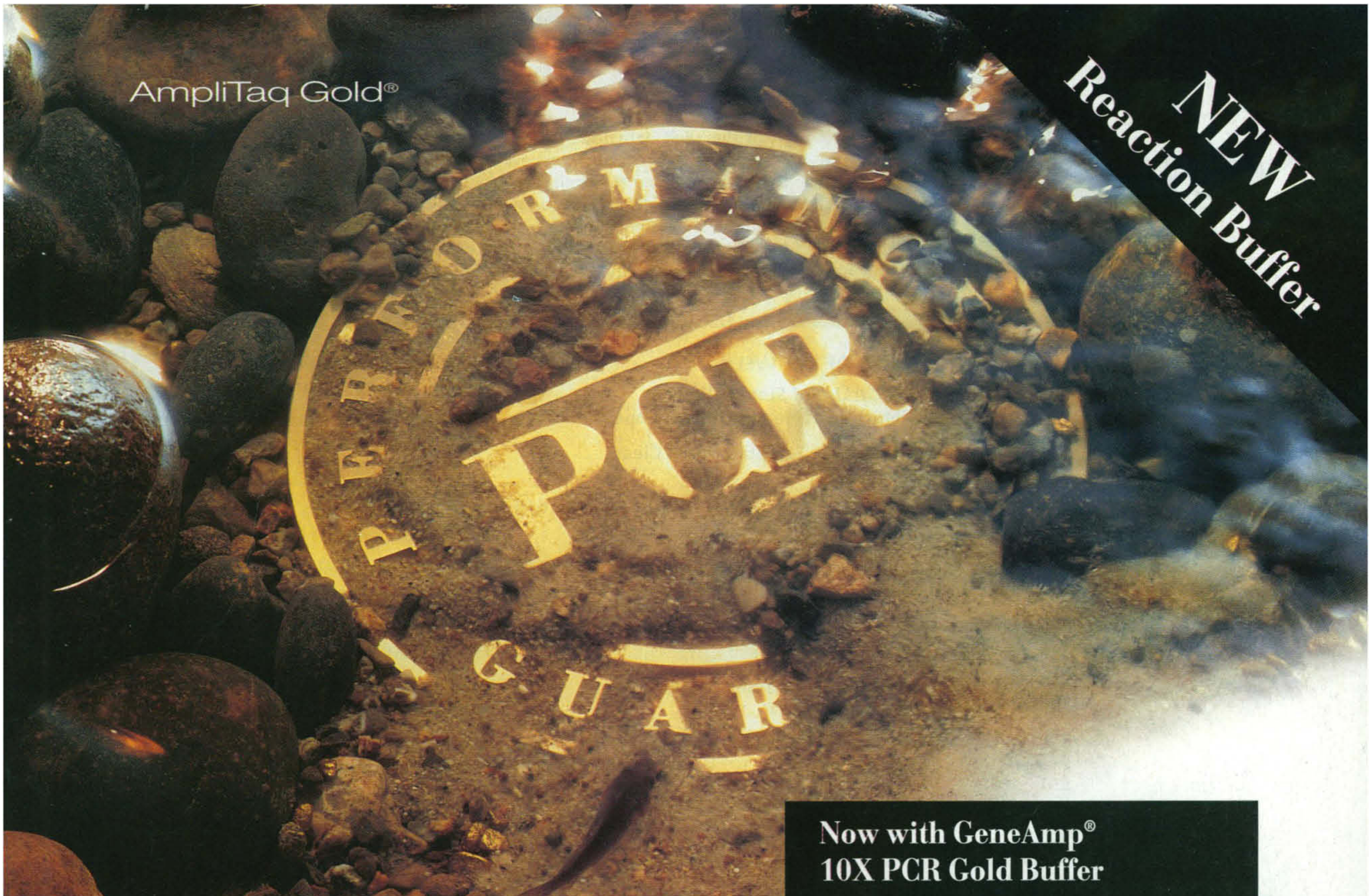


C. elegans
Sequence to Biology

American Association for the Advancement of Science



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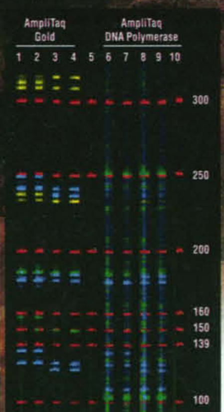
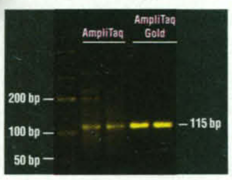


Co-amplification of 8 human STR loci. L1, 2: male control DNA; L3, 4: female control DNA; L5: AmpliTaq negative control; L6, 7: male control DNA; L8, 9: female control DNA; L10: negative control.



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Perkin-Elmer PCR reagents are developed and manufactured by Roche Molecular Systems, Inc., Branchburg, New Jersey, U.S.A.

Roche

VOLUME 282 11 DECEMBER 1998 NUMBER 5396

Science

www.sciencemag.org

COVER A view of the adult nematode *Caenorhabditis elegans* (~1 millimeter long, with two adjacent embryos) against a background of its sequence. The special section (beginning on p. 2011) commemorates the completion of the genome sequence for *C. elegans* and highlights some of the new insights in biology that are now possible. [Photomicrograph: Maria Gallegos, CMB Program, University of Wisconsin-Madison. Graphic manipulation: Cynthia Faber-Smith]

1975

Japan's cloning efforts mulitply

NEWS

NEWS OF THE WEEK

NEWS FOCUS

DEPARTMENTS

RESEARCH

RESEARCH ARTICLE

REPORTS

C. ELEGANS: SEQUENCE TO BIOLOGY

REVIEWS

See related Editorial on p. 1989 and News story on p. 1972.

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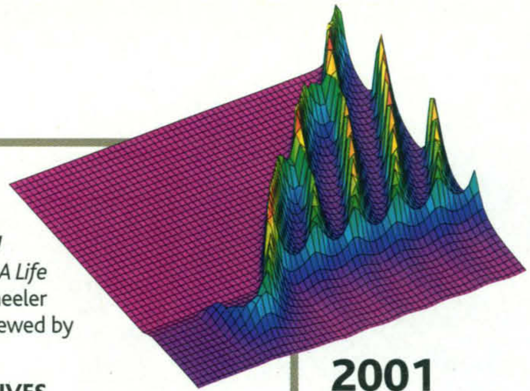
SCIENCE'S COMPASS

EDITORIAL

LETTERS

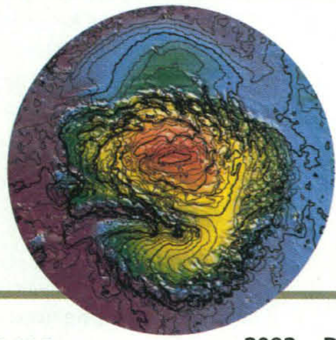
BOOKS AND NEW MEDIA

PERSPECTIVES



2001

The physics of traffic



2053

Less and lower ice on Mars

TECHNICAL COMMENTS

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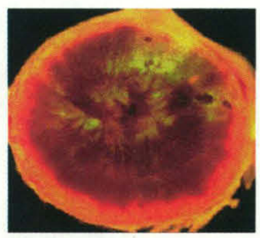

2072

Trophoblast stem cells isolated

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SURVEYING THE MARTIAN NORTH POLE

Much of the current visible inventory of volatiles on Mars resides in its polar caps. Understanding the history of water on Mars requires an accurate measure of the size of the north polar cap and the elevation of the polar basin with respect to the elevation of lower latitudes. The Mars Global Surveyor (MGS) has been examining the northern hemisphere of Mars closely, and Zuber *et al.* (p. 2053) now present an analysis of the topography of the north polar region and the ice cap. The data show that the cap is much smaller than previously assumed (about half the size of the Greenland Ice Sheet), is cut by deep fissures, was once somewhat larger, and resides in a topographic basin that is at a lower elevation than low-latitude regions. This result may negate models in which groundwater flows southward from the ice cap toward the equator. MGS also imaged clouds forming above the ice cap.

A DUSTY, OLD BROWN DWARF

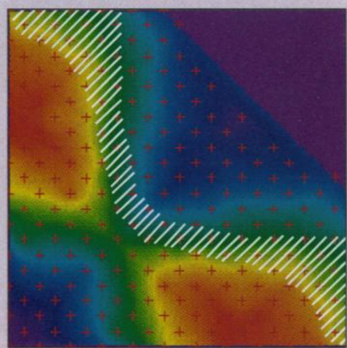
Brown dwarfs are caught in the middle: They are too massive to be planets and not massive enough to be stars. Gliese 229B was the first bona fide brown dwarf identified in 1995 and it remains the coldest brown dwarf (900 Kelvin) that has been studied. Griffith *et al.* (p. 2063) realized that Gliese 229B was too warm to have ice clouds like Jupiter, and too cool to have silicate-rich clouds like some stars. This lack of clouds allowed them to observe Gliese 229B's atmosphere with near-infrared wavelength spectroscopy with the Keck I Telescope. The spectrum suggests the presence of an organic-rich haze in Gliese 229B's atmosphere that probably formed as a result of incident radiation from its primary star, just like the mechanism suggested for the formation of Jupiter's stratosphere. Thus the radiation from a star may cause a brown dwarf to become more planet-like.

IMPACT AND EXTINCTION IN ARGENTINA

Evidence for an impact event in the mid-Pliocene (about 3 million years ago) of South America has been found in the Pampean Formation of coastal, central Argentina. Schultz *et al.* (p. 2061) describe centimeter- to meter-sized glass fragments that contain flow structures and vesicles that are indicative of a dynamic fusion process. These textures are similar to textures seen in impact glasses from known craters. This possible impact event, if it is confirmed by the identification of the impact crater, which should be near to the location of the glassy fragments, seems to be nearly coeval with the regional extinction of endemic fauna in Argentina, as highlighted in a news story by Kerr.

REMNANT FERMI SURFACES IN INSULATORS

High-temperature superconductors (HTSs) exhibit an unusual "*d*-wave" symmetry in the energy gap that separates the superconducting and insulating states. Whether a gap exists depends on the momentum of the elec-



trons, and this behavior is not readily accounted for theoretically. Ronning *et al.* (p. 2067; see the news story by Service) suggest a possible origin for this gap symmetry—it may already be present in the parent insulating state. Photoemission spectra of a Mott insulator related to HTSs, $Ca_2CuO_2Cl_2$, show that a remnant Fermi surface is present (defined in this case as a sharp drop in electron occupancy probability as a function of momentum) and that the *d*-wave shape is similar to that of the HTS superconducting gap.

PLACENTA ORIGINS

In early mammalian development, the blastocyst contains an inner cell mass (ICM), which becomes the embryo proper; and the trophectoderm, a layer of surrounding epithelial cells that specifies the fetal portion of the placenta. An unknown signal from the ICM is required for the maintenance of the trophectoderm. Tanaka *et al.* (p. 2072) have now identified the growth factor FGF4 as this embryo-derived signal. Cell culture conditions that included FGF4 allowed a trophoblast stem cell line to be isolated. This cell line can be used to understand better placental development and placental insufficiencies.

CONNECTING MUSCULAR DYSTROPHY AND LEPROSY

The mechanism of infection by *Mycobacterium leprae*, the bacterium responsible for leprosy, and for a class of viruses known as arenaviruses have been unexpectedly linked to muscular dystrophy (see Perspective by Spear). Rambukkana *et al.* (p. 2076) showed that *M. leprae* uses α-dystroglycan—a protein of the dystrophin complex implicated in muscular dystrophy—to mediate its internalization by its target Schwann cells. Cao *et al.* (p. 2079) demonstrate that arenaviruses, including lassa fever virus, use the same protein as their host cell receptor.

NUCLEAR PROCESSING OF TRANSFER RNA

In protein synthesis, it is important that only mature and functional transfer RNAs (tRNAs) are used; otherwise, the translation process would be defective. Maturation of tRNA includes base modification, processing of the 5' and 3' ends, and splicing. Lund and Dahlberg (p. 2082; see also the Perspective by Hopper) now show that correct folding and end maturation of tRNA are required for efficient export from the nucleus, and they suggest that aminoacylation serves to proofread these tRNAs prior to export. These findings counter the prevailing viewpoint that RNA is transcribed and processed in the nucleus and then aminoacylated in the cytoplasm. The nucleus plays a bigger role than was previously thought.

MEDIATING TOXIC SHOCK

Recognition of lipopolysaccharide (LPS), a product of Gram-negative bacteria, can lead to toxic shock, but animals without a response to LPS cannot effectively clear Gram-negative infections. The protein responsible for transmitting signals from LPS to the cell has been found by Poltorak *et al.* (p. 2085). Two mouse strains known to be defective in their response to LPS had mutations in the toll-like receptor-4 (*Tlr-4*) gene—one strain had a mutation in the coding region and the other lacked transcripts from the gene entirely. *Tlr-4* is thus necessary for LPS signaling in mice; the endogenous *Tlr-2* gene, which in humans can transmit signals from LPS, does not replace *Tlr-4* function in mice.

CONTINUED ON PAGE 1955

THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 1953

SHAPELESS SIGNALING

Many cellular signaling pathways require specific protein-protein interactions mediated by SH3 (Src homology 3) or WW domains (so called because they usually contain two tryptophan or W residues). These domains bind to proline-rich sequences in other proteins. Nguyen *et al.* (p. 2088) explored the requirement for proline in the target binding site and found that the critical requirement is the presence of an N-substituted amino acid, not the side chain shape. This property allows interactions of high specificity but low affinity, which are critical for the transient interactions of signaling proteins. By substituting nonnatural N-substituted amino acids, Nguyen *et al.* could also create ligands that bound selectively to an SH3 domain with 100 times greater affinity than the that of the normal interaction. These results may facilitate drug design strategies directed at protein interactions mediated by SH3 and WW domains.

JNK1 AND T HELPER CELL DIFFERENTIATION

When an antigen initially activates helper T cells of the immune system, the cells differentiate into either type 1 (T_H1) or type 2 (T_H2) cells. The specific choice is influenced by the cytokine milieu. When Dong *et al.* (p. 2092) constructed mice that lacked the kinase Jnk1, their T cells preferentially differentiated into T_H2 cells and had enhanced proliferation. The cells could produce the cytokines that were necessary for T_H1 development but could not down-regulate the production of the T_H2 cytokines, such as interleukin 4 (IL-4), which skewed differentiation. T cells with no Jnk1 selectively accumulated in their nuclei the transcription factor NFATc, which is required for IL-4 transcription and T_H2 differentiation. Thus, Jnk1 may normally function to regulate cell growth and to turn down T_H2 differentiation signals after T cell activation.

INCREASING VITAMINS IN PLANTS

The vitamins and nutrients critical to a healthy diet are not always easily available in the foods that habitually show up on our dinner tables. Shintani and DellaPenna (p. 2098) show how molecular tools can be used to revise a plant's metabolism and dramatically shift its production of important nutrients. The specific case presented results in ninefold increase in vitamin E activity, a nutrient often undersupplied in average diets, in the seed oil of the model plant *Arabidopsis.*

CLONING MANY COWS

The most immediate application of recent advances in cloning technology may well be the application of the procedure to the production of identical herds of animals. Kato *et al.* (p. 2095; see the news story by Normile) report high success rates in production of calves derived from nuclei of single, adult somatic cells. Epithelial cells from the oviduct and cumulus cells from ovarian oocytes were used as sources of nuclei.

TECHNICAL COMMENT SUMMARIES

Pleistocene Speciation and the Mitochondrial DNA Clock

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5396/1955a

J. A. Klinka and R. M. Zink (Reports, 12 Sept. 1997, p. 1666) found that "molecular data suggest a relatively protracted history of speciation events among North American songbirds over the past 5 million years," contrary to that suggested by the "Late Pleistocene Origins (LPO) model."

B. S. Arbogast and J. B. Slowinski comment that the report contains invalid assumptions about estimating "dates of divergence," no measures of error, and no test of whether "a molecular clock holds for their data"—which Arbogast and Slowinski find it does not.

In response, Klicka and Zink discuss the assumptions made in the report (finding that a molecular clock "is valid for this data set"), provide details of their analyses, and maintain that the LPO model of speciation has been falsified.

Proofreading by Isoleucyl–transfer RNA Synthetase

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/282/5396/1955b

O. Nureki *et al.* (Reports, 24 Apr. 1998, p. 578) described the crystal structure of isoleucyl–transfer RNA synthetase (IleRS), "an enzyme with editing activity in translation." Figure 4 of the report was a "stereoview of the IleRS editing site as a ball-and-stick representation."

X. Qiu comments that, "although this is an excellent study, fig. 4 and the discussion of it on the same page (p. 581) do not seem to build a reasonable argument." Qiu cites three reasons why the scenario depicted seems "unlikely."

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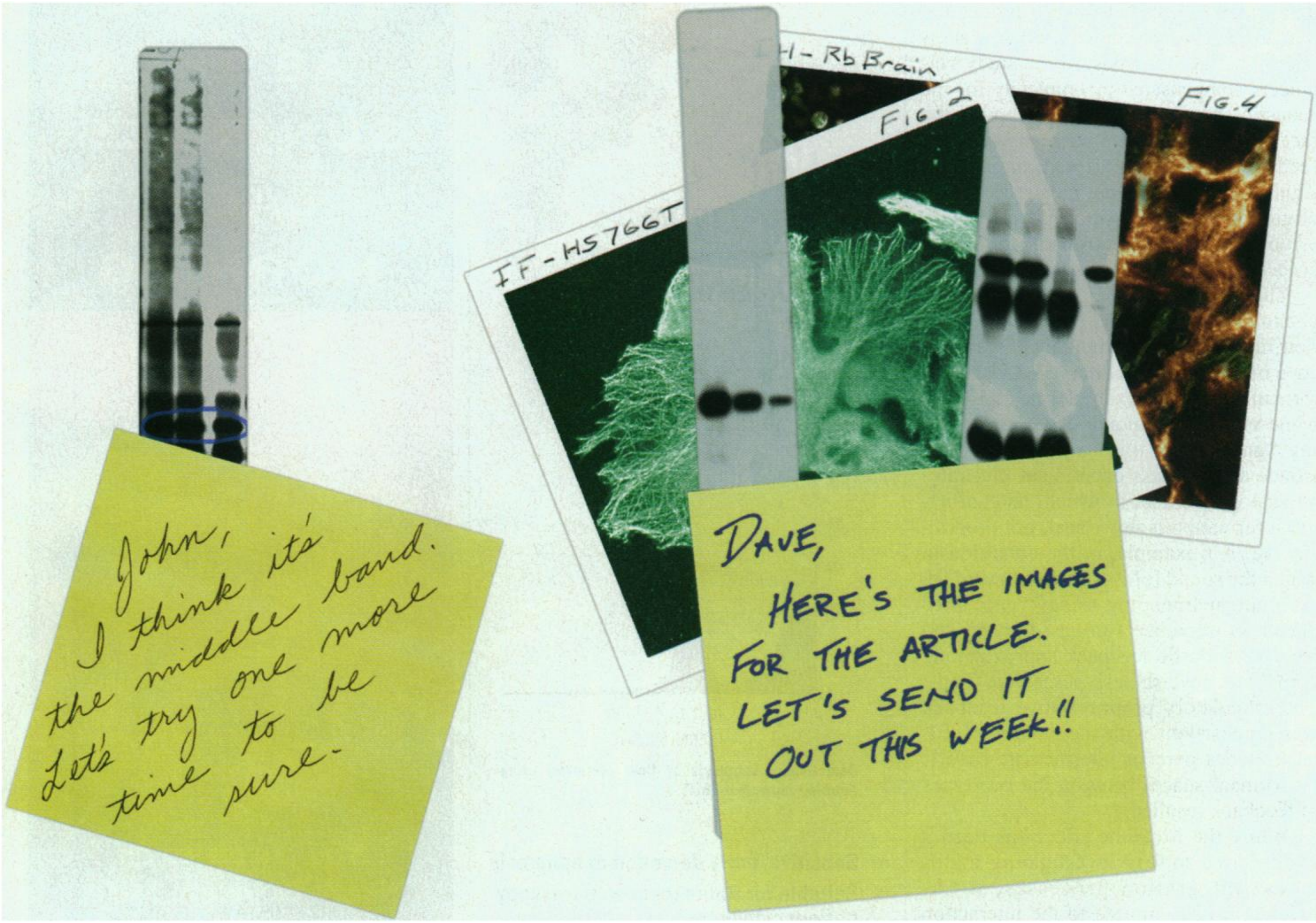
IH - Rb Brain
Fig. 2
Fig. 4
IF - HS766T
John,
I think it's
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Let's try one more
time to be
sure.
Dave,
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for the article.
Let's send it
out this week!!

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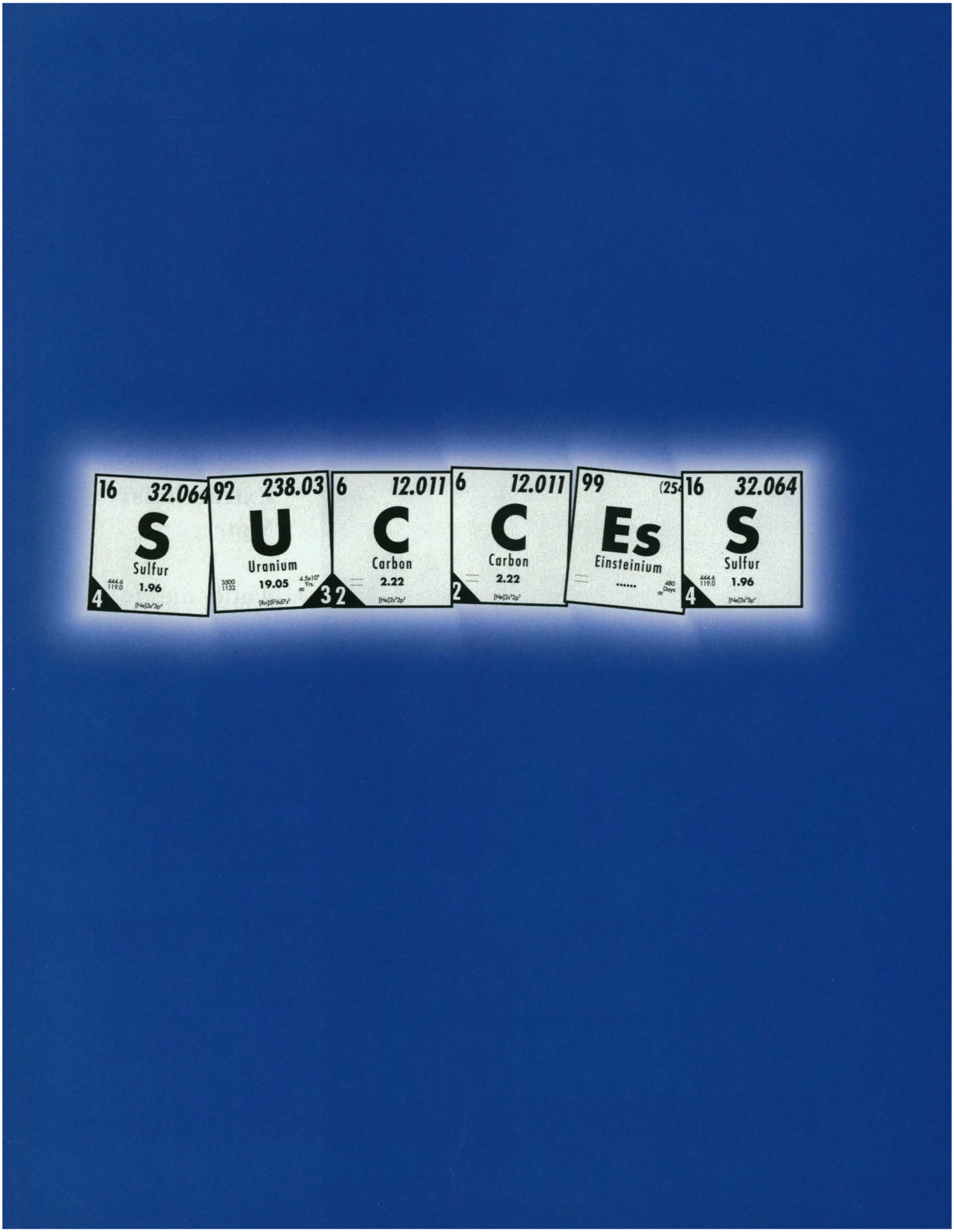
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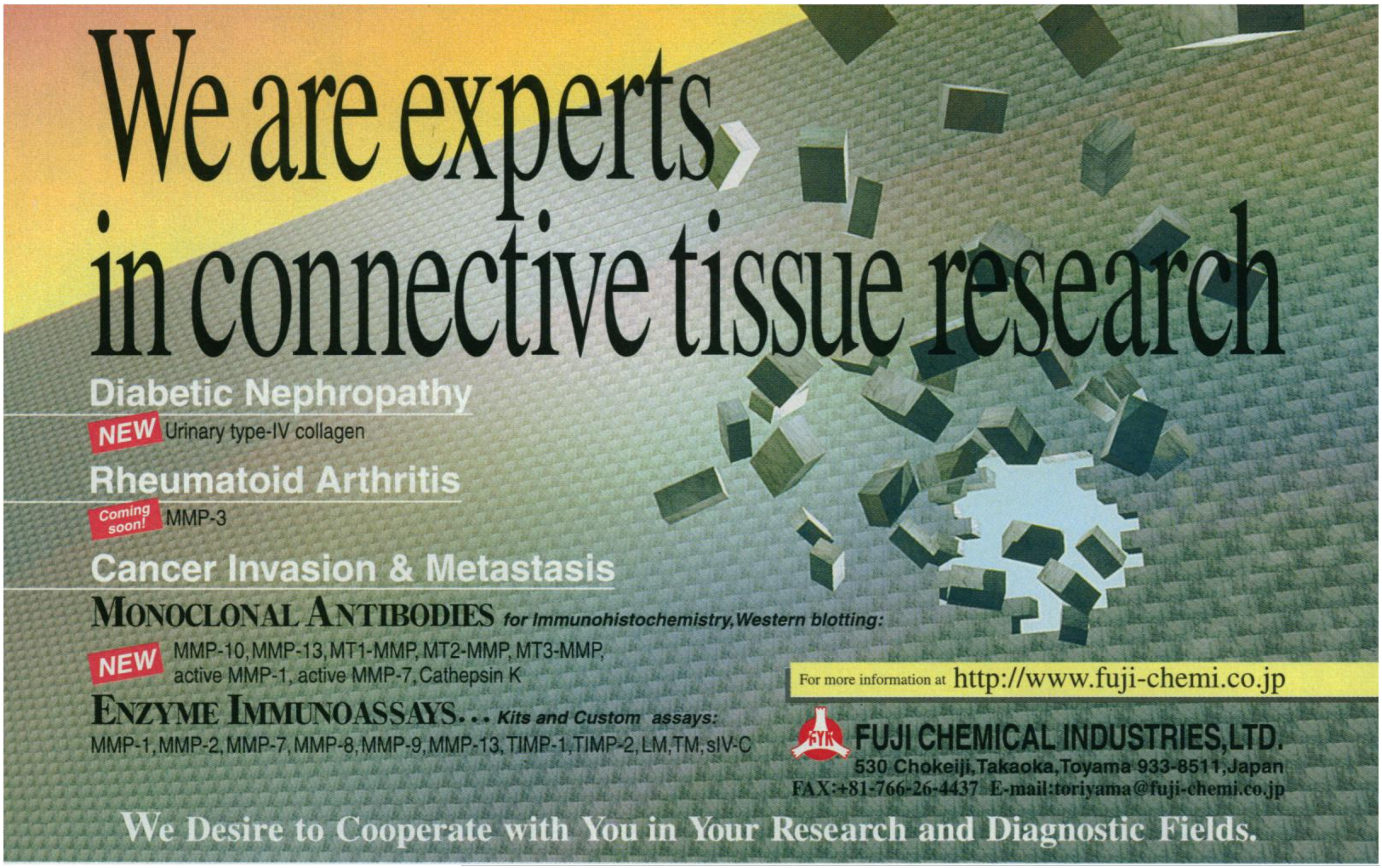

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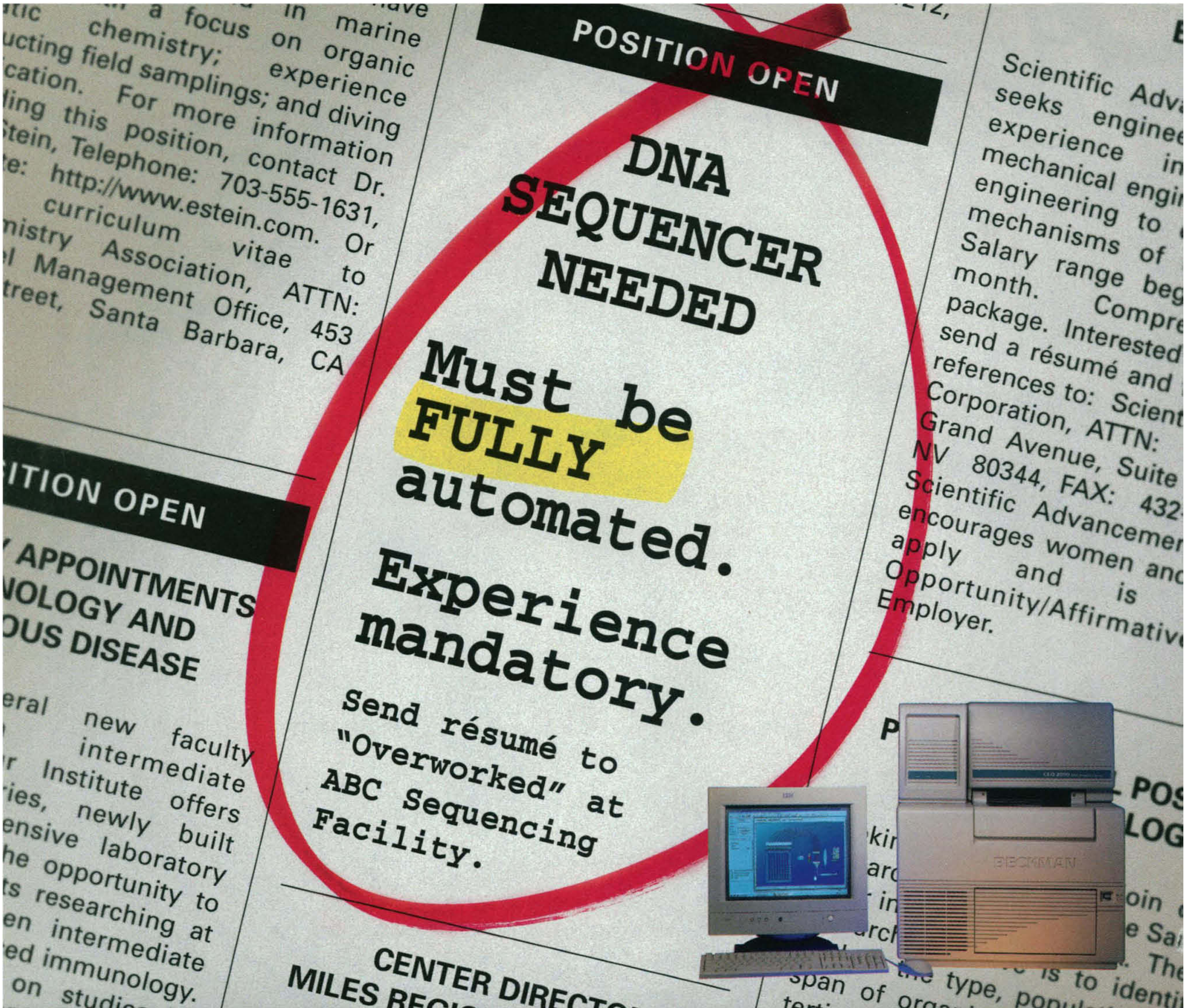

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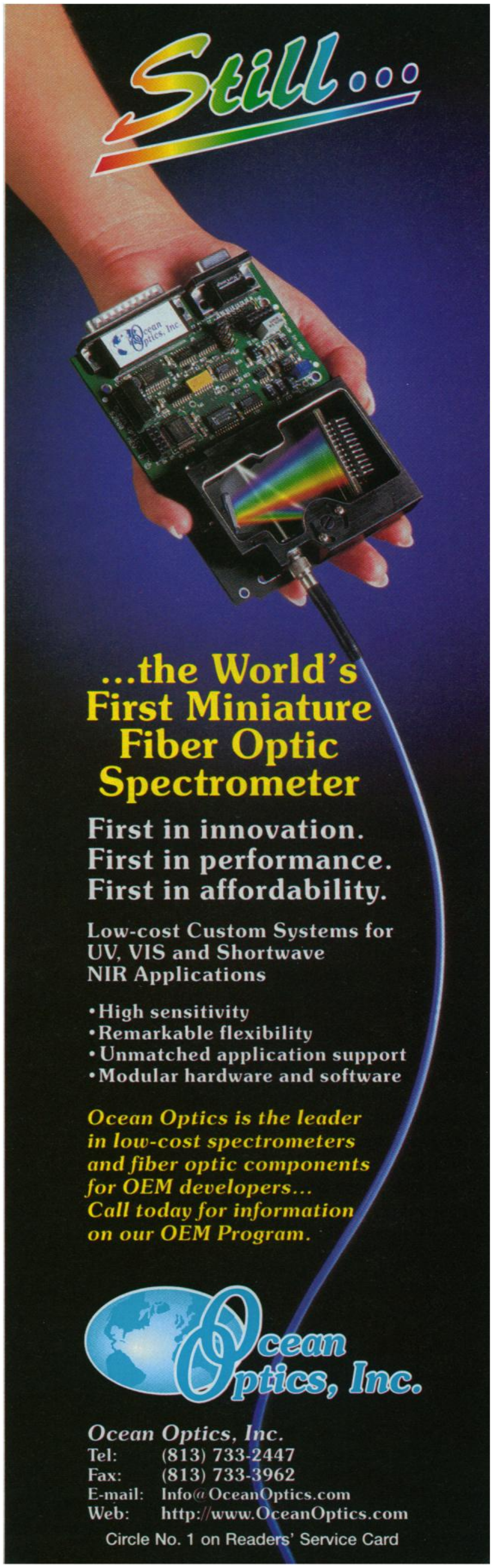

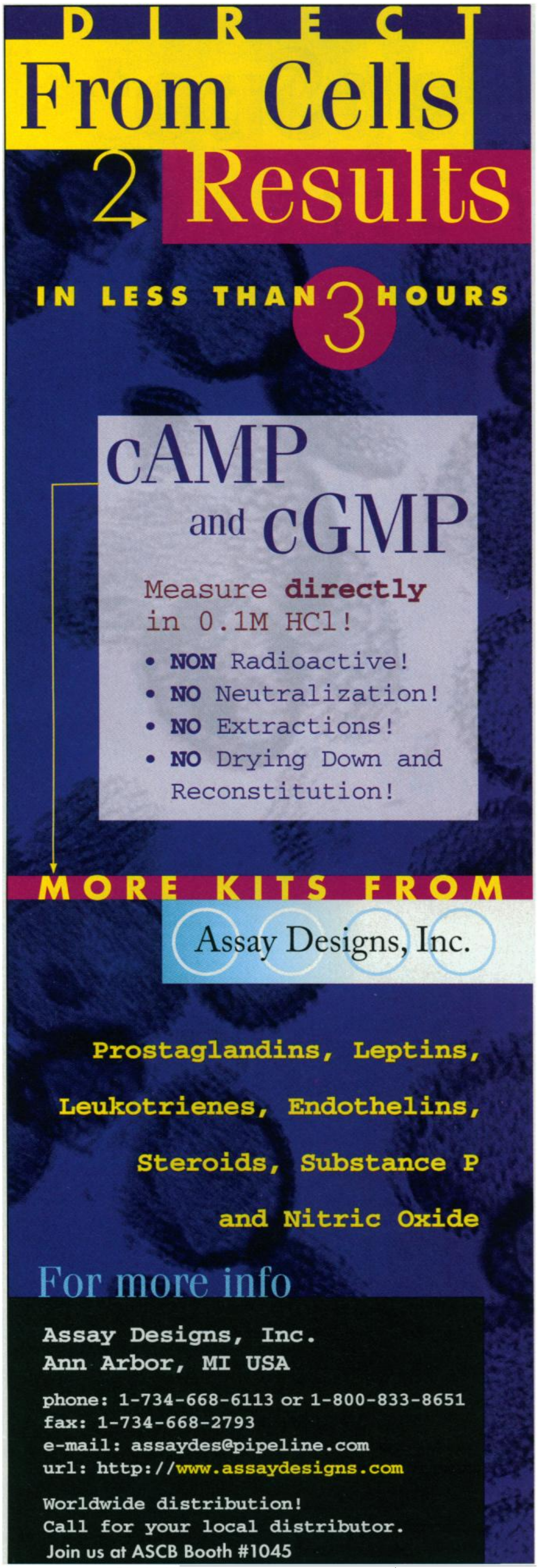

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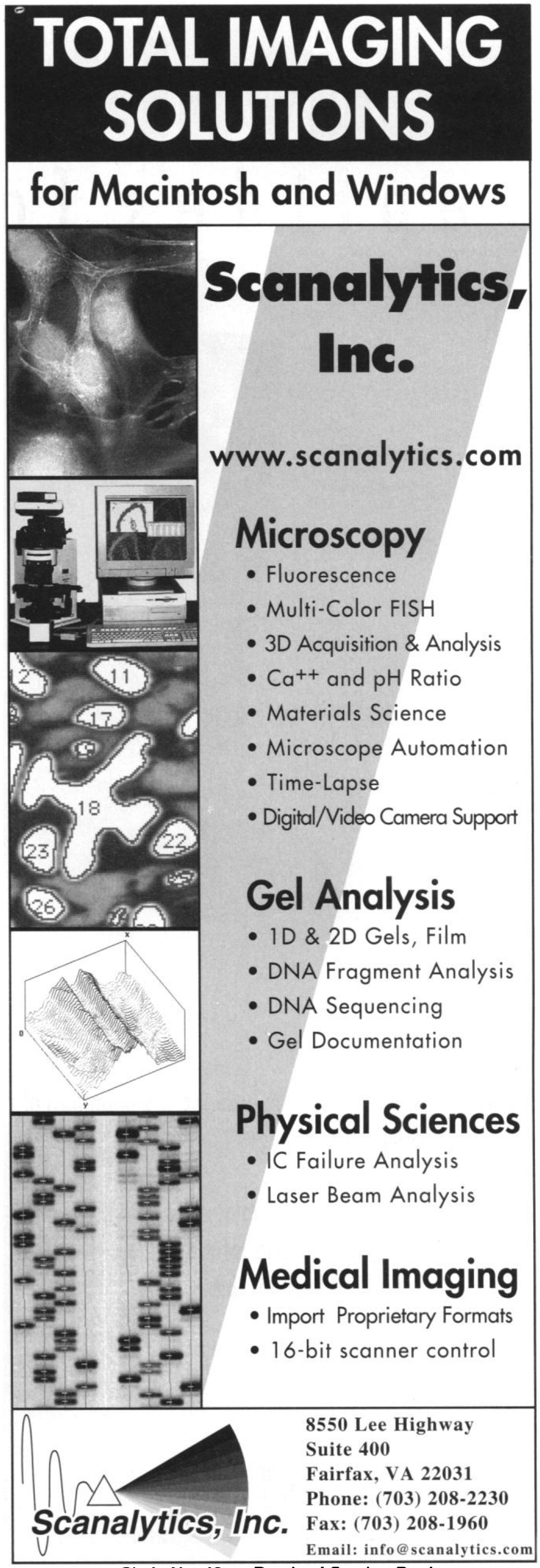

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