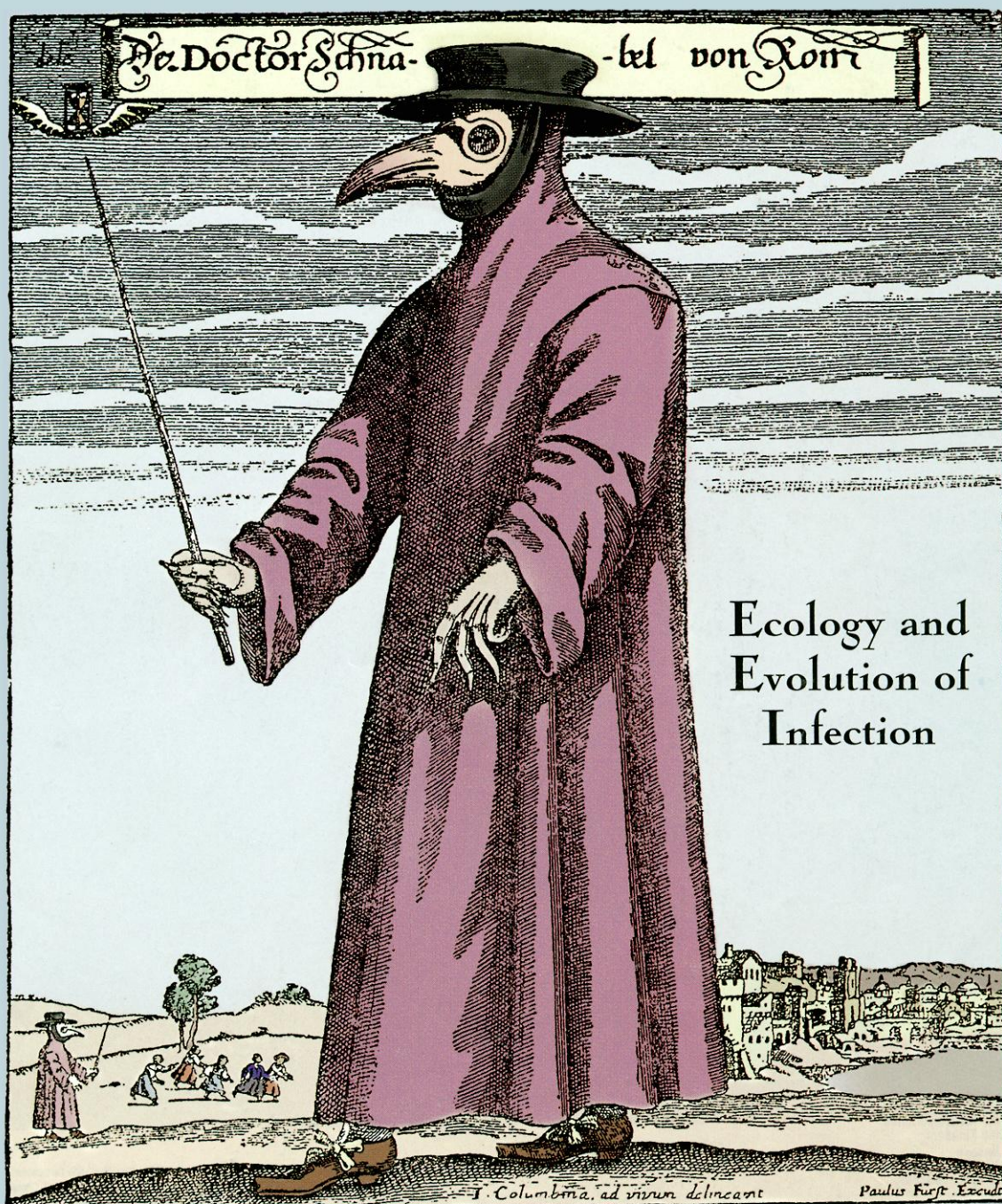


Science

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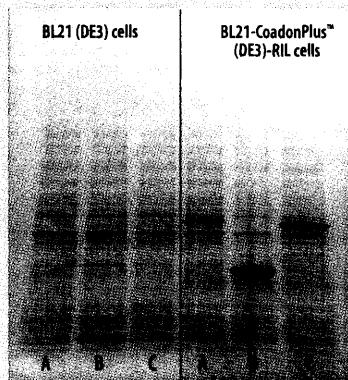
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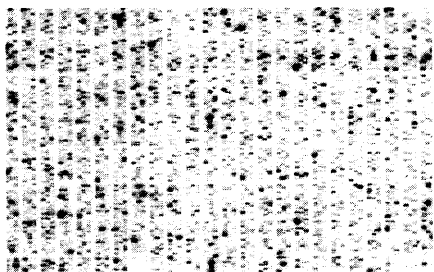
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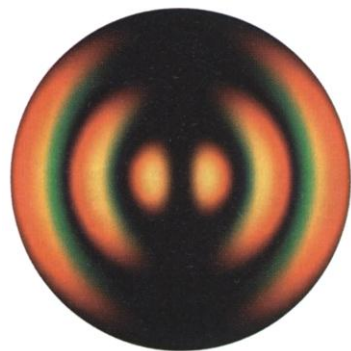
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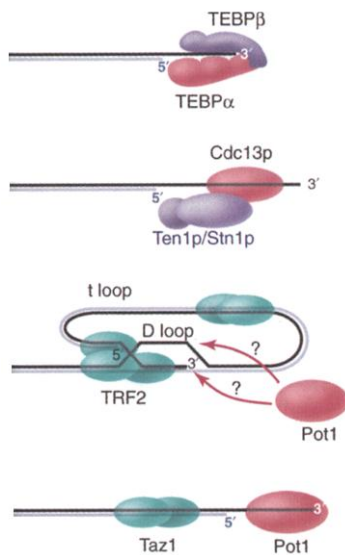
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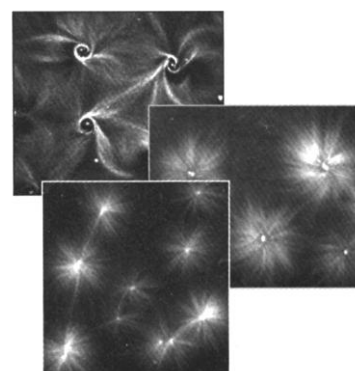
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COVER 1089

The plague doctor in clothing worn to protect from contagion, circa 1656. We are haunted by images of the horrors of disease and death, but with the current influx of data from microbial genomes, we can expect some answers to questions about how microorganisms have evolved, causing much fear. Apart from using these data to design new drugs and vaccines, we can also explore what the molecular signature of a microorganism may mean to a host population and predict more precisely the effects of intervention. [Image: Stock Montage]



1167

Self-organization rules

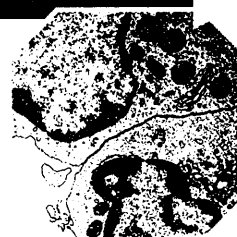
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Extremely Large Variations of Atmospheric ^{14}C Concentration During the Last Glacial Period J. W. Beck *et al.*

Large variations in the atmospheric abundance of carbon-14, measured in a stalagmite, indicate that the carbon cycle has changed substantially over the past 45,000 years.

Requirement of *CHROMOMETHYLASE3* for Maintenance of CpXpG Methylation A. M. Lindroth *et al.*

The gene *CHROMOMETHYLASE3*, a cytosine methyltransferase, maintains gene silencing in the plant *Arabidopsis* by hypermethylating key regions of the genome.

Physiological Regulation of the Immunological Synapse by Agrin A. A. Khan, C. Bose, L. S. Yam, M. J. Soloski, F. Rupp

PERSPECTIVE: **Agrin—Bridging the Gap Between the Nervous and Immune Systems** A. Trautmann and E. Vivier

Agrin, a protein known to be required for neuromuscular synapse formation, is demonstrated also to contribute to the generation of the immunological synapse.

TECHNICAL COMMENTS

"Majorite" and "Silicate Perovskite" Mineral Compositions in Xenoliths from Malaita

Collerson *et al.* (Research Articles, 19 May 2000, p. 1215) presented evidence suggesting that xenoliths from the island of Malaita, southwest Pacific, may have come from depths greater than 470 km, in view of the presence in those rocks of transition zone and lower mantle mineral phases such as majorite and diamond. Neal *et al.*, in a comment, offer alternative interpretations of the mineral chemistry, geothermobarometry, texture, and infrared spectroscopy data consistent with an upper mantle origin for the xenoliths. They conclude that "without definitive x-ray data . . . the deep-mantle interpretation for the mineral compositions reported by Collerson *et al.* . . . remains highly equivocal." Collerson *et al.* respond that obtaining such "definitive x-ray data" is "physically impossible," as the Malaita majorites and perovskites would not be expected to have preserved their original crystallography. They go on to suggest several reasons why it is unlikely that the majoritic chemistries reported in their original study instead represent orthopyroxenes, as suggested by Neal *et al.*

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/292/5519/1015a

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Perspective: CREB Signaling—Timing Is Everything S. Impey and R. H. Goodman

A focus on the controversy surrounding the activity-dependent regulation of gene expression in neurons.

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UK: Doorstep Challenge—Put the Candidates on the Spot P. Cotgreave

With a general election on its way, the director of Save British Science challenges scientists to make sure that the issues that matter to them are on the political agenda.

Canada: Out of the Frying Pan L. Addicott

Earlier this year, Dalhousie University introduced an employment service catering specifically to graduate students. Find out what the organizers hope to achieve.

US: Alternative Career Anxiety—A Reckoning with Lingering Doubts L. Lab-Rat

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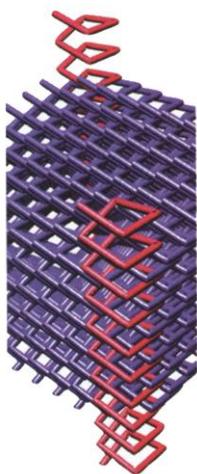
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Making a Full Recovery

Industrial catalysts generally fall into two categories—soluble compounds (homogeneous catalysts) that are often well defined but can be difficult to recover from solution, and insoluble materials (heterogeneous catalysts) that are readily recovered but whose surface reactions can be difficult to understand. Xi *et al.* (p. 1139) have used a tungsten oxide cluster to catalyze olefin epoxidation as a soluble species, at least as long as the oxidant, hydrogen peroxide (H_2O_2), holds out. When the oxidant is used up, the catalyst precipitates for ready recovery. The H_2O_2 can be generated in situ from air with a secondary catalytic system. This approach, when applied to the synthesis of propylene oxide, a major commodity chemical, could avoid the formation of unwanted by-products made in current industrial production.

Spiraling into a Photonic Band Gap

Photonic band gap (PBG) crystals are artificial materials designed with periodic fluctuations of the refractive index on length scales of optical wavelengths. In these materials, energy gaps open up that prohibit the propagation of light of particular wavelengths and thus can be used to guide light. To date, most designs have been based on the popular diamond-like or woodpile structures, but fabrication techniques have not been amenable to spatially extended three-dimensional structures. Toader and John (p. 1133) present a blueprint for an alternative PBG crystal structure based on a square-spiral structure that could be deposited over large scales. Their calculation also indicates that the structure should be functional even if defects are present.



Complete Archean Ophiolite

Ophiolites consist of layers of magnesium- and iron-rich rocks formed by a magmatic intrusion associated with extensional tectonics, such as an oceanic spreading center. Although ophiolites are relatively rare, complete sequences have been noted through much of Earth's history from the Proterozoic to Phanerozoic, and a few incomplete ophiolites were found in older rocks of the Archean. Kusky *et al.* (p. 1142; see the Perspective by Karson) found a complete ophiolite sequence of Archean age (about 2504 million years old) in the northern part of the Chinese craton near the village of Dongwanzi. The complete Dongwanzi ophiolite indicates that the fundamental processes of

1136 Nanotube Crystals

Most synthesis methods for carbon nanotubes produce entangled, poorly ordered mats, and nanotubes with different chirality are usually found within one sample. Directed growth methods show more success for creating uniform, ordered nano- and microstructures, but usually the ordered assemblies that form contain only tens of nanotubes. Schlittler *et al.* (p.1136) report the synthesis of micrometer-scale nanotube crystals containing up to several thousand individual nanotubes. Thermolysis of nanopatterned precursors was used to generate the crystals, each of which consists of an ordered array of nanotubes with identical diameter and chirality. ✕

plate tectonics were operating earlier in Earth's history than had been previously recognized.

A Dominant Population

One theory for the origins of modern humans is that they emerged from Africa about 100,000 years ago and replaced extant populations even as far away as northern Europe, Asia, and Indonesia. A second theory is that there were large degrees of inter-

breeding with extant populations that had a much larger role in future generations. Ke *et al.* (p. 1151; see the news story by Gibbons) provide strong support for the first theory in an extensive analysis of three Y chromosome markers characteristic of African origins in more than 12,000 males from 163 populations in East Asia. All of the individuals in their survey carried at least one of the three markers. Thus, there seems not to be even a minimal contribution to the gene pool from previous Asian hominids.

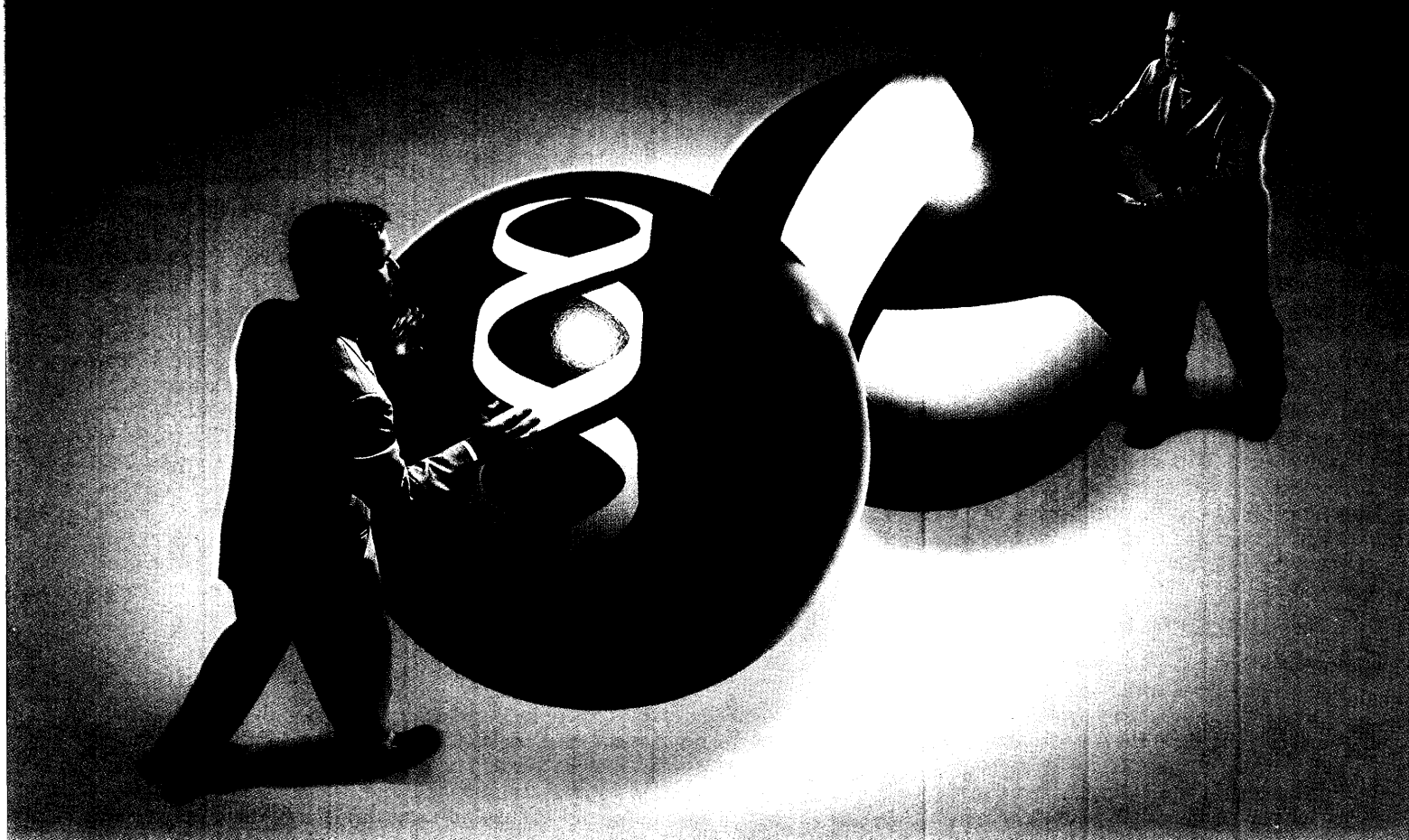
Fighting Foot-and-Mouth Disease

In early February 2001, an epidemic of foot-and-mouth disease began in northern England. By early April, more than 1000 farms across Great Britain had been infected, and hundreds of thousands of cows, sheep, and pigs were slaughtered. Ferguson *et al.* (p. 1155) use data supplied to several groups of epidemiologists by the U.K. Ministry of Agriculture, Fisheries and Food as a basis for modeling the future spread of the disease under various different scenarios of treatment, including selective culling and vaccination. They conclude that the best option for controlling the current epidemic is extensive culling of animals in the immediate vicinity of infected farms. ✕

Rock Cake for Bugs

The New Albany Shale is a remnant of Late Devonian mud that is rich in carbon in the forms of natural gas and resistant organic matter, or kerogen. When such sedimentary rocks are exposed, the carbonaceous material is weathered by several chemical and physical processes. Petsch *et al.* (p. 1127) now show that bacteria also process kerogen. They have isolated microorganisms from cores and monitored their consumption of kerogen in powdered, sterilized rock by measuring the incorporation of ^{14}C versus ^{13}C isotopes (^{14}C is absent in ancient organic matter). At least three-quarters of the carbon assimilated by their bacterial cultures originated from the rock. Until now, kerogen was not thought to be bioavailable, but this work shows that bacterial consumption of organically rich sediments may be a significant factor in weathering and, over geological time scales, may have made a significant contribution to global biogeochemical carbon cycles. ✕

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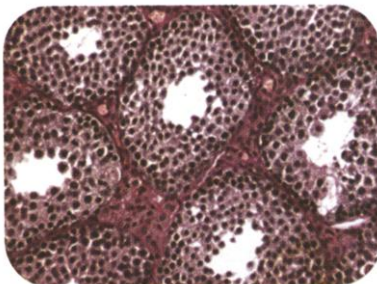
Statins are drugs that are widely used to lower cholesterol levels by inhibiting the enzyme HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase (HMGR) that catalyzes the committed step in cholesterol biosynthesis. Istvan and Deisenhofer (p. 1160) have determined structures of the catalytic portion of human HMGR bound to six different statins at resolutions of 2.3 angstroms or better. The statins bind to the enzyme active site and thus sterically prevent substrate binding. The binding pocket rearranges to accommodate statin molecules, and residues near the carboxyl terminus become disordered.

Synergy Between Selector and Signaling Proteins

Throughout development, complex structures such as organs and appendages form as directed by spatial and temporal cues. Studies have begun to define these cues, but we currently do not know how the various cues are integrated. Using the *Drosophila* wing imaginal disk, Guss *et al.* (p. 1164; see the Perspective by Affolter and Mann) examined the relation between the selector proteins and signaling factors that influence wing-specific genes. Wing development requires DNA binding by both selector proteins and signaling proteins for the specification of a developmental field.

Fertility Factor

It had been suggested at one time that all transcription machinery included the TATA-binding protein (TBP). Subsequently, TBP-related factors (TRF) were found whose function was unclear but might represent tissue-specific factors. Recent studies in *Xenopus* and *Caenorhabditis elegans* showed that TRF2 is required for early development, and that elimination of this factor leads to embryonic lethality. In contrast, Zhang *et al.* (p. 1153) now show that when mice lack functional TRF2, the animals are generally healthy but the resultant males are sterile because of a defect in spermatogenesis. Hence, TRF2 in mammals may represent a tissue-specific factor for sperm development. ✕



Let's Get Organized

Cellular architecture is governed by a network of intracellular fibers known collectively as the cytoskeleton, and one of its major components is the microtubule network. Surrey *et al.* (p. 1167) examined the types of structures that microtubules together with microtubule-based motors could construct in the absence of other cellular structures. They observed the self-assembly of several types of complex structures at steady state, including asters and vortices whose formation depended on the ratio and type of motors and microtubules. They also developed a computer simulation that faithfully predicted the observed structures.

Cap in Hand

In ciliated protozoa, the ends of chromosomes, or telomeres, are bound to capping proteins that are thought to protect the telomeres from degradation. Baumann and Cech (p. 1171; see Perspective by de Lange) have identified long-sought homologs of these proteins in fission yeast and in humans. These proteins, called Pot1 (for protection of telomeres), bound to telomeric DNA in a sequence-specific manner. Deletion of the *pot1* gene in fission yeast caused immediate loss of telomeric DNA and chromosome circularization—a phenotype more dramatic than that caused by loss of telomerase, the enzyme that synthesizes new telomeres.

The Roots of Drug Cravings

Even after long periods of being drug-free, persons addicted to cocaine can exhibit craving behavior. In an animal model, Vorel *et al.* (p. 1175; see the news story by Holden) observed that electrical theta burst stimulation of the ventral subiculum but not the cerebellum or the medial forebrain bundle could elicit strong cocaine-seeking behavior. The stimulated ventral subiculum fibers are glutamatergic, and these results suggest that glutamate receptor antagonists could block the cravings and help in treating addiction.

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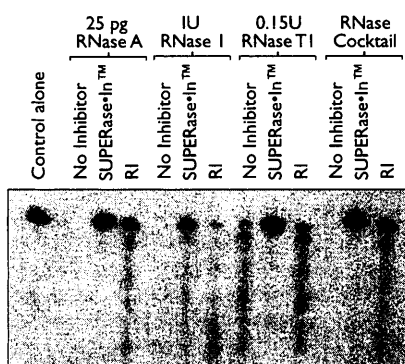
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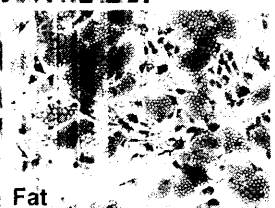
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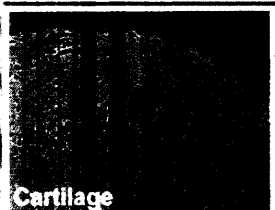
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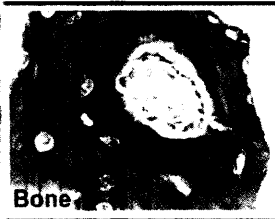
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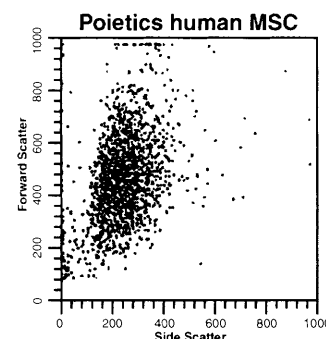
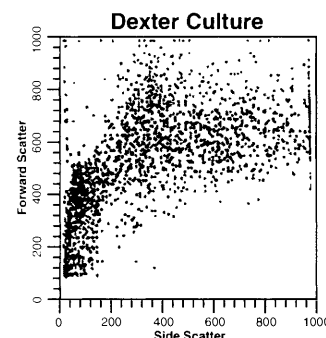
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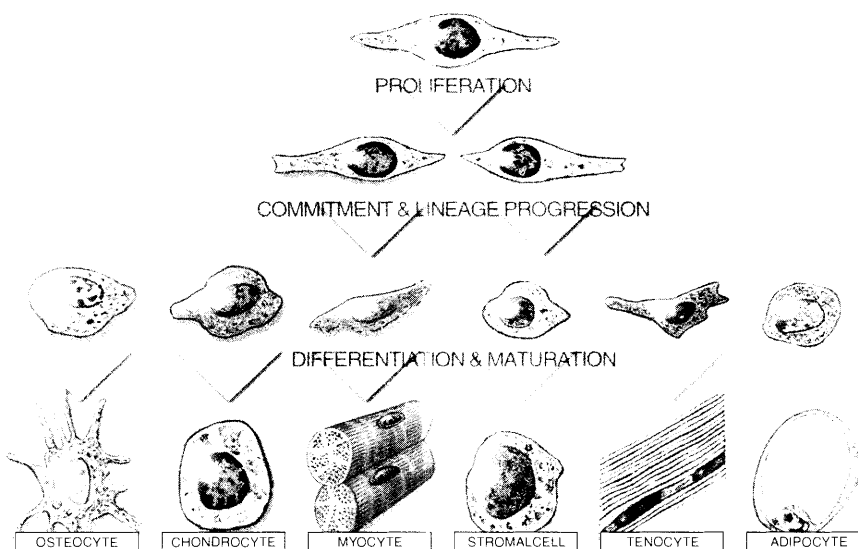
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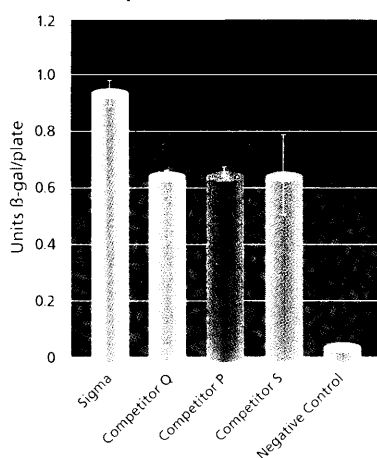
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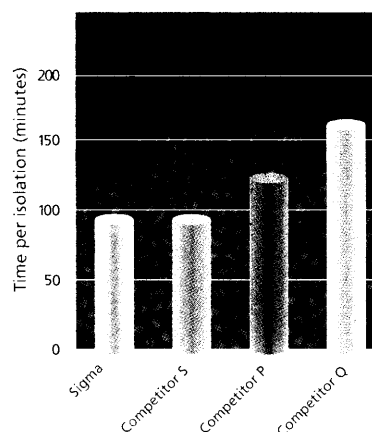


Comparison of Transfection Efficiency



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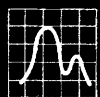
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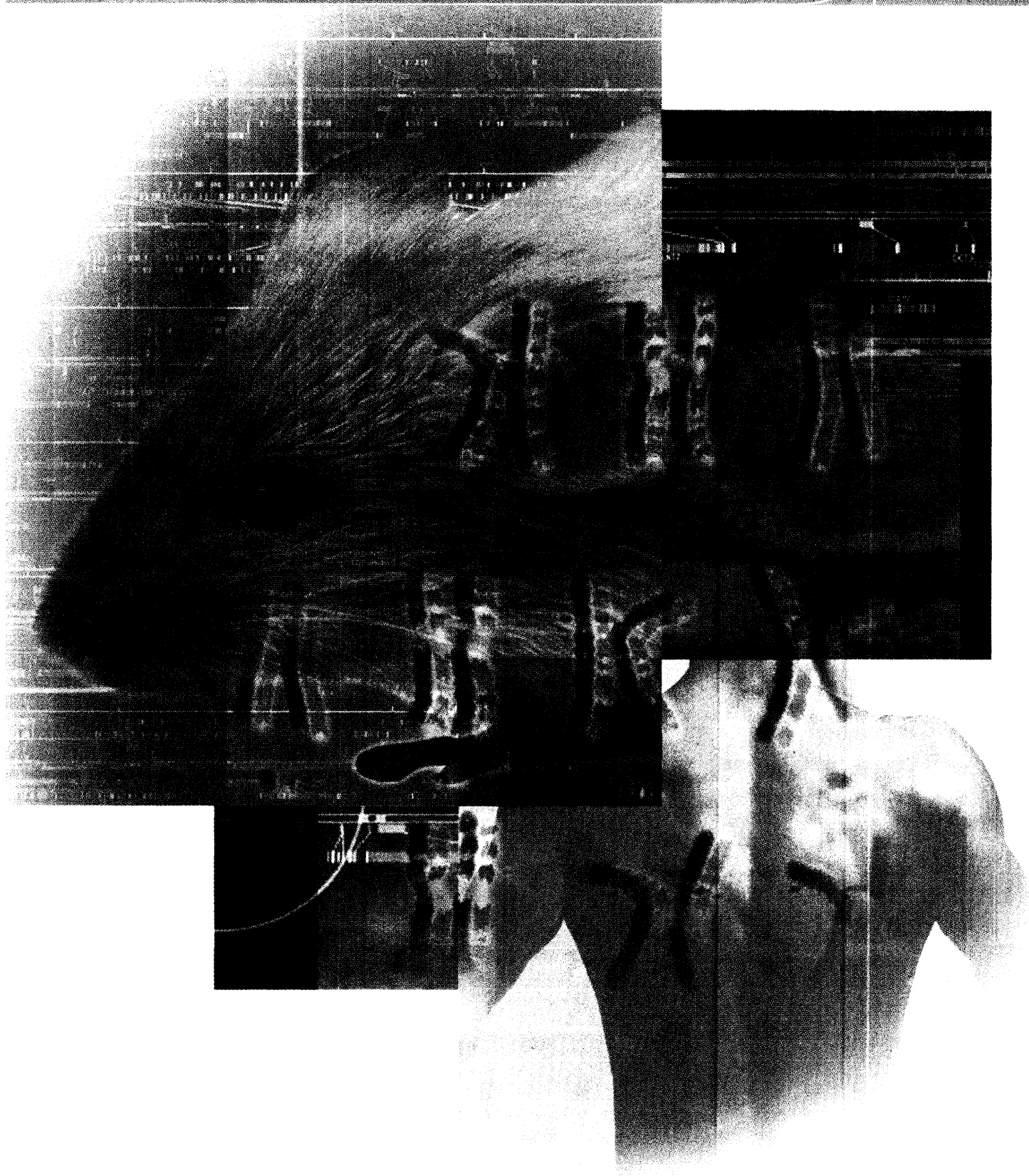
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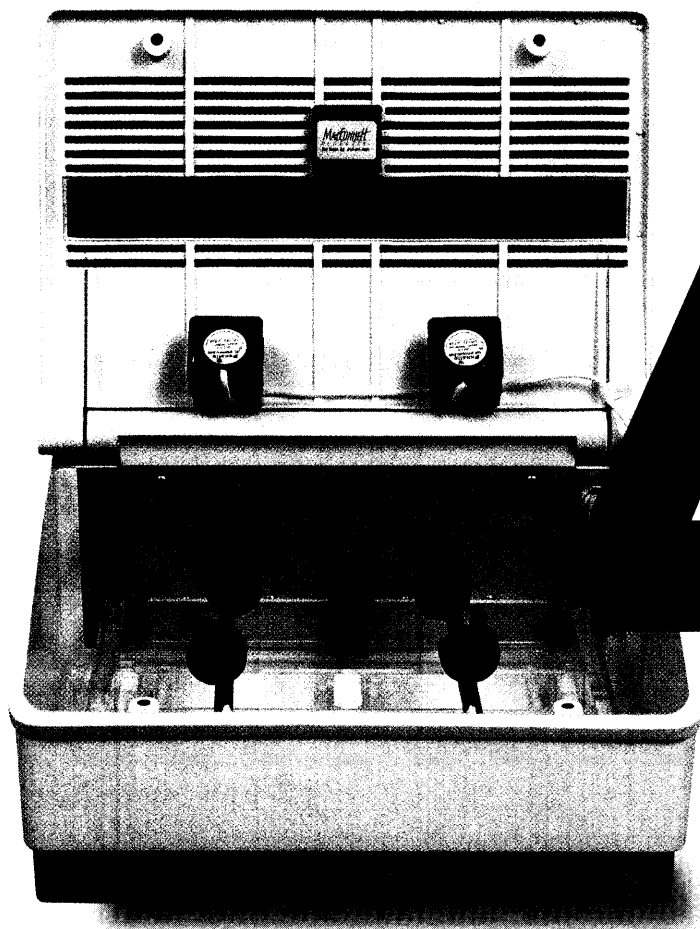
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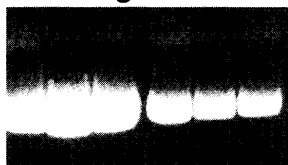
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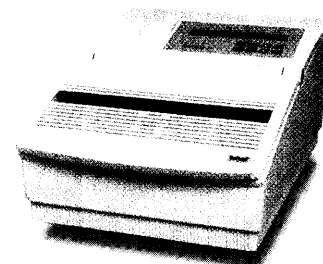
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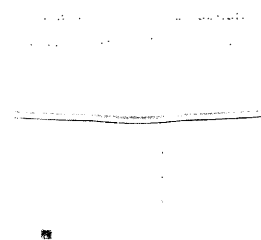
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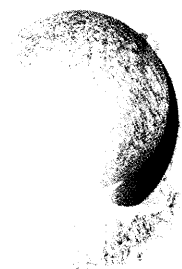
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Embryo day 13

1. Telencephalon/Diencephalon
2. Mesencephalon (Midbrain)
3. Rhombencephalon (Hindbrain)
4. Spinal cord

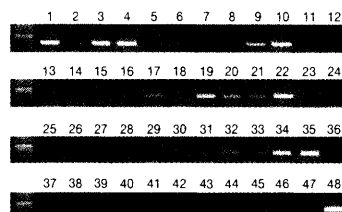
Embryo day 15

5. Telencephalon
6. Diencephalon
7. Midbrain
8. Pons
9. Medulla
10. Spinal cord

Embryo day 18

11. Frontal cortex
12. Posterior cortex
13. Entorhinal cortex
14. Olfactory bulb
15. Hippocampus
16. Striatum
17. Thalamus
18. Hypothalamus
19. Midbrain
20. Pons
21. Medulla
22. Spinal cord

HOX 3.1



Postnatal day 7

23. Frontal cortex
24. Posterior cortex
25. Entorhinal cortex
26. Olfactory bulb
27. Hippocampus
28. Striatum
29. Thalamus
30. Hypothalamus
31. Cerebellum
32. Midbrain
33. Pons
34. Medulla
35. Spinal cord

Adult 5 week

36. Frontal cortex
37. Posterior cortex
38. Entorhinal cortex
39. Olfactory bulb
40. Hippocampus
41. Striatum
42. Thalamus
43. Hypothalamus
44. Cerebellum
45. Midbrain
46. Pons
47. Medulla
48. Spinal cord



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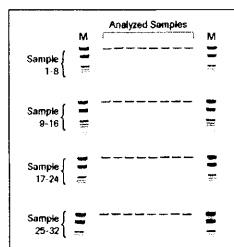
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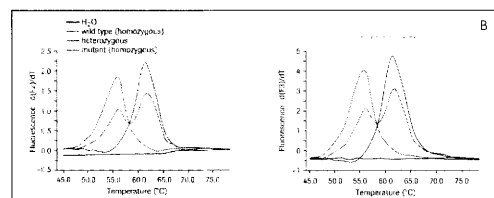
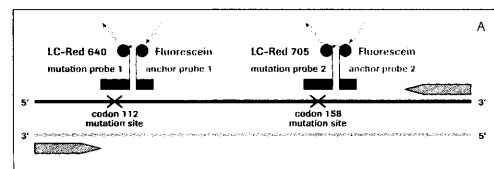
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A. Schematic of the PCR. **B.** Melting curve analysis was performed on different genotypes at codons 112 and 158 of the Apo E sequence (in channels 2 and 3) to discriminate wild type, heterozygous, and mutant genotypes.



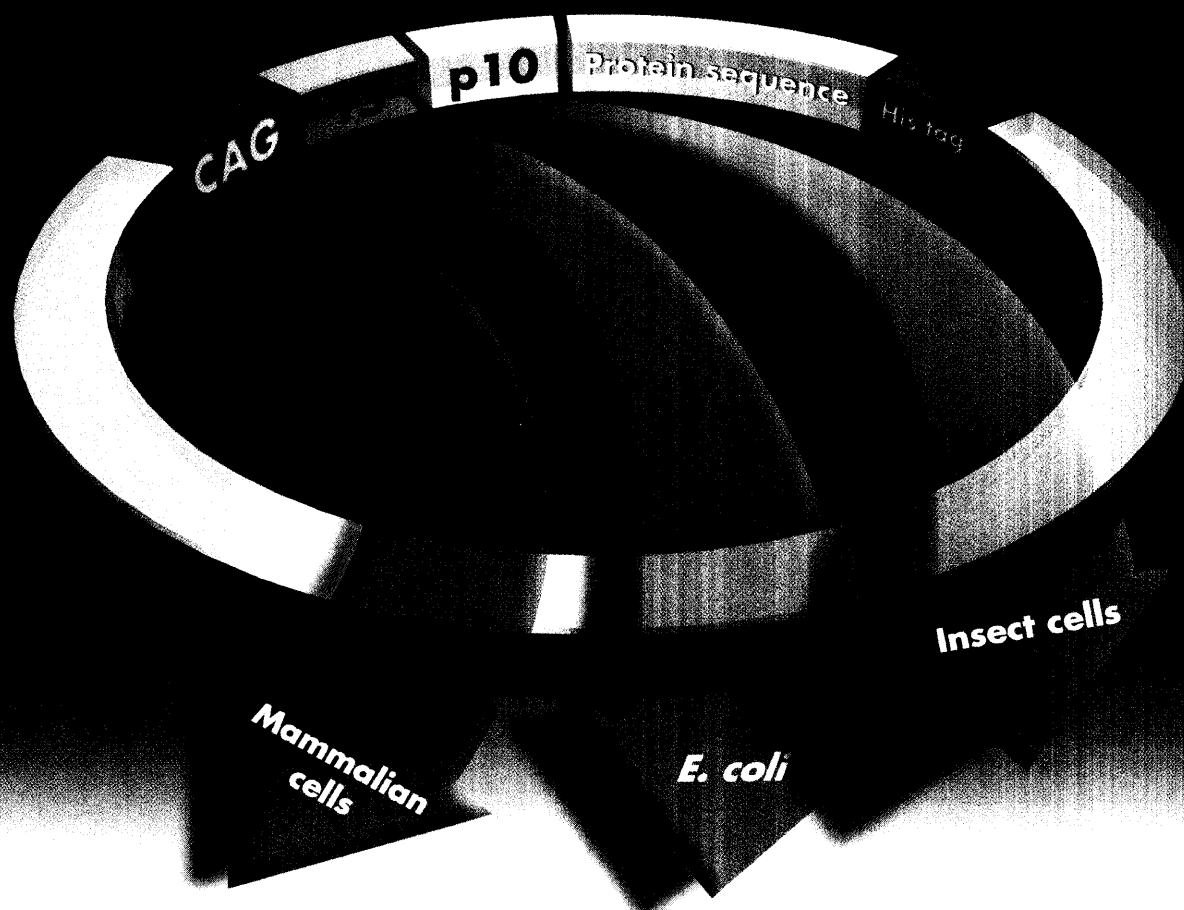
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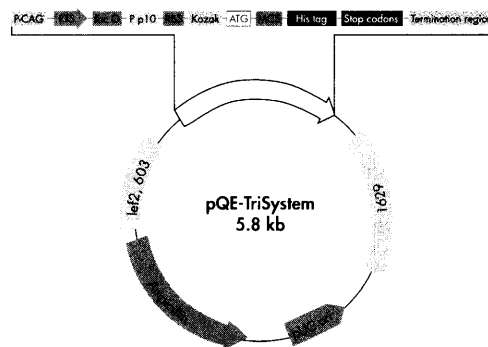
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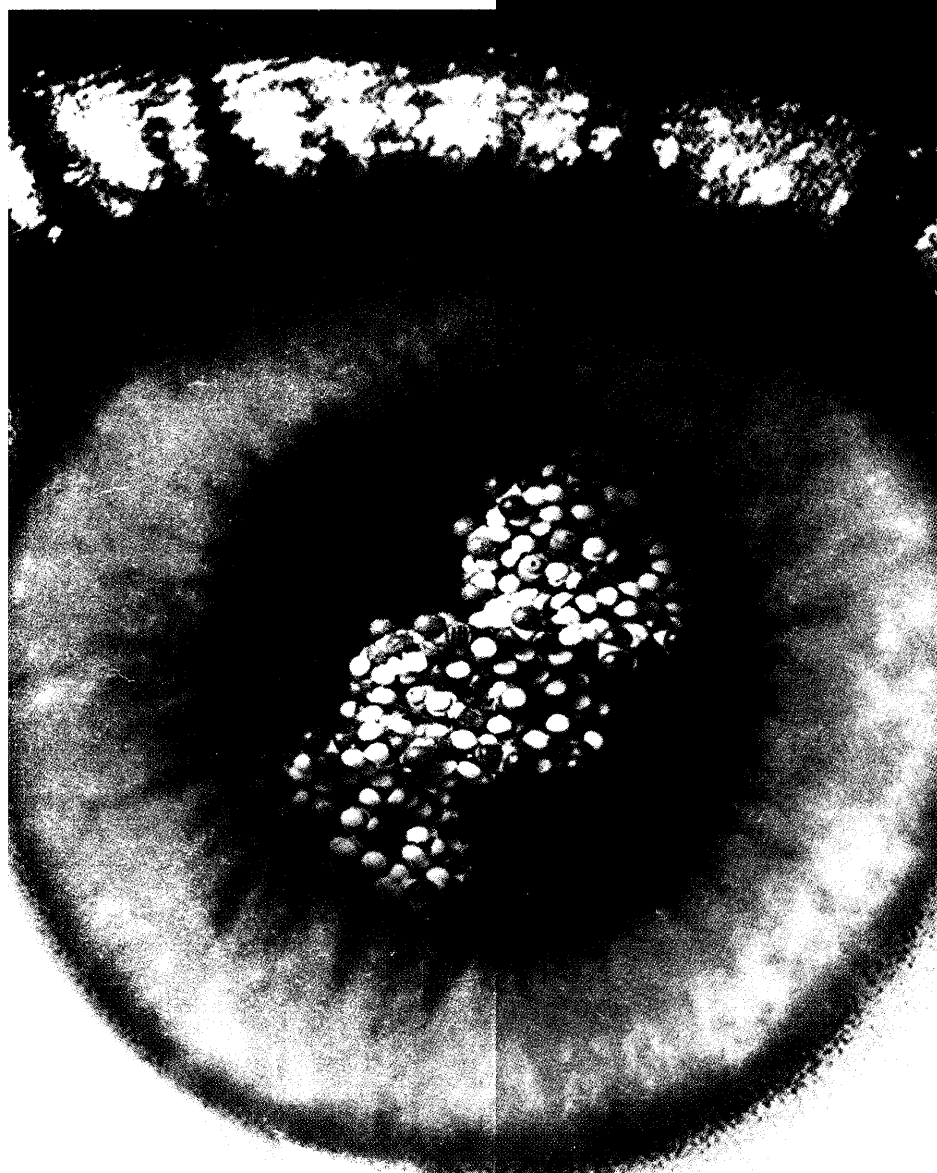
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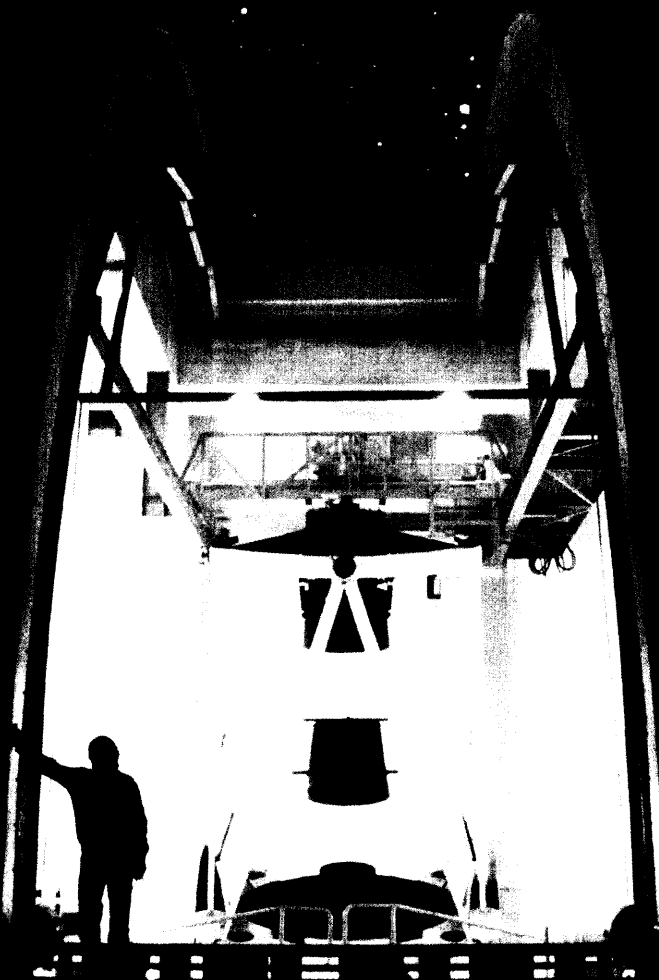
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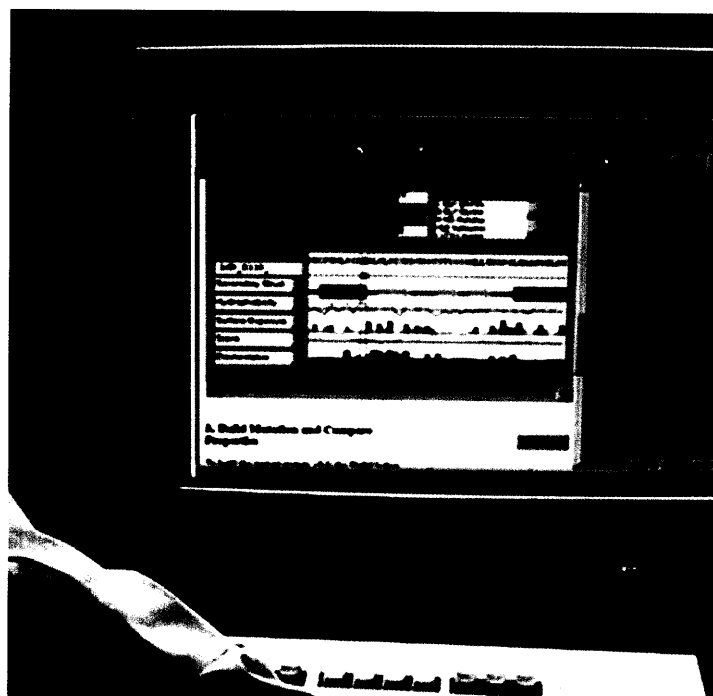
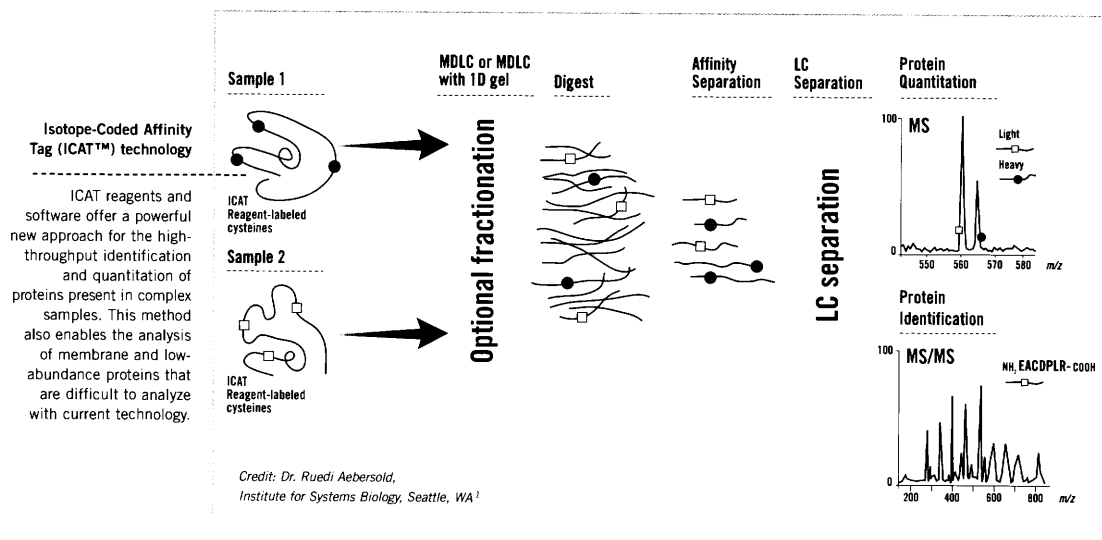
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APPLICATIONS

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(sample tracking, chromatographic fractionation, protein depletion, protein enrichment)

LABELING AND QUANTITATION

(relative abundance comparison, differential display)

PROTEIN SEPARATION

(ion exchange, reversed phase, affinity chromatography, electrophoresis)

SAMPLE PROCESSING

(MALDI plate spotting, sample dilution, matrix addition, robotics)

IDENTIFICATION

(protein identification, peptide mass fingerprinting, sequence tags, *de novo* sequencing)

CHARACTERIZATION

(post-translational modifications, protein analysis, N-terminal processing)

PROTEIN FUNCTION ASSAYS

(epitope mapping, protein-protein interactions)

PROCESS AND INFORMATION MANAGEMENT

(data mining, experiment tracking, bi-directional instrument control)

APPLIED BIOSYSTEMS

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Shawn P. Gigg, Rodrik Rist, Scott A. Gerber, Frantisek Jurecek, Michael H. Gell, Ruedi Aebersold. 1999. Quantitative analysis of complex protein mixtures using isotope-coded affinity tags. Nature Biotechnology 17:994-999.

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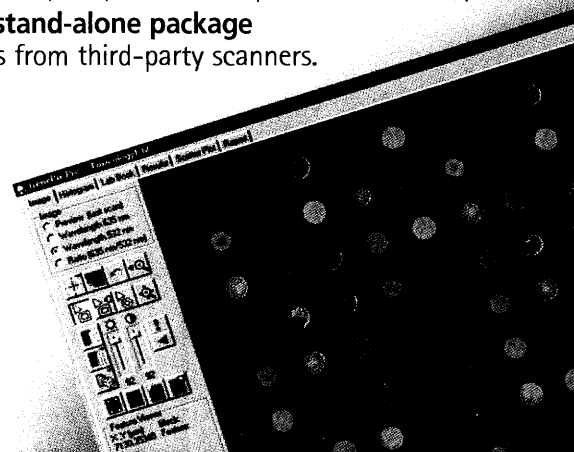
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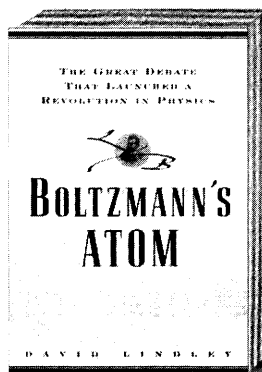
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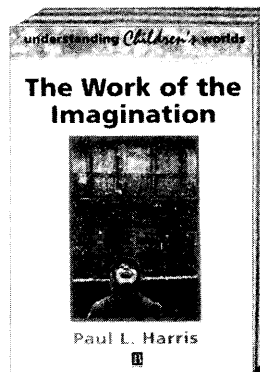
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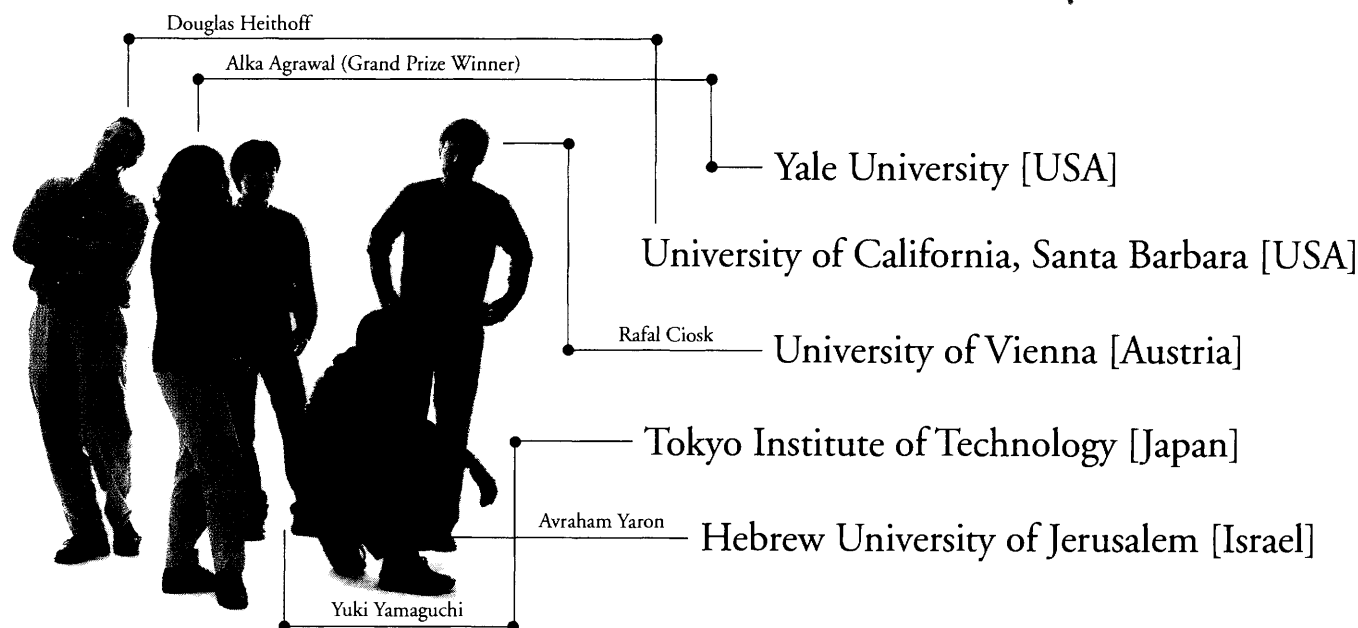
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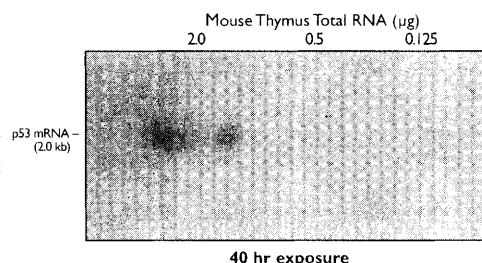
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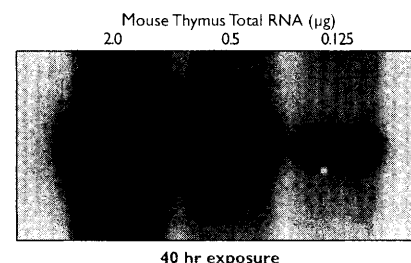
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1. *Molecular Cloning: A Laboratory Manual*, 1989. Sambrook, J. Fritsch, E.F., Maniatis, T. Cold Spring Harbor Laboratory Press.

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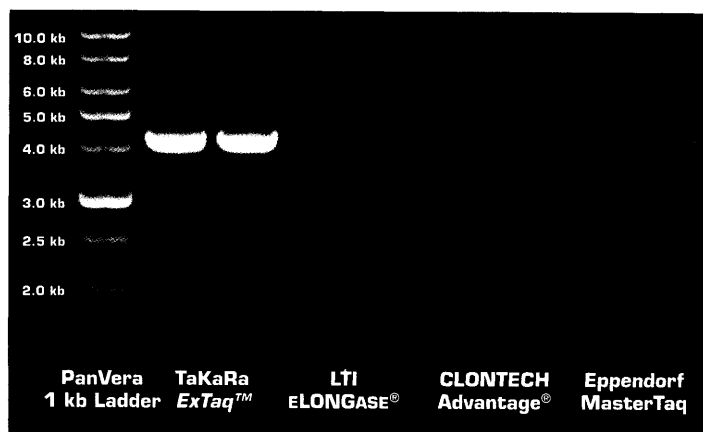
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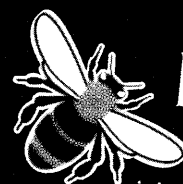
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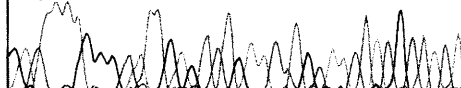
when you can

Fig. 1. Fluorescent sequencing results of a 100 bp pUC18 PCR fragment sequenced with a -20 Fwd primer using the DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech). Data generated for USB by Cleveland Genomics (clevelandgenomics.com), a research service company. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up. Base miscalls in (b) are due to inherently low yields of short PCR products when using columns.

Fig. 2. Autoradiograms of a 20.7 kb Lambda PCR fragment sequenced with MBL202 Fwd primer using USB's Thermo Sequenase Radiolabeled Terminator Cycle Sequencing Kit. PCR clean-up performed with: (a) ExoSAP-IT; (b) a column designed for PCR clean-up.

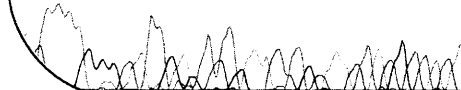
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Fig. 1(a)



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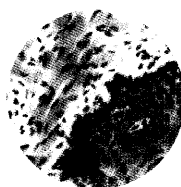
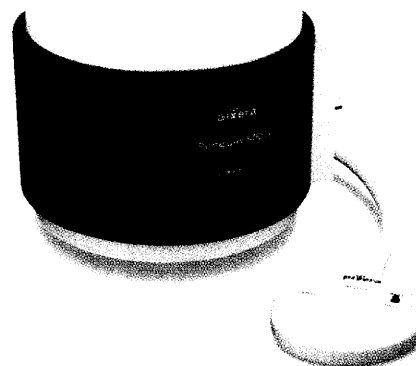


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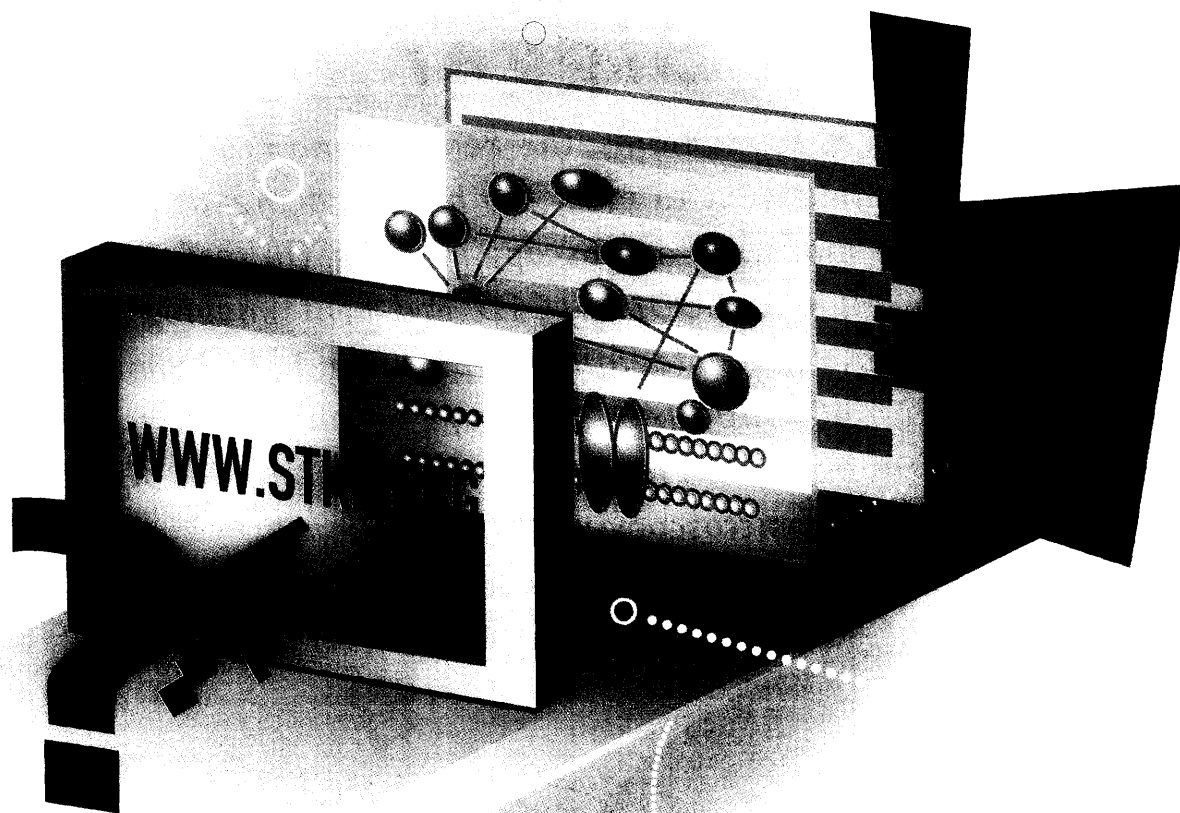
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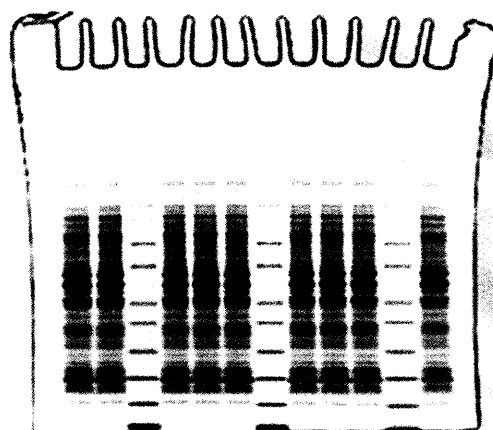
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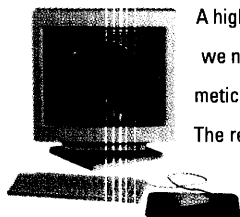
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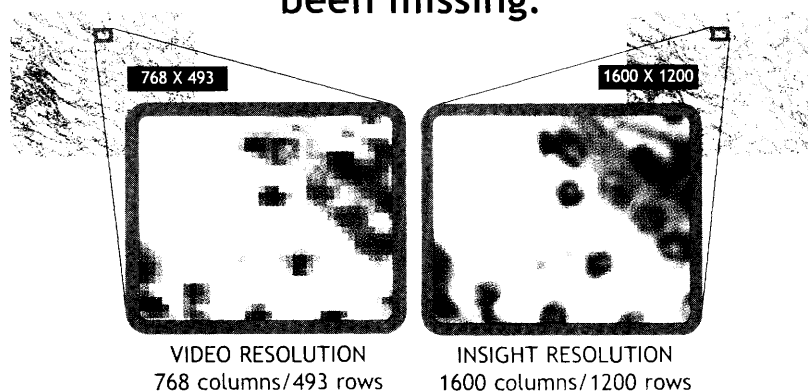
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