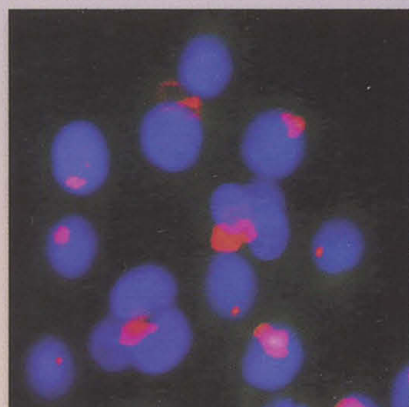


Silence Your Genes

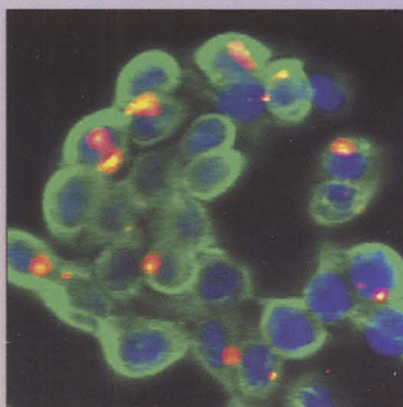
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GAPDH siRNA

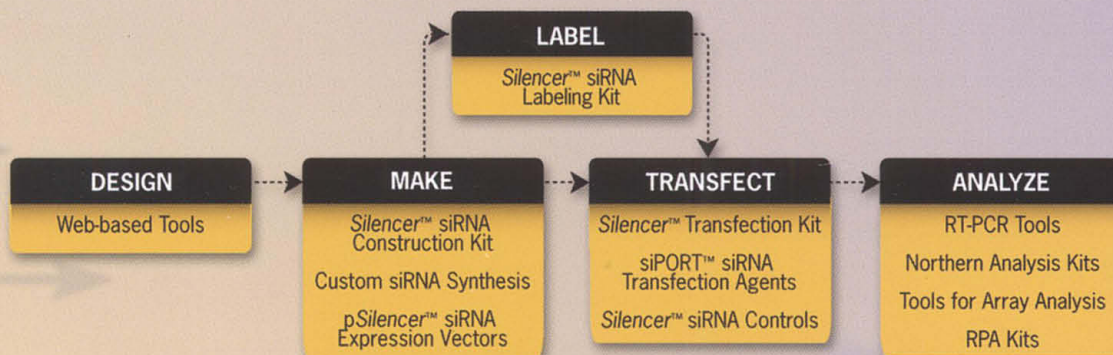


GAPDH Scrambled Control

siRNA Silencing of GAPDH Gene Expression. siRNA to human GAPDH (Cat #4602) and a scrambled control were fluorescently labeled with Cy3 using the *Silencer*[™] siRNA Labeling Kit (Cat #1632), transfected into HeLa S3 cells, and analyzed by fluorescence microscopy. **LEFT:** siRNA silencing of GAPDH expression. **RIGHT:** Control siRNA had no effect on GAPDH protein levels. **RED:** Cy3 labeled siRNA; **GREEN:** Anti-GAPDH antibody detected with fluorescein labeled secondary antibody; **BLUE:** DAPI stained nuclei.

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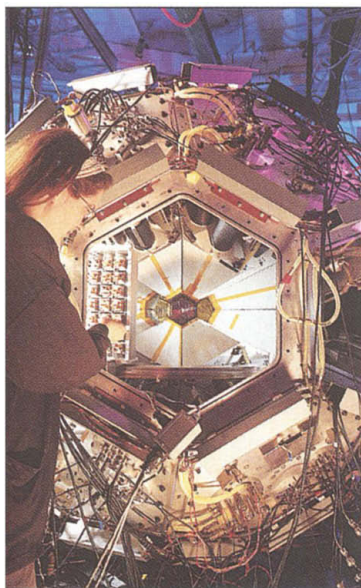


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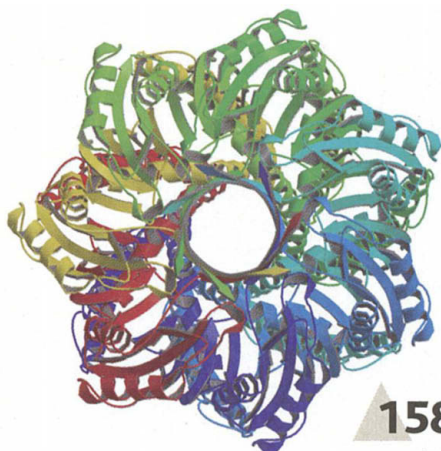
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One for you, two for me



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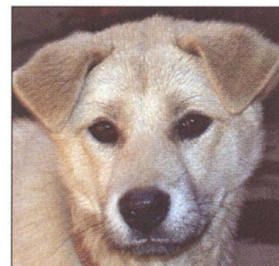
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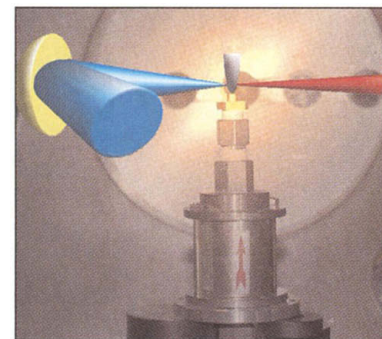
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Accelerating electrons with laser pulses



COVER 1610

A Chinese native dog, showing one of many morphological types. Although extreme variation in morphology is seen among dog breeds worldwide, they may all have originated about 15,000 years ago from the single East Asia gene pool. [Photo: Y. Zhang, D. Pan, and L.-Y. Luo]

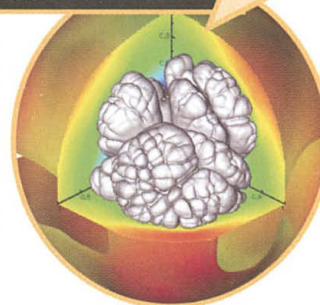


New on Science Express

Turbulent flame triggers supernova

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CONTENT HIGHLIGHTS AS OF 22 NOVEMBER 2002

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SCIENCE EXPRESS

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Mutations in the *DJ-1* Gene Associated with Autosomal Recessive Early-Onset Parkinsonism V. Bonifati *et al.*

Mutations in the *DJ-1* (PARK7) gene have been identified in two families with a rare early-onset form of Parkinson's disease.

▼ NPAS2: A Gas-Responsive Transcription Factor E. M. Dioum *et al.*

¹⁵⁶⁷ Activity of the heme-containing mammalian transcription factor NPAS2 is regulated by carbon monoxide levels in vitro.

Thermonuclear Supernovae: Simulations of the Deflagration Stage and Their Implications V. N. Gamezo, A. M. Khokhlov,

E. S. Oran, A. Y. Chtchelkanova, R. O. Rosenberg

Modeling of a Type Ia supernova explosion shows that a central turbulent flame ignites the stellar boom.

TECHNICAL COMMENTS

Are 100,000 "SNPs" Useless?

Bailey *et al.* (Reports, 9 August 2002, p. 1003), in a study of segmental duplications within the human genome, noted that unrecognized duplications can lead to paralogous sequence variants being falsely identified as single nucleotide polymorphisms (SNPs)—and estimated, based on their analysis, that "about 100,000 paralogous sequence variants currently contaminate dbSNP," the public SNP database. Hurles comments that nonallelic gene conversion among duplicated segments has been shown to be "capable of generating allelic diversity," and that such variations, far from being mere artifacts of genome assembly, could be etiologically significant even though they might escape detection by "haplotype-based whole genome association studies of complex disease." Bailey and Eichler, in a response, agree that gene conversion is a likely source for "some of the 'SNP' abundance" in the public database, but argue that artifacts in the public assemblies provide "the most prosaic explanation" for the observed enrichment of SNPs in the database.

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/298/5598/1509a

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career resources for scientists

CANADA: Cutting-Edge Vaccine Research H. Wilson

The Veterinary Infectious Disease Organization is a unique training site for graduate students.

US: Vintners Go High-Tech A. Sreenivasan

Wine growers in California use new technologies to improve their crops.

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NETHERLANDS: Going Dutch—But Who Will Pay the Research Bill? H. Meijers

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Growth hormone thins and strengthens the elderly, but at a cost.

NOTEWORTHY THIS WEEK: BAD Time for Suicide M. Beckman

Growth factors save cells by foiling mitochondrial disrupter.

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signal transduction knowledge environment

REVIEW: Regulation of Growth Factor Receptors by Gangliosides E. A. Miljan and E. G. Bremer

Membrane composition influences receptor activity.

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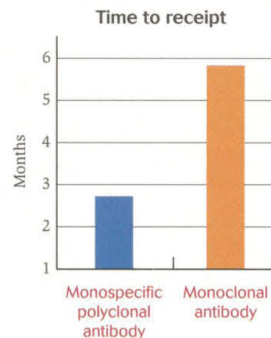
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THIS WEEK IN Science

edited by Phil Szuromi

Describing the Densest Matter

Nucleon-nucleon interactions make it difficult to compress ordinary matter here on Earth beyond an approximate saturation density of about 2.7×10^{14} grams per cubic centimeter. However, this limit is exceeded by objects in space such as neutron stars (densities about nine times the saturation density) and supernovae (densities about four times the saturation density). Danielewicz *et al.* (p. 1592) have developed a new theoretical equation-of-state model, which relates densities to pressure and temperature conditions, for supersaturated matter based on recent high-density nuclear collision experiments. They limit the range of possible pressure and temperature conditions that may exist in neutron stars and supernovae, which not only constrains the concentrations of neutrons versus protons in these objects but also their dynamical behavior. **X**

Bacteria and Groundwater Arsenic

In an attempt to prevent cholera and other water-borne diseases, Bangladesh encouraged the use of groundwater, which had the unintended effect after several years of exposing a large part of the population to arsenic present as a contaminant. The uncertain origin of the arsenic has hampered remediation efforts. In a study in southern Bangladesh, Harvey *et al.* (p. 1602; see the news story by Stokstad) rule out several suggested mechanisms and show that young organic carbon is being carried into aquifers by the extraction of groundwater for agriculture. Dissolved carbon is likely feeding bacteria, which liberate arsenic bound in solids in the aquifer back into the groundwater.

Digging into Dog Domestication

The origins of how humans and dogs developed their association, and when and where this occurred, is the subject of three reports (see the news story by Pennisi). Dogs and wolves (and some primates) are social animals that must comprehend and respond to their own species. Hare *et al.* (p. 1634) compared the performance of wolves and dogs in interpreting human signals (such as looking, pointing, and tapping) that relate to food location. Unlike wolves, dogs exhibit this skill that helped them interpret human communication. Some studies argue that the domestication of dogs from wolves occurred as a single event, and others favor multiple events and distinct Old and New World origins. The fossil record offers evi-

1596 Laser Accelerators

The probing of grand unification theories and fundamental interactions within atoms will require the ability to go beyond the energies of particle accelerators available today. However, with the maximum attainable energies of conventional accelerators being limited by the breakdown fields of the materials used in construction, other routes are being developed, especially the use of laser-plasma interactions. Malka *et al.* (p. 1596), using intense femtosecond laser pulses interacting with a jet of helium gas, show that a new acceleration mechanism opens up the forced laser wake field regime, where emitted electrons can attain energies greater than 200 million electron volts.

And in Brevia ...

A study of a perennial grass found around hot springs by Redman *et al.* (p. 1581) revealed that it harbors a fungus that confers heat resistance, and that neither organism can live in the hot soils without the other.



dence that domestication occurred about 13,000 years ago in the Near East, whereas molecular clock data imply an earlier date. Leonard *et al.* (p. 1613) analyzed mitochondrial DNA (mtDNA) from ancient aboriginal North and South American dog remains and argue for a single Asian origin for dogs. Dogs migrated to the Americas with their human companions via the Bering Strait about 12,000 to 14,000 years ago, but these indigenous breeds appear to have been replaced by larger European breeds during the colonial period. Savolainen *et al.* (p. 1610; see the cover) collected mtDNA sequences from 38 Eurasian wolves and 654 domestic dogs sampled across Asia, Europe, Africa, and the Arctic America to assess the number and location of dog

domestications. The higher genetic diversity in dogs from East Asia compared to Southwest Asia and Europe suggests that dogs originated in East Asia. This phylogenetic analysis, when interpreted in light of archaeological data, suggests that domestic dogs originated around 15,000 years ago, with several origins from wolves.

Primitive Primates

The origins and evolution of the euprimates—those primates that share many modern primate characteristics such as larger brains, grasping hands, convergence of the eyes for improved binocular vision, and fingernails—has been obscure in part because of limited earlier fossil material. Euprimates appear about 55 million years ago and evolved eventually to include the anthropoids and hominoids. Bloch and Boyer (p. 1606; see the Perspective by Sargis) now describe an earlier fossil plesiadapiform based on a nearly complete skull and large part of its skeleton. The fossil exhibits traits that in some ways are more primitive than the euprimates, but also has several derived features, including clear nails and the ability to grasp. These results suggest that these groups shared a common origin and that grasping evolved before orbital convergence.



Pulled Sideways

Bacteria lack rigid cell walls and must respond rapidly to salt-induced gradients in osmotic pressure. In *Escherichia coli*, the mechanosensitive channel proteins MscL and MscS open in re-



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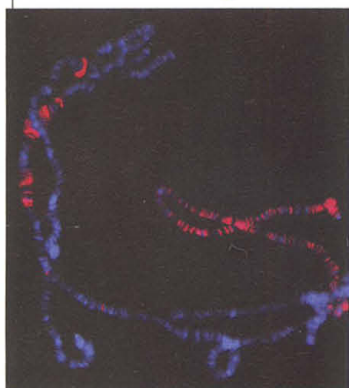
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sponse to pressure applied perpendicularly to the membrane, which has the effect of pulling laterally on the membrane-embedded proteins. Bass *et al.* (p. 1582; see the Perspective by Bezanilla and Perozo) provide the crystal structure of MscS and describe how the transmembrane helices might reorient themselves as a result of being pulled sideways. The authors also propose how changes in transmembrane electrical potential might trigger movement of positively charged arginines and voltage-gate the osmolyte flux.

Pass the Photosynthesis Genes

Photosynthesis completely transformed Earth by introducing oxygen into the atmosphere. Raymond *et al.* (p. 1616; see the news story by Pennisi) made a comparative sequence analysis of genomes from the five branches of photosynthetic bacteria known today to address the origin and evolution of photosynthesis and found that it entailed lateral gene transfers. This work draws attention to an emerging caveat, namely, many core genes for specific metabolic processes are uncharacterized, yet they appear to be of paramount importance to the evolution of certain cellular innovations.

Controlling Chromatin Spreading



Dosage compensation involves the propagation in cis of altered chromatin architecture and gene activation states over much of the X chromosome. The male-specific lethal (MSL) complex, which includes the *roX1* and *roX2* non-coding RNAs, is responsible for such spreading on the X chromosome in the fruit fly *Drosophila*, but the mechanism by which the spreading occurs is not fully understood. Park *et al.* (p. 1620) show that a limiting concentration of the *roX* RNAs relative to the MSL complex is critical for effective spreading to occur. This condition apparently ensures that MSL complexes are completed by the addition of nascent *roX* RNA while the RNA is still tethered to the DNA template, thereby limiting spreading and dosage compensation to the X chromosome.

RNA Polymerase I in Action

The kinetics of the RNA polymerase I RNA (pol I), the enzyme that transcribes ribosomal RNA, have been revealed by combining photobleaching microscopy of living cells with computational modeling. Dundr *et al.* (p. 1623; see the news story by Couzin) followed the entry of its subunits into the nucleolus, complex assembly, and elongation. The pol I subunits rapidly exchanged between the nucleoplasm and transcription site in the nucleolus, and the polymerase complex bound to the promoter as distinct subunits rather than as a preassembled unit. The assembly of the polymerase is a relatively inefficient process that occurs via metastable intermediates.

Seeing and Touching an Object

When observers combine different sources of information perceptually, do they preserve or discard the original sources? Hillis *et al.* (p. 1627) show that cues are combined within the visual modality in such a way that certain information is lost, and differences that should be obvious are simply not seen. However, this loss does not occur when cues from different modalities, vision and touch, are combined.

B Cell Immunodeficiency

Several cytokine receptors utilize the common cytokine receptor γ chain (γc), and mutations in γc result in the condition known as X-linked severe combined immunodeficiency (XSCID). Lack of signaling through the interleukin-7 (IL-7) and IL-15 receptors leads to a loss of natural killer and T cells in XSCID patients, although the cause of the B cell defect is not established. Ozaki *et al.* (p. 1630) observed that B cells from mice lacking IL-21 receptor had altered antibody production. When combined with a loss of IL-4 signaling, a severely impaired immunoglobulin G response was observed that is strikingly similar to that seen in XSCID individuals.

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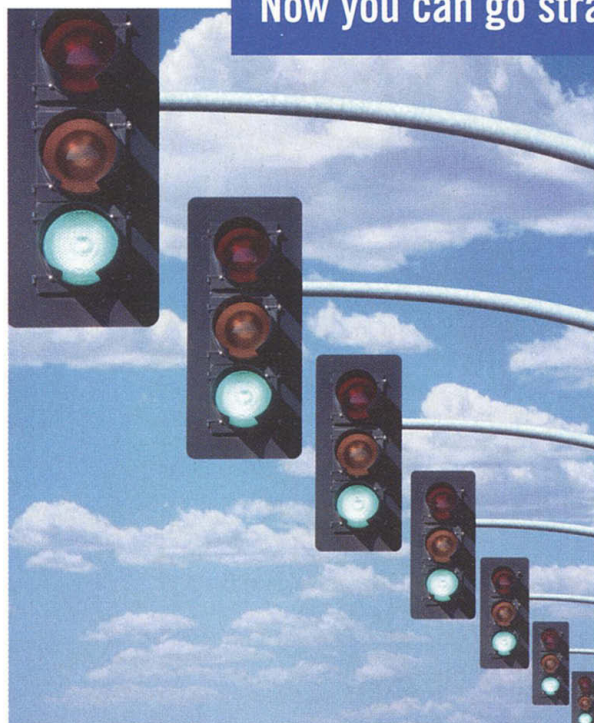


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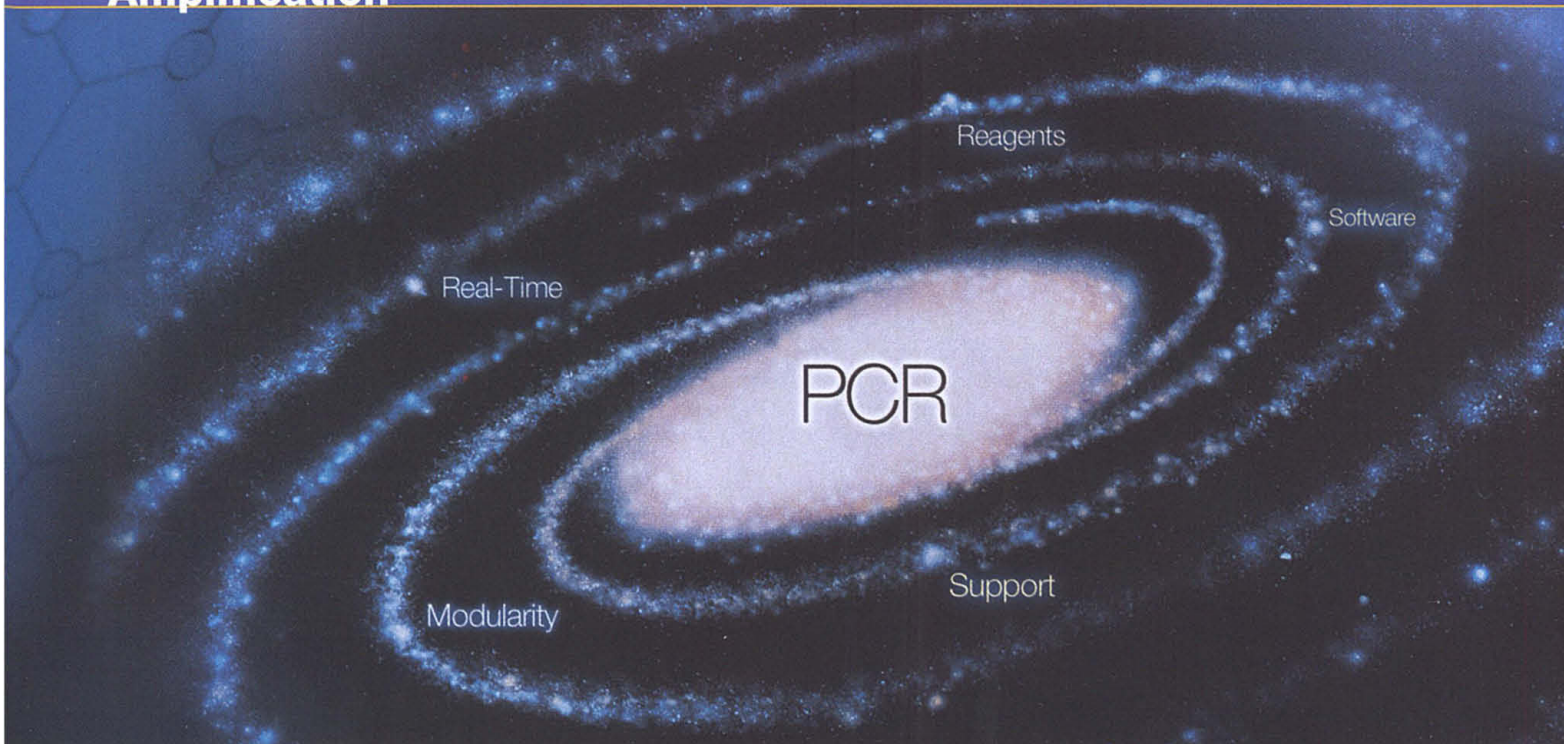
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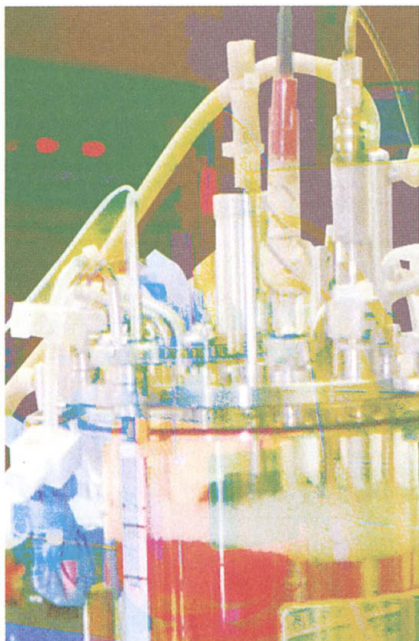


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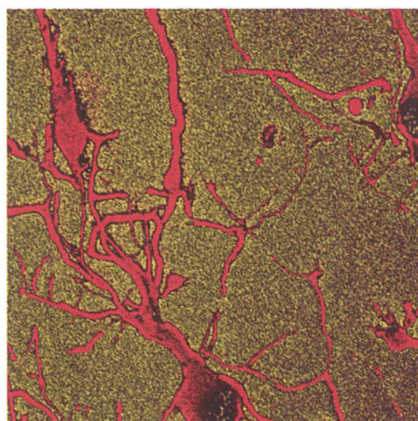


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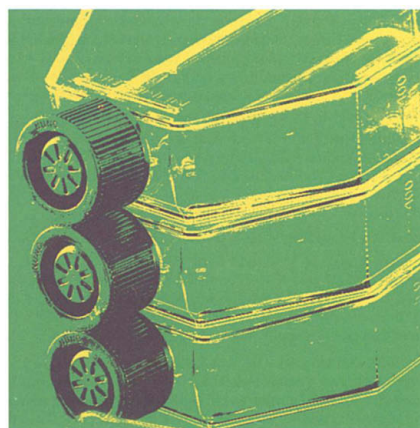


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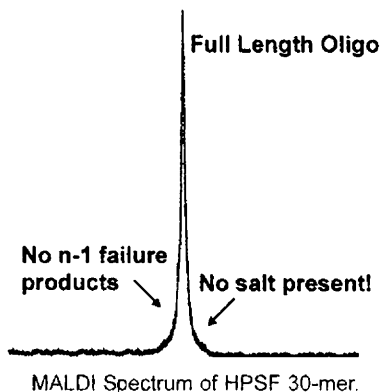
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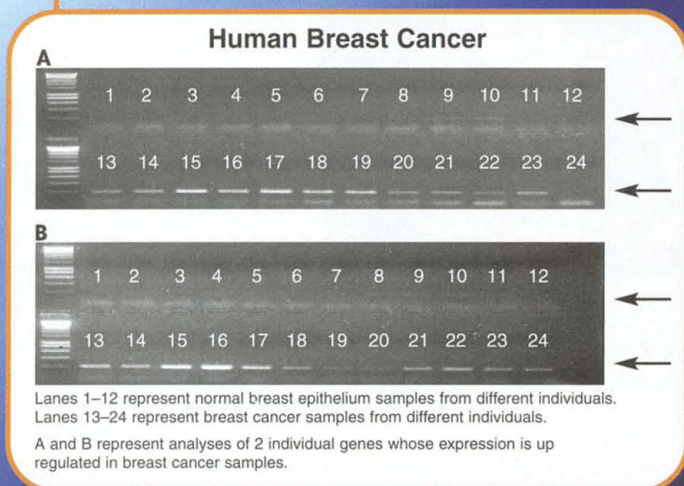
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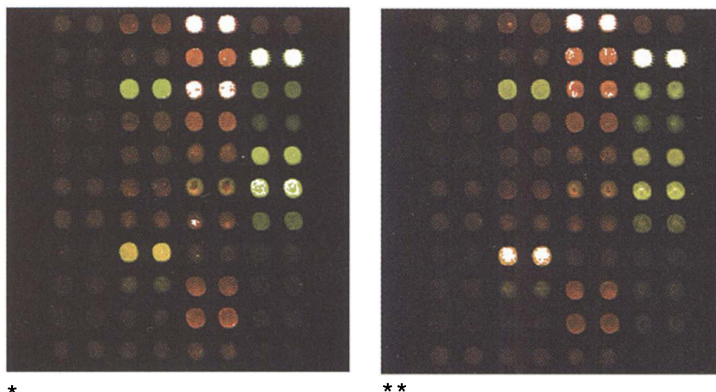


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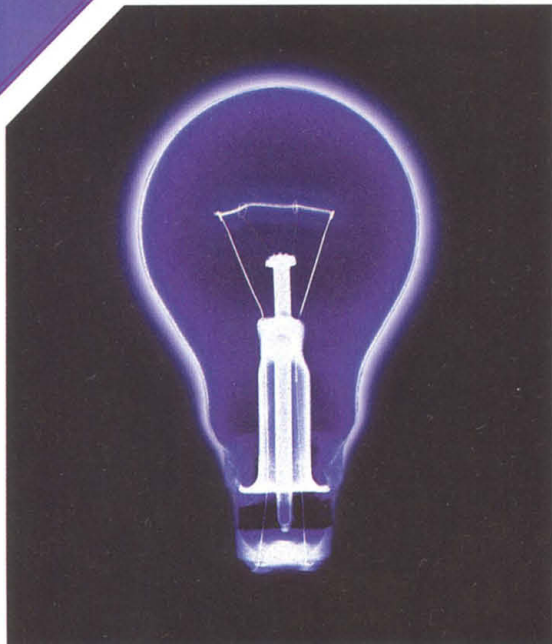
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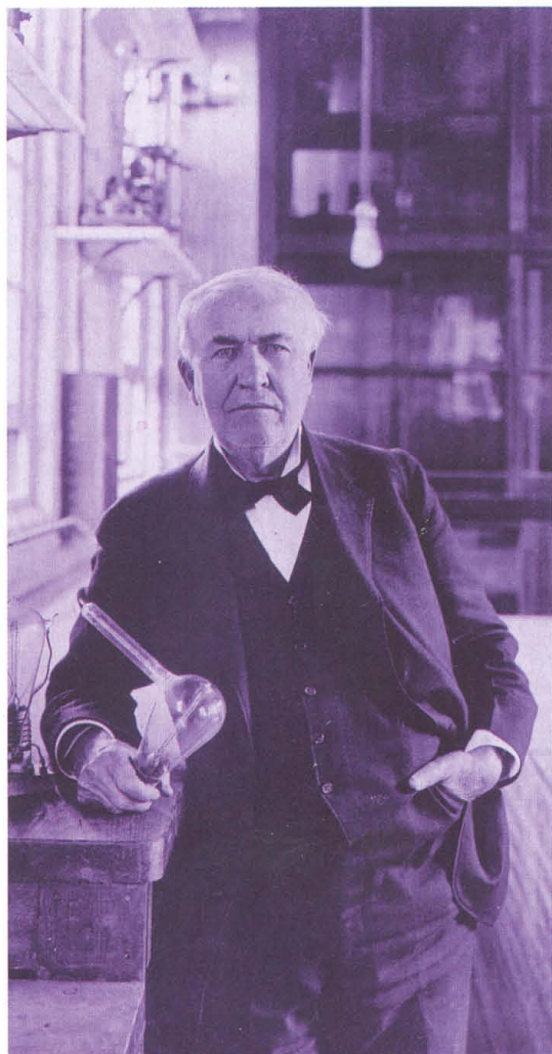
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AWARDS AND HONORS

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- 1990 Magna Cum Laude
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PUBLICATIONS

1. John Doe, Gustave Hall, and Sossity Rapparell. Coordinate Regulation of HLA Class II Gene Expression. *Complex. Molecular Immunology*, Vol. 66, No. 11/12, pp. 490-511, 1998.
2. John Doe and Sossity Rapparell. Identification of Alternatively Spliced Transcripts by RNA Sequencing. *Lines from a Bare Lymphocyte Syndrome Patient*. [In Preparation]

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