18 February 2000

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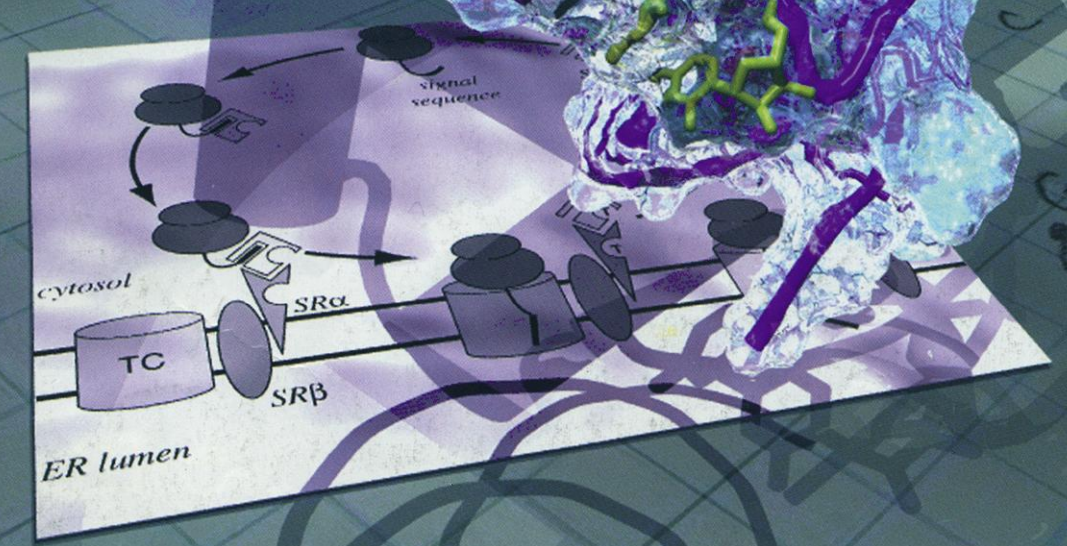

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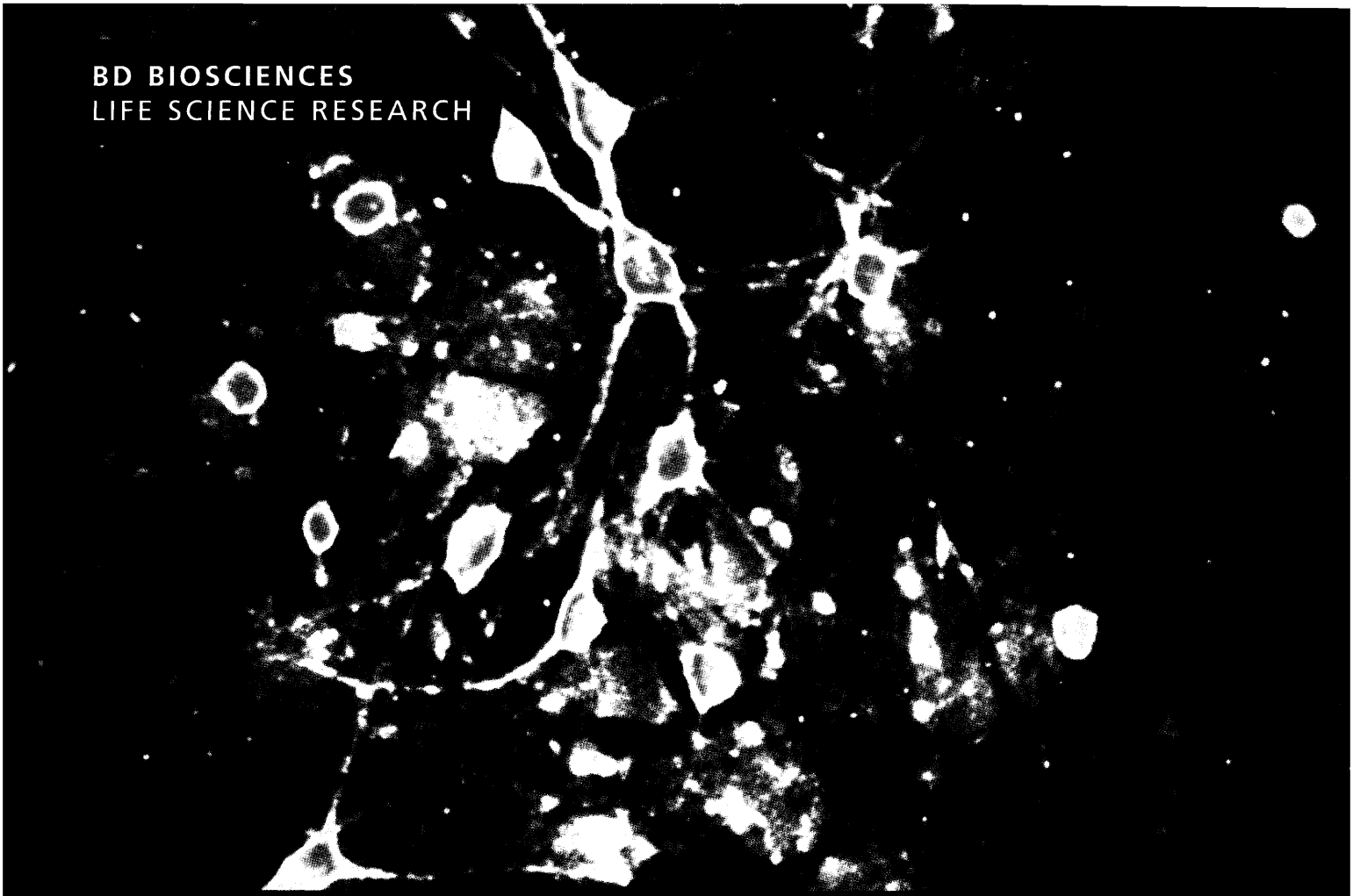

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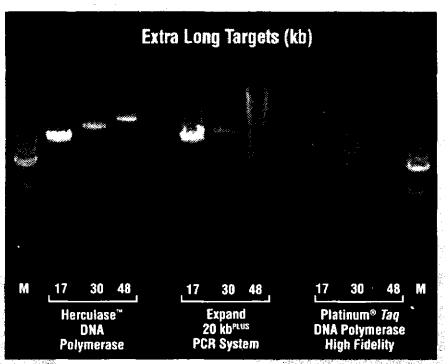

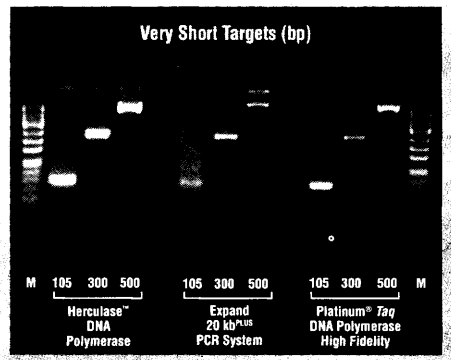

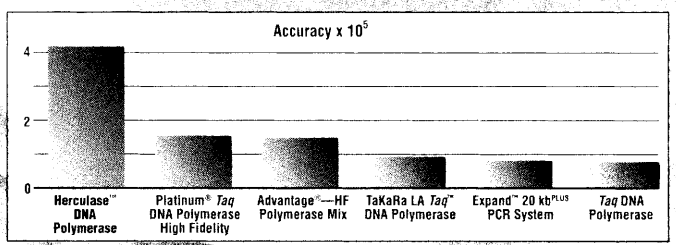

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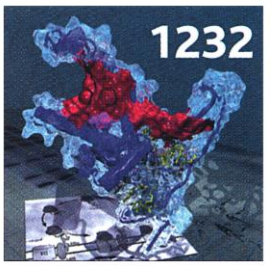

COVER Molecular surface representation of the RNA-protein core of the signal recognition particle (SRP) from the bacterium *Escherichia coli*. The proposed signal sequence binding groove, highlighted in red against the glassy molecular surface, is made up of protein and RNA, whose backbones are depicted in dark blue. The domain of the SRP is universally conserved (shown in yellow for the RNA), suggesting a common mechanism for signal recognition in all life. [Image: R. T. Batey and R. P. Rambo]

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Exploring the link between science and advocacy

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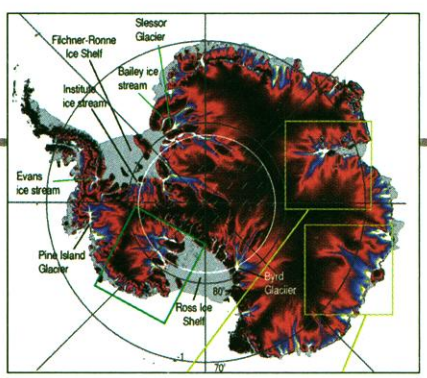

1248

Antarctic ice sheet balance velocities

1217

Structure at the billion light-year scale

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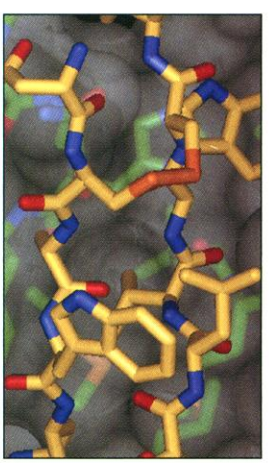

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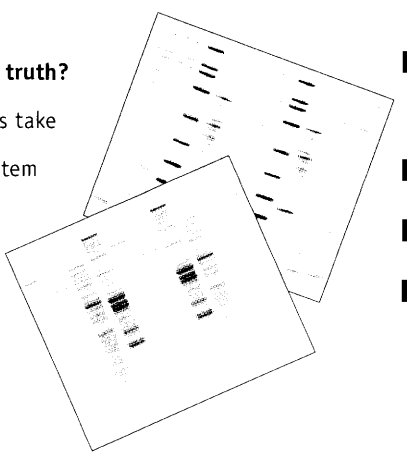

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BLACK HOLE SUN

An accretion disk of rapidly spiraling gas and particles may form around a black hole. This disk can give off intense x-ray emissions as the gravitational energy of the material is lost before it is swallowed by the black hole. Modeling by Zhang *et al.* (p. 1239) of the low- and high-energy x-ray spectra of two Galactic superluminal sources, GRS 1915+105 and GRO J1655-40, suggests that the high-energy x-ray emissions are related to a very hot and thin corona around the disk, and that the low-energy x-ray emissions are related to Compton scattering of central disk photons in a warmer disk layer that encompasses the colder central disk. This modeled structure resembles the structure of the solar atmosphere, which suggests that similar physical processes may account for the formation and stability of accretion disks in general.

GETTING THEIR IRON

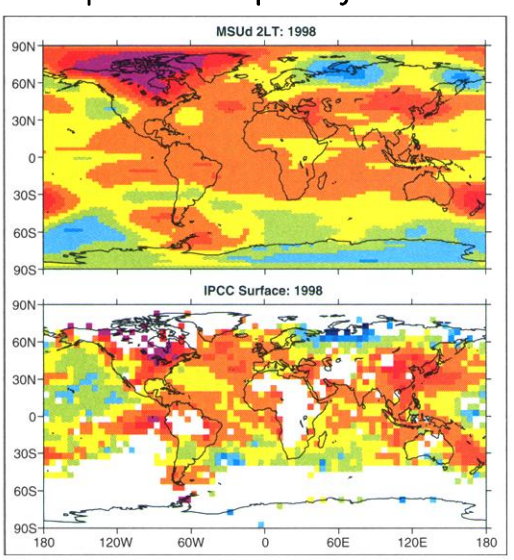
Marine microorganisms have evolved sophisticated mechanisms for sequestering iron, which is often only present in trace amounts in the surrounding seawater. Like terrestrial microorganisms, they secrete siderophores, low-molecular-weight compounds that scavenge iron from the environment and facilitate its uptake into the microbial cells. Martinez *et al.* (p. 1245) show that two families of siderophores isolated from different genera of marine bacteria spontaneously form vesicles upon addition of Fe(III). This iron acquisition mechanism may be a distinctive feature of marine bacteria.

RECOGNIZING A STOP SIGN

Proteins that are destined for integration into a membrane or for secretion across a membrane generally carry a signal sequence at their amino-terminus—a stretch of ~20 amino acids containing both hydrophobic and basic side chains. As the nascent peptide emerges from the ribosome, the signal sequence is bound by the signal recognition particle, a complex of protein and RNA, and protein synthesis is halted momentarily. The entire assembly is then ferried to a membrane where peptide synthesis continues with co-translational membrane insertion. Batey *et al.* (p. 1232; see the cover and the Perspective by Walter *et al.*) describe the 1.8 angstrom structure of the core of the signal recognition particle that reveals the intimate contacts between two RNA loops and two protein helices docked into the minor groove of the RNA.

ON THE GROUND AND IN THE AIR

Satellite-based microwave measurements of lower tropospheric temperatures have shown no change or even a slight cooling trend since 1979, which conflicts with ground-based observations of surface temperature that indicate warming. A research article and a report discuss how these different measurements can be reconciled (see the Perspective by Parker). Santer *et al.* (p. 1227) show that approximately 30% of the difference in the trends of satellite-based measurements of lower tropospheric temperature and ground-based measurements of surface temperature for the past 20 years can be explained by the different spatial coverage of the methods. Their model results show that the remaining differences are greater than can be explained by natural variations alone, and that the best model simulation is one that includes the influences of anthropogenic factors and volcanic aerosols. Gaffen *et al.* (p. 1242) have collected vertical temperature profiles of the tropical troposphere made with weather balloons during this period and found that both satellite and surface measurements apparently are correct. The differences between the two time series are due to variations in the vertical temperature profile of the troposphere.



LIVER TRANSPLANT LIFELINES?

Many liver transplant patients die each year because of the chronic shortage of suitable donor organs. Two reports discuss successful approaches in rodent models of liver disease that may one day buy human patients time by slowing liver damage (see the news story by Hagmann). Transplantation of hepatocytes, which can provide temporary metabolic support, is hampered by a similar shortage of transplantable hepatocytes. Kobayashi *et al.* (p. 1258) have constructed a line of hepatocytes that can be reversibly immortalized and therefore grown up in large quantities in vivo. Subsequent removal of the immortalizing gene minimized possible oncogenic side effects. Transplantation of the cells was effective in treating rats with acute liver failure. In an independent study, Rudolph *et al.* (p. 1253) suggest a different therapeutic strategy for prolonging the life of patients awaiting liver transplants. Mice with abnormally short telomeres (the DNA sequences at the end of chromosomes) are especially prone to develop liver cirrhosis when the liver is injured. The development of cirrhosis in these mice was prevented by the administration of a gene encoding an essential component of telomerase, the enzyme that makes telomeres.

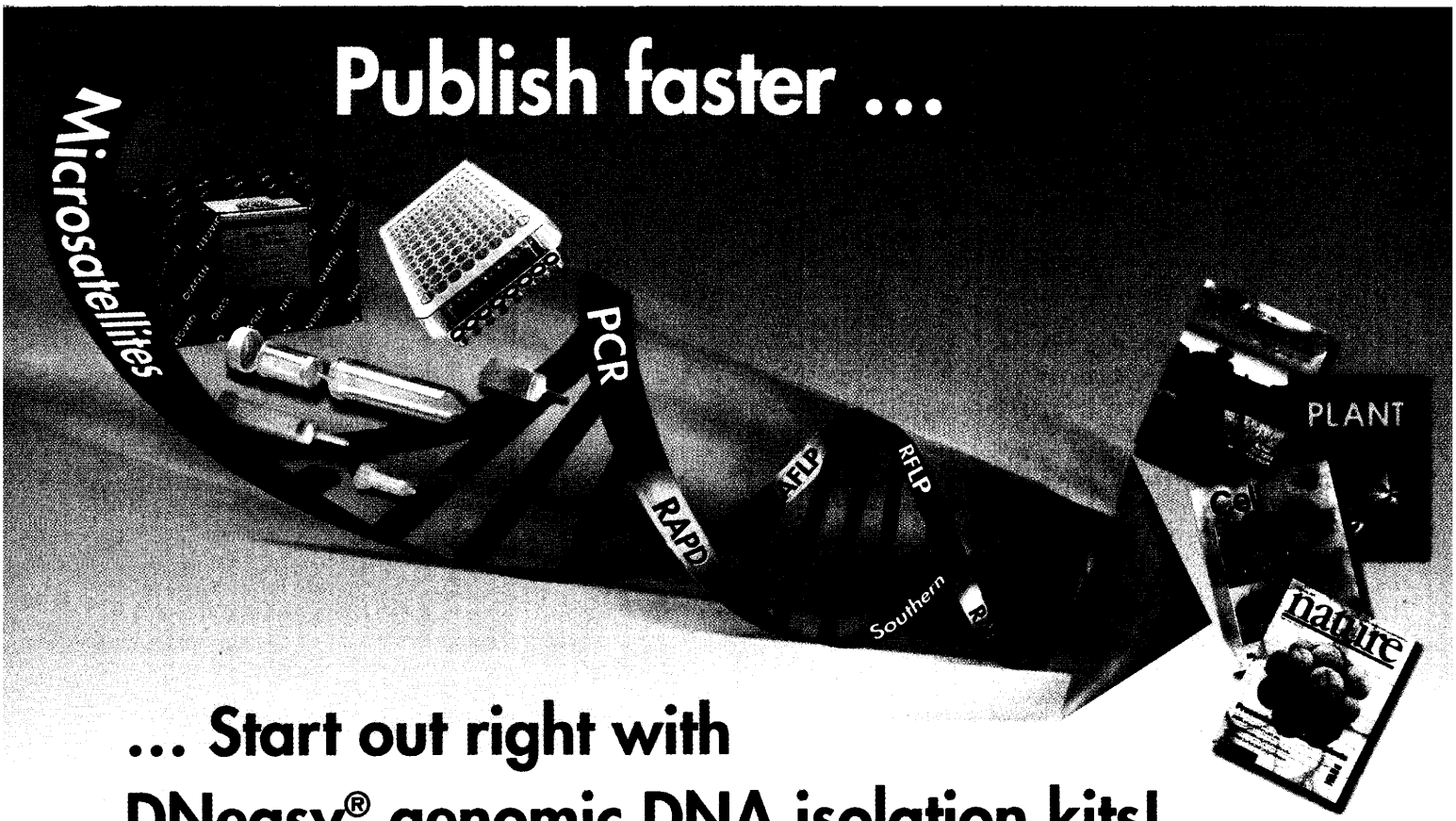
STEROID RECEPTORS HIT AND RUN

In the presence of hormone, steroid receptors modulate transcription by binding to specific response elements in chromatin and recruiting co-activators or co-repressors. McNally *et al.* (p. 1262) have observed the interaction of glucocorticoid receptor, labeled with green fluorescent protein, with response elements in living cells. With ligand continuously present, the receptor exchanges rapidly between chromatin and the nucleoplasmic compartment. This finding is inconsistent with the classic view that the receptor remains bound to chromatin as long as ligand is present. Instead, it supports the "hit and run" mechanism in which the receptor interacts transiently and recruits secondary factors to form a stable complex that modulates transcription.

IMAGES REMEMBERED

What differentiates the familiar image from the unfamiliar one? Henson *et al.* (p. 1269) have examined this age-old

CONTINUED ON PAGE 1167



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THIS WEEK IN *SCIENCE*

CONTINUED FROM PAGE 1165

question in psychology by using functional brain imaging to measure the amount of neuronal activity triggered by single presentations of stimuli. What they find is a complex interplay between the factors of repetition and familiarity; that is, the second viewing of an unfamiliar drawing portraying a possible object would generate an enhanced neural response that would reflect the process of creating an internal memory. If the drawing could not represent an object or if it recalled an already memorized object, however, the neural response would decline, as a simple manifestation of stimulus repetition.

A HOT SPOT FOR PROTEIN BINDING

Are there regions within proteins with characteristics that make them particularly well suited to interaction with other proteins? DeLano *et al.* (p. 1279) addressed this question by selecting peptides from a randomized library that would bind to the constant fragment (Fc) of immunoglobulin G. Although it should have been possible to isolate peptides that interacted with virtually any part of the Fc molecule, selection for interactions of high affinity yielded primarily a single peptide. In biological contexts, the Fc fragment binds four other proteins that all have very different structures. However, these proteins all bind to the same site on the Fc molecule, as did the peptide found during selection. The nature of this preferred binding site—its accessibility, hydrophobicity, and limited number of sites for polar interactions—helps define the essential properties of such interaction domains. Understanding these characteristics in more detail should be useful for predicting protein function or design of interacting ligands.

MITOCHONDRIA MAKE THE CUT

Mitochondria, the powerhouses of the cell, exist in multiple copies in eukaryotic cells. They possess their own genome that is essential both for their efficient functioning and for their propagation from generation to generation during cell division. However, the division process itself that produces daughter mitochondria is not well understood. Beech *et al.* (p. 1276; see the Perspective by Martin) discovered the existence of a protein encoded by a nuclear gene of an alga that is targeted to the mitochondria and is likely to play a role in mitochondrial division. The protein is related to a bacterial protein known to be involved in bacterial division, and thus this finding may provide a missing link in our knowledge of mitochondrial evolution.

DOUBLE TAKE

Mutations are generally thought to occur through substitutions of single nucleotides in DNA. Averof *et al.* (p. 1283) now document the occurrence of double-nucleotide substitutions in a wide range of organisms at a rate that is higher than would be expected by chance. These doublet substitutions may take place at different rates in different cell types and at different sites, with implications for models of molecular evolution and phylogenetic reconstruction as well as mutational mechanisms of human disease.

TECHNICAL COMMENT SUMMARIES

Peg3 and the Conflict Hypothesis

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/287/5456/1167a

In a mouse study, Li *et al.* (Reports, 9 Apr., p. 330) found that the paternally expressed imprinted gene *Peg3* regulates fetal growth and maternal behavior in offspring. That observation, Li *et al.* suggested, may be consistent with the parental-conflict hypothesis for genomic imprinting. Hurst *et al.* comment that the maternal-behavior connection may not fit with the conflict model. "[T]he paternally expressed *Peg3* affects the behavior of daughters, not of the current mate," note Hurst *et al.*, and genes transmitted to the daughter from either parent have the same chance of being transmitted to the daughter's offspring. Smits *et al.*, in a separate comment, concur: "The confusion may have arisen from the involvement of three generations, whereas the classical theory of parental conflict deals with two generations only."

Li *et al.* respond that *Peg3*'s effect on maternal behavior may indeed not fit easily into the conflict hypothesis, but that the effect of the imprinted gene on fetal growth in utero clearly does. Judging the evolutionary significance of imprinting for behavior, they conclude, will require additional experiments.

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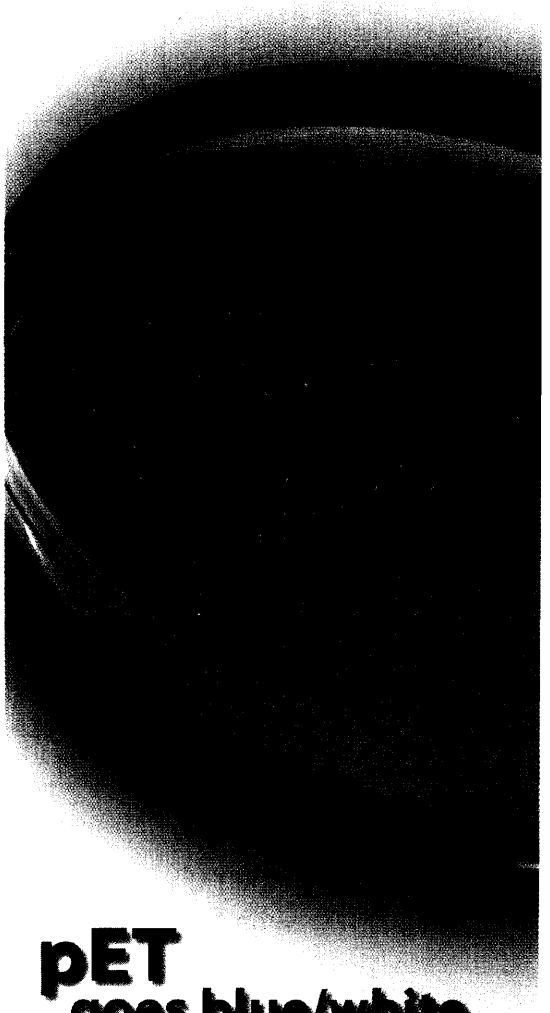

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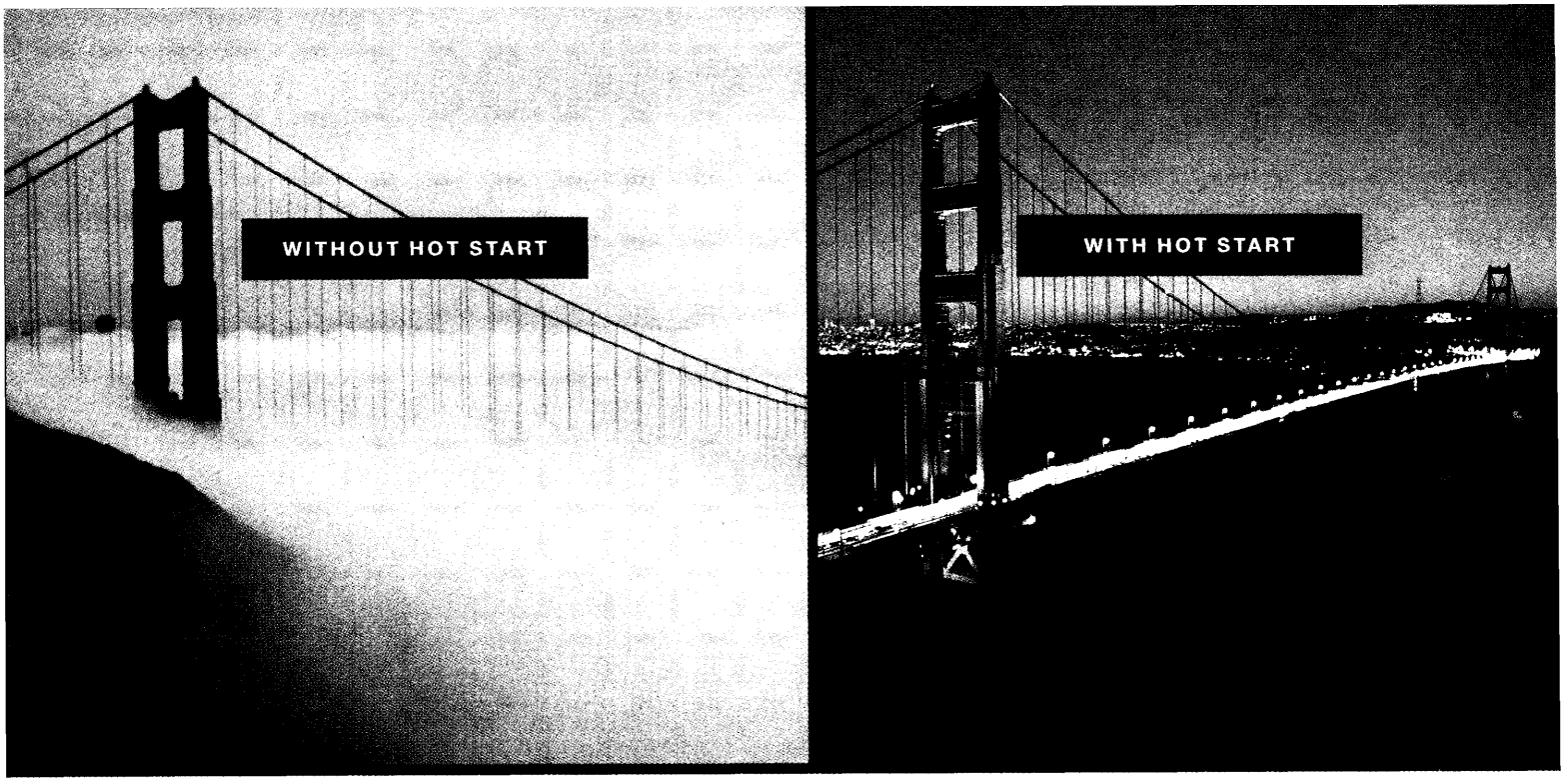

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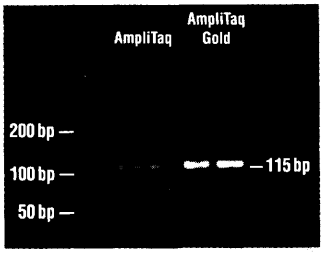

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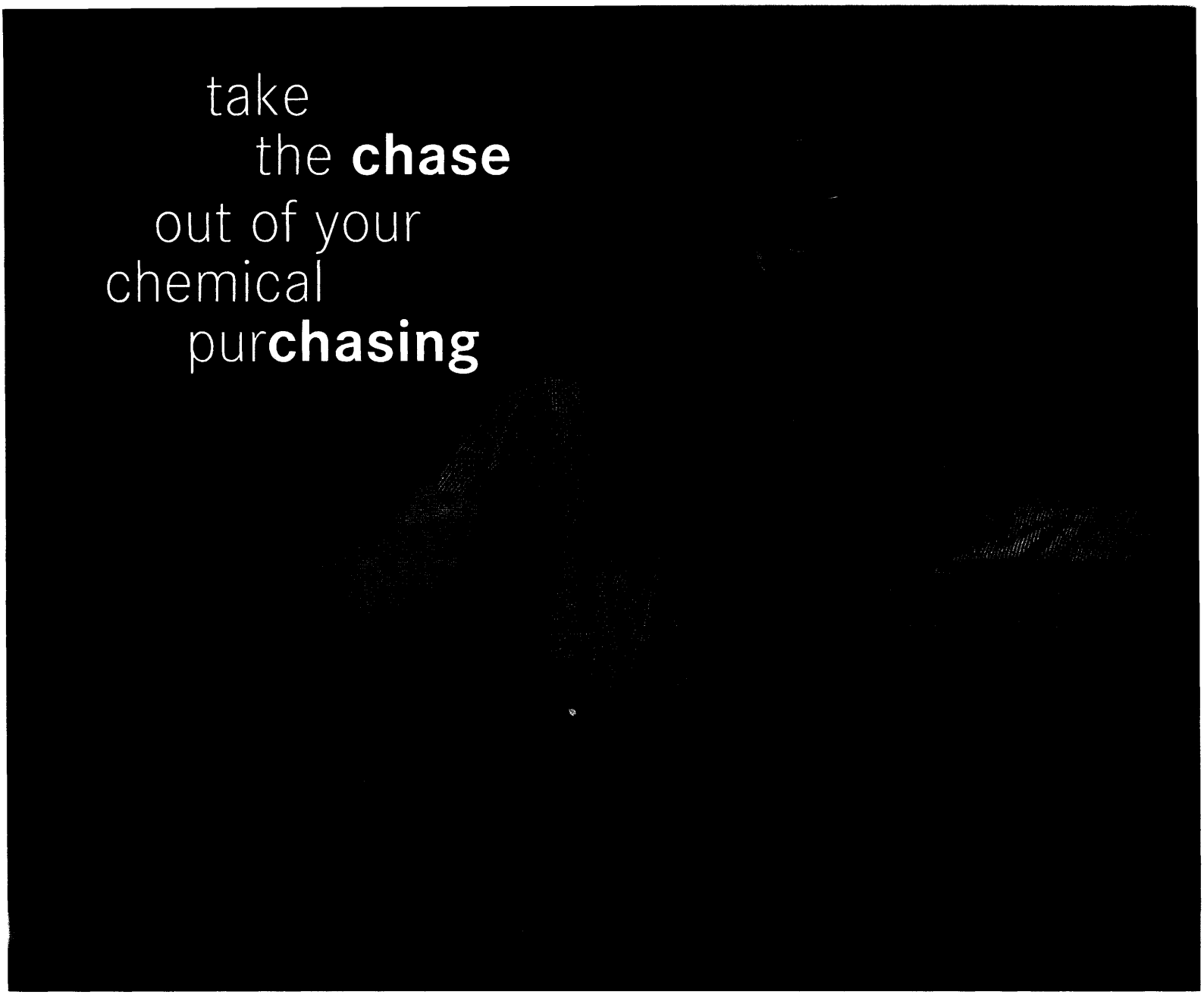

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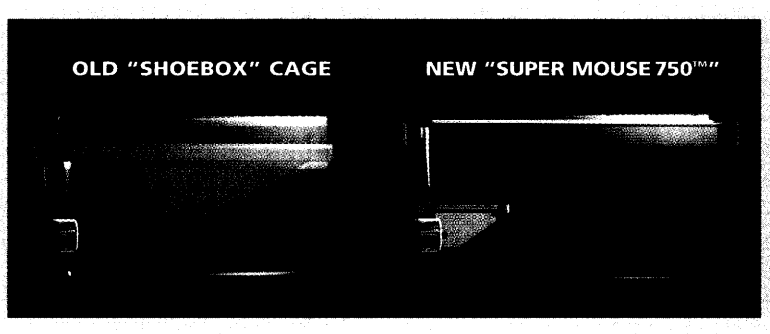

*Guide for the Care and Use of Laboratory Animals, Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, 1996.

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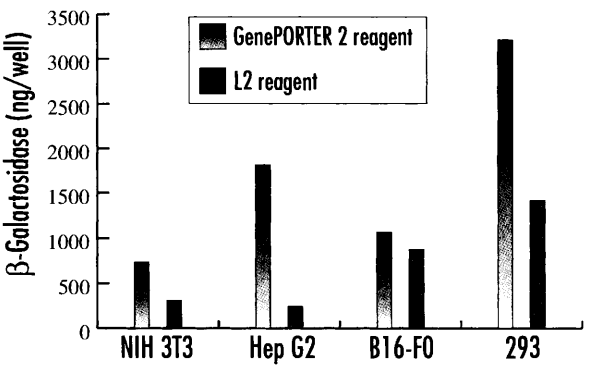

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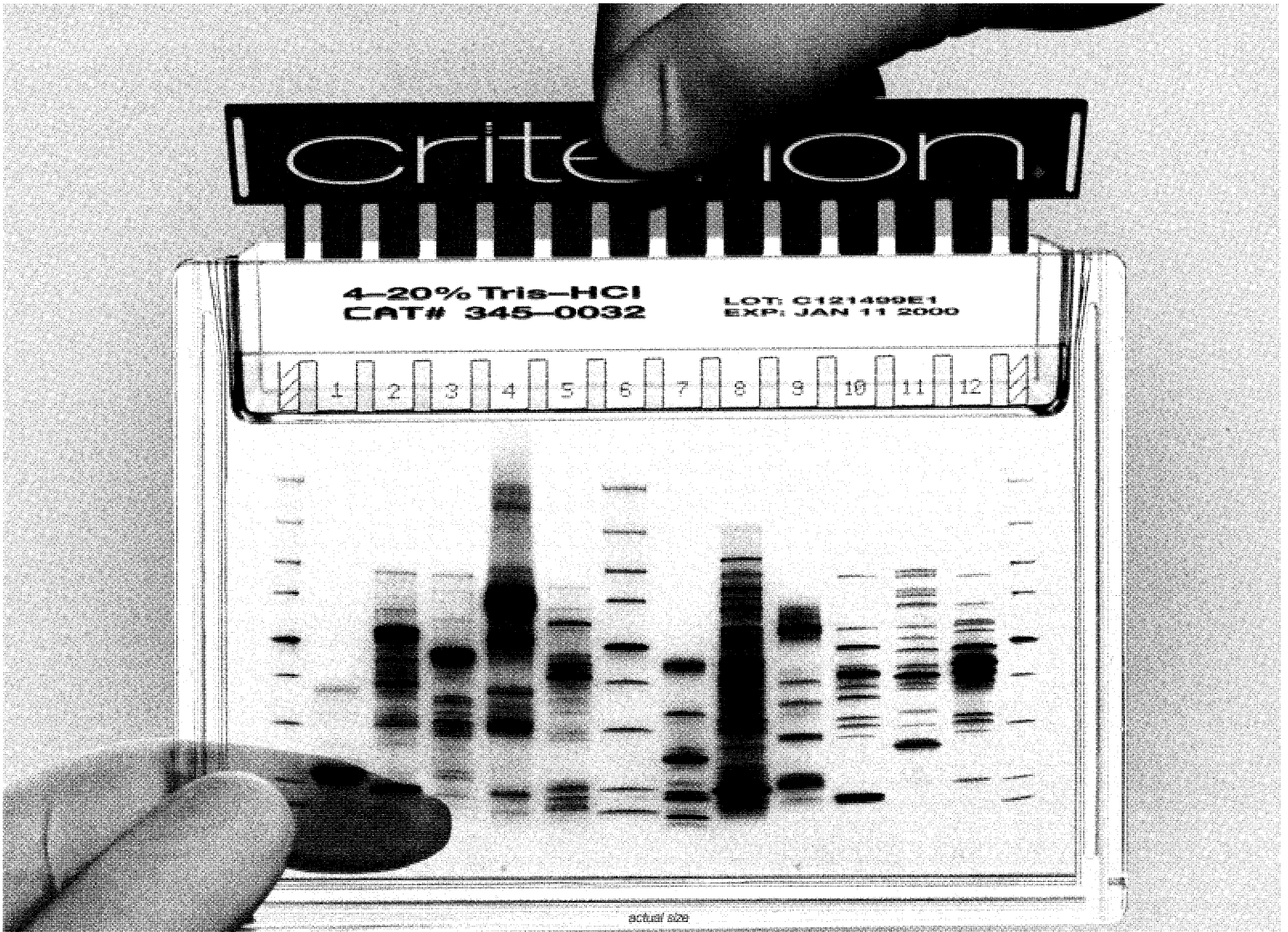

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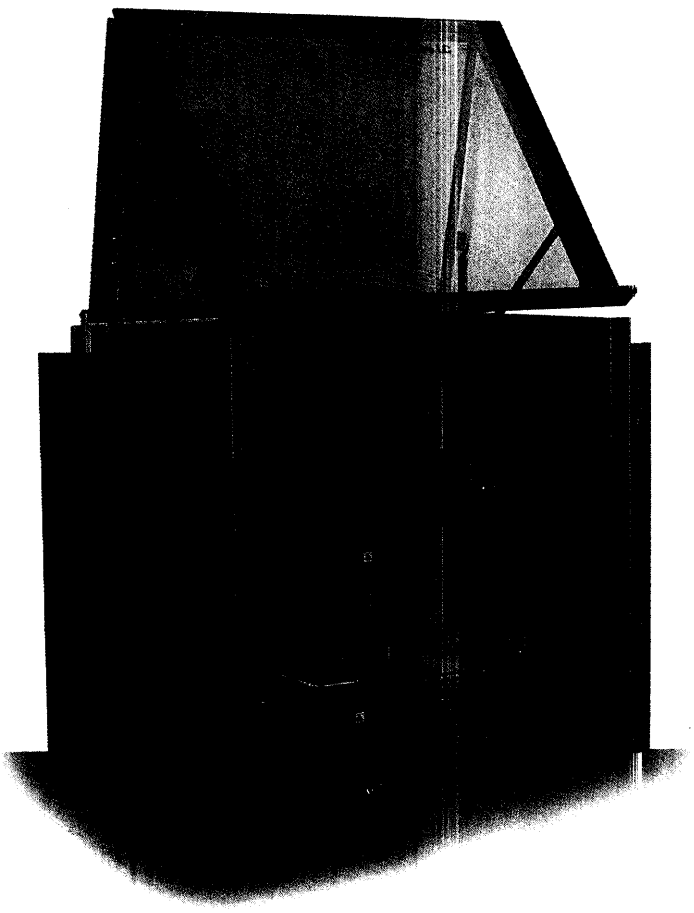

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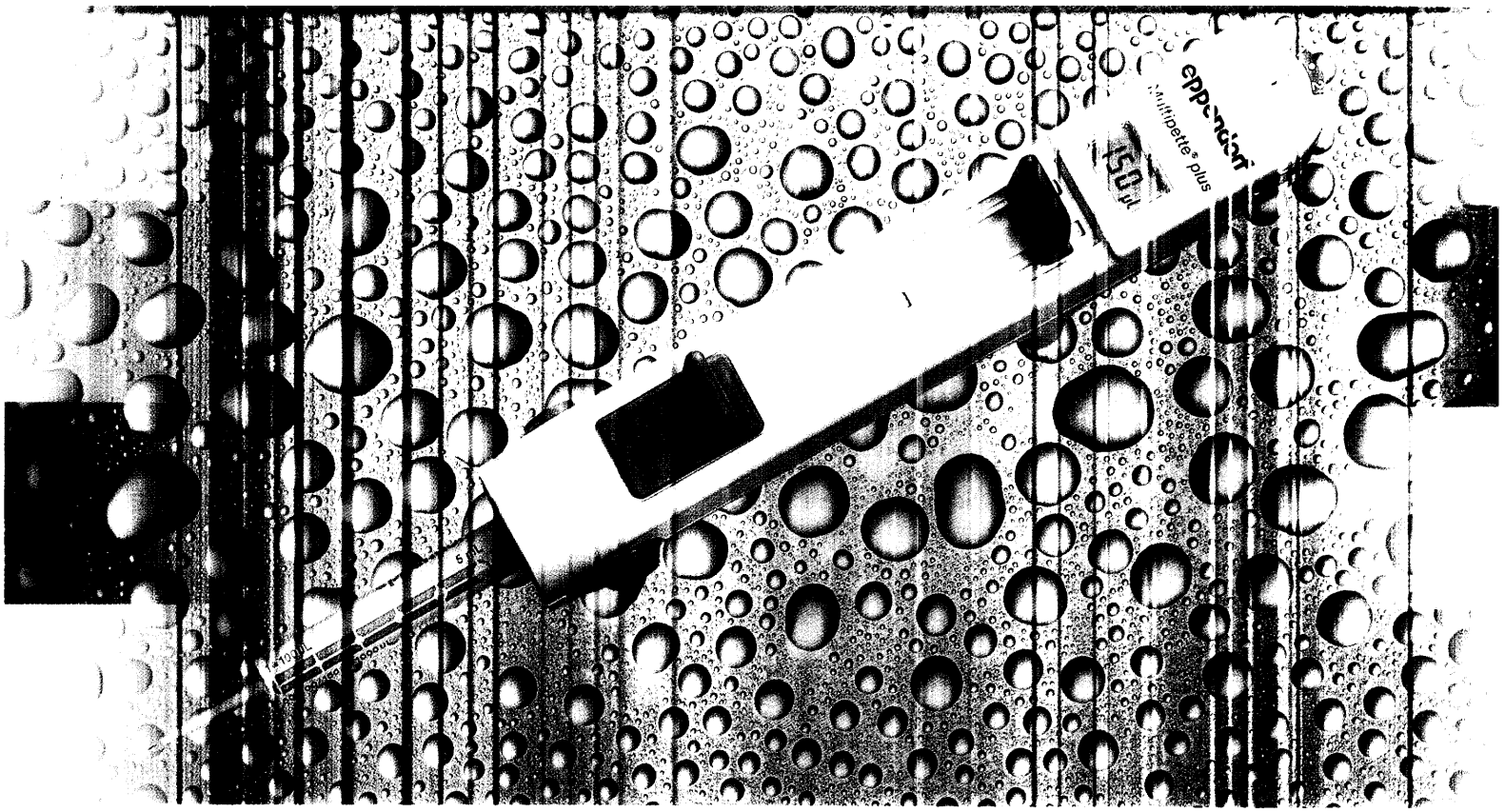

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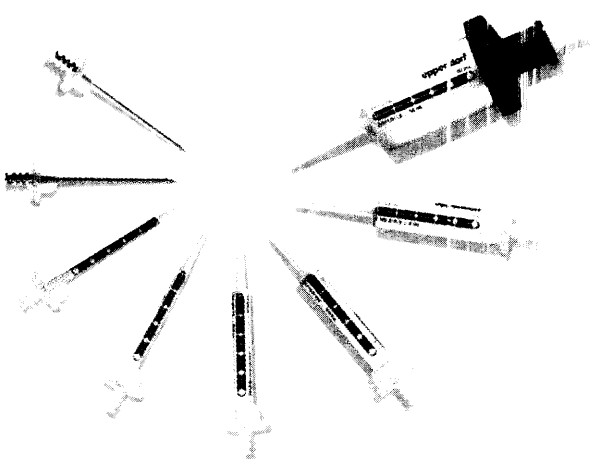

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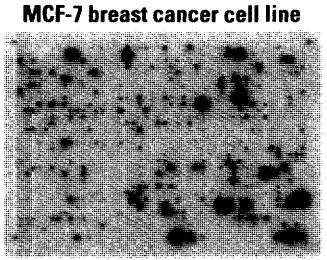

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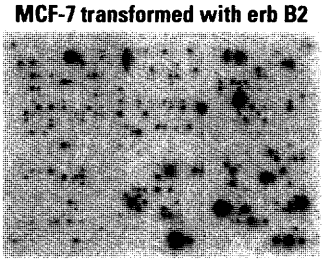

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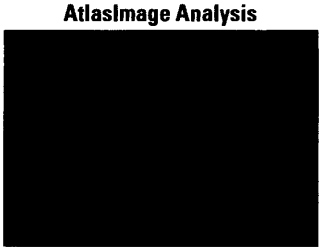

AtlasImage 1.0 was used to compare hybridization patterns obtained with the Atlas Human Cancer 1.2 Array. Red indicates up regulation greater than 2-fold and blue indicates down regulation greater than 2-fold.

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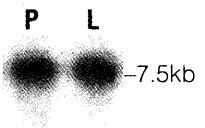

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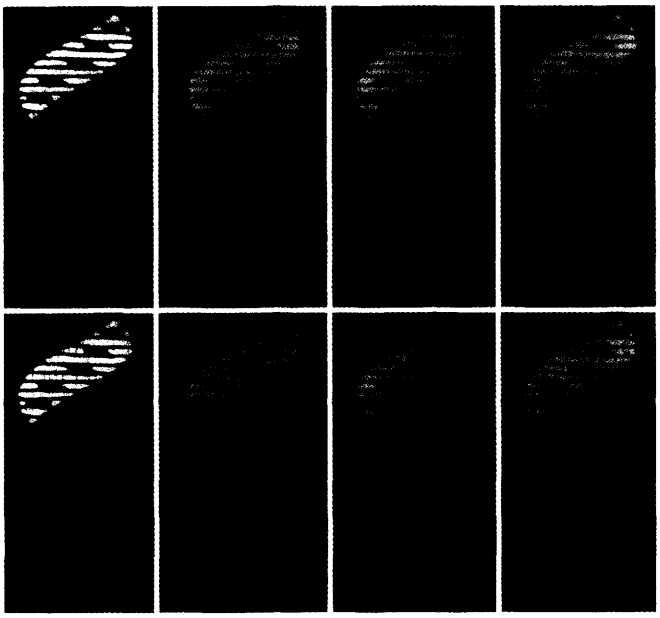

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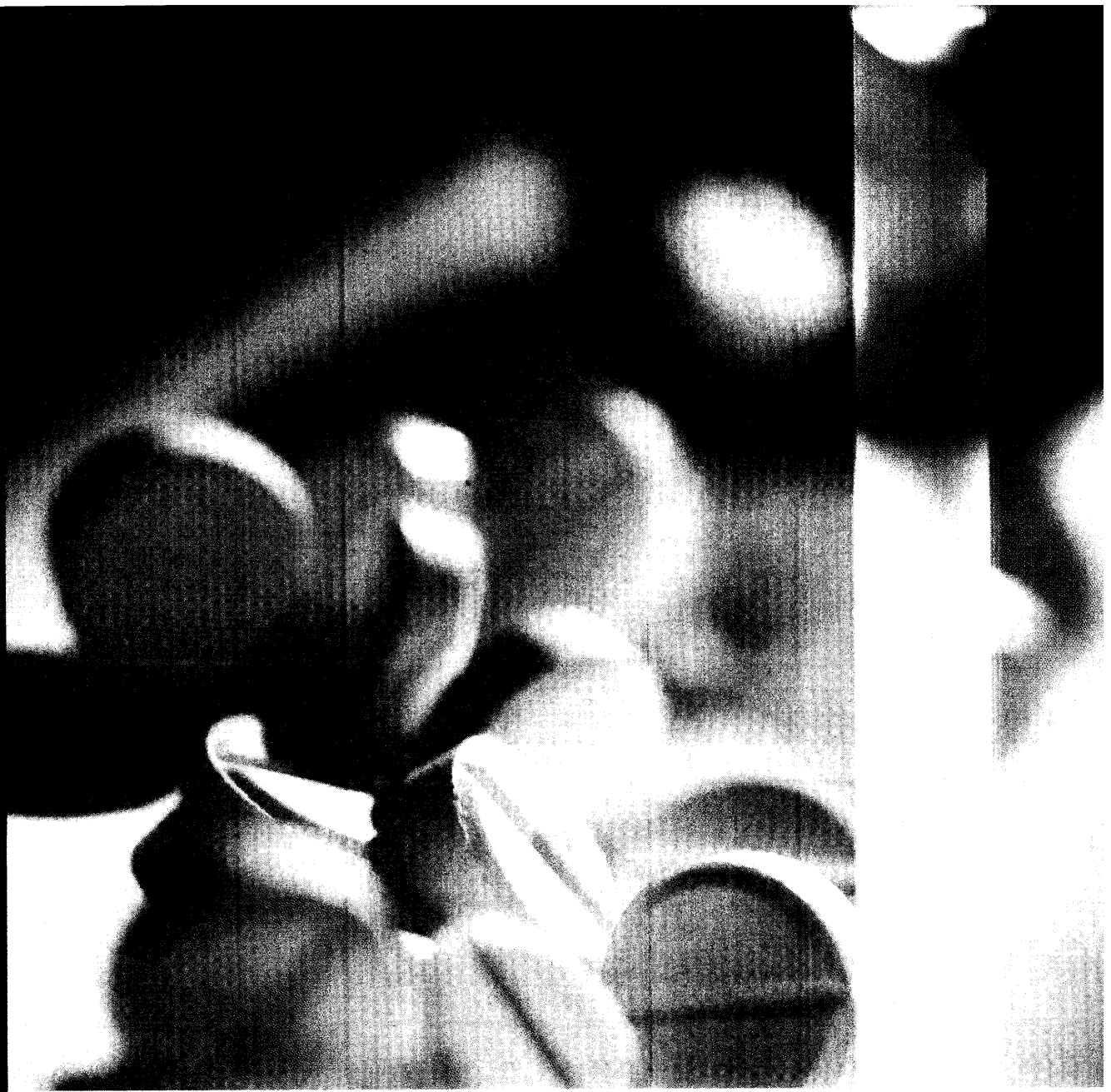

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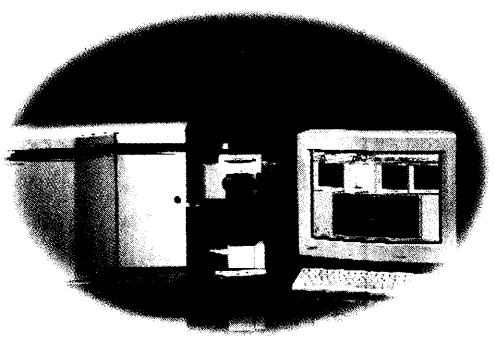

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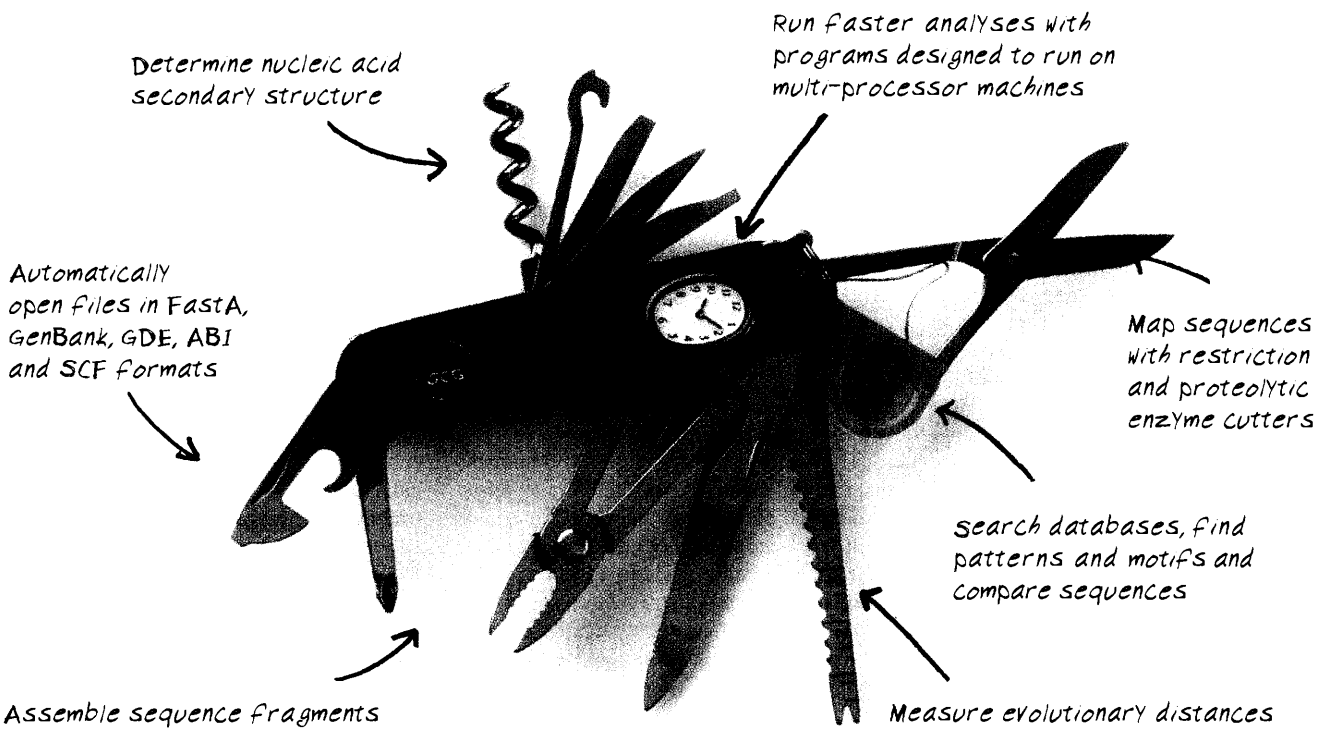

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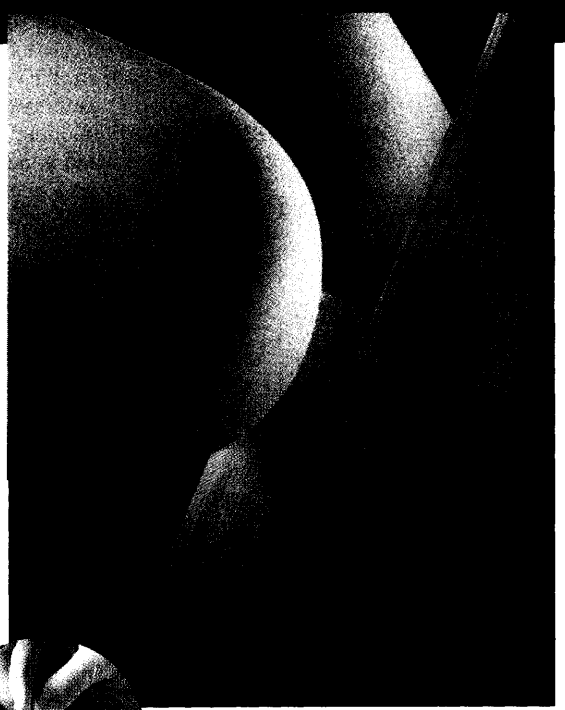

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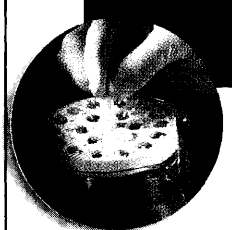

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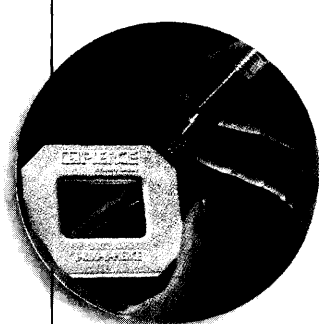

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