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**Women's
Health
Research**

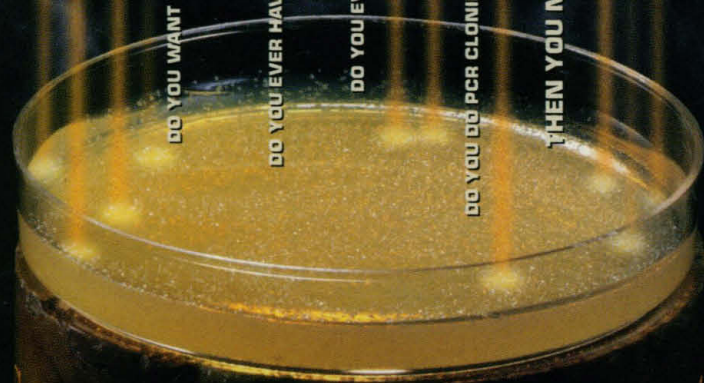


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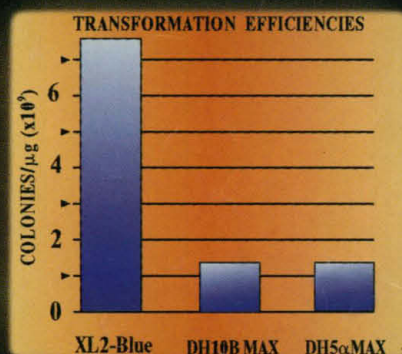
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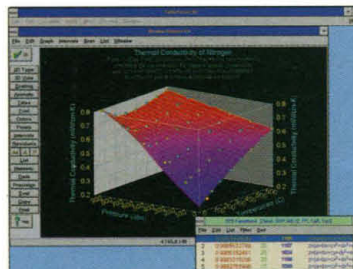
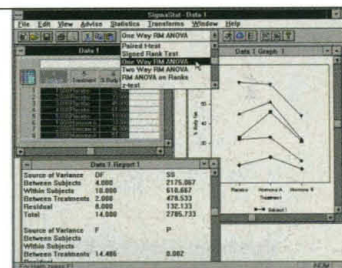
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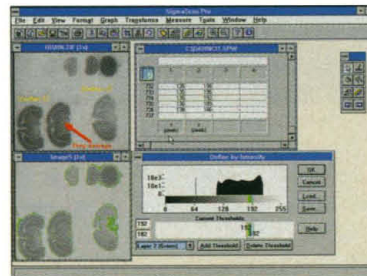
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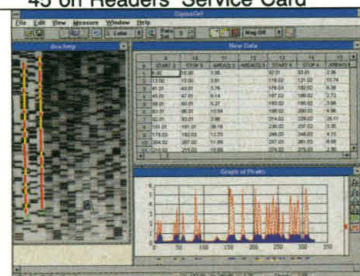
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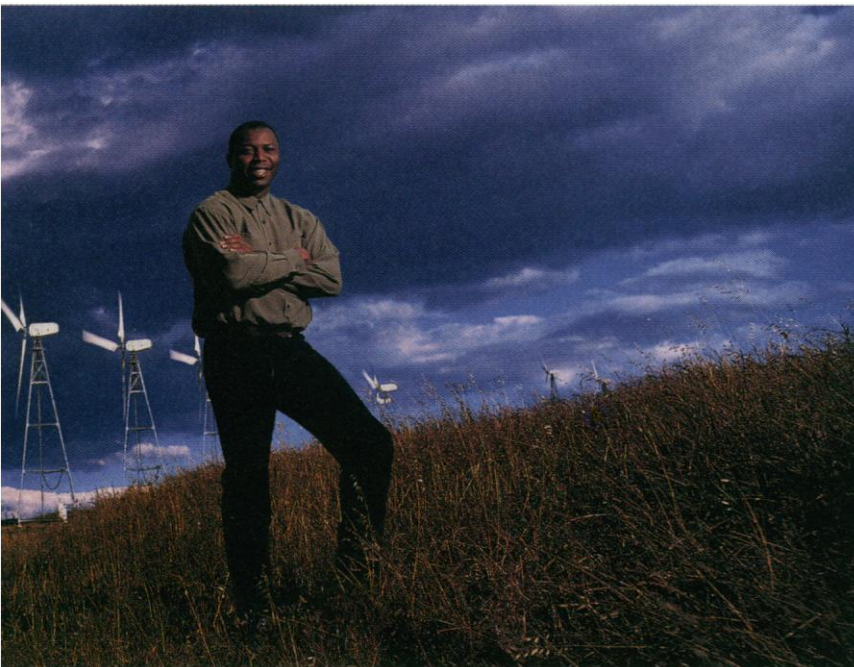
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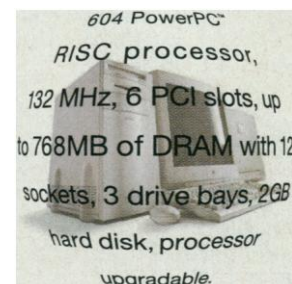
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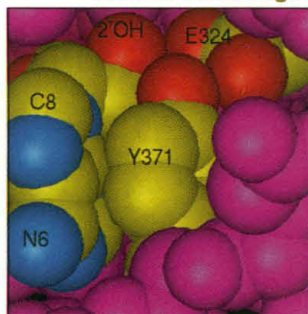


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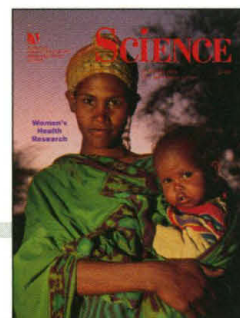
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This Somali mother and child are emblematic of one of the major policy questions dealt with in this issue's special section (beginning on page 765) on women's health research: In developing countries, how much money should be allocated for infant health and how

much for the prevention of maternal mortality? Elsewhere, the section addresses the subtle gender-based differences in patterns of disease and responses to therapy in developed nations. [Photo: Peter Menzel]



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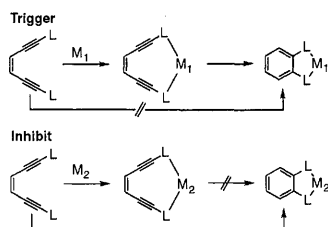
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Suddenly cyclic

Enediyne molecules, in which a carbon-carbon double bond bridges two triple bonds, can cyclize to form an aromatic species with two unpaired electrons; such diradicals can cleave DNA and can be effective antitumor agents. Warner *et al.* (p. 814) have found that when the ligand (L) is diphenylphosphine,



platinum or palladium ions can be used to accelerate this Bergman cyclization reaction and mercuric ions can be used to inhibit it. Such control may find application in targeting the action of such drugs.

Basalt beginnings

Two isotopic systems are becoming increasingly useful as tracers of the origin and evolution of mantle plumes, the presumed progenitor of Earth's voluminous flood basalt provinces. Whether plumes originate from deep in the lower mantle is unresolved. Basu *et al.* (p. 822) report that olivine crystals in the Siberian flood basalts, which is the largest flood basalt province and formed 253 million years ago, contain high ratios of helium-3 to helium-4, thought to be indicative of derivation from undegassed mantle. Walker *et al.* (p. 819) propose that the rhenium-osmium isotopic system in basalts might provide a tracer for the involvement of Earth's core in plumes, in that rhenium, in particular, and osmium are enriched in Earth's core relative to the

Settling Spain in the early Pleistocene

When did humans first migrate into western Europe? Fossils had been found that dated to about 500,000 years ago, much younger than fossils in neighboring regions. Now Carbonell *et al.* (p. 826) describe hominids and associated lithic technology from a deep layer of the Gran Dolina cave site in north-central Spain that on the basis of the paleomagnetic stratigraphy, as described by Parés and Pérez-González (p. 830), are greater than 780,000 years old, the age of the most recent field reversal (see the related news story by Gutin, p. 754).

mantle so that even small additions of core material to plumes could be detected.

Protein folding and chaperonin asymmetry

In two related papers in this issue Engel *et al.* (p. 832) and Hayer-Hartl *et al.* (p. 836) have examined what form the chaperonin protein complexes that act in protein folding have when they are in the process of performing their function. Two complexes have been identified made of multiple chaperonin subunits, one of which forms a bullet-like shape and one of which looks more like a football in the electron microscope. Only the bullet-shaped, asymmetric complex is capable of participating in productive, energy-dependent protein folding reactions. The data together provide the basis for a detailed model of the chaperonin reaction cycle.

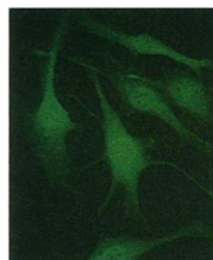
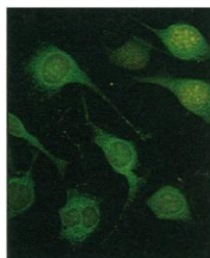
Given the Nod

Development of root nodules in leguminous plants is stimulated by nodulation (Nod) factors produced by symbiotic bacteria. By application of synthetic Nod factors to cells of a nonleguminous plant, Röhrig *et al.* (p. 841) show that the developmental pathway normally triggered

by the bacteria shares at least some steps of its signal transduction mechanism with pathways in the nonleguminous plant regulated by endogenous plant growth factors. Analysis of a range of synthetic Nod factors indicated that the fatty acyl substituent was more effective in trans than in cis orientation.

Sodium regulation and cystic fibrosis

Airway epithelial cells from patients with cystic fibrosis (CF) fail to secrete Cl^- because of a



defect in the cystic fibrosis transmembrane regulator (CFTR). Cells from patients with CF also have an abnormally high rate of Na^+ absorption, and this also contributes to the inadequate hydration of airway secretions

associated with CF. Stutts *et al.* (p. 847; see the Perspective by Al-Awqati, p. 805) provide evidence that this alteration in Na^+ channel function is also a result of modification of the CFTR. Their data show that the CFTR functions decrease the permeability of epithelial Na^+ channels. Thus the CFTR appears to be a critical regulator of ion transport serving both as a Cl^- channel itself and as a regulator of Na^+ channels.

Sound delivery

Drug delivery directly through the skin has several advantages over oral delivery, including avoidance of the effects of gastrointestinal metabolism, but the low permeability of skin to most compounds limits this approach. Mitragotri *et al.* (p. 850) found that the use of low-frequency ultrasound increased the permeability of human skin to many compounds, including proteins such as insulin and interferon γ , by several orders of magnitude, thus offering a potential alternative to injections.

Feature presentation

Processing in the visual system decomposes stimuli into features such as shape, color, or spatial location. How then are these features recombined to form a unified percept? Although neuronal mechanisms that would serve to bind together the cortical representations of these features have been proposed, biological evidence for these mechanisms has been scarce. Friedman-Hill *et al.* (p. 853) describe the analysis of a human patient who exhibits severe deficits in feature binding as a result of bilateral parietal-occipital lesions.

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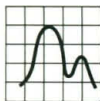
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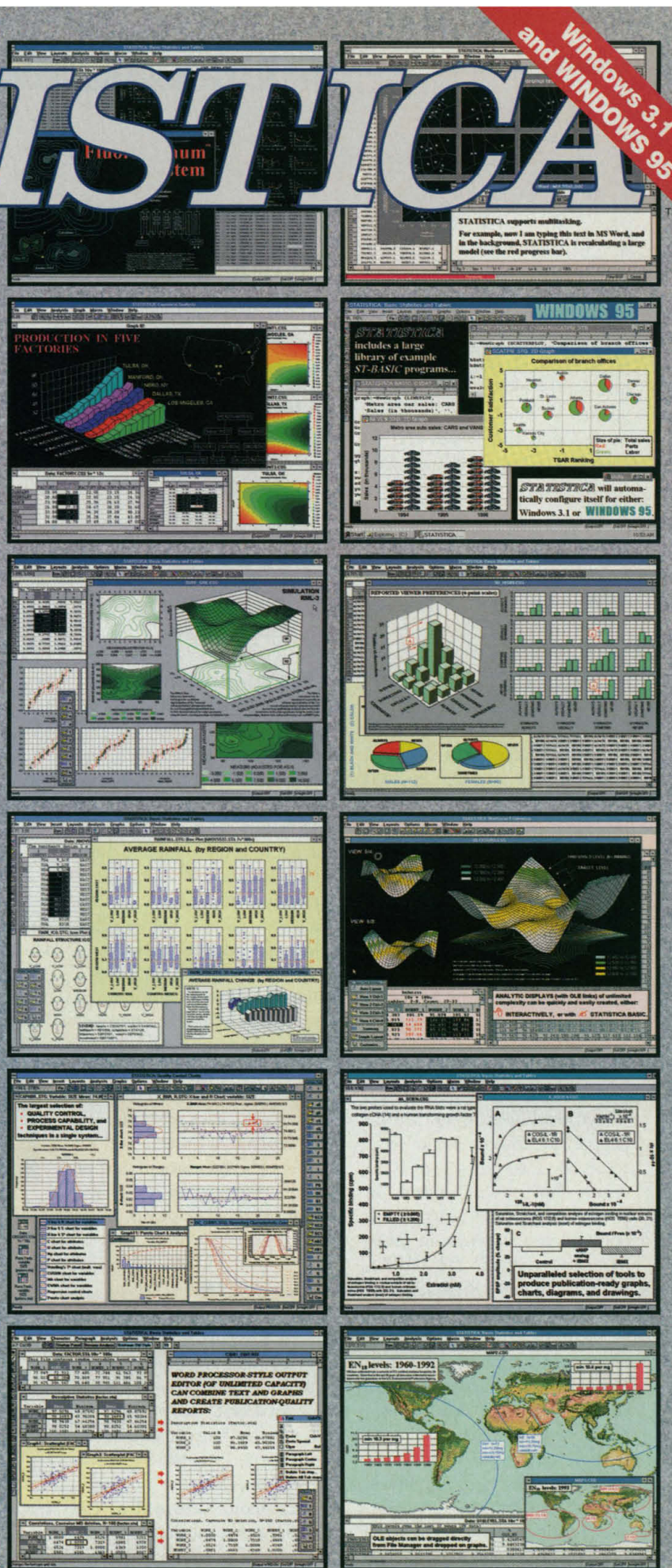
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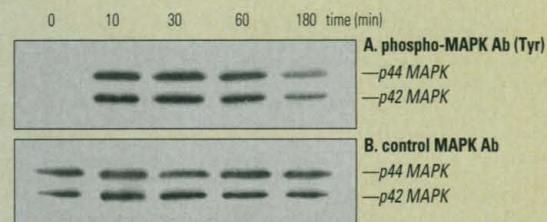
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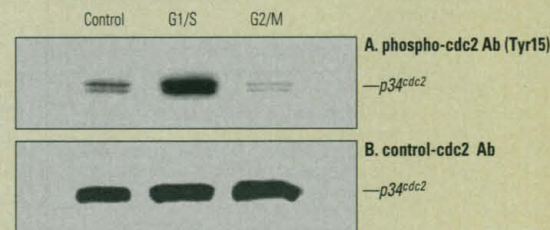
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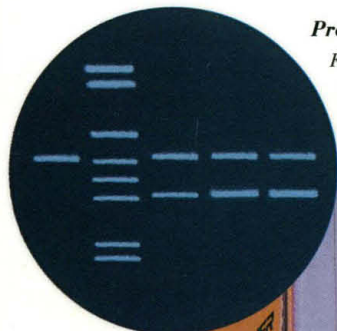
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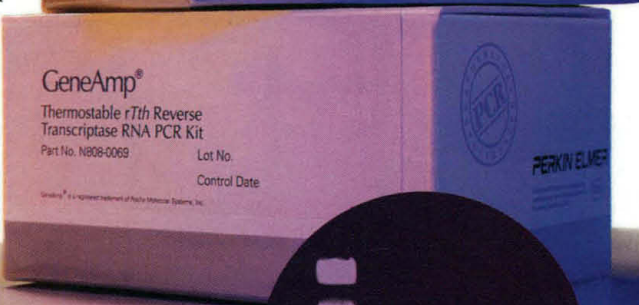
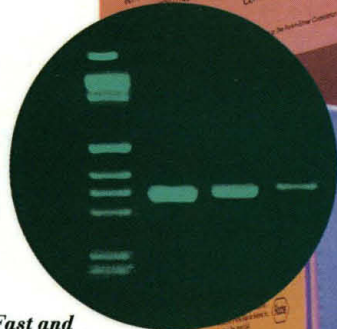
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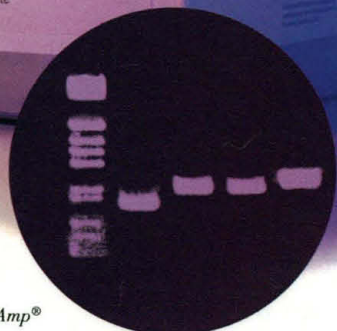
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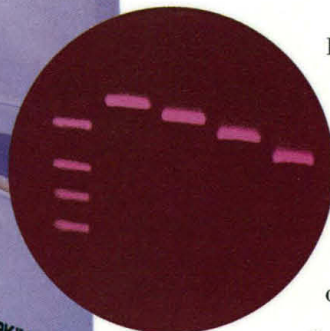
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References

1. Fodde, R., and Loosekoot, M., *Human Mutation*, 3, 83, (1994).
2. Fischer, S.G. and Lerman, L.S., *Proc. Natl. Acad. Sci., U.S.A.*, 80, 1579 (1983).
3. Borresen, A. L., et al., *Proc. Natl. Acad. Sci., U.S.A.*, 88, 8405 (1991).

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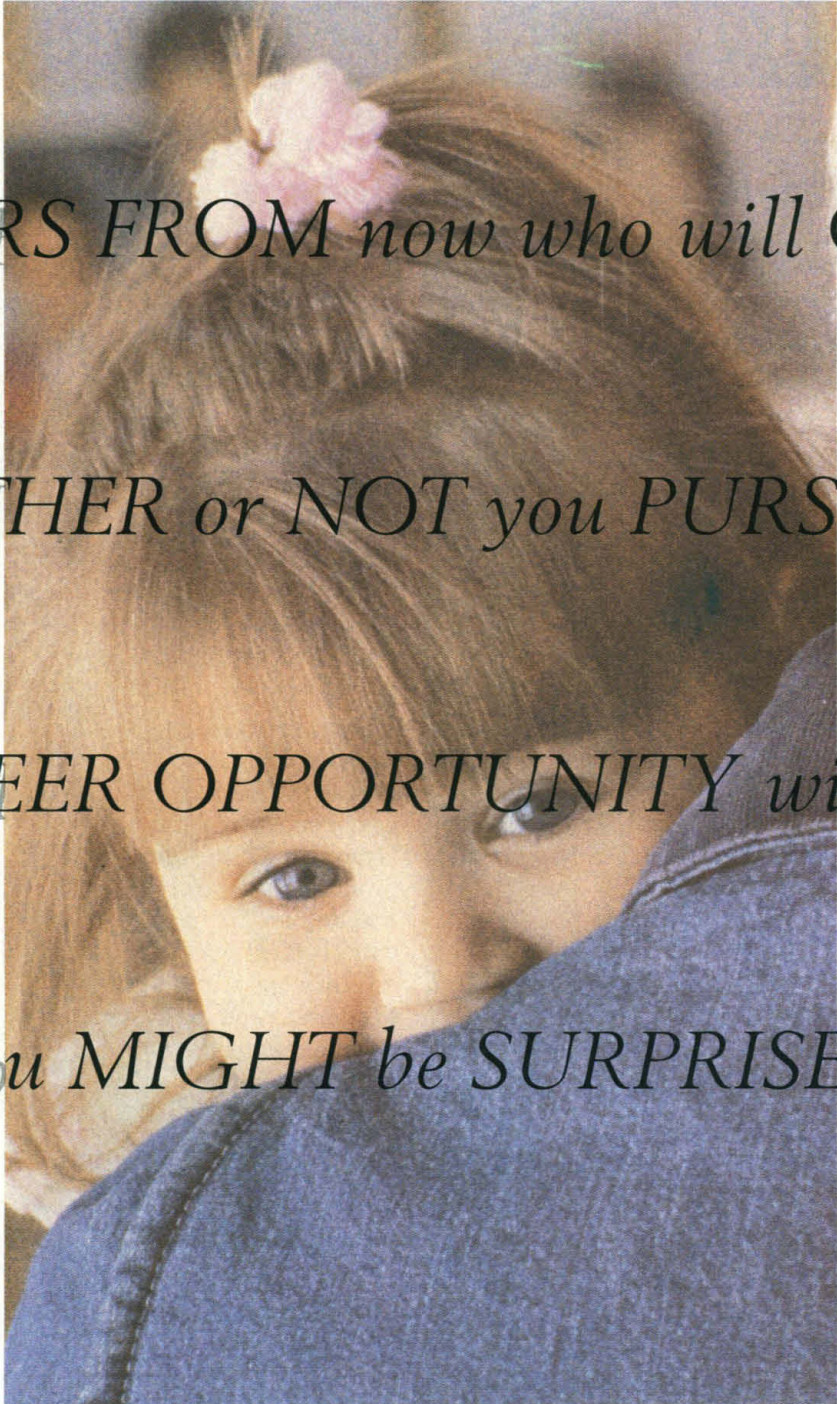
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WOMEN'S HEALTH CARE RESEARCH

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Department of Defense Research Programs for Women

Breast Cancer Research Program

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Congress has allocated \$150 million to execute the 1995 Department of Defense Breast Cancer Research Program (BCRP).

Congressionally mandated since 1992 and managed by the U.S. Army Medical Research and Materiel Command, the goals of the BCRP, derived from recommendations of the National Academy of Sciences' Institute of Medicine (IOM), emphasize the need for a broad-based research agenda encompassing all areas of prevention, detection, treatment, and quality of life research.

The 1995 appropriation of \$150 million supports efforts in three areas: \$115 million for a multi-disciplinary research program based on IOM recommendations, \$20 million to improve and verify the accuracy of breast imaging, and \$15 million to improve patient-centered care in three dedicated breast cancer centers.

Significant execution milestones for this year's program include:

1 Jun 1995 ► Release of Broad Agency
Announcement (BAA)
8 Sep 1995 ► Proposal Receipt - Training
13 Sep 1995 ► Proposal Receipt - Research
and Breast Imaging
15 Sep 1995 ► Proposal Receipt - Cancer
Centers
30 Sep 1996 ► Awards Completed

Defense Women's Health Research Program

The ultimate goal...to minimize the health risks unique to women's service in the Armed Forces by fully integrating gender-specific concerns.

Congress allocated \$40 million for 1995 to support a coordinated medical research effort within DoD on women's health issues.

The DoD's Defense Women's Health Research Program (DWHRP) focuses research on gender-specific issues to enhance U.S. Armed Forces readiness, operational effectiveness, and sustainability.

The program strategy, as developed with guidance from the IOM, will focus on four broad research areas: factors affecting the health and work performance of military women, psychological issues impacting on military women, health promotion and disease prevention, and access to and delivery of health care. The research agenda will also include epidemiologic research on military-specific operational hazards pertaining to women, and data- and knowledge-base development.

Execution milestones for the 1995 program include:

31 Jul 1995 ► Publication of IOM
Recommendations
3 Aug 1995 ► Release of BAA - Intramural
15 Sep 1995 ► Release of BAA - Extramural
2 Oct 1995 ► Proposal Receipt -
Intramural
15 Nov 1995 ► Proposal Receipt -
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20 Nov 1995 ► Awards - Intramural
30 Sep 1996 ► Awards - Extramural



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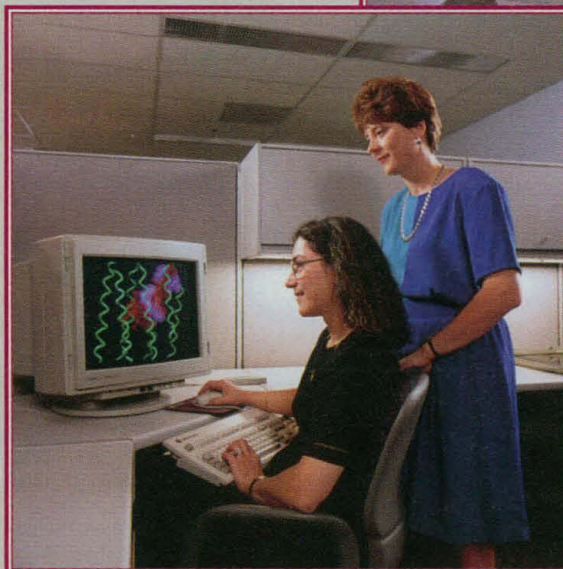
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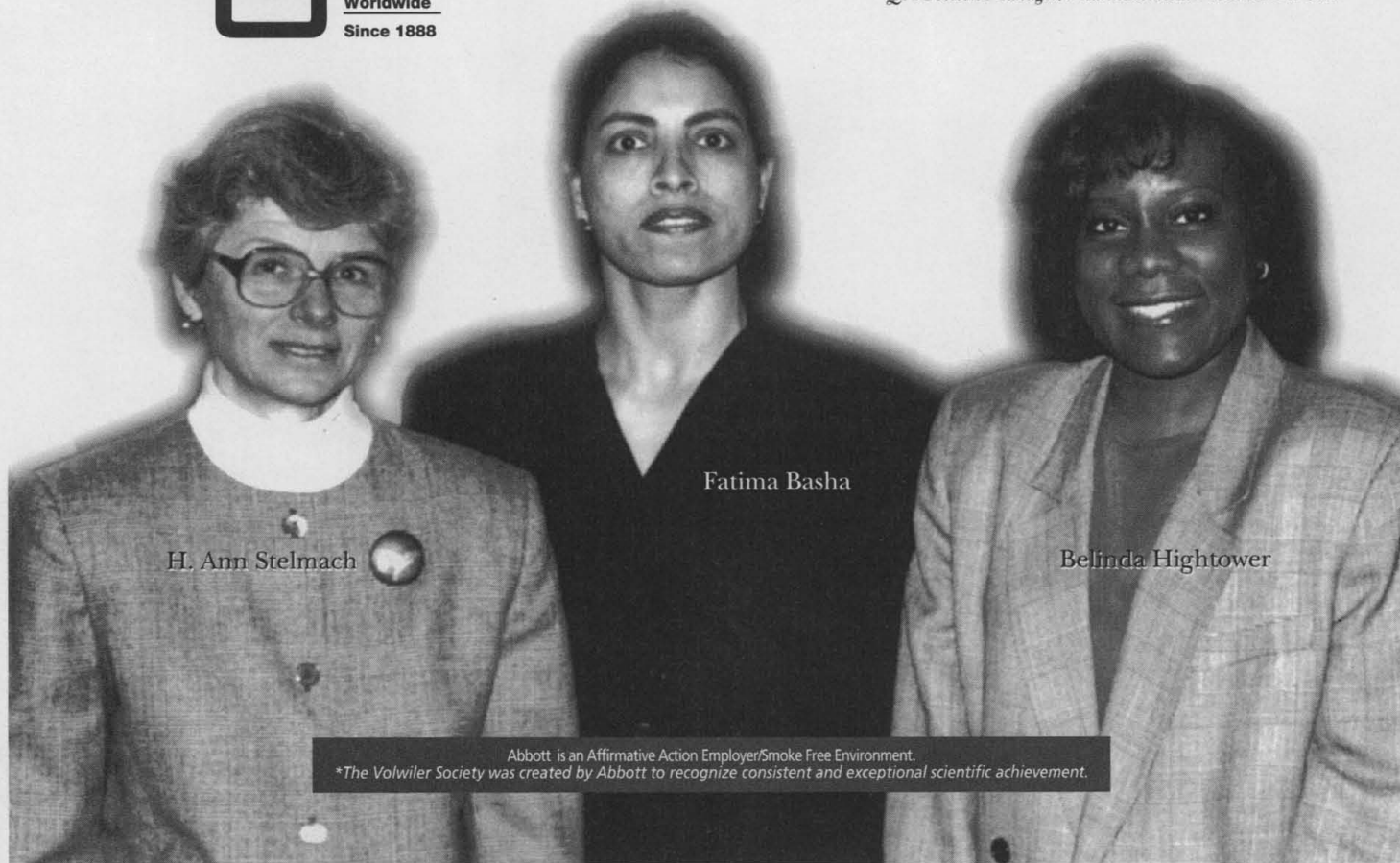
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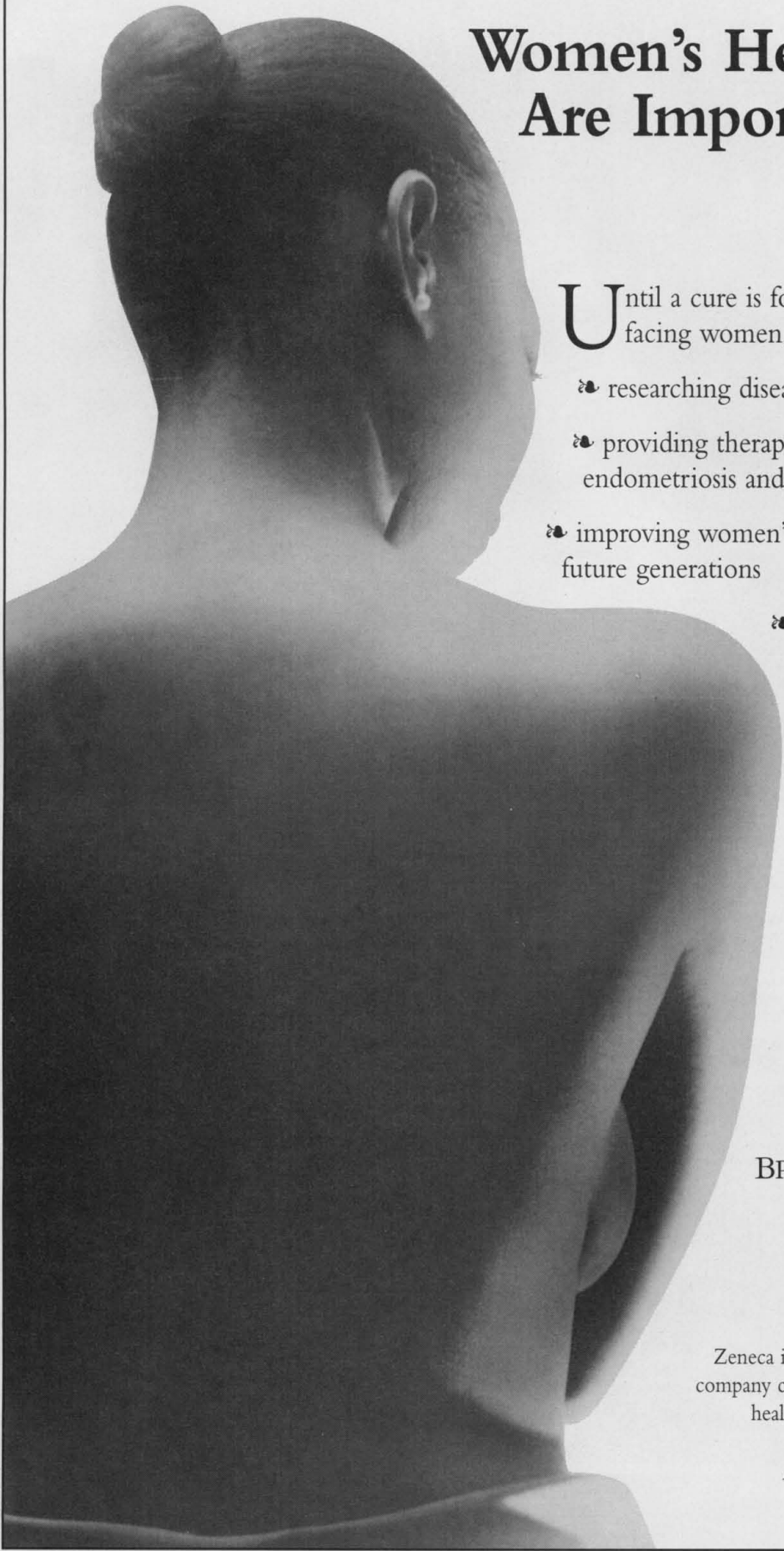


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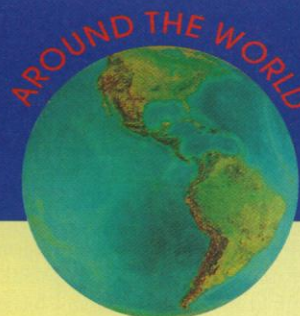
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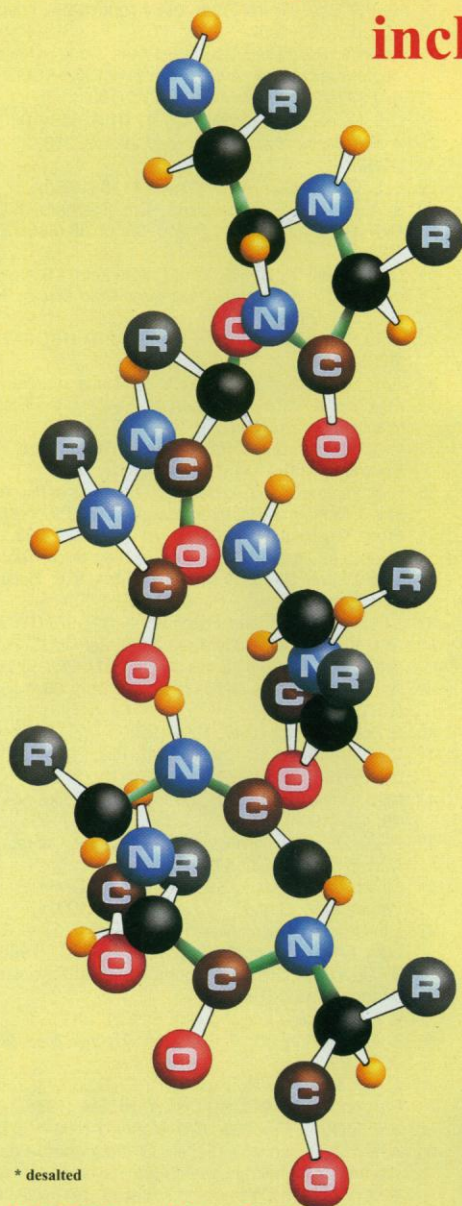
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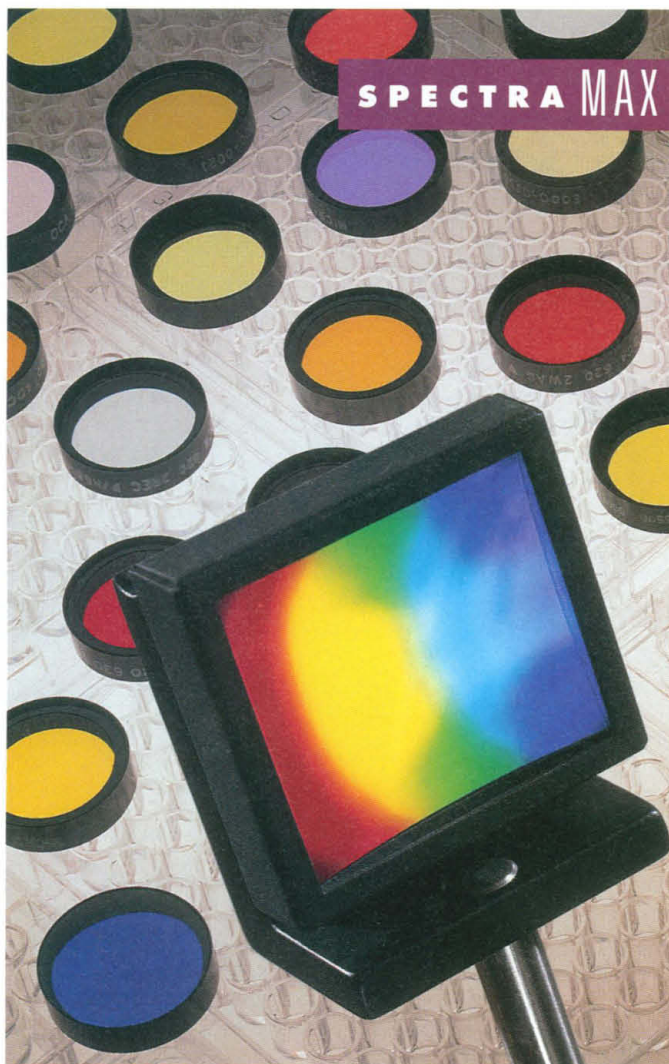
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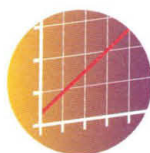
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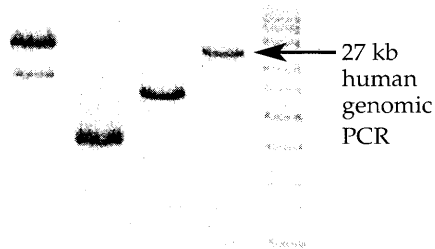
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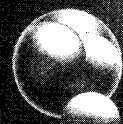
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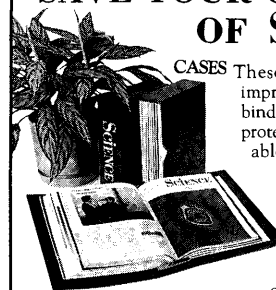
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