AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Bush & Clinton on Science

SCIENCE

16 OCTOBER 1992 $6.00
VOL. 258 • PAGES 369–516

Take the Strain Out of Protein Expression

Take charge of protein expression! Take a break from the strain. Try TOPP cells.

It's Time for a Change of Host... To Stratagene's New TOPP™ Cells

- Produce hard-to-express proteins
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- Compatible with common expression vectors

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Different TOPP strains benefit different proteins. For example, TOPP 2 and TOPP 3 cells prove far superior to *E. coli* K-12 in producing the human Fab antibody protein (see figure). TOPP strains 2, 3, 5, and 6 enhance expression of tenascin, a human extracellular-matrix protein. Because all six TOPP strains are *E. coli*, commonly used expression vectors like the pBluescript® II phagemid and pUC can be transformed and propagated in these cells.

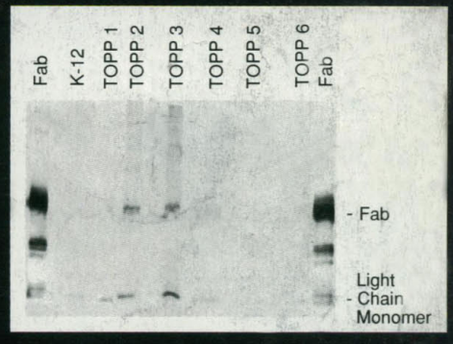

Figure:
Expression of Fab antibody protein in *E. coli* K-12 and TOPP™ Cells.

Call Stratagene Technical Services at 1-800-424-5444 to discuss how TOPP cells can help with your protein expression.

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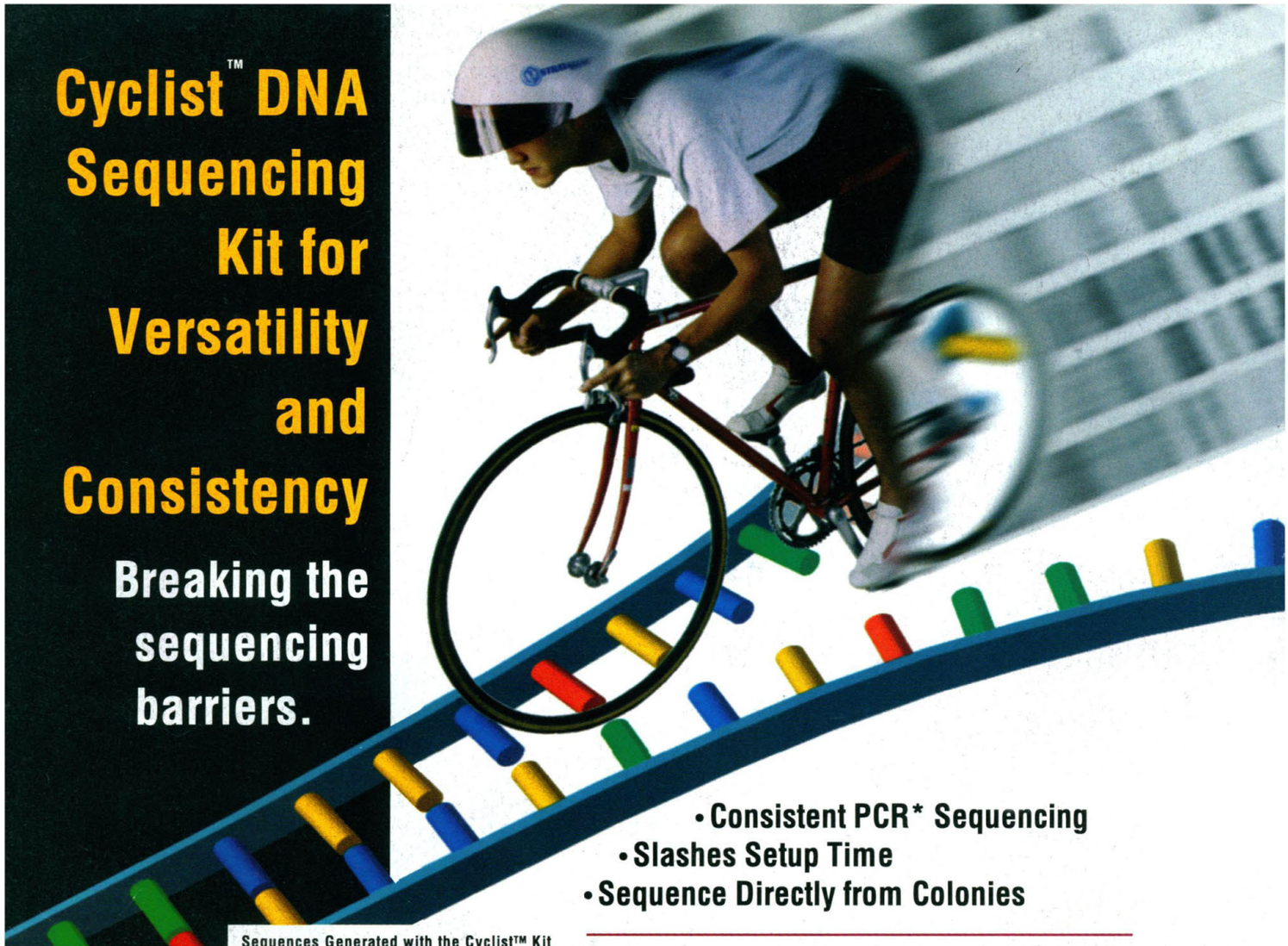
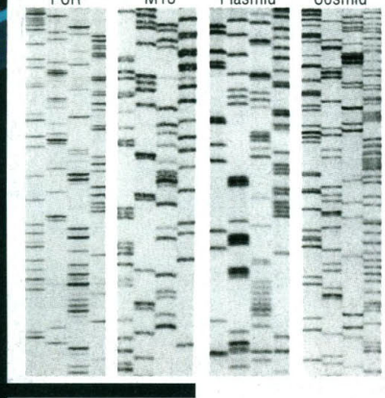


- **Consistent PCR* Sequencing**
- **Slashes Setup Time**
- **Sequence Directly from Colonies**

Sequences Generated with the Cyclist™ Kit



The basic reaction consisted of reaction mix (buffer and nucleotides), template, primer, ^{33}P-dATP radiolabeled nucleotide and *Taq* DNA polymerase aliquoted to the four termination tubes containing dideoxynucleotides. An initial denaturation at 95°C for 5 minutes was followed by 30 cycles at 95°C for 30 seconds, 55°C for 30 seconds and 72°C for 60 seconds in Stratagene's SCS-2 Temperature Cycler.

Now you can generate high quality sequence data directly from PCR products, bacterial colonies, cosmids and lambda plaques - rapidly and reliably - with Stratagene's new Cyclist™ DNA Sequencing Kit. Template preparation is minimal, so setup is remarkably fast.

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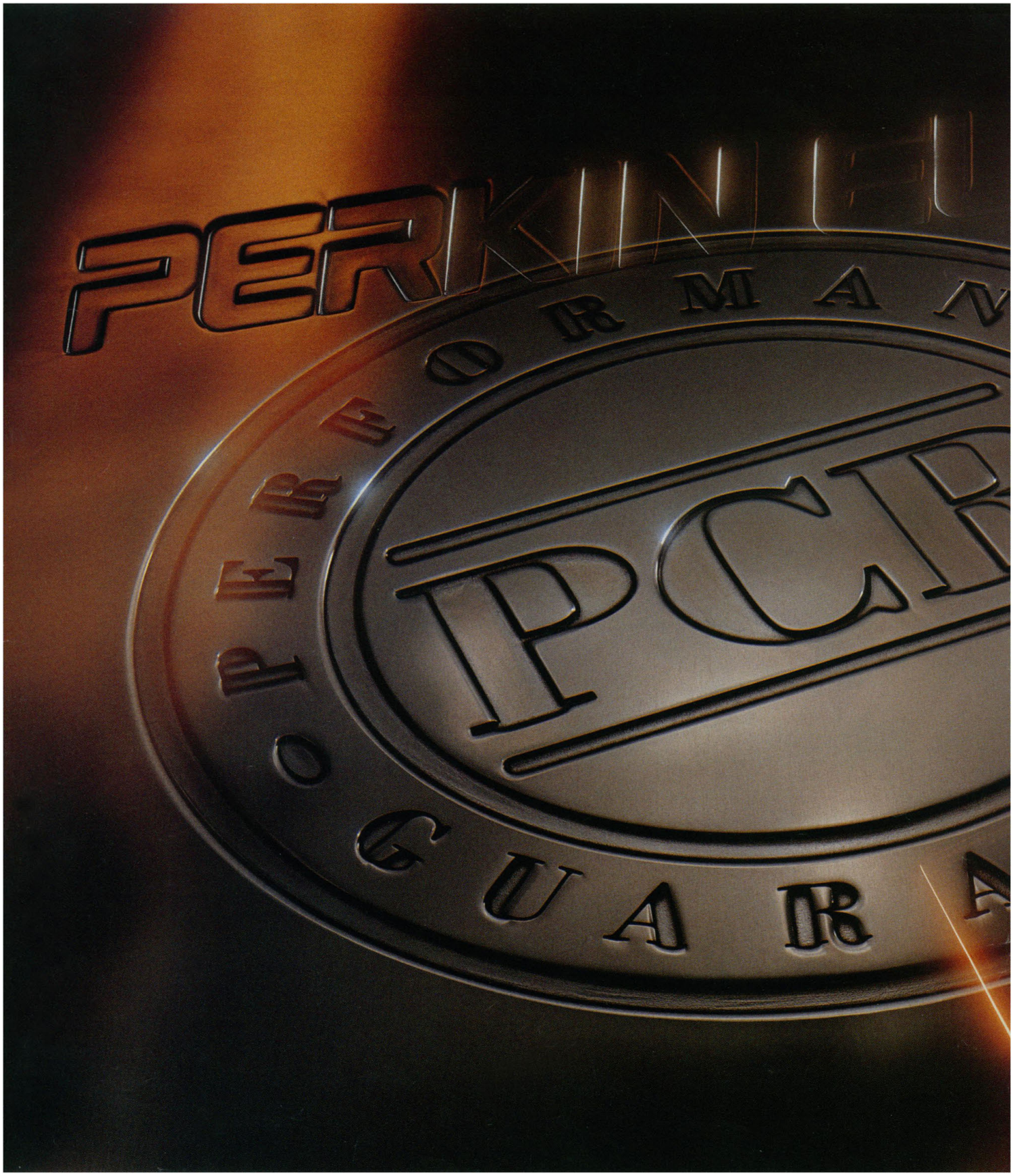
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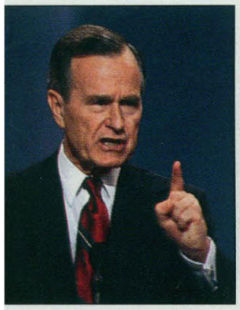

Bush and Clinton address *Science* questions **384**

398, 457 & 461

Aging flies and models of mortality

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NEWS & COMMENT

RESEARCH NEWS

PERSPECTIVE

ARTICLES

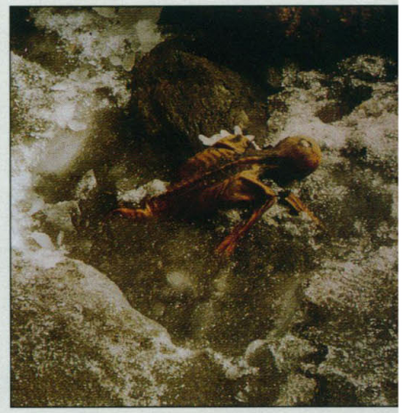
RESEARCH ARTICLES

DEPARTMENTS

COVER

Representation of the entropy distribution in a nascent neutron star about 20 milliseconds after the collapsing core of its parent star stiffens and bounces. The shocked region experiences hydrodynamic instabilities that violate spherical symmetry and that may be central to the eventual understanding of supernovae and pulsars. See page 430. The entropy values span the spectrum from purple through blue and red, with the highest values represented by red; the black core shows the inner dense stable region. [Image: Adam Burrows and Bruce A. Fryxell]

REPORTS



455 Frozen in time

◩ Indicates accompanying feature

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Science is indexed in the *Reader's Guide to Periodical Literature* and in several specialized indexes.

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For information Circle #17

For a demonstration Circle #18

edited by PHIL SZUROMI

Macroscopic tunneling

Everyday experience suggests that some events are impossible, such as throwing a ball through a window without breaking the glass. Quantum mechanics revises this classical physics description in terms of probabilities; energetic barriers only decrease the probability of observing such events. In some macroscopic systems, such as superconducting Josephson junctions, quantum effects are regularly observed. Awschalom *et al.* (p. 414) review another macroscopic system that displays quantum tunneling effects. Quantum tunneling effects are seen in the magnetic dynamics of ferritin, an iron storage protein.

■

DNA repair enzyme

Endonuclease III of *Escherichia coli*, a prototypic DNA repair enzyme, excises oxidized pyrimidines and introduces single-strand nicks at excision sites. Kuo *et al.* (p. 434) describe the atomic structure of this enzyme in its free state and in complex with thymine glycol, an inhibitor. This enzyme displays an unusual fold (a six-helix barrel domain) and contains an iron-sulfur cluster that appears to be involved in the proper positioning of the enzyme along the DNA strand.

■

Nylon stackings

Thin films are an important part of many technologies, and epitaxial films—those whose structure aligns with that of the substrate—are especially interesting. Sano *et al.* (p. 441) find that thin films of nylon 6 could be epitaxially grown on graphite. Scanning tunneling microscopy was used to probe the surface structure of the films. In contrast to previous efforts in which films were fabricated by epitaxy of one-dimensional chains, the films of nylon represent epitaxy of two-dimensional sheets. Hydrogen bonding can be used to control the orientation of macromolecules in epitaxially grown films.

■

Prehistoric profile

More than 5000 years ago, a man, aged between 25 and 40, froze to death in the Tyrolean Oetztaler Alps; last autumn his mummified body was recovered from glacial ice. Seidler *et al.* (p. 455) present anthropological details of the "man in ice." Because the mummy must be kept under simulated glacial conditions, the more extensive examinations, such as of the skull, were made by rotated computer tomography and plastic reconstruction. Because bodies trapped in glacial ice are often transformed into white grave wax, mummification (dehydration) likely took place before the body was enclosed in ice.

■

Atherosclerotic mouse

Changes in the genes that encode proteins involved in lipid metabolism, such as apolipoprotein E (apoE), have been identified as one of the factors in atherosclerosis. Lipoprotein particles that contain apoE are cleared from the bloodstream by receptors in the liver. Zhang *et al.* (p. 468) used gene targeting to inactivate the *apoE* gene in mice. In such mice, the plasma cholesterol was five times greater than normal. Deposits rich in foam cells were present in the proximal aortas of 3-month-old mice and by 8 months severe occlusions of the coronary artery ostium occurred. This mouse provides an in vivo model for testing drug and genetic therapies.

■

A star is born

Supernova explosions are among the most violent events in nature, yet a clear understanding of how they happen has been elusive. When its thermonuclear fuel is exhausted, a star may begin to collapse. The collapsing matter should bounce; the expanding shock wave then causes the supernova explosion. In computer simulations, however, the shock wave stalls—a dead end that is called the "supernova problem." Burrows and Fryxell (p. 430; cover) report numerical studies revealing the presence of a violent hydrodynamic instability that drives large-scale convection. Although detailed radiative transfer calculations are still necessary, this instability may be a way out of the supernova problem.

Gated porins

Entry of molecules through the outer membrane of Gram-negative bacteria into the periplasmic space is controlled by porins, which are nonspecific, and by receptor proteins that are specific for a number of ligands. Rutz *et al.* (p. 471) present evidence that these two distinct transport systems may be related. The ferric enterobactin receptor (FepA) requires the cytoplasmic membrane protein TonB for proper function. Mutants of FepA that lacked certain cell-surface peptides no longer accelerated the uptake of specific ligands but instead formed porin-like, nonspecific channels that were independent of TonB. The high sequence homology of the ligand-specific outer membrane receptors that require TonB suggests that all of them use TonB to facilitate the entry of the specific ligand and block the nonspecific entry of other molecules into their channel.

■

Kinase kinase

The receptors for many peptide growth factors are tyrosine kinases. These receptors initiate intracellular signals in the form of cascades of phosphorylation reactions. Mitogen-activated protein (MAP) kinases participate in this cascade. They are activated by phosphorylation on tyrosine and threonine residues and are themselves serine-threonine kinases. Crews *et al.* (p. 478) report the cloning of MEK, a kinase that phosphorylates and activates MAP kinase. MEK has similarity to Byr1, a protein kinase from yeast that participates in signal transduction in response to mating pheremones.

■

Immunosuppression and heat shock proteins

Deoxyspergualin (DSG), like cyclosporin A and FK506, is an immunosuppressant, but its mode of action differs; for example, the inhibitory effects of DSG on the generation of killer T cells cannot be reversed by administering interleukin-2. Nadler *et al.* (p. 484) show that DSG specifically binds to heat shock cognate Hsc70, the constitutive member of the heat shock protein 70 family. Although these different classes of immunosuppressants may induce distinctive pathways, ultimately heat shock proteins may be involved in the action of both types of immunosuppressants.

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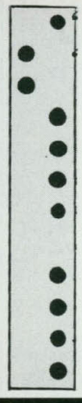

Analysis of PCR amplified material: Human genomic DNA PCR amplified using CFTR exon 9 primers, dot blotted onto Hybond™-N+, hybridized with cystic fibrosis mutation allele specific oligonucleotides prepared using the ECL 3'-oligolabelling system. 2 minute exposure to Hyperfilm™-ECL
Data supplied by A E Shrimpton and D J H Brock, Human Genetics Unit, Western General Hospital, Edinburgh, Scotland.

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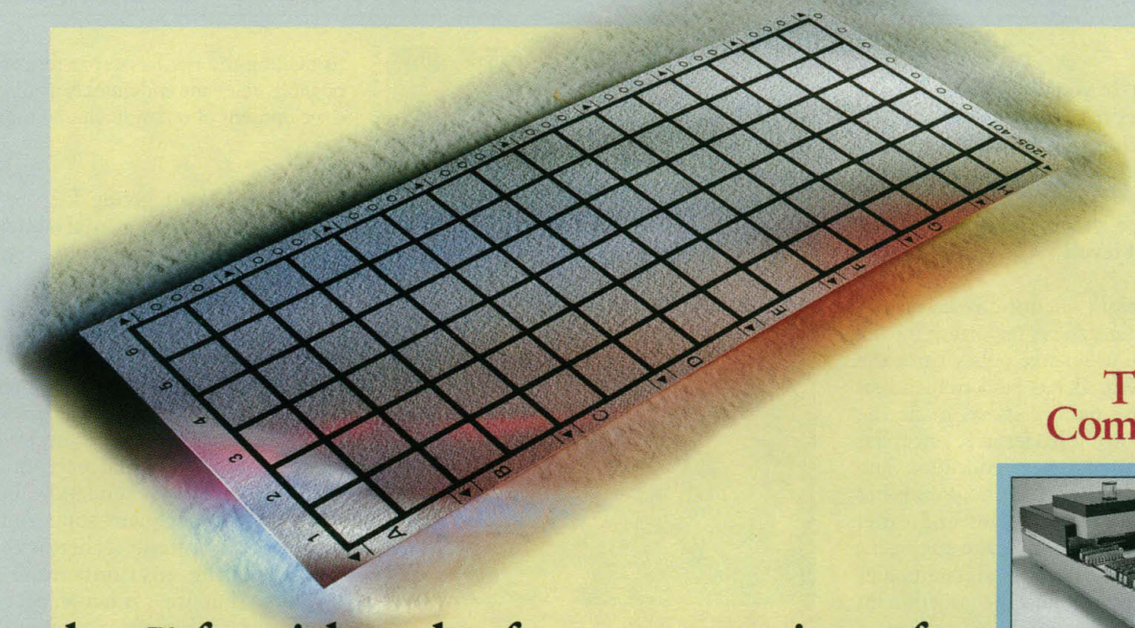

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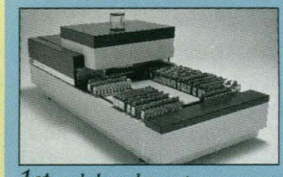

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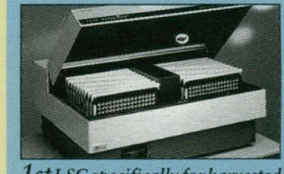

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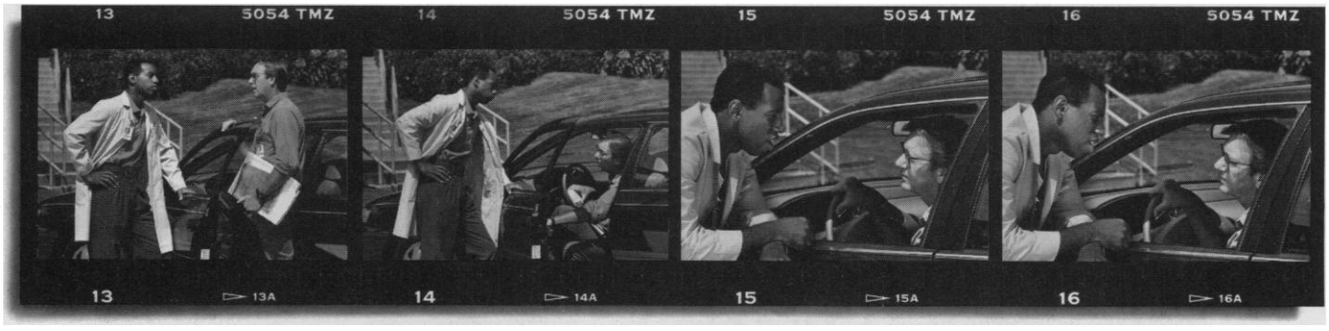

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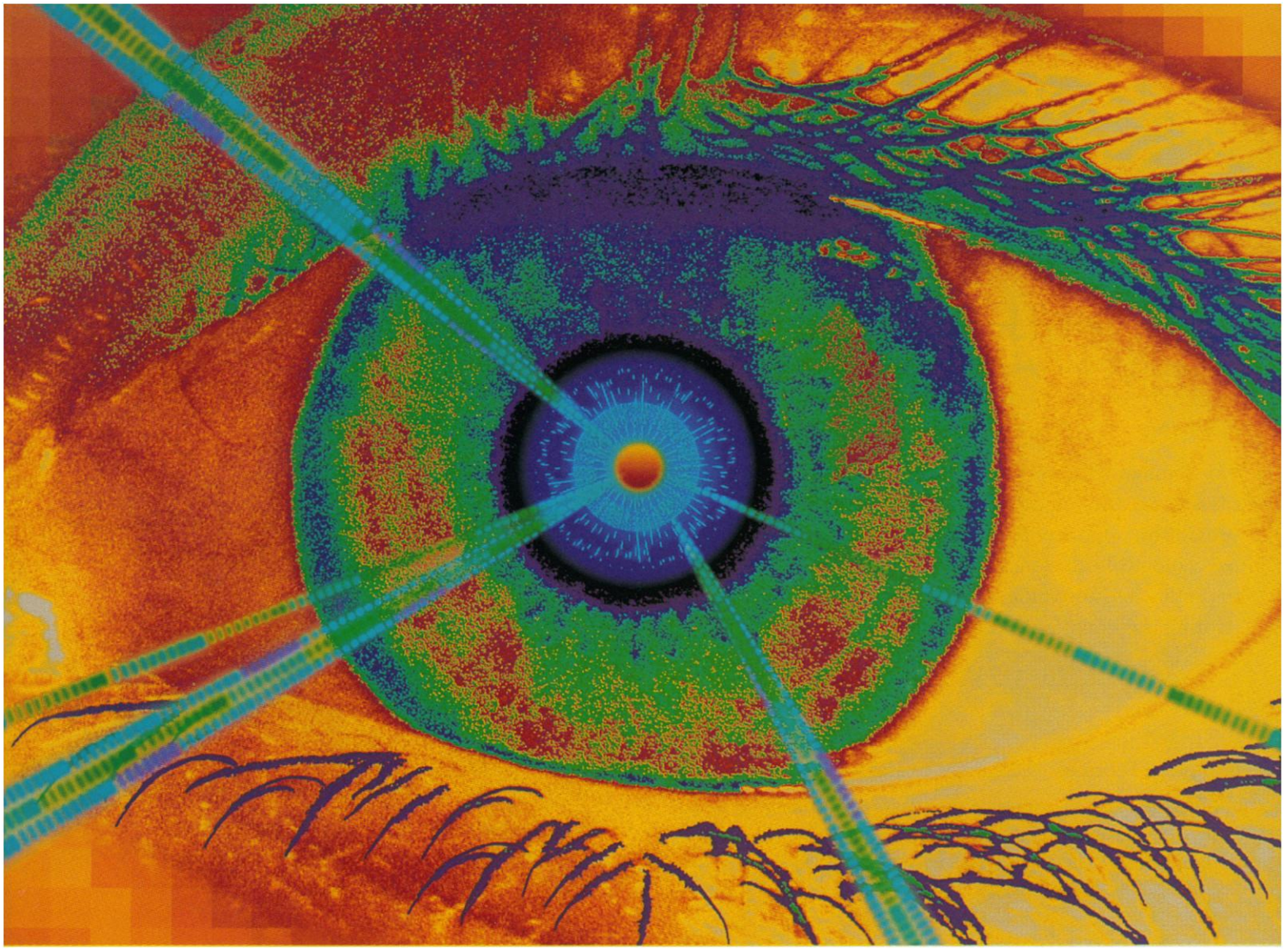

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This seminar will explore questions regarding the definitions, causes, hazards, and treatments of human obesity. It will provide an opportunity for scientists, medical clinicians, and psychological clinicians to hear first-hand from top researchers in the field about the state of the art in understanding and treating this complex and prevalent condition.

Introduction

Friday, 12 February, 9:00 am–9:20 am

Seminar Organizers: **David B. Allison,** *Columbia Univ College of Physicians and Surgeons*; **F. Xavier Pi-Sunyer,** *Columbia Univ College of Physicians and Surgeons* and *President, American Diabetes Assn*

Basic Science

Friday, 12 February, 9:20 am–12:40 pm

Harry Kissileff, *Columbia Univ College of Physicians and Surgeons*
Hunger, satiety, nemiety, and palatability: Studying elusive constructs

Rudolph L. Leibel, *Rockefeller Univ*
Evaluating the "Set-Point" hypothesis

Claude Bouchard, *Laval Univ*
Genetics and obesity: What genetic analyses do and do not tell us

Etiology

Friday, 12 February, 1:40 pm–5:00 pm

David B. Allison, *Columbia Univ College of Physicians and Surgeons*; **Steven B. Heymsfield,** *Columbia Univ College of Physicians and Surgeons*
Do the obese overeat?

James O. Hill, *Vanderbilt Univ*
The role of physical activity in the development and maintenance of obesity

Stanley Heshka, *Columbia Univ College of Physicians and Surgeons*
Is obesity associated with a reduced metabolic rate?

Health and Treatment, Part I

Saturday, 13 February, 9:00 am–12:20 pm

F. Xavier Pi-Sunyer, *Columbia Univ College of Physicians and Surgeons* and *President, American Diabetes Assn*
The health hazards of obesity

George Bray, *Louisiana State Univ*
"Healthy," "ideal," "desirable," and "reasonable" weights: What are they, how do they differ, and when are you there?

Steven B. Heymsfield, *Columbia Univ College of Physicians and Surgeons*
The health hazards of weight loss: What we know, what we think we know, and what we ought to know

David Williamson, *Centers for Disease Control*
The health hazards of weight variability: Epidemiological perspectives

Health and Treatment, Part II

Saturday, 13 February, 1:20 pm–4:40 pm

James O. Hill, *Vanderbilt Univ*
The benefits and use of exercise in obesity treatment

David B. Allison, *Columbia Univ College of Physicians and Surgeons*
If we live in a deterministic world, why can't we predict treatment outcome?

L. Arthur Campfield, *Hoffman-LaRoche, Inc.*
Simple solutions for complex problems? Occam's Razor, the FDA, and the pharmacological treatment of obesity

Panel Discussion

Saturday, 13 February, 4:40 pm–5:00 pm

Moderator: **Steven B. Heymsfield,** *Columbia Univ College of Physicians and Surgeons*

Register Now!
Use the form on the facing page.

American Association for the Advancement of Science

Seminar Registration Form

Human Obesity ✧ 12–13 February ✧ Boston

First name (as you would like it to appear on your badge) _____ Last name (as you would like it to appear on your badge) _____

Institution/company (will appear on badge, subject to abbreviation) _____

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If registering at student rate, check here ❑ and attach a copy of your student ID card.

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Payment Method[3]: ❑ Check enclosed ❑ VISA ❑ MasterCard (no other cards accepted) ❑ Original institutional purchase order attached

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Mail to: AAAS☆93, P.O. Box 630285, Baltimore, MD 21263. **Or fax** (credit card payments only) to 202-289-4021.

❑ Check this box to receive prices and descriptions of other AAAS☆93 seminars and symposia.

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(22 January 1993 Deadline)

Regular	❑ $200
Student[2]	❑ $100
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Retired	❑ $100

Important Notes

[1] **Seminar fee** covers admission to Human Obesity, but does not include admission to any other AAAS☆93 sessions. Registrations received after 22 January 1993 will not be processed, but you may register on site beginning 11 February. On-site rates are $30 higher than advance rates for regular registration, $10 higher for students, and $20 higher for all others.

[2] **Special rates:** To qualify for student rate, you must attach a copy of your student ID card. To qualify for postdoc or K–12 teacher rate, you must provide the name and phone number of your department chairperson or principal in the space provided. *Registrations received without appropriate verification will be charged at the regular rates.*

[3] Cancellations must be received in writing by 22 January 1993. No refunds will be made for cancellations received after this date. Refunds are subject to a $25 cancellation charge and will be processed after the seminar. C D

Hotel Reservation Form

Seminar at AAAS☆93 ✧ February 1993 ✧ Boston

Send confirmation to:

Name _____ (last name) (first name)

Institution/company _____ (if part of address)

Address _____

City/state/zip/country _____

Phone _____ Fax _____

Other occupant(s) of room _____ (name)

_____ (name) / _____ (name)

Special housing needs: ❑ Wheelchair-accessible room ❑ Nonsmoking room

❑ Other _____

Late Arrivals (after 4 pm) must be guaranteed with a deposit for the first night plus 9.7% occupancy tax, either by a major credit card or check (payable to the appropriate hotel).

❑ Check enclosed ❑ Credit card _____ (credit card company)

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✦ **Reservations must be received at the appropriate hotel by 18 January 1993.** (Housing requests received after this date are conditional on room availability.)

✦ Reservation changes and cancellations must be made directly with the hotel.

✦ Children under 18 stay free in same room as parents.

✦ Check-in time is 4 pm; check-out time is 12 noon.

Room Rates:

Check appropriate box for your choice of hotel and room. Add 9.7% occupancy tax to rates shown.

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Attn: Reservations, 110 Huntington Avenue, Boston, MA 02116

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❑ Double (2 persons, 1 bed)	$ 99
❑ Triple (3 persons, 2 beds)	$109
❑ Quad (4 persons, 2 beds)	$119

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[Specify main hotel or tower] ..... main / tower

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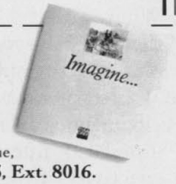

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