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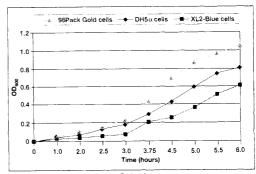




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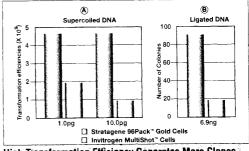
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# cience

Volume 291

2 February 2001

Number 5505

**SCIENCE ONLINE** 783 785

THIS WEEK IN SCIENCE

**EDITORIAL** D. Kennedy

789

"Accepted Community Standards"

**EDITORS' CHOICE** 791

795 **NETWATCH** 

**CONTACT SCIENCE** 798

**NEW PRODUCTS** 895



812 Unsolvable mystery?

### **N**EWS

	NEWS OF THE WEEK	809	PROTEIN FOLDING: Virtual Molecules Nail Bacteria's Weapon	
802	SEISMOLOGY: Tectonics, Design Combine for Indian Disaster—More Coming	809	PHILANTHROPY: Gates Gives Booster Shot	
803	BIOINFORMATICS: Hughes to Build Own Tech Research Center	811	to AIDS Vaccines  PALEONTOLOGY: Doubts Raised About	
805	ORGANIC CHEMISTRY: Sugars Join the Automation Rush		Dinosaur Heart	
805	SCIENCESCOPE		News Focus	
806	WOMEN IN SCIENCE: College Heads Pledge to Remove Barriers	812	MEDICINE: Gulf War Illness: The Battle Continues Congress Explores the Scientific Fringe	
<b>▼ 806</b> 878	MICROBIOLOGY: Bakers' Yeast Blooms Into		Restoring Faith in the Pentagon	
5/5	Biofilms	817	ACADEMIC HARASSMENT: Women Faculty	
	RICE GENOME: Syngenta Finishes,		Battle Japan's Koza System	
	Consortium Goes On	819	GERMAN UNIVERSITIES: Humboldt Hits the	
808	MATH EDUCATION: Academy Report Aims to Quiet Debate		Comeback Trail A Strong University Grows Stronger	
	•		Teaming Up to Woo Young Hotshots	
808	REPRODUCTIVE BIOLOGY: Cloning: Could Humans Be Next?	823	RANDOM SAMPLES	

### **SCIENCE'S COMPASS**



831 The meaning of our genome

### 827 **LETTERS**

Sequence Data: Posted vs. Published R. W. Hyman. Atmospheric Ethics A. H. Westing. Response P. Baer, J. Harte, B. Haya, A. Herzog, N. Hultman, D. M. Kammen, R. B. Norgaard, J. Holdren, L. S. Raymond. Safety of Low-Cyanide Cultivars A. I. Robertson. Einstein's Motivation J. R. D. North. Museum Collections and Conservation Efforts W. J. Kress, S. E. Miller, G. A. Krupnick, T. E. Lovejoy. Corrections and Clarifications

### **ESSAY**

831 Is the Genome the Secular Equivalent of the Soul? A. Mauron

### BOOKS ET AL.

**HISTORY OF SCIENCE: Victorian Sensation** 833 The Extraordinary Publication, Reception, and Secret Authorship of Vestiges of the Natural History of Creation J. A. Secord, reviewed by D. L. Hull

PHYSICS: Einstein's Unfinished Symphony 834 Listening to the Sounds of Space-Time M. Bartusiak, reviewed by M. Visser

### **PERSPECTIVES**

**▼** 835 **NEUROBIOLOGY: Sniffing Out Odors with** 889 Multiple Dendrites Y. Yoshihara, H. Nagao, K. Mori

837 **COSMOLOGY: In Support of Inflation** A. Gangui

**▼**839 **AGING: When Do Telomeres Matter?** 868 J. W. Shay and W. E. Wright 872

**▼ 840** 854 **SEMICONDUCTORS: Toward Functional** Spintronics H. Ohno

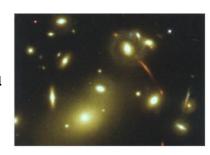
▼ 841 **CHEMISTRY: Aromatic Metal Clusters** D.-K. Seo and J. D. Corbett

842 Nota Bene Texas Elephants Stomp to Victory

### **REVIEW**

843 **NUCLEAR STRUCTURE: Protein Dynamics:** Implications for Nuclear Architecture and Gene Expression T. Misteli

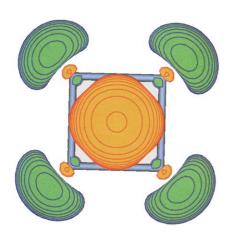
834 Gravitational effects



### RESEARCH

### **REPORTS**

849 Microstructured Magnetic Materials for RF Flux Guides in Magnetic Resonance Imaging M. C. K. Wiltshire, J. B. Pendry, I. R. Young, D. J. Larkman, D. J. Gilderdale, J. V. Hajnal



859

Aromatic without carbon

- 851 Functional Nanoscale Electronic Devices Assembled Using Silicon Nanowire Building Blocks Y. Cui and C. M. Lieber
- ▼ 854

  \*\*Room-Temperature Ferromagnetism in Transparent Transition Metal—Doped Titanium Dioxide Y. Matsumoto, M. Murakami, T. Shono, T. Hasegawa, T. Fukumura, M. Kawasaki, P. Ahmet, T. Chikyow, S. Koshihara, H. Koinuma
- First Solvation Shell of the Cu(II) Aqua Ion: Evidence for Fivefold Coordination
   A. Pasquarello, I. Petri, P. S. Salmon, O. Parisel,
   R. Car, E. Tóth, D. H. Powell, H. E. Fischer, L. Helm, A. E. Merbach

▼859 Observation of All-Metal Aromatic
 841 Molecules X. Li, A. E. Kuznetsov, H.-F. Zhang,
 A. I. Boldyrev, L.-S. Wang

- 862 Inland Thinning of Pine Island Glacier, West Antarctica A. Shepherd, D. J. Wingham, J. A. D. Mansley, H. F. J. Corr
- 864 Scale Dependence in Plant Biodiversity
  M. J. Crawley and J. E. Harral

▼868 Lack of Replicative Senescence in

839
872 Cultured Rat Oligodendrocyte Precursor
Cells D. G. Tang, Y. M. Tokumoto, J. A. Apperly,
A. C. Lloyd, M. C. Raff

**▼872** Lack of Replicative Senescence in Normal Rodent Glia N. F. Mathon, D. S. Malcolm, M. C. Harrisingh, L. Cheng, A. C. Lloyd

875 Control of Fusion Pore Dynamics During Exocytosis by Munc18 R. J. Fisher, J. Pevsner, R. D. Burgoyne

▼878 Bakers' Yeast, a Model for Fungal Biofilm 806 Formation T. B. Reynolds and G. R. Fink

881 Molecular Analysis of Commensal Host-Microbial Relationships in the Intestine L. V. Hooper, M. H. Wong, A. Thelin, L. Hansson, P. G. Falk, J. I. Gordon

884 Protein Design of an HIV-1 Entry Inhibitor M. J. Root, M. S. Kay, P. S. Kim

▼889 Dynamic Optimization of Odor

835 Representations by Slow Temporal

Patterning of Mitral Cell Activity

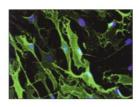
R. W. Friedrich and G. Laurent

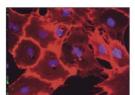


**COVER 878** 

Bakers' yeast forms a large floral structure called a mat (~7.5 centimeters in diameter), which is made up of millions of yeast cells. The cells form these multicellular structures with a reproducible pattern when grown on the surface of semi-solid media. A cell surface glycoprotein, Flo11p, is required for mat formation and adherence to plastic. [Photograph: F. Frankel]

872
Immortal brain cells













**889**Representation of smell in the brain



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Automated Solid-Phase Synthesis of Oligosaccharides O. J. Plante,

 ▼ E. R. Palmacci, P. H. Seeberger
 805 Carbohydrate synthesis, normally a manual process, has now been automated in a manner analogous to that for nucleic acids and peptides.

An Iron-Regulated Ferric Reductase Associated with the Absorption of Dietary Iron A. T. McKie et al.

A cytochrome b-like protein is implicated in the control of whole-body iron homeostasis.

Recovery of Infectious Ebola Virus from cDNA: Transcriptional RNA Editing of the GP Gene and Viral Cytotoxicity V. E. Volchkov, V. A. Volchkova, E. Mühlberger, L. V. Kolesnikova, M. Weik, O. Dolnik, H.-D. Klenk

A new, safe lab technique for studying the deadly pathogen is yielding intriguing, potentially invaluable insights into its molecular biology.

### **TECHNICAL COMMENTS**

Dinosaur with a Heart of Stone

Using computerized tomography (CT), Fisher et al. (Reports, 21 April 2000, p. 503) interpreted an object found within the rib cage of a fossil ornithischian dinosaur as a fossil heart. Rowe et al. comment that the object "fails both geological and anatomical tests" of such an identification, arguing that it is more likely an ironstone concretion, that preservation of soft tissues is extremely unlikely in the sedimentary environment in which the putative heart fossil was found, and that the object lacks most "of the...anatomical structures of an actual heart." Russell et al. respond that fossils of soft tissues have indeed been reported from the Hell Creek Formation, where the object was found, that the position of the object within the fossil skeleton supports the heart interpretation, that CT imaging allows identification of large-scale structures consistent with that hypothesis, and that identifying the object as a fossil heart "need not assume structural identity with a crocodile heart or the preservation of relatively thin-walled structures." The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/291/5505/783a

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Perspective: Ras GTPases: Singing in Tune M. Symons and Y. Takai Report from a meeting on the Ras superfamily.

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In Next Wave's February special feature issue, our global editorial team fills you in on the job prospects and encouraging research funding situation in Europe and North America for the emerging science of nanobiotechnology. Top nanobiotechnologists from around the world share their impressions of the field—and the potential that it holds for up-and-coming scientists.

### US: Establishing a Postdoctoral Association at Brown University D. Bucci

How postdocs at Brown got together to form an association that could represent their interests and needs to the university's administration.

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Practical grant-writing tips designed to maximize the chances that your proposals in Germany are funded.

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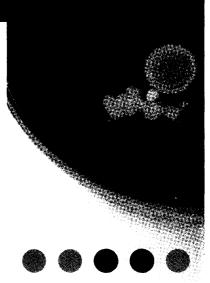
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# THIS WEEK IN Science

edited by Phil Szuromi

### Magnetic in the **Radio Range**

Microstructured materials can show unusual optical properties, as exemplified by photonic band gap materials and materials that exhibit negative refractive index. Wiltshire et al. (p. 849) now show how an array of spiral-wound capacitors (rolled-up aluminized Mylar) can be used to direct magnetic flux. This material is nonmagnetic in a dc field but is designed to be magnetic in an applied radio-frequency (RF) field. It can be used to guide magnetic flux to the receiver coils used in nuclear magnetic

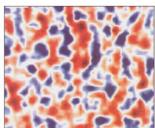
resonance and magnetic resonance imaging.

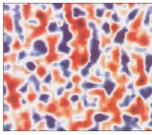
### **Transparent Magnets**

For the field of spintronics, in which electronic spin and magnetic interactions between host and carrier determine device op-

eration, great effort is being expended in developing materials with enhanced functionality. Matsumoto et al. (p. 854; see the Perspective by Ohno) report the finding of a transparent ferromagnet based on cobalt-doped titanium dioxide. The material, a thin film of  $Ti_{1-\nu}Co_{\nu}O_{2}$  in the anatase phase with (0 < x < 0.08), remains

ferromagnetic above room temperature.





### **Nanowire Toolbox**

Their ability to readily dope silicon nanowires during the growth process into electron or hole carriers make them attractive candidates as building blocks for nanoscale electronic architecture. Cui et al. (p. 851) explore the potential of these materials by fabricating and demonstrating a range of functional devices that consist of simple junctions of crossed nanowires with active areas of  $10^{-12}$  to  $10^{-10}$ cm<sup>2</sup>. The ability to fabricate diodes, bipolar transistors, and elementary logic devices such as inverters highlights the role these materials will play in a "bottom-up" approach to nanoscale electronics.

### **Copper Surprise**

Determining the solvation shell of ions in water can be tricky even for relatively simple systems. For example, it has long been assumed that the Cu<sup>2+</sup> ion attracts six water ligands in a distorted octahedral structure, but while the nearest-neighbor copper-oxygen bond lengths are well characterized, the more distant bond lengths have eluded characterization. Pasquarello et al. (p. 856) have performed a combined neutron diffraction and ab initio calculation study and show that the Cu<sup>2+</sup> aqua ion only has five water ligands with similar bond lengths. There are no distal Cu-O bonds, which would explain the previous difficulty in trying to pin them down.

### **How Metals Square with Aromaticity**

Aromatic molecules are usually carbon ring systems, although they may contain heteroatoms such as boron or nitrogen. Molecules are considered aromatic if they are cyclic, planar, and conjugated and have (4n + 2) delocalized  $\pi$ -electrons. Li et al. (p. 859; see the Perspective by Seo and Corbett) report a series of unusual aromatic molecules that contain only metal atoms. The molecules contain a square Al<sub>4</sub>-unit that fulfills both the structural and the electronic criteria for aromaticity. Other group-13 elements may form similar species.

### Thinning Ice

The West Antarctic Ice Sheet contains enough water to raise sea level by 5 meters if it were to melt completely. Most permanent Antarctic ice discharge is provided by ice streams, so glaciologists (and the rest of us) would like to know sooner rather than later if ice loss by streaming is accelerating. The Pine Island Glacier, which has the largest rate of discharge of all of the West Antarctic ice streams, could be a preliminary indica-

tor. Shepherd et al. (p. 862) provide evidence from satellite altimetry and interferometry that ongoing inland thinning due to ice dynamics is occurring. The acceleration of ice flow from the interior due to ice stream dynamics is a distinct possibility. If the present rate of thinning continues, the currently grounded Pine Island Glacier will be afloat in 600 years.

### **How Plant Diversity Scales**

The relation between species richness and area is an important component of ecological studies. Crawley and Harral (p. 864) provide detailed evidence that the relation varies with spatial scale. using data on plant species gathered at different spatial scales in Britain ranging from 0.01 square meter to 1000 square kilometers. Slopes of the species-area relation (logarithm of species richness versus logarithm of area) were steepest at intermediate scales, where the matrix of habitats with distinct floras tends to maximize richness in any given area. The shallowest slopes were at the smallest spatial scales, where individual plants would be expected to interact strongly with each other, and at the largest scales, where few new habitats are added.

### **Eternal Youth** for Rodent Cells

Cells grown in culture dishes usually only divide a certain number of times before they senesce, a state in which cells cannot undergo apoptosis and have a distinctive phenotype. Now, through careful adjustment of culture conditions, indefinite normal growth of two types of rat cells appears to have been achieved. Tang et al. (p. 868) achieved 60 days of normal growth for oligodendrocytes, and Mathon et al. (p. 872) report 50 passages for Schwann cells. Fibroblasts in the same conditions senesce in three to four passages. This demonstration that rodent cells are not universally subject to replicative senescence is discussed in a Perspective by Shay and Wright. They point out that the especially long telomeres in rodent cells may allow

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**CONTINUED ON PAGE 787** 

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### **Fusion Pore Dynamics**

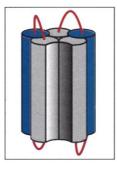
Cellular secretion involves the fusion of membrane-bounded secretory vesicles with the cell surface. Details of the cellular fusion machinery have become clearer during the last few years. Fisher *et al.* (p. 875) looked at the role played by one protein in the fusion machinery, Munc18. Rather than playing a direct role in fusion itself, Munc18 appears to be important in the late stages of the fusion process for the expansion of the fusion pore that is required to make fusion irreversible.

### **Rising Film Maker**

Many bacteria and fungi can grow as aggregates of cells that adhere to a solid surface. When these so-called "biofilms" form on medical devices, such as orthopedic implants, they can significantly increase the rate of infection because, in this protected microenvironment, the pathogens are more resistant to antimicrobial drug therapy. The mechanisms underlying the development of fungal biofilms are especially mysterious because most pathogenic fungi are not genetically well defined. Reynolds and Fink (p. 878; see the cover and the news story by Helmuth) have discovered that the well-studied baker's yeast *Saccharomyces cerevisiae* can undergo the initial steps of biofilm formation in the laboratory and that the cell surface glycoprotein Flo11p is required for this process. The ability to study biofilm formation by classical genetics and whole-genome approaches may help to identify new targets for therapy of fungal infections.

### Adding One to a Gang of Five

Infection by HIV-1 requires fusion of the viral and cellular membranes. This is facilitated by formation of a trimer-of-hairpins structure, having as its core a six-helix bundle that serves to bring together the amino- and carboxyl-terminal regions of the gp41 ectodomain. Now Root et al. (p. 884; see the news story by Helmuth, 12 Jan.) have designed a small protein, called 5-Helix, that binds tightly and specifically to peptides from the carboxyl-terminal region of gp41; 5-Helix inhibits membrane fusion and, thus, infection by HIV-1 viruses with a variety of envelope proteins. These results suggest that 5-Helix may be the basis for a new class of anti-HIV-1 agents and strategies for vaccine development.



### **Picking Out Odors**

Odor representations in the olfactory bulb are not stationary but change while the stimulus is present. Friedrich and Laurent (p. 889; see the Perspective by Yoshihara et al.) recorded from mitral cells in the olfactory bulb of the zebra fish. Responses of these neurons to odors became progressively transformed during the time course of stimulus presentation. This transformation was not due to sharpening of individual mitral-cell tuning profiles. Instead, odor representation appeared to become more evenly distributed at later times during stimulation. Temporal patterning reduced the similarity between ensemble activities and made each odor representation more specific over time. These data provide an important step in our understanding of how olfaction differs from other sensory modalities.

### Flora Facilitating Fauna

The gut is the largest organ in a mammal and is populated by a bulky and complex flora that influences the physiology and the development of the entire host animal. Hooper et al. (p. 881) have started to dissect some of the complex interrelations between the gut tissue of the host and the organisms that colonize it by following the establishment of Bacteroides thetaiotaomicron in the intestine of germ-free mice. The presence of the bacterium influences several basic functions, from nutrient uptake and maintaining the integrity of the intestinal mucosal barrier to the metabolism of alien substances.

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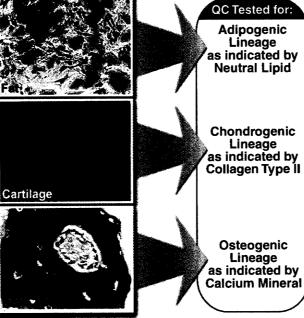


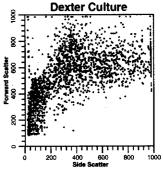
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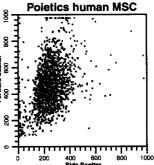
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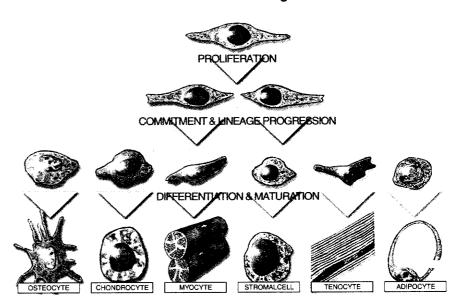
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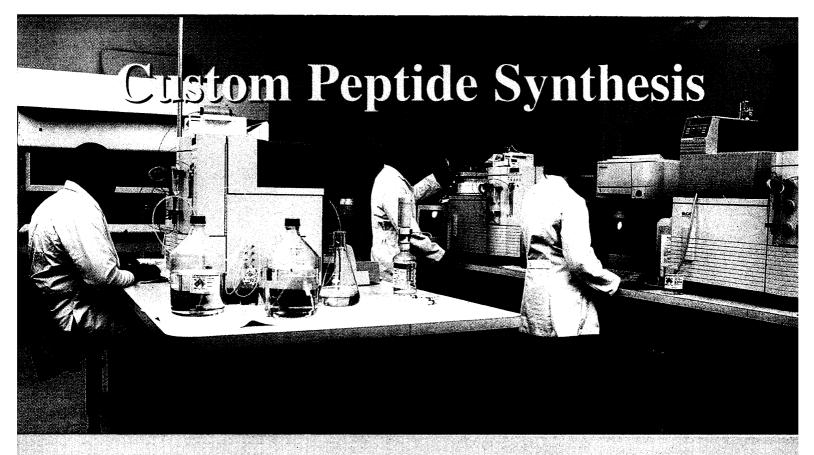
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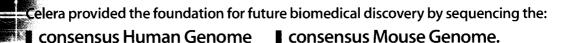
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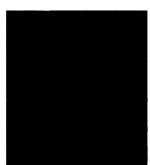
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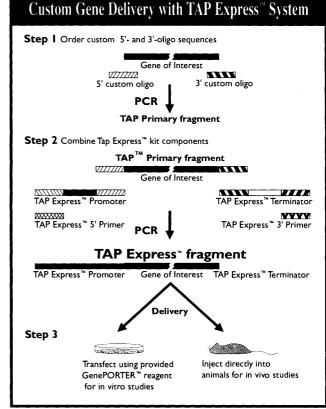
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# CALL FOR LETTERS OF INTENT TO APPLY FOR A RESEARCH GRANT FOR 2002 AWARD YEAR

(Deadline for receipt of letter of intent is 30 March 2001)

The new HFSP research grant program places special emphasis on **novel**, **innovative**, **interdisciplinary approaches to basic research** focused on the elucidation of complex mechanisms of living organisms. The general areas in which applications will be considered are the neurosciences and molecular approaches to biological functions, with the involvement of other disciplines such as chemistry, physics, mathematics, computer science and engineering. Significant new ideas, techniques and discoveries often arise at the boundaries between disciplines. To stimulate novel, daring ideas and innovative approaches, preliminary results are not required in research grant applications. Applicants are expected to develop new lines of research through the collaboration; projects must be distinct from applicants' other research funded by other sources. HFSP supports only international, collaborative teams, with an emphasis on encouraging scientists early in their careers.

A new application procedure has now been introduced for research grants: International teams of scientists interested in submitting applications for support must first submit a letter of intent online via the HFSP web site. The guidelines for potential applicants and further instructions are available on the HFSP web site (www.hfsp.org).

Research grants provide support for basic research (up to 3 years) carried out jointly by research teams in different countries. The principal applicant must be from one of the member countries\*. Preference is given to intercontinental teams. The size of the team should normally be 2 – 4 members with not more than one member from any one country.

### TWO TYPES OF GRANT ARE AVAILABLE:

**Young Investigators' Grants** are for teams of scientists who are all within 5 years of establishing an independent laboratory and within 10 years of obtaining their PhDs. Successful teams will receive a standard amount of \$250,000 per year for the whole team.

**Program Grants** may be applied for by independent scientists at all stages of their careers, although the participation of younger scientists is especially encouraged. Up to \$500,000 may be applied for per year for the whole team, including approximately \$100,000 per team member per year plus some additional funds for essential equipment related to the collaboration.

\*Current member countries are Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Italy, Japan, Luxembourg, the Netherlands, Portugal, the Republic of Ireland, Spain, Sweden, Switzerland, the United Kingdom and the United States.

### Deadline for Receipt of Letters of Intent 30 MARCH 2001

(invitations to submit full applications will be issued at the end of June 2001)

Note: This deadline applies only to Research Grants. The Long-term Fellowship deadline will continue to be 1 September 2001 and the call for applications will appear in May 2001.

The guidelines are available on the HFSP web site (www.hfsp.org)

# Test results not quite what you were expecting?



# Signal Transduction Antibodies

### (Phosphorylation Site-Specific)

Antibody targets and

number of site-specific antibodies

Akt/PKB		JAK1	1
Bad	)	JAK2	- 1
CB1	i	JNK	1
cdc2	1	p38	1
c-Raf	)	p53	1
Cyclin E	i	Paxillin	3
EGF-R	-	PKR	2
elF-2α	!	PLCy-1	- 1
EIF4E	i	Pyk2	5
ERK1/2	i	Rb	-
ERK5	1	RON	- 1
FAK	11	Src	- 3
GSK-3β	2	STAT1	2
ΙκΒ-α	i	STAT3	3
Insulin-R	2	Syndecan-4	1
Integrin β-3	1	Tau	1.4
IRS-1	1		

### Why settle for less?

- Affinity purified both negative and positive selection
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- Rigorously tested in multiple applications and cell lines
- Sample and bulk pricing
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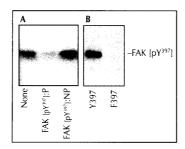


Figure A: FAK pY<sup>397</sup> PSSA analysis illustrating that only the phosphopeptide blocks the Western signal. Figure B: FAK pY<sup>397</sup> PSSA analysis illustrating the absence of a Western signal with the FAK  $(Tyr \rightarrow Phe(F^{397}))$  mutant.

# Testimonial from the field...

"When testing at the same concentrations, the signal for your antibody was similar to the competitors; with your background being 3-4 fold less. I would like to request a quote for 50 mg of the dual-p-JNK antibody. And if you have the stock, a quote for 100 mg of the antibody."

Pharmaceutical Researcher



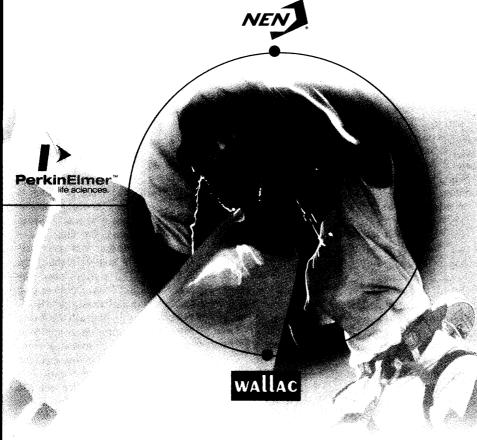
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Drug Discovery

Research

Genetic Screening

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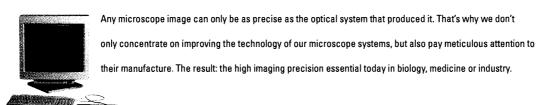


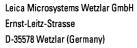
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why do I have to wait 24-48 hours for gene expression?

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Peptides

Proteins

Antibodies

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### Applications:

- · in vivo delivery of antibodies, enzymes, regulators
- · delivery of inhibitory peptides
- · organelle labeling
- · protein half-life studies
- · transient complementation studies



Actin filament labeling of human fibroblast (HS68) cells using anti-actin antibody delivered by CHARIOT. (65% transfection efficiency)

FIG. 2 Cells are fixed

FIG. I Cells are not fixed



FIG. 3 CHARIOT delivery of a 10 kDa protein, labeled with lucifer yellow at the C-terminus, to the nucleus of human fibroblast (HS68) cells. Cells are not fixed. (70% transfection efficiency after 30 min, incubation)

### **CHARIOT** Advantages

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- Serum independent
- No need to generate fusion proteins
- Fast and efficient
- Non-cytotoxic
- Non-covalent complex

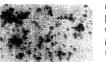


FIG. 4 CHARIOT delivery of a 119 kDa β-galactosidase protein into COS cells. Cells are fixed and stained 2 hours post-transfection. (60% transfection efficiency)

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Molecular Biology

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Tools for Gene Discovery

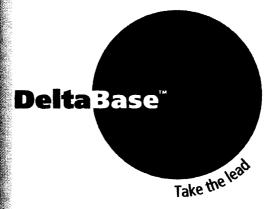
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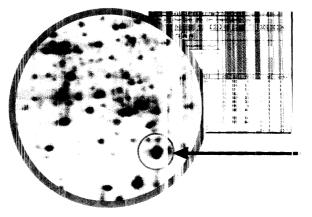
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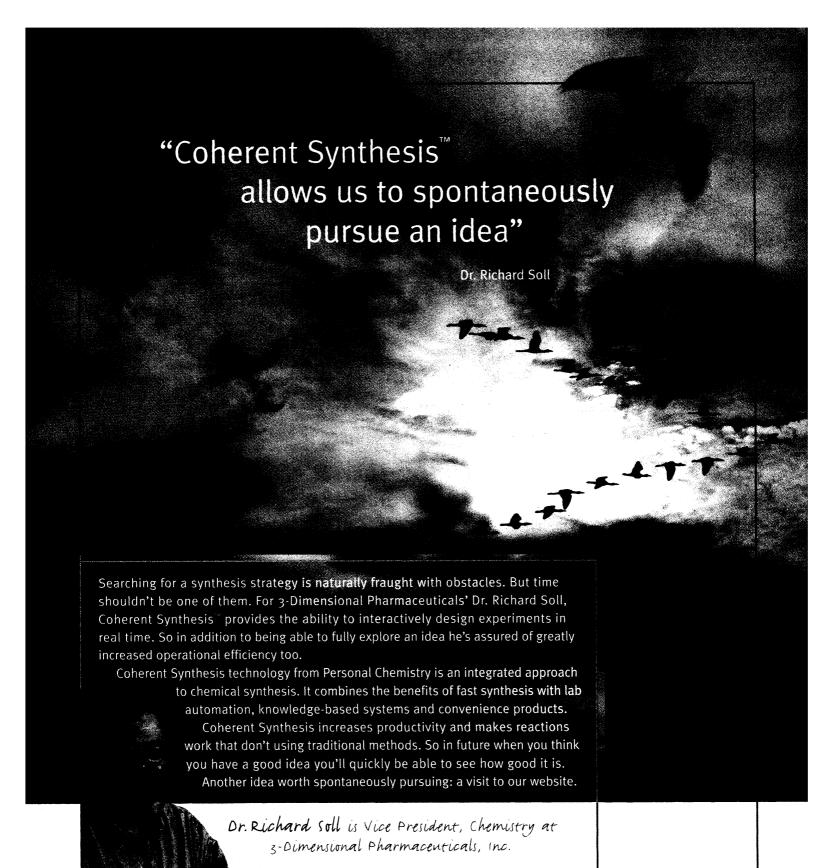
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