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NEWS FOCUS

Engineering a New Green Revolution



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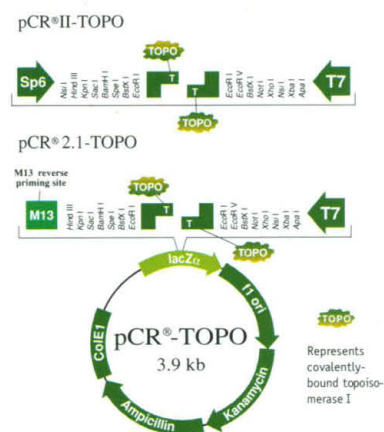
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Cover The cover photograph illustrates a range of rice varieties. Such diversity provided the grist for plant breeders who developed today's high-yielding strains. Now the world needs another boost in grain harvests, and agricultural researchers are pinning their hopes on biotechnology. See the News stories beginning on page 310. [Photo: International Rice Research Institute and Consultative Group on International Agricultural Research]



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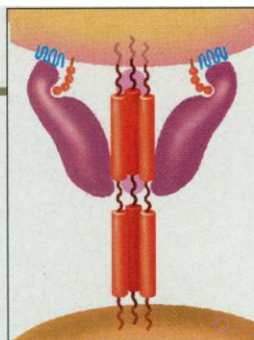
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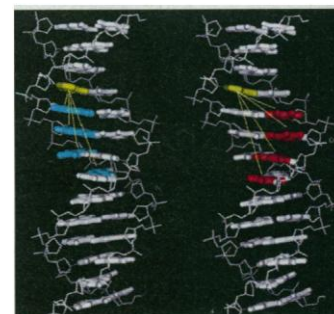
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Running the bases in DNA electron transfer

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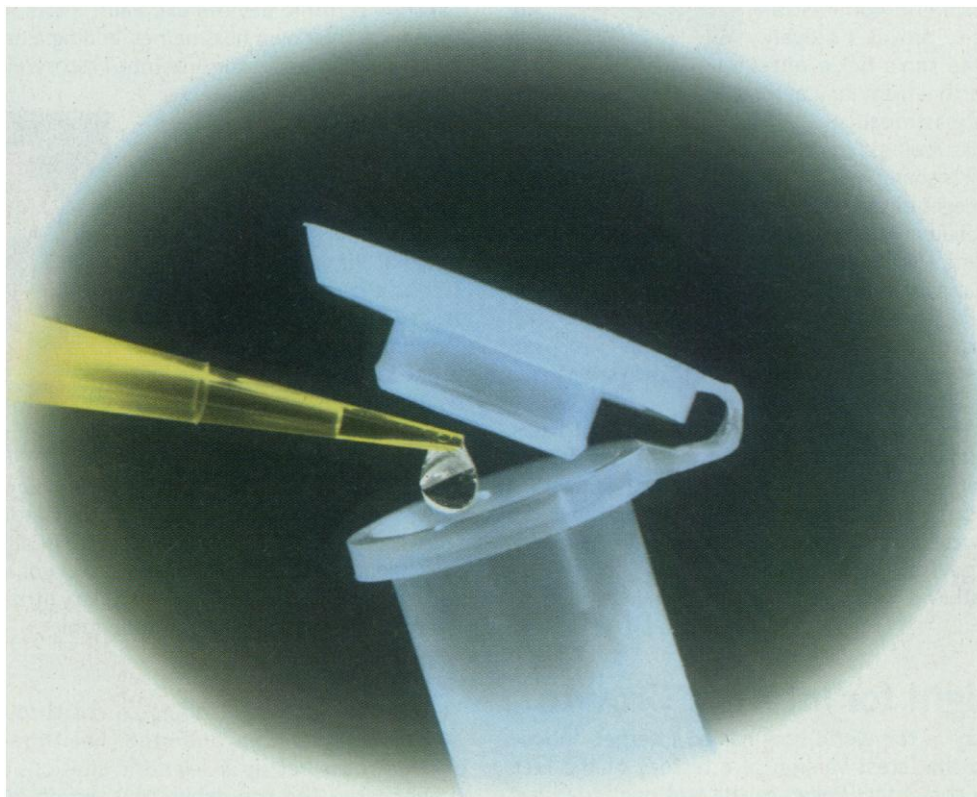


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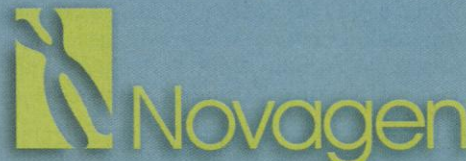
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MASS-INDEPENDENT ISOTOPE FRACTIONATION

Exchange of isotopes as part of a chemical process (reaction or diffusion) almost always reflects the relative masses of the isotopes involved. However, several gases—notably ozone, carbon dioxide, nitrous oxide, and carbon monoxide—and some meteorite grains and minerals seem to preserve a mass-independent relation among the isotopes. As discussed by Thiemens (p. 341) in a review, this effect can be used as a tracer or to provide information on the origins or sources and sinks of the gases, even though the mechanism responsible for the mass-independent fraction may remain obscure. One example of such an effect is the enrichment in the atmosphere of the heavier isotopes (^{17}O and ^{18}O) in ozone relative to the background levels. Asymmetric molecules (such as $^{16}\text{O}^{17}\text{O}^{18}\text{O}$) carry the highest enrichments, whereas symmetric molecules (such as $^{17}\text{O}^{17}\text{O}^{17}\text{O}$) are slightly depleted. Most explanations for this observation invoke kinetic effects induced by molecular symmetry. Mauersberger *et al.* (p. 370) now report rate coefficients for a range of ozone selection channels with different isotopic compositions. The results suggest that the collision process itself, rather than molecular symmetry, determines the enrichment.

NEUTRAL HYDROGEN ON IO

Io, Jupiter's closest large satellite, creates an enigmatic oxygen- and sulfur-rich plasma torus around Jupiter through the satellite's active volcanism and interaction with Jupiter's strong magnetic field. Roesler *et al.* (p. 353) used the Hubble space telescope imaging spectrograph to obtain far-ultraviolet images of neutral oxygen, sulfur, and hydrogen Lyman- α emission of Io's extended atmosphere. The temporal and spatial variations of the oxygen and sulfur suggest that volcanic emissions must be altered or accelerated by the jovian magnetic field, the plasma torus, or both. The hydrogen signal localized near each pole of Io was unexpected and may be produced by hydrogen-rich polar frost, dissociation of hydrogen concentrated at the poles by the jovian magnetic field, or reflection of the solar hydrogen Lyman- α radiation from Io's surface.

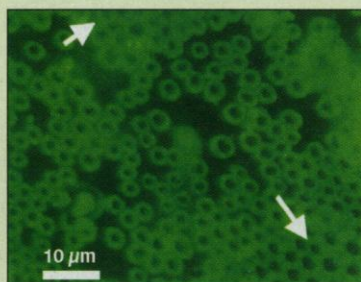
STILL WATERS FIX LEAST

One commonly predicted effect of climate change induced by greenhouse gases is an increase in the stratification of the South-

ern Ocean, a major area of primary production. Arrigo *et al.* (p. 365) show that this change may further hinder the ability of the plankton communities to decrease atmospheric CO_2 by fixation. Their studies of the plankton dynamics in the Ross Sea off Antarctica show that diatoms (which form silicate, not carbonate bodies) dominate in highly stratified waters, whereas *Phaeocystis antarctica* assemblage, which consume a much greater amount of CO_2 , dominate in mixed regions.

ORDERED POROUS POLYMERS

Unusual morphologies often result when two different polymer types are joined in one molecule. Rod-coil diblock copolymer, for example, join a rigid polymer based on conjugated monomers (such as polyphenylquinoxaline, PPQ) with a flexible polymer that forms coils (such as polystyrene, PS).



Jenekhe and Chen (p. 372) show that PPQ-PS diblock copolymers, when placed in solvent (carbon disulfide) that dissolves only the flexible coil, form micelles with diameters of a few micrometers. Solvent evaporation produces a well-ordered porous material that may have several applications, including use as a photonic band gap material.

AN OMNIVOROUS HOMINID?

Early hominids were thought to forage mainly in wooded areas for fruits and C_3 plants (for example, trees, bushes, and herbs). Sponheimer and Lee-Thorp (p. 368; see the Perspective by Kohn and the news story by Vogel) present carbon isotopic evidence from the enamel of teeth from *Australopithecus africanus*, which suggests that this 3-million-year-old ancestor ate more than fruits and leaves. The enamel shows enrichment in ^{13}C consistent with a diet that includes C_4 plants (for example, grasses and sedges) found in more open grasslands, animals that consumed C_4

plants, or both. Thus, *A. africanus* may have had a more diverse diet that included ranging into open grasslands or preying on small, vulnerable mammals without the apparent use of any tools.

INTERBASE ELECTRON TRANSFER IN DNA

Studies of electron transfer through DNA have produced conflicting results, from ultrafast "molecular wire" behavior over many base pairs [characterized by β values of 0.1 per angstrom ($\text{\AA}^{-1}$) or less] to strongly distance-dependent transport more typical of proteins (β values nearer to $1 \text{ \AA}^{-1}$). One confounding issue in several previous studies showing ultrafast behavior is that the donors and acceptors have been species intercalated into DNA. Kelley and Barton (p. 375) now study electron transfer in DNA molecules that incorporate fluorescent analogs of adenine (1, N^6 -ethenoadenine and 2-aminopurine). Electron transfer rates deduced from fluorescence quenching by guanine or deazaguanine bases yielded β values ranging from 0.1 to $1.0 \text{ \AA}^{-1}$. They conclude that stacking interactions and reactant energetics strongly influence the distance dependence and that electrons are preferentially transported between bases on the same strand.

FREEZING EPITOPES FOR HIV-1 VACCINES

The initial interactions between the human immunodeficiency virus-type 1 (HIV-1) envelope protein gp120 and the host cell result in a series of conformational changes in the viral envelope that result in cell-virus fusion. LaCasse *et al.* (p. 357; see the Perspective by Montefiori and Moore) used formaldehyde fixation of cells expressing viral envelope protein co-cultured with cells expressing CD4 and the coreceptor CCR5 to capture an intermediate structure. This epitope complex, which has been "frozen" on the expressing cell, was used as an immunogen in a mouse model. Unlike the currently available recombinant gp120 vaccine candidates, the "fusion-intermediate" immunogen stimulated production of antibodies that neutralized a broad array of primary HIV-1 isolates.

PUTTING PATHWAYS TOGETHER

Although the biochemical signaling pathways through which cells respond to various stimuli have generally been elucidated as linear chains of reactions, such pathways interact to form a complex network. Bhalla and Iyengar (p. 381; see the Perspective by

CONTINUED ON PAGE 299

THE LOUIS-JEANTET PRIZE FOR MEDICINE

The 1999 laureates are

Adrian P. BIRD

Institute of Cell and Molecular Biology, University of Edinburgh, United Kingdom
for his work on DNA methylation and gene regulation

Herbert JÄCKLE

Max-Planck-Institute for Biophysical Chemistry, Göttingen, Germany
for his work on developmental biology in *Drosophila*

Jean-Louis MANDEL

Institute of Genetics and Molecular and Cellular Biology, CNRS/INSERM,
Strasbourg, France, for his work on human molecular genetics

The Louis-Jeantet Foundation for medicine awards the three laureates the global sum of CHF 2'100'000, equally divided between them.

The Louis-Jeantet Prize for medicine is not intended to honour past accomplishments but to encourage innovative research. Candidates must be engaged in basic or clinical biomedical research in the European countries members of the Council of Europe. The Prize is awarded each year to one to three researchers or research groups. Since its inception in 1986, the Prize has encouraged forty-four researchers.

Call for nominations

Nominations for the 2000 Louis-Jeantet Prize for medicine will be accepted until February 15, 1999. Candidates must be nominated by scientists, physicians or institutions having detailed knowledge of their research. Self-nominations are not accepted. Selection is made by the Science Committee of the Foundation.

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The name(s) of the laureates of the 2000 Louis-Jeantet Prize for medicine will be announced in January 2000.
The Prize Ceremony will take place in Geneva (Switzerland) in April 2000.

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THIS WEEK IN SCIENCE

CONTINUED FROM PAGE 297

Lisman and Fallon) used computation methods to model networks that comprised up to four individual signaling pathways. All of the model parameters were derived from experiment. The results show that such networks can have properties not present in the individual pathways that may be critical for proper cellular regulation. Combinations of common signaling pathways showed, for example, the capacity to remain activated after an initial stimulus was removed and had specific requirements for the amplitude and duration of a signal to reach a threshold for activation. Such coordination may provide a mechanism for storing information.

CHANGE FOR THE BETTER

Mutations, generally deleterious and occasionally advantageous, provide the grist for adaptive evolution. De Visser *et al.* (p. 404) have investigated the complex relation between the rate at which new mutations arise and the course of adaptive evolution in bacterial populations evolving in the laboratory. In small or well-adapted populations, their evolution is limited by the rate at which they can produce new mutations. In large or poorly adapted populations, the rate of new mutations has little effect on the rate of evolution. Thus, a hypermutable phenotype can be advantageous in the right circumstances.

IMMUNE-DEFICIENCY LINK

Mice and humans who lack Bruton's tyrosine kinase (Btk) have an immunodeficiency that primarily affects B cell development and production of serum immunoglobulin. Suzuki *et al.* (p. 390) and Fruman *et al.* (p. 393) generated mutant mice, or mice in which only lymphocytes were affected, that were deficient in the p85 α regulatory sub-

unit from phosphoinositide-3 kinase (PI3K). These mice had a phenotype similar to that of the Btk deficient mice.

HYPERACTIVITY PARADOX

Psychostimulant drugs have been used for many years to treat children with attention-deficit hyperactivity disorders (ADHD). This therapy was introduced after empirical observations without an understanding of this paradoxical effect. Gainetdinov *et al.* (p. 397; see the news story by Marx) analyzed mice lacking the dopamine transporter gene. These animals showed striking similarities in their behavior to ADHD children and could also be calmed down by psychostimulants. The paradoxical effect depends on normal serotonergic neurotransmission. These findings may serve as a useful model to develop new therapies to improve these widespread childhood behavioral defects.

CANNABIS, OPIATES, AND REWARD MECHANISMS

Much debate has centered around the linkage between cannabis use and subsequent use of opiates. Ledent *et al.* (p. 401) analyzed mutant mice that were lacking the central cannabinoid receptor CB₁. These animals did not respond to any of the cannabis derivatives, and none of the typical CB₁ receptor-mediated effects could be observed. Although opiates had no unexpected behavioral effect, mutant animals showed less addiction and also less severe withdrawal symptoms. It seems as if CB₁ receptors are involved in the manifestation of physical dependence in opiate addiction. This finding may further our understanding of the processes that lead to drug addiction and may also help to develop new strategies to combat drug addiction.

TECHNICAL COMMENT SUMMARIES

Investigating the Possible Use of Fire at Zhoukoudian, China

The full text of these comments can be seen at www.sciencemag.org/cgi/content/full/283/5400/299a

S. Weiner *et al.* (Reports, 10 July, p. 251) reexamined "the oldest reliable evidence for the controlled use of fire by humans" in Layer 10 at Zhoukoudian (the Peking Man site). They found "burned and unburned bones ... present in the same layer with stone tools," but "no ash or charcoal remnants." They concluded that there was only "indirect evidence for burning."

X. Wu comments that Weiner *et al.* "do not fully address the wealth of data collected at the entire site since the 1930s, and they do not adequately account for problems of material transport by water that apply to the particular sample they studied." He states that other studies do "show that fire was used in this site."

In response, S. Weiner *et al.* state that the "demonstration of free carbon" in earlier studies "does not necessarily imply that the organic matter was burned." They agree with Wu that there is "evidence in support of fire use" and that "many open questions" remain, but state that there is not "conclusive, direct evidence for the use of fire by *Homo erectus*."

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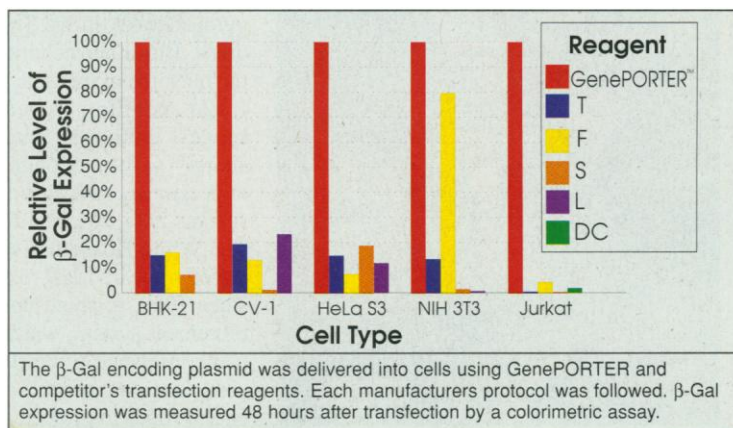
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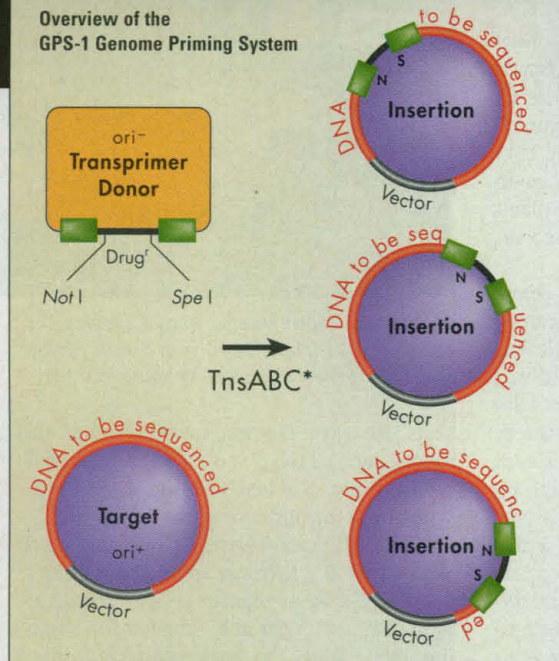
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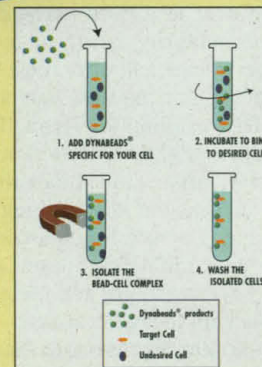
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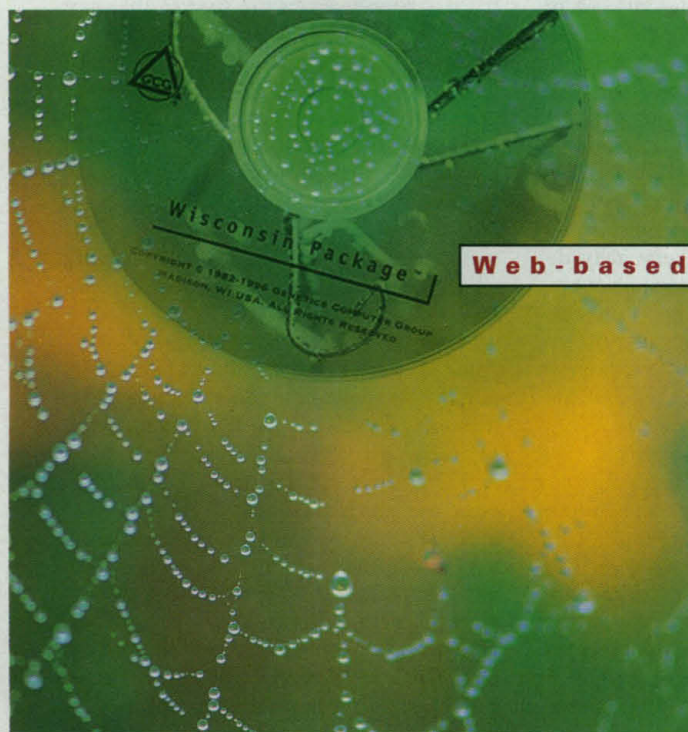


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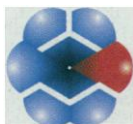
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Request for Proposals

High-throughput Screening and Combinatorial Chemistry Approaches for Cystic Fibrosis Drug Discovery

Application Receipt Date: Open

Developments in the understanding of the cystic fibrosis (CF) basic defect and the role of the CF gene product, CFTR, have enabled scientists to develop strategies for new therapies. The Cystic Fibrosis Foundation (CFF) is soliciting proposals to utilize the growing body of knowledge about CF to develop systems that rapidly discover chemical compounds which correct the function of CF cells. This will be achieved by using the technologies of high-throughput screening (HTS) and combinatorial chemistry (CC).

The CFF will consider proposals for review that address the following issues, but are not limited to:

- developing miniaturization technologies, indicator dyes, marker proteins, cell systems, and related technologies to facilitate the development of HTS technologies related to CF drug development;
- furnishing potential therapeutic agents to evaluate as potential lead compounds for CF drug development;
- creating HTS facilities that serve as resources for evaluating prospective chemical agents resulting from combinatorial chemistry or other entities for evaluation and;
- developing chemical derivatives of existing lead compounds for consideration as candidate drugs.

The application of HTS and CC to develop new anti-*Pseudomonas aeruginosa* drugs will be considered.

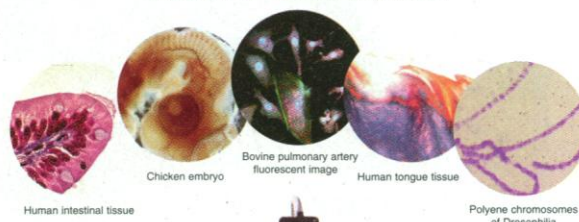
Review and Award: The maximum amount awarded will be \$1.5 million over two years. Each application must contain "milestone achievement objectives" and the appropriate timetable for completion of each. Continued funding for the project will be, in part, based upon milestone attainment.

Submission: An original, plus 20 copies, must be sent to the CFF, Attn: Office of Grants Management, 6931 Arlington Road, Bethesda, MD 20814 (301) 951-4422.



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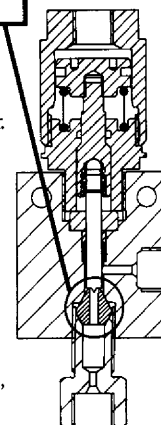
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