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The Commitment to Discovery

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The Results of Our Search

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Scientists at Stratagene have recently cloned Pfu DNA ligase\(^1\). This extremely thermophilic microorganism grows optimally at 95°C and functions superbly in the ligase chain reaction (LCR).\(^2\)\(^,\)\(^3\) Cloned Pfu DNA polymerase* exhibits 12-fold higher fidelity than Tag polymerase.\(^4\)\(^,\)\(^5\) The exonuclease-deficient mutant of Pfu DNA polymerase can be used to directly sequence PCR products with \(^35\)S-dATP.\(^6\) This is just the beginning of Stratagene's commitment to explore thermophilic enzymes and their applications. Just the beginning of the already unmatched line of Stratagene enzymes that can take the heat.

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- **Cloned Tth DNA ligase**: Until now, the only commercially available thermostable DNA ligase. The original LCR technique employs this enzyme. Cat# 600193
- **LCR Kit**: Includes Pfu DNA ligase, reaction buffer, positive and negative control oligonucleotides, control plasmid template and a detailed LCR protocol complete with experimental design and troubleshooting section. Cat# 200520
- **Cloned Pfu DNA Polymerase**: Extremely thermostable. Exhibits 3' to 5' exonuclease-dependent proofreading activity and the highest fidelity of any thermostable DNA polymerase. Cat#'s 600153, 600154, 600159
- **Native Pfu DNA polymerase**: The original high-fidelity Pfu polymerase isolated from the hyperthermophilic archae bacterium, Pyrococcus furiosus. Cat#’s 600135, 600136
- **Exo-minus Pfu DNA polymerase**: The genetically engineered mutant of Pfu polymerase possesses no detectable exonuclease activity. Ideal for cycle sequencing PCR products with \(^35\)S nucleotide analogs and for other high-temperature primer extension reactions that do not require high-fidelity DNA synthesis. Cat# 600163
- **Cyclist**TM Exo-minus Pfu DNA sequencing kit: Contains all the reagents required for cycle sequencing with Exo-minus Pfu. Designed for direct sequencing of PCR products or purified plasmid templates, labeled with \(^35\)S-dATP. Cat# 200326
- **Native Taq DNA polymerase**: Traditionally used for high-temperature primer extension reactions. Stratagene's Taq DNA polymerase is purified using a proprietary technique that makes the enzyme extremely thermostable. Cat#'s 600131, 600132
- **Cyclist™ Taq DNA sequencing kit**: Contains all the reagents required for cycle sequencing with Taq polymerase. Designed for direct sequencing of PCR products, plasmids from colonies or phage from plaques, using \(^32\)P- or \(^33\)P-dATP. Cat# 200325

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REPORTS

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National Institute for Science and Technology

The National Institute for Science and Technology (NIST)* is enjoying substantially enhanced funding and status at a time when most U.S. research and development (R&D) organizations face uncertain futures. Direct federal appropriations for NIST that were $246 million in fiscal 1992 are $520 million this year and are projected to rise to $935 million in fiscal 1995. NIST is expected to be a key federal factor in facilitating improvements in U.S. global economic competitiveness. Rationale for showering funds on NIST includes its special culture in which cooperation with many branches of industry has long been a way of life.

Prior to 1988 NIST was known as the National Bureau of Standards (NBS). Research to create precise weights and measures and distribution of thousands of calibrated samples provided benefits to many companies. The NBS maintained an excellent worldwide reputation. However, during much of the Cold War its budget was static. Direct appropriations were about $200 million a year in 1990 dollars. Many of the staff of 3000 found it necessary to seek and obtain funds from other government agencies as the Department of Defense. The change in NBS's fortunes began in 1988. Congress perceived that the United States was lagging in global competition. It passed legislation changing the name to NIST and mandating an emphasis on improving U.S. technology.

New programs were initiated at NIST. They included a Manufacturing Extension Partnership (MEP) and an Advanced Technology Program (ATP). These initiatives were well-chosen mechanisms for responding to the needs of the times. Plans for them were carefully made and then they were launched on a pilot scale. The MEP responds to a national need to upgrade the capabilities of hundreds of thousands of small manufacturing companies. Many of them need guidance in utilizing computer-based manufacturing and other advances in technology. By 1992 seven Manufacturing Technology Centers were established. These are located in areas with relatively high concentrations of industrial firms. They are managed by local sponsors and draw on expertise from a wide variety of sources, including universities. They are partially supported by federal funds channeled through NIST. They have already established a record of effectiveness. Their number is being increased.

The ATP began in 1990 with an initial $10 million allotment. The Clinton Administration has expanded support and has stated an intention to recommend that the annual appropriation be $750 million in fiscal 1997. The broad objective of the ATP is to promote rapid commercialization of high-risk technologies. ATP relies on industry to suggest, define, and implement R&D programs having potential substantial long-term economic impacts. A large number of companies apply to participate. Selection criteria used by NIST are designed to identify recipients who have excellent R&D plans and a vision of how success in them would be translated into competitive marketable products. The companies also must furnish half of the funds to implement R&D programs which are to be conducted in their facilities. Once they receive awards, their progress is monitored. Awards to individual companies are limited to $2 million over 3 years. Awards to members of joint ventures can be for up to 5 years. Past awards have been made in a broad spectrum of technologies, including agriculture, biotechnology, microelectronics, machine tools, and information technology.

Latest awards, made 25 April, involve a 5-year government investment of $745 million in five new R&D programs. The ATP had received more than 550 project proposals since last October. Based on ideas in more than 150 of the proposals, the five new program areas were selected. These included Tools for DNA Diagnostics and Computer Integrated Manufacturing for Electronics.

With only a tiny fraction of the U.S. R&D budget, NIST is expected to perform the next thing to miracles. Although participation in and management of new programs will require extensive attention, there will be only a small increase in total staff. Some personnel will be diverted from basic research to projects closely related to technology. The ongoing research program at NIST will receive support for improved facilities.

NIST is the focal point of a major experiment in government-industry collaboration. Staff members who have central roles have high morale and the thrill of participating in an important mission.

Philip H. Abelson

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LETTERS

Geological Models

As the lead author and the Department of Energy monitor for one of the reports (1) cited by N. Oreskes et al. in response to letters (15 Apr., p. 329) about the issue of validation and verification of codes and models (2), we take exception to their representation of our work. The Yucca Mountain Site Characterization Project has long recognized that “verification” in the common sense is not possible for models of long-term geological processes. Thus, we have restricted the use of the term to the verification that codes which embody models accurately implement the mathematical equations that describe the model, without regard to the verity of that model. This can be done.

We use the term “validation” in the sense of provisional acceptance, as E. J. Rykkel Jr. points out in his letter (p. 330). It is certain that there will be debate over who should decide the acceptance criteria, as pointed out by Oreskes et al. (Articles, 4 Feb., p. 641), and there certainly has been in the arena which they appear to criticize, that is, the radioactive waste management community. To the extent the public cares to listen, the caveats have been far better presented than Oreskes et al. indicate with their selective citation. Warnings about the possibility of absolute proof are even embodied in the regulations.

As scientists involved in the difficult task of supporting credible policy decisions, we are regularly made aware of the limitations of our models by the scientific community. The statements of Oreskes et al. are, we feel, exaggerated.

Jean L. Younker
Jeremy M. Boak
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References

SIDS Research

Ginger Pinholster (News & Comment, 8 Apr., p. 197) suggests that pioneering sudden infant death syndrome (SIDS) research by Alfred Steinschneider may be called into question because the mother of two SIDS victims is now charged with having murdered her babies. In 1972, Steinschneider described five infants with severe apneic episodes who subsequently died from SIDS (1). He suggested that SIDS may be due to apnea.

These murder charges do not refute Steinschneider’s ideas. SIDS is the most common cause of death in infants between the ages of 1 month and 1 year, yet its cause remains unknown. Leading hypotheses about the cause of SIDS are related to brain-stem dysfunction, especially neurologic control of breathing and sleep-wakefulness. The relation between control of breathing, apnea, and SIDS is currently being investigated, and many studies support an association between SIDS and respiratory dysfunction. Thus, one should not conclude that the “apnea hypothesis of SIDS” is unpopular, has been disproved, or that it is of little scientific interest.

Child abuse exists, and it is a serious pediatric problem. Similarly, SIDS exists, and it is a serious pediatric problem. Occasionally, infants whose deaths were originally attributed to SIDS are found to have died from child abuse. These deaths, and those described in the article, are tragic, but they represent child abuse. That child abuse exists does not decrease the credibility of legitimate scientific inquiry into the cause of true SIDS deaths. Steinschneider’s ideas have inspired 20 years of sustained SIDS research in which the relation between SIDS and apnea has been investigated, and that research continues today.

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References

Embargo on Biomaterials

The article “New challenges in biomaterials” (25 Mar., p. 1715) by N. A. Peppas and R. Langer points out significant opportunities for the creation and characterization of biomaterials that are essential com-
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Fire and Ice... and Worms?

May I point out that the "Wärmertod" referred to in the Vignette from Karl Sigmund's book Games of Life: Explorations in Ecology, Evolution, and Behaviour (Oxford Univ. Press, New York, 1993) in the issue of 29 April (Book Reviews, p. 727) means "death of the worms." This is not at all identical with the once-predicted Wärmertod, the hypothetical death of a universe coming into perfect thermal equilibrium. It is highly probable that the Wärmertod would be preceded by a Wärmertod, although it must be noted that these hardy animals did manage to survive the Wärm-Eiszeit.

Lucien F. Trueb
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Neue Zürcher Zeitung,
8021 Zurich, Switzerland

Corrections and Clarifications
In the Perspective "α-Helical coiled coils: More facts and better predictions" by C. Cohen and D. A. D. Parry (28 Jan., p. 488), the second sentence of the second paragraph of column 1 on page 489 should have read, "The structural motif is indeed a left-handed three-helix bundle with left-handed chain connectivity."

Correction
29 April (p. 734)
and
13 May (p. 911)
issues of
Science
The talk being given by Dr. Harold Varmus at the Science/HUGO Human Genome 1994 meeting on Monday, 3 October, in Washington, D.C., is entitled "Manipulating Cancer Genes in the Mouse."

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<th>Product</th>
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<td>SUPERscript™ II RNase H⁻ Reverse Transcriptase &amp; Buffer</td>
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<td>18038-067</td>
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- Gentle technique maintains biological activity
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HERE'S AN EXAMPLE.

The American Cancer Society predicts that at least 85 million people living in the U.S. today will have some form of cancer. This year alone, more than 200,000 American women will be diagnosed with breast or ovarian cancer. Clearly, cancer is one of our most widespread and devastating health problems. Which is why thousands of researchers around the country are studying ways to prevent and treat the disease.

NEEDED:
GOOD TUMOR SAMPLES TO STUDY.

One of the keys to this research is the ability to reproduce cancer cells in the laboratory in the same way they grow in the body.

If we can replicate the cells, we can try out different drugs to see how the cells react. This, in turn, could lead to new and better treatments.

But under conventional Earth laboratory conditions, human cells are extremely difficult to grow. The cells either do not last long in culture, or they show growth characteristics that are not representative of the way cells develop in the body.

However, when these cells are allowed to form a three-dimensional arrangement in reduced gravity conditions, cells assemble next to one another, form cellular bridges, and join together much as they do in our bodies.

In other words, if we can grow cells in the microgravity of space, or in simulated microgravity here on Earth, we might be able to create many of the cell samples we need for advanced cancer research.

A TOOL DEVELOPED FOR SPACE HELPS ACHIEVE CELL GROWTH ON EARTH.

The Rotating Wall Vessel, a "bioreactor" created to grow cells and tissue in space, is already generating new insights into several forms of cancer.

The vessel was originally designed by scientists at Houston's Johnson Space Center. The idea was to mimic microgravity in order to protect delicate cell structures from breaking apart during launches and landings of the space shuttle.

Much to the surprise of scientists around the country, the Rotating Wall Vessel works fairly well on Earth, as well.

The vessel's simulated microgravity allows organized, three-dimensional clusters to be grown that are superior to cells grown by conventional lab methods.

Today, researchers at Harvard, MIT, the University of South Florida, the University of Texas at Houston, the University of Texas at San Antonio, and several other institutions are using the device for Earth-bound research.

THE SPACE STATION COULD BE ONE OF OUR MOST USEFUL CANCER RESEARCH TOOLS.

As good as current bioreactor samples are, they offer only a hint at what could be achieved aboard the Space Station.

The Station will provide scientists with research conditions that are impossible to duplicate on Earth. It will allow us to expand today's cancer research by performing experiments for extended periods of time in a true microgravity environment.

Today, even with simulated microgravity, we can't grow cell clusters as large as we'd like. Typically, sizes no greater than a fraction of an inch in diameter are possible.

Long-term, large-sized, advanced cellular development will be attained only in the near-zero-gravity environment the Space Station offers. This weightless condition will allow for months of uninterrupted, three-dimensional cellular growth.

We can't, of course, predict that the Space Station will produce a cure for cancer.

But we can ensure that the Station is built and equipped to facilitate promising areas of research.

And we can say without doubt that what we learn in space will help improve the lives of millions of people living on Earth today.
SUCCESSFUL SYSTEMS DESIGN REVIEW IS MAJOR MILESTONE.

In late March, the Space Station Program Office completed a comprehensive design review of all Space Station systems.

By successfully completing the Systems Design Review, the Space Station team demonstrated that it was ready to move from design work to full-scale production of flight hardware.

Altogther, 200 managers and engineers representing 17 nations were in attendance. After the full-day review, the program managers reported that plans for the International Space Station are maturing rapidly, and the orbiting research facility is on track for assembly to begin in 1997, as scheduled.

By incorporating approximately 75 percent of the hardware that was in development for Space Station Freedom, NASA has been able to maintain the nation’s investment-to-date, yet redesign the Space Station to be less expensive and more capable.

Since the transition from the Freedom program began last fall, more than 1,500 technical issues have been resolved. By the close of SDR, only 17 minor issues remained open. All of these issues are expected to be resolved by the end of June.

The Space Station will orbit the Earth every 90 minutes. And its observation angle will cover 85% of the world. So astronauts will be able to view and record most volcanoes, storms, and environmental changes within minutes or hours of occurrence.

MEMBERS OF VEST COMMITTEE HIGHLY IMPRESSED WITH STATION PROGRESS.

Shortly after the conclusion of the Systems Design Review, 15 former members of the Vest Committee met in Houston for their own review of the Space Station’s status.

Led by Dr. Charles Vest, President of MIT, the committee was created by the White House last year to make recommendations on the Station. In its June 1993 assessment, the panel was highly critical of the way the program was being handled.

But after the recent briefing, Vest said, “There has been an absolute sea change in the management and organization of this program.” He went on to say, “I can state with confidence that the high-level conclusions were self-evident and overwhelmingly positive.”

Another former member, Professor Bradford Parkinson of Stanford, said, “The changes wrought by Dan Goldin and an outstanding new project management team have won us over. Given our original skepticism, this turnabout is quite remarkable.” He also said, “I believe this project deserves to be strongly supported by the Administration.”

We’ll have more comments from former Vest Committee members in our next Progress Report.
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- The Award carries a $5,000 prize

1993 Award Winner: Science Theatre
Michigan State University

For additional information, contact: Amie Hubbard, Project Director, American Association for the Advancement of Science, 1333 H Street, NW, Washington, DC, 20005, telephone (202) 326-6760 or fax (202) 371-9849.

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