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PCR OPTIMIZATION



Four primer/template sets were PCR-amplified using either standard *Taq* polymerase buffer (10mM Tris, 50mM KCl and 1.5mM MgCl₂) or individually optimized Opti-PrimeTM buffer systems. Lane 1: 1 ug of lambda Hind III/phi x 174 Hae III marker. Lanes 2&3: 105- bp PCR product of a human Gaucher's disease gene. Lanes 4&5: 150-bp PCR product of Bluescript® vector MCS. Lanes 6&7: 230-bp PCR product of an Epstein Barr viral nuclear antigen gene. Lanes 8&9: 1700-bp PCR product of a *lacl* target gene from a transgenic mouse. Lanes 2,4,6 and 8 are of primer/template sets amplified using standard *Taq* polymerase buffer. Lanes 3,5,7 and 9 are of primer/template sets amplified using individually optimized Opti-Prime kit buffers.

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COVER

Science presents a largely white face to the world. In this issue, a special news section beginning on page 1089 reviews attempts to add color to that face. By creating job opportunities in academia and industry, and by becoming scientific policy-makers, minority scientists are making some inroads. But obstacles such as a lack of role models, economic hard times, and some cultural values held by both majority and minority groups are strewn across a far-from-finished canvas. [Painting: Camille Przewodek]

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This Week in Science

edited by PHIL SZUROMI

Picosecond STM

High spatial resolution is the most familiar attribute of the scanning tunneling microscope. Picosecond time resolution can be achieved by taking advantage of the nonlinearity of the current-voltage response of the tip. Nunes and Freeman (p. 1029) converted optical pulses from a laser delay line into voltage pulses with photoconducting switches. When the pulses are coincident at the junction, the current is much greater than the simple sum of currents arising from each pulse. This excess current provides a time-dependent signal. Optically excited processes such as photoconductivity and reduction of superconducting gap voltages can be followed with this instrument.

Bacterial bushings

Flagellar bacteria have to anchor their rotating flagellum to a static outer membrane in such a way that the torque generated by the flagellum is dispersed effectively and thus does not rupture the membrane at the site of attachment. Engelhardt et al. (p. 1046) propose that an Archimedian spiral structure, the basal disk, serves these functions. Assembly of a spiral, compared to concentric rings, uses only a single point of growth and is less restricted by the size of the building blocks.



Electrical lighting on Jupiter

Radio-frequency emission from Jupiter's magnetosphere is correlated with the phase of Io, the innermost of the Galilean satellites. This phenomenon has been attributed to the generation of electric currents by Io's motion through the planet's

Unraveling trends in ultraviolet radiation

Although large decreases in stratospheric ozone levels in the Arctic and Antarctic springtime have been recognized for several years and lesser decreases have been reported elsewhere recently, the expected increase in the flux of ultraviolet-B (UV-B) light reaching the Earth's surface has been difficult to detect. One reason is that yearly variations in cloudiness and pollution can obscure local trends. Such interferences can be accounted for by monitoring the entire UV-B spectrum. Kerr and McElroy (p. 1032; see news story by Appenzeller, p. 991) report measurements from Toronto that show that UV-B levels increased up to 35 percent per year in winter and 7 percent per year in summer since 1989 in conjunction with observed decreases in column ozone levels over Toronto. No trends in intensity were seen at other wavelengths, as would be expected if a change in cloudiness, for example, was the cause.

magnetic field. Observations by Connerney et al. (p. 1035) of patches of infrared emission near Jupiter's poles lend weight to this suggestion; the emission is attributed to excited H₃⁺ and arises at the points where magnetic flux tubes connected to Io complete a current loop through Jupiter's magnetosphere. Detailed modeling based on these observations should help to clarify the origin of Jupiter's decameter-wavelength radio emission, which is still poorly understood.

Turning on hormones

Plant development is controlled by phytohormones, but the activity of those hormones must be confined to the appropriate time and place. Inactive phytohormone conjugates are stored in the seed endosperm and transported to various parts of the seedling. Brzobohatý et al. (p. 1051) analyze the function of a Bylucosidase that is localized in the growing parts of the root tip and is able to cleave, and therefore activate, the phytohormone conjugates that are transported there from the endosperm. The enzyme does not, however, cleave another type of phytohormone conjugate thought to be a permanently inactivated form of the hormone.

Calcium memories

Increased concentrations of intracellular calcium, [Ca²⁺]_i, cause release of secretory vesicles docked at the cell surface. Von Rüden and Neher (p. 1061) present evidence that the $[Ca^{2+}]_{i}$ also controls conversion of secretory vesicles into a form that is docked or ready for release. Increased [Ca²⁺], enhanced recovery of a secretory response after release-ready vesicles had been depleted. Hormones that cause Ca2+-dependent secretion often cause sustained increases in [Ca²⁺], of moderate magnitude that do not cause release. These sustained increases in [Ca²⁺], appear to enhance subsequent secretory responses by increasing the size of the pool of vesicles ready for release.

Intersecting paths

In many cell types, proliferation is inhibited by agents that increase the intracellular concentration of adenosine 3',5'-monophosphate (cAMP) and consequently activate the cAMPdependent protein kinase. Many growth factors activate a signal transduction pathway that includes the guanosine triphospate binding protein Ras. Activation of Ras leads to activation of a series of protein kinases including Raf and mitogen-activated protein (MAP) kinases. Cook and McCormick (p.1069) and Wuetal. (p. 1065) have localized a point at which these antagonistic pathways interact. They found that increased concentrations of cAMP inhibited activation of Raf and MAP kinases by Ras. Inappropriate activation of Ras appears to contribute to certain human cancers. These results reveal how hormones and other agents that increase concentrations of cAMP might counteract activation of Ras (see news story by Marx, p. 988).

Following directions

Gap junctions are structures that allow direct passage of small molecules between cells. More than a decade ago it was suggested that passage in both directions need not be equal. Robinson *et al.* (p. 1072), using intact retina, have performed



experiments that support this claim. Fluorescent dyes injected into astrocytes spread to either oligodendrocytes or Müller cells, yet dyes injected into either of the latter cell types rarely pass into astrocytes. This directional aspect of gap junction connections may provide another means of communication.

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gram contains powerful new image analysis features: Freehand regions of interest can be drawn on any area of an image, allowing users the flexibility to count, measure, and classify particles within irregular regions of interest. Other new features include new particle measurements (for a total of 56 measurements), enhanced particle counting, new filters, and new frame grabber support. Data Translation. Circle 137.

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The current issue of SynChro-Notes newsletter discusses "Ion Exchange Chromatography— The Untapped Technique," which has excellent potential for resolution of proteins. Syn-Chrom. Circle 144.

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PE Thermal Analysis Systems Overview highlights a line of systems that provide complete solutions for materials characterization requirements. Perkin-Elmer. Circle 149.

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Bruce S. Duncan, Ph.D., Research Associate, Department of Molecular Biology (left), is pictured with Arthur J. Olson, Ph.D., Professor, Department of Molecular Biology, and Director, Molecular Graphics Laboratory.

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A study by the National Action Council for Minorities in Engineering (NACME) concluded that AT&T's CRFP significantly affects the graduate experience and subsequent career paths of the Fellows. As Willetta Greene-Johnson, a 1987 graduate of the University of Chicago and current Professor of Chemistry at Chicago's Loyola University said, "CRFP was a definite, positive experience. The program helped me make my decision to pursue science as a career. My summer job at the Labs gave me an opportunity to see how 'real science' was done."

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Committed To Train Of Scientists And

The National Institutes of Health is the world's largest institution committed to biomedical research. The NIH intramural research program, which brings together more than 4,000 doctoral level scientists and a clinical center that is home to half of all research beds in the country, has traditionally provided exceptional postdoctoral training opportunities in both the basic and clinical biomedical sciences. In addition, the NIH is fully committed to helping prepare the upcoming generation of scientists by providing programs for graduate, medical, and college students. Programs for college faculty and secondary school teachers are also available to help the nation's professors and teachers better prepare the next generation of scientists.

The National Institutes of Health also seeks to ensure that the upcoming generation of scientists reflects the rich cultural diversity of this Nation's citizenry. The NIH and the Minority Officers Liaison Council of the United States Public Health Service are committed to achieving this goal and enhancing the training experience and career development of all postdoctoral fellows at the NIH.

The following descriptions introduce the various postdoctoral and other educational opportunities available at the National Institutes of Health. Minorities are especially encouraged to explore the various training opportunities which are available and to contact the Office of Education for additional information.

Postdoctoral Training Programs

Laboratory Research Training

Postdoctoral fellowships are available to conduct fundamental biomedical research in a wide variety of disciplines at the NIH. Initial appointments are usually for two to three years. Candidates should have either a graduate doctoral degree (e.g., PhD, MD/PhD) or a professional degree (e.g., MD, DO, DDS, DMD, or DVM) accompanied by previous laboratory research experience. Current postdoctoral openings at the NIH are posted on the NIH **EDNET Bulletin Board's POSTDOC** conference which is available via modem . In addition, the NIH welcomes applications for anticipated openings nine months to a year in advance. A catalog featuring research descriptions of NIH scientists has been developed to assist prospective fellows in this process and the catalog is available from the NIH Office of Education. Research descriptions may also be accessed on the NIH Gopher server on Internet. Individuals interested in pursuing research training through the Clinical Investigator Pathway of the American Board of Internal Medicine may contact the NIH Office of Education for additional information.

Clinical Research and Subspecialty Training

Subspecialty training at the NIH allows physicians to become boardcertified specialists who are also prepared for careers in academic medicine. In-depth training in clinical and/or basic research complements the fellow's clinical training in the following programs which are accredited by the Accreditation Council on Graduate Medical Education or by boards in their respective disciplines: Allergy and Immunology, Anatomic Pathology, Critical Care Medicine, Dermatology (third year), Diagnostic Immunology, Endocrinology and Metabolism, Gastroenterology, Hematology, Infectious Diseases, Medical Genetics, Medical Oncology, Nuclear Medicine, Oral Medicine, Pediatric Endocrinology, Pediatric Hematology/Oncology, Psychiatry (fourth year), Radiation Oncology, Reproductive Endocrinology, Rheumatology, and Transfusion Medicine. Programs in Clinical Chemistry and Clinical Microbiology offer credit toward board certification on an individual basis.

Re-Entry Postdoctoral Training

A new program has been developed at the NIH to assist individuals with terminal degrees (e.g., MDs, PhDs, MD/PhDs, etc.) who have had to delay or postpone their research careers because of family responsibilities. Research training, supported by

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ing The Next Generation Clinical Researchers.

courses and workshops, is provided to assist participants in their retraining and eventual re-entry into research careers.

Accessing Information on Postdoctoral Training Electronically

The NIH EDNET Bulletin Board's POSTDOC conference may be accessed by Internet (cu.nih.gov) or via modem (1,3014022221 or 1,8003582221). The settings for modem access are "7,Even,1". When connected to NIH, type in ",vt100" at the connect message, "F5E" at initial, and "AJL1" at account.

An electronic version of the Postdoctoral Research Fellowship Opportunities catalog may be accessed via the network-based (Internet) Gopher Information System. To access the NIH Gopher server, Gopher client software (available via anonymous ftp "boombox.micro.umn.edu") must be running on your computer and configured to point to "gopher.nih.gov" and port "70". Select *Grants and Research Information* to reveal the NIH Office of Education directory.

Graduate Student Programs

Students interested in doctoral training in genetics are encouraged to consider the NIH-George Washington University (GWU) **Graduate Pro**gram in Genetics. NIH and GWU faculty provide didactic instruction and dissertation research is conducted in NIH laboratories. Full tuition and stipend support are provided.

Medical and Dental Student Programs

The Summer Research Fellowship Program provides eight to ten weeks of basic research training for students in the summer following their first or second year. In addition, nineteen different Clinical Electives are available for third and fourth year students, providing clinical and clinical research experiences unduplicated elsewhere.

Undergraduate Student Programs

Students can participate in stateof-the-art biomedical research through the **Summer Internship Program**. The summer program also provides workshops on career pathways and strategies for a successful scientific career, as well as a weekly seminar series. In addition, juniors or seniors who are preparing for careers as secondary science teachers may participate in the **Pre-Service Teacher Program** to gain experience in biomedical research, the use of new technologies, and the teaching of of bioethical issues.

Secondary School Teacher Programs

Several summer programs provide opportunities for teachers to participate in laboratory research, including an **In-Service Teacher Program**. It offers teachers from schools with predominately minority enrollments an in-depth course in molecular biology before the research experience begins. Training in the teaching of bioethics and use of electronic databases is also provided.

To find out how the NIH can play a role in your research train-

ing, please contact the NIH Office of Education for information on any of these programs.



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 $\sqrt{50}$ provide students with maximal choice and flexibility in selecting a research specialization, the basic science departments at UCLA offer a combined recruitment, admission and first-year program. This initiative, known as UCLA ACCESS to Programs in the Molecular and Cellular Life Sciences, represents a simple, flexible mechanism for maximizing research choices throughout the first year of graduate study. As part of this program, students are able to select research projects from 150 faculty mentors according to changing perceptions, interests and goals without regard to traditional departmental boundaries. Ethnic, gender and cultural diversity are both a strength and a priority at UCLA and we solicit and encourage applicants who will increase and strengthen our diversity.

All Ph.D. students are fully supported through a variety of sources including the following federally sponsored pre-doctoral training programs:

Cellular and Molecular Biology, Genetics, Atherosclerosis, Tumor Cell Biology, Biotechnology, Tumor Immunology, Microbial Pathogenesis, Chemistry/Biology Interface Training

For information and application materials:

UCLA ACCESS Molecular Biology Institute, University of California, Los Angeles Los Angeles, CA 90024-1570 (800) ATG-UCLA or (310) 206-5280

R & D Scientists at Pfizer Central Research

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DR. RICARDO OCHOA, DIRECTOR

As Director of Pathology in the Drug Safety Evaluation Department, I lead a team of veterinarians trained in toxicologic pathology.



Our major responsibilities are to evaluate the safety of new drug candidates in all therapeutic areas.

This is challenging work and I would certainly like to encourage members of minority groups to seriously consider this field. After work I am a dedicated long distance runner and find southeastern Connecticut ideal for this activity.

DR. EDNA GARCIA, RESEARCH SCIENTIST

Pfizer liked my years of team experience as an engineer and medical technologist, coupled with my mass spectrometry research. But, as a native Texan with over 300



years of family ties there, I had to look closely at the company and the community before I committed to Pfizer. I've found that working with structurally unique molecules is very satisfying. It's been a pleasure living here, too. People

are quite friendly, and the rural atmosphere has been really good for me and for my family.

MS. JANET GREEN, BIOMETRICIAN

As a clinical research biometrician, I work closely with new agents that are potential candidates for regulatory approval. It's very interesting working here - no one is looking over your shoulder; you can use your own initiative. Outside of Pfizer, I'm president of the local



women with science and math careers and prepare them for entering the workforce.

DR. DANIEL YOHANNES, **RESEARCH SCIENTIST**

Medicinal Chemistry. The focus of our research is to design small molecules to improve cognition in the treatment of Alzheimer's disease, and I also work closely with my colleagues in biology, to define the activity profile of new drug candidates. Good teachers along the way nurtured my

interest in science...and Pfizer offers me another such opportunity.

Ms. Gwendolyn Robinson, ASSOCIATE SCIENTIST

I study behavioral effects of new compounds for anxiety, Alzheimer's disease, and psychosis and support other disease studies as well. It's a challenging field and I feel I have the freedom necessary to select the studies appropriate to the project. As a student, my favorite subject was zoology, so it is not surprising that my career at Pfizer has been focused on studying behavior. I've raised three children here, too and like the

schools, the coast and the change of seasons. DR. DAVID BLACKWELL,

SENIOR RESEARCH SCIENTIST

While an intern in the summers for a pharmaceutical company, I developed a strong interest in toxicology. As a veterinarian, I now work in the General Toxicology Group within the Drug Safety Evaluation Department. My technical responsibilities

include evaluating the safety profile of compounds designed to treat human diseases. I feel a strong sense of responsibility in this role people's lives depend on it.

DR. JOHN VINCENT, ASSOCIATE DIRECTOR I have a varied background in clinical medicine, with a PhD degree in Clinical Pharmacology. As a member of

the Early Clinical Research Group, I am responsible for designing and carrving out



studies to determine the safety, toleration and pharmacokinetics of new drug candidates. I've found Pfizer to be a fascinating place; its quality and its openness are remarkable. And that holds true for the communities here as well. I have children involved in scouting for example, and they clearly have found a home.

As a research-based, global health care company, Pfizer's mission is to create innovative products that improve the quality of life around the world. If you are interested in joining our dynamic scientific team, please send your

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Inquiries and/or resumes should be addressed to: Southwest Research Institute, Personnel Department #723, 6220 Culebra Road, P.O. Drawer 28510, San Antonio, Texas 78228-0510.





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MEMORIAL SLOAN-KETTERING CANCER CENTER

The Memorial Sloan-Kettering Cancer Center offers postdoctoral training fellowships in basic laboratory and clinical research. Stipends provided are based upon level of postdoctoral experience. For additional information write to program directors listed below.

CLINICAL SCHOLARS TRAINING PROGRAM IN BIOMEDICAL RESEARCH

Richard A. Rifkind, MD - Director

This two-year postdoctoral fellowship program provides training for a select group of physicians who have completed their clinical training and demonstrate a commitment to careers in biomedical research. Training opportunities are available in the research programs of: molecular biology, cell biology and genetics, cellular biochemistry and biophysics, immunology and molecular pharmacology and therapeutics.

SURGICAL ONCOLOGY RESEARCH TRAINING PROGRAM Murray F. Brennan, MD - Director

The program seeks to strengthen academic surgical oncology research by training surgical fellows in laboratory research related to biology of human cancer. Research opportunities include areas such as metabolism, neurophysiology, molecular biology, cell biology, immunology, immunology, immunology and genetics.

PSYCHIATRIC AND PSYCHOLOGICAL RESEARCH TRAINING IN AIDS

Jimmie Holland, MD - Director

This training program seeks to address the urgent need to recruit and train more investigators to conduct research on the mental health aspects of the AIDS epidemic. The program draws upon a faculty involved in investigations of psychiatric, neuropsychological, and behavioral aspects of AIDS/HIV infection in diverse populations (gay men, women, intravenous drug users and minority group members). The methods used to train new investigators include didactic seminars, apprenticeship with experienced investigators, and supervised conduct of independent research.

PSYCHIATRIC AND PAIN RESEARCH TRAINING IN CANCER Jimmie Holland, MD - Director

This training program seeks to address the urgent need for a cadre of investigators with expertise in the supportive care areas of pain, psychological distress, supportive/palliative care, psychoneuro-

immunology and behavioral medicine. The training program is open to psychologists and physicians with training in psychiatry, neurology, medicine and oncology. Its world reknown faculty is involved in research of the psychiatric, neuropsychological, behavioral, neuroimmunological and pain related (clinical and laboratory) aspects of patients with cancer. The curriculum to train these clinical investigators includes didactic seminars, apprenticeship with experienced clinical investigators in pain, psychiatry, psychology and neurology and closely supervised conduct of independent research.

GASTROINTESTINAL ONCOLOGY RESEARCH

Sidney J. Winawer, MD - Director

The program offers opportunities for basic and applied research in Gastrointestinal Cancer. A number of interrelated groups are working on collaborative efforts and jointly participate. This affords the trainees an excellent opportunity to study a wide spectrum of biological, molecular genetic, immunological and pharmacological approaches to gastrointestinal cancer and its etiology. There is special emphasis on cancer prevention, nutrition and inheritance.

CANCER CHEMOTHERAPY TRAINING PROGRAM John Mendelsohn, MD and George Bosl, MD - Co-Directors

The Oncology/Hematology Fellowship Program provides qualified physicians with comprehensive clinical training necessary for certification in Internal Medical subspecialties of Oncology and Hematology and research training designed to prepare the trainee for an academic research career. Through the Cancer ChemotherapyTraining Program, clinical and laboratory scientists from Memorial Hospital and the Sloan-Kettering Institute provide opportunities in and supervision of basic and applied research training in gene expression, growth factor modulation, differentiation, drug resistance, gene transfer, and clinical trials methodology after the completion of clinical training.

IMMUNOLOGY RESEARCH TRAINING PROGRAM Kenneth O. Lloyd, PhD - Director

The program offers training in areas of modern immunology. These include human and mouse immunogenetics, function and mechanism of action of T lymphocytes, biology of B lymphocytes, and molecular control of HLA antigen genes. Another interest is in T cell development and selection in the thymus and in the peripheral circulation. The Program also has strong efforts in tumor immunology, with an emphasis on an analysis of the immune response in tumor cancer antigens, the production of human and mouse monoclonal antibodies to tumor antigens and the clinical application of these antibodies.

HEAD AND NECK TRAINING PROGRAM - SURGICAL ONCOLOGY Stimson P. Schantz, MD - Director

This is a two year program with dedicated clinical and research training opportunities in head and neck oncology. A specific focus will be placed on cancer prevention and detection strategy for tobacco-induced cancer.

ENDOCRINE AND METABOLIC RESEARCH TRAINING PROGRAM Martin Sonenberg, MD, PhD - Director

The objective of the Endocrine Research Training Program is to develop research physicians and scientists who will contribute to an understanding and management of endocrine and metabolic diseases. We are integrating the training programs of 17 faculty members of 4 neighboring institutions, Memorial Sloan-Kettering Cancer Center, The Rockefeller University, the New York Hospital-Cornell Medical Center and The Population Council. Areas of research include: mechanism of hormone action, hormonal control of growth and differentiation, regulation of testicular function, neuroendocrine control of neural gene expression, control of membrane channel function, biochemical genetics and metabolism of atherosclerosis, hormonal control of bone metabolism, anti-receptor antibodies in cancer treatment.

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