Michael W. Berns Receives Lifetime Achievement Award

Michael W. Berns, the Arnold and Mabel Beckman Professor, Professor of Biomedical Engineering, Developmental and Cell Biology, and Surgery, and co-founder (with Arnold O. Beckman, 1900-2004) of the Beckman Laser Institute at UCI, was awarded the 2006 Biomedical Optics Lifetime Achievement Award at the annual meeting of SPIE’s International Symposium on Biomedical Optics (BiOS) held in January 2006 at San Jose, California. Before an audience of approximately 500 engineers and biomedical scientists, Dr. R. Rox Anderson, Director of the Wellman Center for Photomedicine at Harvard University, presented the award to Dr. Berns “for his contributions to the development and growth of laser microbeam technology, a major step towards establishing new tools for understanding laser interactions with biological tissues, which have resulted in significant improvements in diagnosis and treatment of disease.” Additionally, Dr. Anderson remarked that Michael is generally considered the “father of laser microbeams,” having started his work as early as 1969 with publication of a seminal paper in Nature magazine describing how the laser can be used to perform subcellular surgery on chromosomes. Over the past 35 years, Dr. Berns has published over 400 articles and written and/or authored six books.

The Vascular Birthmarks Foundation honored BLI Associate and Medical Director J. Stuart Nelson as “Physician of the Year” for 2005 for his research, inventions, and training that have improved the lives of individuals affected by a port wine stain.

The principal goal of Dr. Nelson’s research has been to develop new approaches for the characterization and treatment of port wine stain birthmarks. His research is interdisciplinary in nature combining expertise in optics, electrical and mechanical engineering, and medicine. He has been awarded nine patents for developing biomedical devices from the Patent and Trademark Office, United States Department of Commerce. The “dynamic cooling device” methodology developed by Dr. Nelson and colleagues at the Beckman Laser Institute has now been incorporated into more than 12,500 laser devices. This unique approach to skin cooling, used in conjunction with pulsed dye laser treatment of port wine stain birthmarks is now the standard of care used worldwide.

In addition to Dr. Nelson’s research, teaching, and faculty responsibilities at BLI, he is engaged in university-based clinical research and patient care.

(Nelson continued on p. 6)
Happy Birthday to a Vision

The Beckman Laser Institute is approaching its 20th birthday! So it is appropriate to reflect over these past twenty years and, in particular, on the “vision” that the founders had.

In many ways, that original vision has been achieved. The BLI has become world renown for its basic and applied research in lasers and photonics. Its clinical treatment program has become recognized worldwide for research and treatment of vascular birthmarks, especially for children. In the area of inventions, the BLI program has generated 132 invention disclosures, has three associated spin-off companies at various stages of development and, for the fiscal year of 2005, has the No. 1 ranking in revenue generating patents at UCI and the No. 2 ranking in the entire UC system: the dynamic cooling technology developed by Dr. J. Stuart Nelson and colleagues. This technology has already generated a total of $30 million in royalty and licensing revenues.

With respect to inventions, an even larger benefit to BLI is accruing because of Arnold Beckman’s shrewdness when he pledged the original gift for the building in 1984. He conditioned that gift upon UCI agreeing to allocate to the program any future patent royalty money that BLI generated. Arnold Beckman’s astute “crystal ball” foresaw a time when state, federal, and private money would be so tight, that a program with a flow of funds from its own inventions would be able to out-compete its competition, not only for faculty and student talent, but also to position its programs in new exciting directions long before other programs could get dollars via the slow government grant process.

We are currently poised at an exciting frontier where the boundaries among disciplines blur, and the traditional compartmentalization of research and training is stultifying as well as counter-productive. Arnold Beckman saw this in his crystal ball and took a chance. At the opening dedication of the BLI building in 1986, he said, “This is an experiment and only time will tell if it will be successful.” Let’s not forget his vision as we move through the 21st century.

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Newsbriefs

ELECTED FELLOW OF AIMBE
Director Bruce J. Tromberg, Ph.D., has been elected a Fellow of the American Institute for Medical and Biological Engineering (AIMBE). He was nominated and elected by The College of Fellows for outstanding achievements in medical and biological engineering. A formal induction ceremony was held during the Institute’s Annual Event in Washington, DC, on March 2, 2006, to induce the 98 new members. Over the years, AIMBE Fellows have helped to revolutionize medicine, engineering and related fields that enhance and extend the lives of people all over the world.

CRPF MEDICAL ADVISORY BOARD MEMBER
Dentistry Director Petra Wilder-Smith, Ph.D., D.D.S., has accepted an invitation to serve on the Medical Advisory Board of the Cancer Research and Prevention Foundation (CRPF). Since 1985, the Foundation has provided more than $80 million in support of cancer prevention research, education and outreach programs nationwide and has played a pivotal role in developing a body of knowledge that is the basis for important prevention and early detection strategies.

RESEARCHERS PUBLISH STUDY OF PROTEIN MOLECULES
Zifu Wang, Ph.D., director of UCI’s Optical Biology Imaging Facility, and Michael W. Berns, Ph.D., the Arnold and Mabel Beckman Chair in Laser Biomedicine, recently reported on research involving Fluorescence Correlation Spectroscopy (FCS), a method that gives researchers a clear picture of how proteins dynamically interact with each other in live cells in real time. Wang, Berns and colleagues used FCS to demonstrate how fast a protein molecule moves around to bind to and escape from other molecules during the birth of a new cell. This knowledge may help scientists understand the cause of diseases, such as cancer, and design new pharmaceutical products. This work appears in the July 2006 issue of Biophysical Journal.

FIRST WEST COAST PORT WINE STAIN CONFERENCE
The Beckman Laser Institute (BLI) and the Vascular Birthmarks Foundation (VBF) co-sponsored the first West Coast Port Wine Stain Conference held at the BLI and the Fairmont Newport Beach hotel on October 7-8, 2005. Over 170 individuals were in attendance. The purpose of the conference was to provide information and support for families affected by port wine stains, hemangiomas and other vascular lesions. Past conferences have been held exclusively on the East Coast, and BLI Medical Director J. Stuart Nelson said, “I am pleased that BLI had this opportunity to provide this event to the many families who otherwise would not know about the excellent program available to them at BLI and

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Shared Instrumentation Grant Awarded

A ssociate Professor Vickie LaMorte, Ph.D., and her co-PI, Tatiana Krasieva, Ph.D., have been awarded a $500,000 Shared Instrumentation Grant from the National Institutes of Health to purchase a new Zeiss LSM 510 META NLO microscope. Additional funds for the remaining cost of the $750,000 system were arranged by Dr. LaMorte through Beckman Laser Institute and the Department of Biomedical Engineering.

The new Zeiss LSM 510 META NLO laser-scanning microscope is a state-of-the-art system. Housed on the platform of a Zeiss inverted Axiovert 200 M microscope, it combines standard fluorescence confocal imaging at six different excitation wavelengths with multi-photon fluorescence/second harmonic generation. The excitation source for this modality is a novel femto-second Chameleon Ultra laser (Coherent Inc.), which is tunable over an extremely wide range of wavelengths: from 690 to 1040 nm. One of the unique features of this system is its ability to detect second harmonic generation signals in both transmitted and reflected geometry. META detection provides fast, reliable and precise separation of the emission signals for multiple-labeled samples with widely or almost completely overlapping emission spectra of fluorophores on a pixel-by-pixel basis. Specifically, the new Zeiss META imaging system with two photon capabilities will enhance Dr. LaMorte's ability to examine protein-protein interactions occurring within a single cell. Coupled with Fluorescence Resonance Energy Transfer or FRET-based methodologies, this system will provide spectral separation of the GFP molecules that Dr. LaMorte and her lab use to tag the proteins they are interested in examining with pixel-by-pixel resolution. In combination with the subcellular imaging volume that can be achieved by two photon excitation, they will have resolution of these cellular events that was not obtainable with the previous existing systems. Not only will Dr. LaMorte and her lab be able to determine if two proteins interact in vivo within the confines of the cell but now they will be able to see precisely where this interaction is occurring within the cell's architecture. Ultimately, by mapping a protein's dynamic interplay with other proteins in the cell, a fundamental understanding of how this protein contributes to normal and diseased states will be achieved.

The system will be housed and supported within the well-established NIH Biomedical Technology Resource Center (Laser Microbeam and Medical Program, LAMMP) at the Beckman Laser Institute and will be used by a group of 13 multi-disciplinary investigators representing ten departments at the University of California, Irvine. The LAMMP facility is dedicated to defining and understanding broad issues related to the use of light as a tool to selectively perturb, monitor, and image physiology in cells and tissues. According to Dr. Krasieva, manager of the LAMMP facility, all of the original proposed projects were initiated as pilot/feasibility studies using a multi-photon excitation laser scanning system that she and her colleagues built themselves and/or a 14-year-old LSM 410 confocal system. Now that the original projects have expanded in scope and require frequent and often heavy use of laser scanning microscopy, there was an urgent need for a commercial-grade, user-friendly confocal/multi-photon microscope to be housed and managed within the facility. The Zeiss META instrument will ideally accommodate the researchers' needs, which range from low-light-level endogenous signal detection of both fluorescence and second harmonic generation (SHG) in tissues to cellular FRET-based imaging.

Dr. LaMorte expects that the Zeiss META instrument will have a significant overall benefit to the UCI research community and beyond based on the existing strong impact of the LAMMP and its dissemination of new discoveries to colleagues and collaborators.

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other supporting institutions.”

The conference was made possible through generous contributions from UCI Research Associates (Athalie Clark Research Award); the Board of Directors of BLI, Inc.; Ms. Patricia Beckman; Candelia Corp.; UCI Medical Center; Richard and Betty Kasper; Mary Roosevelt; BLI Director Bruce Tromberg, Ph.D.; and Dr. Stuart Nelson. VBF Founder and President Linda Rozell-Shannon commented, “This was our most successful family/physician conference ever and we are looking forward to the next conference at BLI in 2007.”

ELECTION AND PRESENTATION

Dentistry Director Petra Wilder-Smith, Ph.D., D.D.S., has been elected to the
Douglas C. Wallace, a founder of the field of human mitochondrial genetics, has received a $2.25 million award from the Doris Duke Charitable Foundation to study how metabolic disorders may be triggered by genetic changes in the mitochondria, the power plants of human cells.

“Our receipt of this prestigious award is the direct consequence of UCI’s vision of becoming a world leader for the new biomedical discipline of mitochondrial medicine,” said Wallace, director of the Center for Molecular and Mitochondrial Medicine and Genetics (MAMMAG) at UC Irvine and National Academy of Sciences member.

With the Doris Duke Clinical Interfaces Award, which will provide funding for five years, Wallace will lead a multidisciplinary team of UCI researchers, which include physicians Dr. Ping Wang, Dr. Lee-Ming Chuang and Dr. Jay Gargus; biomedical engineer Bruce Tromberg, director of the Beckman Laser Institute; and atmospheric chemists Donald Blake and F. Sherwood Rowland, who received the Nobel Prize in Chemistry in 1995.

The team will study genetic variation in the DNA of mitochondria and its association with the various symptoms of the metabolic syndrome (the risk factors behind diabetes, obesity, hypertension, high cholesterol and cardiovascular disease). Wang, Chuang and Gargus will collect mitochondrial samples from metabolic syndrome patients of Chinese heritage in Taiwan and in Southern California. Wallace's team at MAMMAG then will conduct extensive molecular and biochemical studies of these samples to see if variations in mitochondrial DNA as well as environmental factors affect individual predispositions to the clinical symptoms of metabolic syndrome.

At the same time, Gargus and Wallace will work with Blake, Rowland and Tromberg to develop rapid, non-invasive methods to diagnose metabolic syndrome. Atmospheric chemists Blake and Rowland will use their expertise with breaking down the components of gases to perfect a breath-analysis system that can evaluate changes in the breath chemistry of mitochondrial metabolic syndrome patients. Tromberg is working on an infrared laser system that can evaluate certain aspects of mitochondrial physiology by shining light directly into the skin.

“By correlating the results of these cutting-edge technologies with those of MAMMAG's molecular and biochemical analyses, our consortium hopes to not only extend our knowledge of the role of mitochondrial defects in the metabolic syndrome but to perfect simple, non-invasive diagnostic tools that will permit the rapid identification of mitochondrial patients within the doctor's office,” Wallace said.

**UCI Team to Study Mitochondrial Role in Diabetes, Obesity and Cardiovascular Disease**

Executive committee and as member-at-large for the Diagnostic Systems Group of the International Association for Dental Research (IADR), the most prestigious dental research organization worldwide. Dr. Wilder-Smith also gave a lecture entitled, “Non-invasive Imaging in the Oral Cavity: Current Status and Future Potential,” on June 16, 2006, to the planning committee on research priorities at the National Institute for Dental and Craniofacial Research in Washington, DC.

**VASCULAR BIRTHMARKS AND MALFORMATIONS DIAGNOSTIC AND TREATMENT CENTER**

This year the Beckman Laser Institute (BLI), in collaboration with the University of California Irvine Medical Center (UCIMC), established the Vascular Birthmarks and Malformations Diagnostic and Treatment Center (VBMDTC). The VBMDTC is comprised of a multidisciplinary team of medical specialists designed to provide accurate diagnosis and current treatment options for patients and their families who are affected by vascular birthmarks or malformations, including port wine stains, hemangiomas, arteriovenous malformations, and lymphatic malformations.

The multidisciplinary team headed by J. Stuart Nelson, M.D., Ph.D., Medical Director of BLI, consists of such specialists as anesthesiologists, dermatologists, head and neck surgeons, ophthalmologists, orthopedic surgeons, plastic surgeons and radiologists. Comprehensive services offered by the VBMDTC include: consultation, diagnosis, second opinion, treatment, on-going assistance to primary-care and specialist physicians, information about vascular birthmarks or malformations, information on support and networking groups, and information about insurance coverage and other matters relating to receiving care.

The VBMDTC will hold quarterly outpatient clinics for evaluation of patients in which representatives from each key medical discipline will meet with patients and their families. The team will form a consensus on diagnosis and treatment, which

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George E. Hewitt

IN MEMORIAM

George E. Hewitt passed away on June 10, 2005. He was one of the earliest friends and supporters of the Beckman Laser Institute and served on the Board of Directors from its inception until 2003. Mr. Hewitt, a pioneer in civilian applications of radar, began his relationship with UCI and its students in 1983 when he established the George E. Hewitt Foundation for Medical Research to support postdoctoral fellows pursuing biomedical science at a number of universities. Director Bruce Tromberg began his career at BLI as a Hewitt Fellow in 1990. Mr. Hewitt’s generous support of UCI culminated in March 2000 with a $5 million gift from him and his wife, Dottie, who died in December 1999, to construct the Dottie and George Hewitt Research Hall, completed in 2003. The building houses researchers who focus on such areas as how cells react to microbial disease-causing agents, how viruses work, and ways to prevent and treat major infections. They also study how the immune system works and how it sometimes turns on itself to cause certain immune disorders such as arthritis and multiple sclerosis. The faculty and staff at BLI remember George Hewitt as a friendly, outgoing person with a perennial smile who would talk to anyone and everyone. He was an extremely successful businessman and scientist, much in the same mold as Arnold Beckman. And also like Dr. Beckman, he was unassuming and felt his greatest contribution to the world was as a philanthropist.
Researchers at UC San Diego and UC Irvine have captured on video for the first time chemical signals that traverse human cells in response to tiny mechanical jabs, like waves spreading from pebbles tossed into a pond. The scientists released the videos and technical details that explain how the visualization effect was created as part of a paper published in the April 21, 2005, issue of *Nature*.

Researchers working at the UCSD Department of Bioengineering developed a novel molecular “reporter” system which allowed the dynamic visualization of the activation of an important membrane-associated protein called Src. Peter W. Wang, lead author of the paper and a postdoctoral researcher at UCSD spent two years designing the reporter molecules to light up selectively only when Src was activated and not other proteins.

Wang and his co-workers studied the effect of mechanical stimuli on Src activation. Using technology developed at the Beckman Laser Institute by its founding director Michael W. Berns, Wang and Elliott Botvinick, a former Beckman fellow, attached small, sticky beads to cells and gently tugged the beads to and fro with laser power acting as invisible “tweezers.” As the laser tweezers moved the beads in one direction, a video camera attached to a specially equipped microscope recorded the dynamic movement of biochemical signals in the opposite direction in the form of a signature pattern of fluorescent light.

“We had no idea what to expect,” said Wang. “It was amazing when we first saw these incredible waves spreading across the cells. We expected to see a signal where the tweezers were pulling the beads, but we did not envision such a directional wave propagating away from the beads.”

Src is one of a large group of enzymes called kinases that attach a phosphate molecule to one or more target proteins in the cell. This phosphorylation reaction typically switches the target protein from inactive to active status. Many diseases can result either when a kinase gene is mutated and can’t properly phosphorylate its targets or when a normal kinase becomes overactive or not sufficiently active. Indeed, Src has been shown to play a key role in cell growth and development and in theogenesis of cancer, atherosclerosis, and many other disease conditions.

According to Shu Chien, Professor of Bioengineering and Medicine at UCSD and senior author of the paper, “This study amounts to a proof of principle that if we can visualize the activation of one kinase, we can do the same for many others using the same approach.” Not only are those additional studies expected to reveal temporal and spatial patterns of kinase activation, but Chien also predicted that there will be practical spin-offs, such as a diagnostic test for many cancers.

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**Berns (cont’d from p. 1)**

edited six books that have been translated into several languages, including Chinese, Japanese, and Serbo-Croatian.

Dr. Berns joined the faculty of the Department of Developmental and Cell Biology at UCI in 1972 where he first served as departmental vice-chair and then Chair. In 1994, he received the UCI medal, the highest honor awarded at the University of California campus. In addition to being the co-founder of the Beckman Laser Institute, he was the founding director of the Center for Biomedical Engineering at UCI which is now the Department of Biomedical Engineering.

Dr. Berns was recently recognized as being in the top 5% nationally of NIH funded scientists for total funds received over the past 25 years, as well as in the top 20% nationally for patents awarded to medical school faculty who have been funded by the National Cancer Institute of the National Institutes of Health.

Following presentation of the lifetime achievement award, Dr. Berns presented a lecture entitled, “Laser Scissors and Tweezers in Space and Time,” a summary of the past, present and future research of his students and collaborators.

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**Nelson (cont’d from p. 1)**

direct clinical practice with a focus on serving patients with pediatric port wine stain birthmarks and other hypervascular dermatoses. He is also a member of the panel of experts on the Vascular Birthmarks Foundation website, responding to families who have inquiries concerning the diagnosis and treatment of port wine stains.
ARRIVALS

David Abookasis, Ph.D., joins BLI as a postdoctoral scholar to work on non-invasive optical imaging for quantitative assessment of traumatic brain injury.

Jeffrey Beckwith has joined BLI as the payroll/personnel coordinator.

Katherine Bhan, Ph.D., has been hired at BLI as a postdoctoral scholar to collaborate with Dr. Jerry Spanier and Project Scientist Dr. Carole Hayakawa on research aimed at accelerating the convergence of Monte Carlo photon transport simulations.

Devilyn Callian joins BLI as purchasing assistant.

Yongseok Chae, Ph.D., was hired as a postdoctoral scholar at BLI to work on the development of surgical systems and devices to perform minimally invasive laser surgery of the head, neck, and upper airway.

Muffie (Janet) Cooper is the new Executive Assistant to BLI Director Bruce Tromberg. She comes to BLI via Housing Administrative Services where she was the Management Assistant for the Assistant Vice Chancellor of Housing.

Jinseob Eom joins BLI as a visiting researcher to work on a project entitled, “Frequency Swept Source with a Rotating Slit for Frequency Domain OCT.”

Enrico Gratton, Ph.D., joins the UCI faculty as Professor with a joint appointment at BLI and the Department of Biomedical Engineering.

Hagyong Kihm, Ph.D., has joined the BLI as a postdoctoral scholar within the Laser Microbeam and Medical Program and will focus on the further development of POISe: an interferometric technology that will enable wide-field spectroscopic imaging of thick tissues.

Jae Gwan Kim, Ph.D., has been hired as a postdoctoral researcher to uncover the origins of optical biomarkers detected in clinical breast cancer research studies by performing detailed optical measurements of tumors in animal models.

Shwayta Kukreti joins BLI as an M.D., Ph.D. student of Enrico Gratton, Ph.D., who is developing new spectroscopic analysis methods to uncover optical biomarkers that link optical measurements of breast lesions with tumor biochemistry and histology.

Alice Lee, M.D., is a UCIMC Otolaryngology resident doing research at BLI under the direction of Brian Wong, M.D. Other residents who will be doing research at BLI with Dr. Wong later in the year are Drs. James Ridgway, Paul Holden and Ali Sepehr.

Ryan Lim is a graduate student working with Bruce Tromberg, Ph.D. He is doing multiphoton imaging of collagen and vulnerable plaque in atherosclerosis.

Justin Lotfi has been hired at BLI as a lab assistant to develop standard operating procedures for sterile animal surgery methods and in vivo optical imaging that targets chronic therapeutic monitoring.

Eric Potma, Ph.D., was appointed Assistant Professor of Chemistry at UCI and joint member of the Beckman Laser Institute faculty.

Kana Sato has been hired as a lab assistant to work on the non-invasive diagnostics projects with emphasis on oral cancer and dental de- and re-mineralization.

Jared Stephens is a graduate student who is working in the lab of Michael Berns, Ph.D. He is studying repair of laser-induced DNA damage during mitosis.

Wendy Tanamai is a recent graduate of UCI and was hired at BLI as a lab assistant to help with clinical breast measurements using the Laser Breast Scanner.

Nicole Wakida is a graduate student working in the lab of Michael Berns, Ph.D. Her research involves studying microtubule structure and dynamics in cell motility using a femtosecond laser system.

DEPARTURES

Sean Merritt, Ph.D., has taken a position at Masimo as an algorithm engineer. Payroll/Personnel Manager, Kristen Caplin, has moved to the UCI School of Biological Sciences to become a Senior Personnel Analyst.

Rhong Zhang, Ph.D., has left BLI to be a stay-at-home mom of twin boys.
will be presented to the family. This unique program allows patients to be seen by more than one specialist at the same visit and allows physicians to share their mutual assessments and concerns with patients and their families. Thereafter, patients will be directed to the appropriate medical specialists for treatment and follow-up.

**GRANTS AWARDED**

The UCI Cancer Center has awarded a seed grant for $15,000 to Dentistry Director Petra Wilder-Smith to develop *in vivo* molecular-based imaging in the oral cavity.

The UCI Cancer Center has also awarded a $15,000 seed grant to Assistant Professor Anthony Durkin, Ph.D., for “Quantitative Diffuse Optical Spectroscopy of Benign and Malignant Cutaneous Melanocytic Lesions.” In collaboration with Modulated Imaging Inc., Dr. Durkin has also received a Small Business Technology Transfer (STTR) Phase 1 grant from the National Institutes of Health entitled “Spatially Resolved Tissue Oximager.”

Amy Hellman, a biomedical engineering graduate student, received a $100,000, two-year Graduate Research and Education in Adaptive Biotechnology training grant from the UC systemwide Biotechnology Research and Education Program. These grants are among the highest individual awards given for graduate education and training in the nation. Hellman is researching the development of a laser microbeam/microscope platform for rapid single cell bioanalytics under the direction of Associate Professor Vasan Venugopalan and Nancy Albritton, Professor of Physiology and Biophysics.

**GORDON RESEARCH CONFERENCE**

Affiliated BLI faculty member Vasan Venugopalan, Sc.D., Associate Professor of Chemical Engineering, Biomedical Engineering and Surgery was Chair of the New Technology/Methodology I session at the Gordon Research Conference on Lasers in Medicine and Biology held July 2-7, 2006, in Plymouth, NH. BLI graduate student, David Cuccia, Department of Biomedical Engineering, participated in the session by presenting a talk entitled, “Modulated Imaging: Quantitative Imaging of Intrinsic and Extrinsic Tissue Optical Properties and Chromophores in the Spatial Frequency Domain.” Another affiliated BLI faculty, Eric Potma, Ph.D., Department of Chemistry, gave a talk in the Cellular/Subcellular Imaging and Manipulation session entitled, “Looking at Biology with CARS.”

**STUDENT RESEARCHER TO ATTEND HARVARD MEDICAL SCHOOL**

Chao Li, an undergraduate student working in the lab of Brian Wong, M.D., Ph.D., has accepted a place in the first-year class of the New Pathway Program at Harvard Medical School entering in September 2006. Chao did research on how light and heat interact with human and animal cartilage.■