LASER
BECKMAN LASER INSTITUTE

IN THE NEWS

SUMMER 2005

In Remembrance
ARNOLD O. BECKMAN, Ph.D.
1900-2004

Arnold O. Beckman (front row, fifth from right) and daughter, Patricia Beckman (front row, fourth from right), celebrate Dr. Beckman's 100th birthday with BLI staff.

Newsbriefs

ELECTED FELLOW OF AIMBE

Zhongping Chen, Ph.D., has been elected Fellow of the American Institute of Medical and Biological Engineering (AIMBE) for "outstanding contributions and leadership in the field of biophotonics and optical imaging." Prof. Chen was inducted in an official ceremony held on February 17, 2005, at the National Academy of Sciences in Washington, DC. AIMBE Fellows represent members of the bioengineering community who have made significant and leading contributions to their discipline in science and education. The number of Fellows is limited to the top 2% of the total number of individuals active in medical and biological engineering.

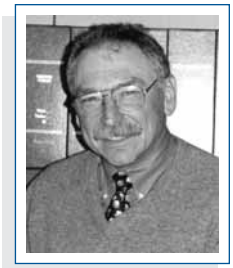
STUDENT WINNERS OF RESEARCH AWARDS

Vi Nguyen, an undergraduate 199 senior in the lab of Dentistry Director Petra Wilder-Smith, is the winner of the DSG/Eastman Kodak Student Research Award for 2005 for the abstract titled, "Early detection of dental caries using optical coherence tomography." The DSG/Eastman Kodak Award is given

(additional Newsbriefs continued on p. 3)

From the Beginning

by Michael W. Berns, Ph.D., Co-Founder



I first met Dr. Beckman on a rainy day in December 1980. He was one of a handful of Orange County CEOs who came to a laboratory open house that I was having to celebrate the opening of the Laser Microbeam Program (LAMP) funded by the National Institutes of Health. This was a facility that I had built in Steinhaus Hall on the UCI campus for the purpose of providing new state-of-the-art laser microbeam technology to the scientific community.

What impressed AOB the most was the fine precision with which we could manipulate organelles (in this case, chromosomes) with a focused laser beam. He remarked many times over the years that the combination of lasers with microscopes seemed to him to have a lot of "potential" for a wide variety of research areas – and this looked like it was truly on the "cutting edge."

Dr. Beckman with laser in hand at BLI.

After that first meeting, which definitely seemed to create some chemistry between us, a long and rewarding professional and personal relationship developed between the two of us. Particularly smitten by the fine precision of the laser microbeam (after all, AOB was a world's expert in bio-instrumentation development), he and I had several meetings over the next two years. He became more and more interested in this technology and wanted to support its further development in some way. I suggested that we build a "Laser Institute" on the UCI campus. However, his unwillingness to make substantial charitable donations to the University of California because, as he put it, "I already pay my taxes," presented a tremendous hurdle. So to the creative "drawing board" we went.

The solution was to establish a separate, non-profit corporation that would build and own a building (Beckman Laser Institute) on the UCI campus. The building would then be leased to UCI, and if all went well (i.e., both UCI and the BLI corporation obeyed the terms of the agreements), the building would become the property of the university in thirty years. Such an agreement between UCI and a separate private entity was groundbreaking as no such partnership like this had been entered into before. But the founding Chancellor of UCI, Dan Aldrich, recognized the potential payoff of such an arrangement, and he was a close and trusting friend of Arnold O. Beckman. I remember the day very vividly when Dr. Beckman presented the $2.5 million matching check to Dan Aldrich in his office. These two men (both of whom were well over six feet tall) represented the best of both the business and academic worlds. They both knew that the arrangement was "risky," but they both had such enormous trust in each other that they felt there was a high probability that the venture would prove successful and perhaps even be a model for future private-public partnerships.

So how has the "laser microbeam" that first fascinated Dr. Beckman almost 25 years ago fared with time? This is a relevant question because the "laser microbeam" has morphed into a system that is about to make its debut as an international "star" or, perhaps more modestly, a technology that will be accessible to researchers from anywhere in the world where there is an internet hook-up.

"RoboLase," as we call it, is a fully capable laser microscope that can be operated via a control panel on any standard desktop or lap top computer. Although there are still some bugs to be worked out, proof-of-principle experiments have already been carried out from the East coast of the United States to as far away as Brisbane, Australia, with our collaborator, Prof. Halina Rubinsztein-Dunlop.

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TECHNOLOGY TRIBUTE

Parallel Worlds

by Bruce J. Tromberg, Ph.D., Director

In his book *Imagined Worlds*, the great physicist Freeman Dyson wrote, "New directions in science are launched by new tools much more often than by new concepts." It seems Dyson had Dr. Arnold Beckman in mind when he made this insightful observation. As one of the world's most accomplished and influential inventors of new tools for scientific research, Dr. Beckman inspired a legacy that will long live on at the Beckman Laser Institute.

Dr. Beckman also provided us with many quotable observations, and one in particular captures the essence of the connection between his life's work as a scientist and inventor and the core mission of the five Beckman Institutes at UCI, Caltech, University of Illinois, Stanford, and City of Hope. In his straightforward style, Dr. Beckman observed, "If you're not taking risks, you're probably not doing very much."

While this adage provides the philosophical foundation for all of the Beckman Institutes, it stands as the key thread of connection between Dr. Beckman and the Beckman Laser Institute. It is not an accident that Dr. Beckman was personally involved as co-founder, along with Dr. Berns, of the BLI – the first of all of the Beckman Institutes. His role in our center was special, a reflection of his lifelong passion for invention and an inspiration that remains as palpable today as it was 25 years ago when Dr. Beckman first visited Dr. Berns' laser microbeam lab in Steinhaus Hall.

During the 1930s and 1940s, Dr. Beckman advanced a series of technologies that were based on his own unique ideas and vision as a scientist. Many of these are famously familiar examples: the first pH meter using new vacuum tube technology that was capable of reliably and stably amplifying weak electrical currents; the first precision spectrophotometers, the DU and IR series, that gave scientists access to broadband spectrophotometric measurements ranging from the ultraviolet to the infrared; the first hand-held oxygen analyzers, radiation dosimeters, micrometers, and portable gas analyzers.

Although Dr. Beckman was Caltech's "Professor Beckman" in the early '30s when he conceived of his first high-impact device, the pH meter, these new concepts clearly needed an original framework, an independent structure to nurture their growth and stimulate their success. To accomplish this, Dr. Beckman formed "National Technical Laboratories" in a garage in Pasadena which several years later evolved into Beckman Instruments.

In some ways, the Beckman Laser Institute is like that garage in Pasadena. We began with the promise of a new technology, pioneered by Dr. Berns, based on a new concept: laser

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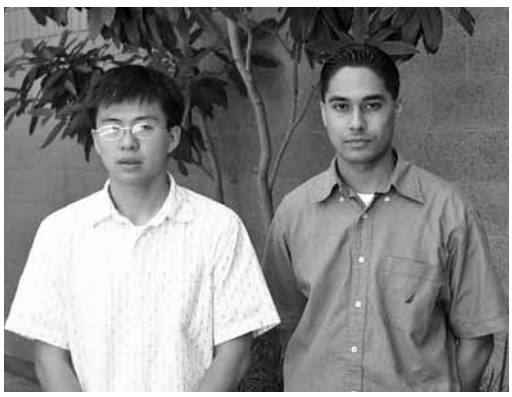
(Newsbriefs cont'd from page 1)



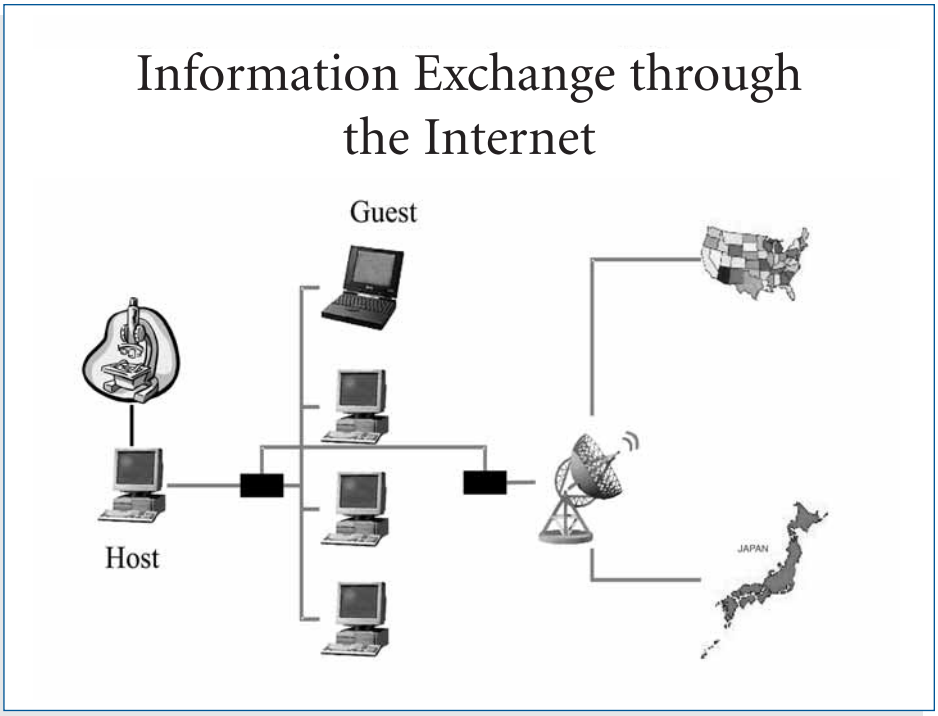
Pictured left to right: Chao Li, Usama Mahmood. Not pictured: Vi Nguyen.

annually for the best abstract submitted by a student for presentation at a Diagnostic Systems Group (DSG) of the International Association of Dental Research (IADR) General Session. The IADR is the most prestigious and comprehensive dental research organization worldwide, and Ms. Nguyen competed against graduate, dental postgraduate and postdoctoral students. She received a plaque and a $1,000 award made available, in part, from a fund donated by the Eastman-Kodak Company to the DSG of the IADR.

Chao Li, a 199 student in Dr. Brian Wong's lab, was awarded a $2,400 fellowship in support of his proposed research project, "Multi-photon microscopy of the extra-cellular matrix peripheral to thermal injury in laser-irradiated hyaline cartilage," for Summer 2005 by the UCI Interdisciplinary Summer Undergraduate Research Experience (ID-SURE) Selection Committee. Mr. Li will present his research results and findings at the UCI Undergraduate Research Symposium scheduled for May 13, 2006. In addition, he is invited to submit a research paper

(additional Newsbriefs continued on p. 8)

From the Beginning *(cont'd from page 2)*



The Robolase microscope is interfaced with other guest-users (UC campuses/ Beckman Centers) via the Internet. It allows for multiple collaborators to work on a single experiment from different centers around the world.

Once fully operational, RoboLase will allow either individual or multiple collaborators to conduct experiments on a sophisticated laser microscope that basically would be too expensive or too complex for them to have in their own labs. RoboLase will also afford a unique opportunity for students at all levels to train on this new technology. It is not surprising that the major achievements of the RoboLase system have been due to the dedicated and "consumptive" effort of Dr. Elliot Botvinick, whose work has been supported through the Beckman Fellows program of the Arnold and Mabel Beckman Foundation.

The unique microscope technology that first interested Dr. Beckman is about to go "virtual" in a way that neither he nor I could possibly have imagined 25 years ago. One of the keys to Arnold Beckman's success was his willingness to take chances on new endeavors that may have seemed risky to an ordinary person. All of us at the Beckman Laser Institute need to be cognizant of the fact that without Arnold Beckman's wisdom and foresight, the Institute would not exist and none of us would be where we are today. ■

(Parallel Worlds cont'd from page 3)

microbeams. In order to support the growth and impact of these tools, a new structure was needed, and the Beckman Laser Institute was born. Ironically, it is difficult to imagine a multidisciplinary center such as ours thriving in a traditional academic environment.

Starting essentially as an extension of Dr. Berns' lab with a few students and postdoctoral fellows, BLI has grown dramatically over 18 years of operation. We have welcomed an incredible group of inventive scientists and engineers who have expanded the use of lasers and optics in biology and medicine, developing new tools and technologies at an extraordinary pace. Today, we have 13 faculty members and approximately 150 affiliated scientists, fellows, students and staff with an annual budget of more than $10 million. And, much like Dr. Beckman's original passion, our mission involves developing state-of-the-art tools for scientific research.

But the connection runs even deeper than that. BLI scientists work on problems that are remarkably similar to the concepts that Dr. Beckman himself pioneered. Clearly, his greatest passion was at the interface between biological and physical sciences. This is precisely where the Beckman Laser Institute is today, thriving in this great intersection and expanding the common link between Dr. Beckman's world and the world of BLI.

Much like Dr. Beckman's pH meter, Dr. Berns' laser microbeam technology was the first platform: informing us of laser interactions with single cells, creating opportunities for subsequent tool development, and stimulating tremendous

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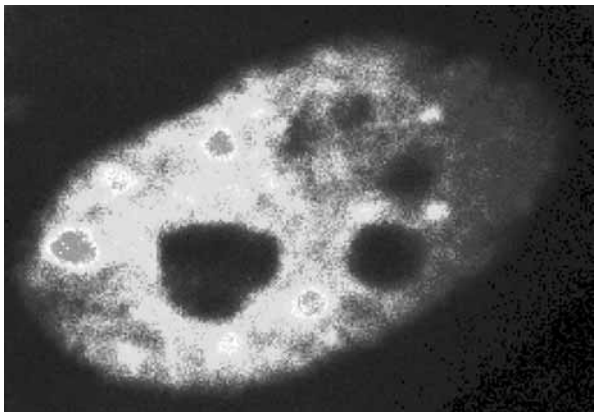
Looking into a Cell

Vickie J. LaMorte, Ph.D., is an Associate Professor at the Beckman Laser Institute. She has been at BLI for the past eight years developing ways to utilize optical techniques to examine the *in vivo* function of nuclear proteins. To do this, she is bridging traditional molecular biology techniques with biophotonics to develop new approaches to monitor a protein's function inside the cell. By utilizing advanced optical microscopy techniques, she is able "to peer into the cell" and monitor what a particular protein is doing.

Through funding from the American Heart Association, she was able to monitor proteins that play a very important role in cholesterol metabolism. Her findings were recently published in the April issue of *Molecular and Cellular Biology* entitled "Spatial Distribution and Function of Sterol Regulatory Element-Binding Protein 1a and 2 Homo- and Heterodimers by In Vivo Two-Photon Imaging Spectroscopy and Fluorescence Resonance Energy Transfer."

Cholesterol is a vital molecule for an array of biological processes as both a structural building block and a precursor to a host of signaling ligands. As important as cholesterol is to the vitality of the organism, it can be deleterious to its survival since there is no way to recover energy and carbon from this molecule. This results in a clinically well-described accumulation and deposition in the blood vessels where the blood flow is impeded. Key players in cholesterol regulation are the members of a family of transcription factors known as the Sterol Regulatory Binding Proteins (SREBPs). Transcription factors are proteins that bind to DNA and act as molecular switches to turn genes on or off. The cellular redundancy of this family of SREBP proteins is under investigation. What regulates these proteins to allow them to have differential roles in the cell and, ultimately, control over when certain genes are switched on or off is key to developing new drugs.



Fluorescence resonance energy transfer detection of SREBP-1a and SREBP-2 heterodimerization in vivo*: a two-photon fluorescence image of a single cell expressing SREBP-1aCFP/SREBP-2YFP in a foci pattern.*

Understanding the molecular dynamics of these SREBP proteins and how they function in the highly organized environment of the nucleus may provide clues to deciphering the cell's requirement for expressing seemingly similar proteins. By utilizing a fluorescent protein found in jellyfish, one can tag these different SREBP proteins and follow their movement within a living cell. This is done by engineering the DNA sequence of the jellyfish protein into the DNA sequence of the protein one wants to track. In essence, a fusion protein is created.

All of these advanced studies require recombinant DNA, and in order to isolate and re-engineer it, one needs the technology that Dr. Beckman developed. Without a *pH meter*, one would not be able to mix solutions that are compatible with the inside of the cell. A *spectrophotometer* is needed to know how much DNA or proteins are in a tube. And without a *centrifuge*, one would not be able to isolate the DNA from the bacterial cells that one commandeers to make the recombinant DNA.

From here, Dr. LaMorte is able to introduce the DNA into the cells with a very thin glass needle. After that, it is up to the cell to read the DNA and make the protein. Once the cell is expressing the glowing protein, Dr. LaMorte can utilize advanced optical tools to monitor this protein in the cell. She is able to know not only where the protein is going but with whom it is talking to along the way. Dr. LaMorte's observations of these proteins indicate a dynamic association between a specific member of this family, SREBP-2 and the PML-containing nuclear body, unlike its sister protein, SREBP-1, which does not appear to associate with this nuclear body. It was also demonstrated for the first time which proteins partner or "talk to each other" and when.

It is sometimes forgotten that basic instrumentation is the first step needed to advance studies like Dr. LaMorte's and her lab. Grateful scientists everywhere offer a special thank you to Dr. Beckman for inventing the basic technological building blocks that are the keystones to research today. ■

CLINICAL TRIBUTE

Perpetuating the Legacy

by J. Stuart Nelson, M.D., Ph.D., Associate Director

When I first arrived at the University of California at Irvine, my main goal was to earn a Ph.D. in cell biology and applied laser biology. I had just received an M.D. from the University of Southern California, and I was anxious to do research and discover how lasers could be applied in the field of medicine. I was accepted into the Ph.D. program of the Department of Developmental and Cell Biology under the supervision of Michael Berns. It was 1981, and Michael's office and labs were located on the third floor of Steinhaus Hall. At that time, Michael was just beginning to interest Arnold Beckman in lasers and their practical possibilities for science. Little did I realize that their eventual collaboration would result in a life-long career for me at UCI and UCIMC.

Because of Dr. Beckman's generous donation, the Beckman Laser Institute and Medical Clinic opened in 1986. Michael was the Director of the Institute. I received my Ph.D. in 1987, and I became the Associate Director in April 1987, a position I still hold today. I decided to specialize in laser surgery on skin and focused my research on discovering the most efficacious ways to treat port wine stain birthmarks.

Port wine stain birthmarks can be, at the least, embarrassing and, at the most, disfiguring in adulthood. The best time to treat a port wine stain is when the patient is young. While some insurance companies no longer regard port wine stain treatment as purely cosmetic, there are many parents who cannot afford to have their children treated by laser. To give these children an opportunity for treatment here at the Institute, the Children's Treatment Fund was established. Donations from the public and private companies have enabled many children to be successfully treated for port wine stains and to feel that they are not different from "normal" children. That the Institute can help improve the lives of these children is extremely gratifying and a prime example of how Dr. Beckman's generosity affects so many people.

Today, I am also the Medical Director of the clinic and I continue to do research on port wine stains. We developed dynamic cooling for lasers that has become the worldwide standard for the treatment of birthmarks in infants. Dr. Beckman, the perennial scientist and inventor, would be proud that here at the Beckman Laser Institute, we have tried to emulate his legacy of creative thinking to effect a practical solution for a scientific problem. ■

(Parallel Worlds cont'd from page 4)

activity in basic research throughout the world. With microbeams as our foundation, BLI was established to nurture the growth of new tools to understand and manipulate laser interactions with biological tissues. And BLI's "dynamic cooling technologies" have dramatically accelerated this process, providing tools that have become among the most successful in the UC system. In fact, Dynamic Cooling Technology is now widely available in nearly 8,000 therapeutic lasers throughout the world.

And the parallels continue…in the 1940s, Dr. Beckman made broadband UV/Vis/IR spectroscopy accessible to the scientific community. BLI has pioneered similar technology for broadband spectroscopy and imaging in turbid media, including biological tissues. Even some of the applications are connected: Dr. Beckman's oxygen analyzer was used in the neonatal intensive care unit to assess incubator oxygen levels and prevent neovascularization in the eye that could lead to blindness. BLI's scientists have developed methods for measuring oxygen in the tissues of neonates and for acquiring high resolution images of blood flow and vessel formation in the retina.

He knew that with tenacity and imagination, from modest beginnings sprang endless possibilities. As Dr. Beckman was well known to say, "Everything in moderation, including moderation itself." Our connection with Dr. Beckman and his vision is further enhanced by the formation of new campus structures, such as the Chao Family Comprehensive Cancer Center and the Department of Biomedical Engineering, which benefit greatly from the resources of the Beckman Laser Institute. The scientists, fellows and students of BLI continue to embrace his spirit, relentlessly introducing new tools for discovery based on lasers and optics into our campus and throughout the world.

Ultimately, we have tried to remain true to Dr. Beckman's legacy. The scientists, fellows, students and staff of the Beckman Laser Institute will be forever thankful for Dr. Beckman's imagination and inspiration, for the height of his expectations and the depth of his passion. ■

Arrivals and Departures

ARRIVALS

Yeh-chan Ahn, Ph.D., has joined the research team of Zhongping Chen, Ph.D., and is working on microchannel flow dynamics.

Kuyoun Baik is a Visiting Graduate Student from Seoul National University, Korea, who is studying optical coherence tomography of acupuncture points with the research team of Zhongping Chen, Ph.D.

Midge Campbell joins BLI as the new Management Services Officer who is in charge of the administrative operations of the Beckman Laser Institute.

Kristen Caplin started at BLI in August 2004 as the Human Resources Manager who is in charge of personnel and payroll.

Roger Chiu Zarate, Ph.D., is part of the research team of J. Stuart Nelson, M.D., Ph.D., participating in projects in electronics and optics.

Sophie Chung is a Visiting Graduate Student from Seoul National University, Korea, who is working with the research team of Bruce Tromberg, Ph.D., and Albert Cerussi, Ph.D., studying high resolution spectroscopy in tissue.

Jenni Frank has joined BLI as the new Contracts and Grants Manager.

Jee Hyun Kim, Ph.D., has been hired to work on a series of projects devoted to determining the influence of port wine stain blood vessel geometry on laser therapeutic outcome. He is part of the research team of J. Stuart Nelson, M.D., Ph.D.

Back row, l. to r.: Jee Hyun Kim, Kristen Caplin, Yeh-chan Ahn.
Front row, from l. to r.: Sophie Chung, Jenni Frank, Midge Campbell, Ang Li.
Not pictured: Kuyoun Baik, Roger Chiu Zarate, Byeong Ha Lee, Sari Mahon, Paula Sweet.

Byeong Ha Lee, Ph.D., a Visiting Associate Researcher from Kwangju Institute of Science and Technology, Korea, has joined the research team of Zhongping Chen, Ph.D. to develop a fiber-based optical coherence tomography system.

Ang Li, Ph.D., joined BLI this year and is working on the development of a new multiple source-detector separation probe for a broad-band frequency domain instrument. He is working with the research team of Bruce Tromberg, Ph.D., and Albert Cerussi, Ph.D.

Sari Mahon, Ph.D., Assistant Project Scientist, is part of the research team of Matt Brenner, M.D., that is developing a fiber optic bundle-based optical coherence tomography probe.

Paula Sweet, Staff Research Associate IV, works on core facility projects for George Peavy, D.V.M., J. Stuart Nelson, M.D., Ph.D., and Bruce Tromberg, Ph.D.

DEPARTURES

Management Services Officer **Cathy Ledray** has moved to the UCI Department of Physiology and Biophysics to become Chief Administrative Officer.

Roman Zorin, Jr. Specialist, is now working at Advanced Bionics as a technical and sales representative.

NEWSBRIEFS

(cont'd from page 3)

for possible publication in next year's UCI Undergraduate Research Journal.

Usama Mahmood, a medical student at UCI, received the Mentored Medical Student Clinical Research Award for 2004-2005 from the UCI General Clinical Research Center. The total award is $20,000. Mr. Mahmood, under the guidance of Brian Wong, M.D., is involved with several projects including clinical optical coherence tomography on laryngeal patients.

GRANT AWARDS

Brian J.F. Wong, M.D., was awarded a Multi-Investigator Faculty Research Grant from the UCI Academic Senate Council on Research, Computing and Library Resources for "Mechanisms accompanying laser-induced chondrocyte proliferation."

Bernard Choi, Ph.D., was awarded the 2004 American Society of Laser Medicine and Surgery (ASLMS) $15,000 Research Grant. Dr. Choi presented his work at the 2005 ASLMS Annual Meeting on March 30-April 3, 2005, at Lake Buena Vista, FL. The grant is available to an ASLMS member with less than five years postgraduate training.

ELECTION TO HONOR MEDICAL SOCIETY

Lynn Leigh Chiu, class of 2005, was elected to the UCI Zeta Chapter of the Alpha Omega Alpha (AOA) Honor Medical Society. The eleven students elected represent some of the best students at the UCI College of Medicine. Ms. Chiu does research with Brian Wong, M.D., and has focused her studies in two areas: photodynamic therapy in the treatment of keloids using a tissue-engineered model and laser cartilage reshaping with cryogen cooling.

IT'S A MATCH

Four researchers at the Beckman Laser Institute have been informed that they have been accepted into residency programs. Three have been working with Brian Wong, M.D. Lynn Chiu has matched into residency at the University of Washington in Seattle in the Department of Otolaryngology – Head & Neck Surgery. James Ridgway, M.D., has matched at UC Irvine, Department of Otolaryngology – Head & Neck Surgery. A postdoctoral fellow, Dr. Ridgway's research has focused mainly on optical coherence tomography (OCT). Kevin Ho has matched at University of Texas Medical Branch in the Department of Otolaryngology – Head & Neck Surgery. The fourth, Misbah Khan, M.D., who has been doing research with J. Stuart Nelson, M.D., Ph.D., has matched with the Department of Dermatology at the University of Medicine and Dentistry New Jersey – Robert Wood Johnson in New Brunswick, NJ. ■

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