

Director's Message	2
Research: Endangered Species	3
Clinical: Laser-Assisted IVF	4

Winter 2001-2002

BLI Patent Soars in Medical Laser Markets

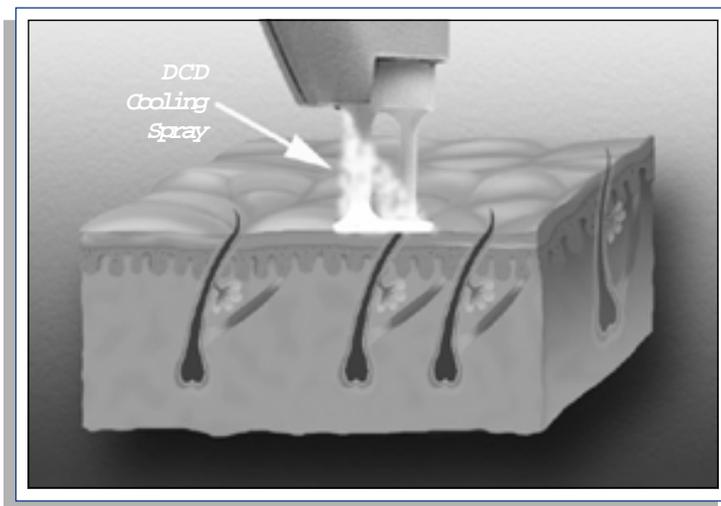
Researchers at the Beckman Laser Institute have scored a major success in the area of technology transfer with the licensing and marketing of a patented cooling device used for many of the most common laser-based medical procedures.

The Dynamic Cooling Device™ (DCD), which provides rapid and spatially selective cooling of the epidermis during laser treatments for a

variety of skin conditions, now ranks third in the University of California system for annual patent royalties. The DCD has earned \$3.8 million in royalties this fiscal year and could see a significant increase in earnings in the coming years as global sales for the device are expected to rise.

J. Stuart Nelson, M.D., Ph.D., Professor of Surgery and one of the inventors of the DCD technology, sees a bright future for this unique device. "Cryogen cooling has become an integral part of laser dermatologic surgery," Nelson says. "The premise is simple, but the design and implementation are extremely elegant."

The DCD delivers short bursts of cooled liquid cryogen to protect against thermal damage as laser energy is delivered through the skin to treat birthmarks, wrinkles, hair removal, and other dermatological irregularities. By protecting the upper layers of skin against heat-related damage, the DCD allows for more thorough and efficacious treatment. "Not only can (see DCD PATENT on p. 7)



The Dynamic Cooling Device™ applies a burst of cooling spray (see arrow) to the skin surface during laser procedures. The DCD patent has earned \$3.8 million in royalties this fiscal year.

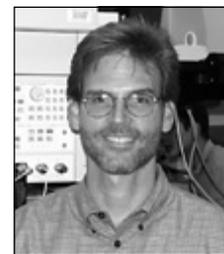
Newsbriefs

TROMBERG GARNERS AWARD

Associate Professor Bruce J. Tromberg, Ph.D., Director of BLI's Laser Microbeam and Medical Program (LAMMP), has received a 2001 *OE Magazine* Technology Innovator Award in the category of medical photonics.

Readers of the magazine nominate candidates in eight categories, then

vote for the engineers and scientists they feel contributed most significantly to the field. Award winners were profiled in the August 2001 issue of the magazine.



TROMBERG

(see NEWSBRIEFS on p. 8)

In Changing Times: A Tribute to George Argyros

by Michael Berns, Ph.D.

Arnold and Mabel Beckman Professor

Back in the 1980s, when Dr. Beckman and I founded the Beckman Laser Institute as a non-profit corporation to support laser biomedical research, I asked him who else we ought to recruit for our Board of Directors. "George Argyros," he said without hesitation. Naturally, we were delighted when George accepted our offer.

Nearly 15 years have passed since then, and it is with considerable sadness that I have learned that George is leaving our Board. He will be sorely missed, but the call and challenge of "national service" as the United States' ambassador to Spain takes precedence. All of us at BLI wish George and his wife, Judie, the best as they embark on a new challenge.

George, during your tenure on our Board your impact has been enormous. Your continued dedication to the ideals and principles of Arnold Beckman and your tough business mind have been crucial to the continued success of the BLI.

Unlike the other four Beckman Institutes/Centers established by the Arnold and Mabel Beckman Foundation, the Beckman Laser Institute has always enjoyed a unique status as a distinct entity, independent from its larger institutional setting (UCI). The Institute has maintained its own Board of Directors, and BLI both raises and invests its own money. This unique structure has allowed us to extend our influence rapidly and

broadly to other members of the academic and scientific community.

Over the past 16 years, the Beckman Laser Institute has gifted and granted funds for innovative laser research to at least twelve institutions in all regions of the United States, ranging from Harvard and the University of Pennsylvania in the Northeast, to Auburn and the University of Tennessee in the South, Oklahoma State University in the West, the University of Wisconsin in the Midwest, Stanford and UC Davis in Northern California, and UC San Diego, the Claremont Colleges, and UC Irvine in Southern California.

Though our corporate home has been on the UCI campus and UCI has benefited the most (over \$15 million) from our generosity over the past 16 years, the BLI has funded innovative research programs nationwide.

George, with your support and commitment to this vision, and with the sustained support of the Beckman Foundation, BLI has achieved its goal of making a *global* impact on medicine, biology, and engineering using lasers and other optical technologies. For that and much more, thank you.

As you embark on your new challenge, we, too, at BLI are embarking on a new and continued challenge to maintain the principles, ideals and vision that Arnold Beckman and I articulated when we formed the BLI non-profit corporation in 1984. Fortunately, as a separate corporation

(which has been funding projects across the United States almost since its inception), we have exciting opportunities for collaboration at a host of first-rate academic institutions. In addition, the construction of a new Beckman Center for Reproduction of Endangered Species (CRES) in San Diego provides another exciting venue for the application of laser and optical tools to the survival of this planet's endangered species (see pg. 3).

With so many new possibilities, it is still our desire to support UCI's laser programs, and we hope the current university administration is amenable although the nature of medicine and oversight are vastly different than even just five years ago. The world is changing, and new chal-

"With your support, BLI has achieved its goal of making a *global* impact."

lenges will require innovative solutions. As we look forward to new and evolving

partnerships, we also look back fondly on the partnerships and cooperation which have helped us to come this far.

George, although you and Judie are going to be immersed in a whole new world of international politics, I know I speak for all of us at the Institute when I say I am delighted that we will still be able to work with you through the Arnold and Mabel Beckman Foundation. Thank you for your support and for a wonderful partnership, and best of luck in your new post! ■

Saving Endangered and Threatened Species

by Michael Berns, Ph.D.

Arnold and Mabel Beckman Professor

Even as a little boy, I hung around the animals. Whether it was a stray cat, a lost dog, or a slithery king snake (I kept five snakes in my grandparents' New York City apartment), these creatures always held a deep fascination for me.

My love of animals continued into college. Though I went to Cornell wanting to become a veterinarian, I spent more time bird-watching and traipsing in the woods and gorges of upstate New York than in class. After spending consecutive summers on dairy farms (part of Cornell's pre-vet curriculum), I realized that I didn't want to spend the rest of my life peering into the backside of cows or trying to stuff a tube down the throat of a horse that clearly would have preferred to kick the daylights out of me.

So I turned to field biology, and I was fortunate to be taken under the wings of two wonderful Cornell biologists (Lowell D. Uhler and William T. Keeton). Both are gone now, but they were my first true mentors. I realize now how lucky I have been to have had mentors throughout my life (Howard Schneiderman and Arnold Beckman being the most recent).

Under Professor Uhler at Cornell, I completed my Masters' thesis on the field biology and developmental biology of "green" frogs that were actually an iridescent blue, like glitter on a young girl's face. It was an exciting challenge to determine why these rare frogs were blue and how

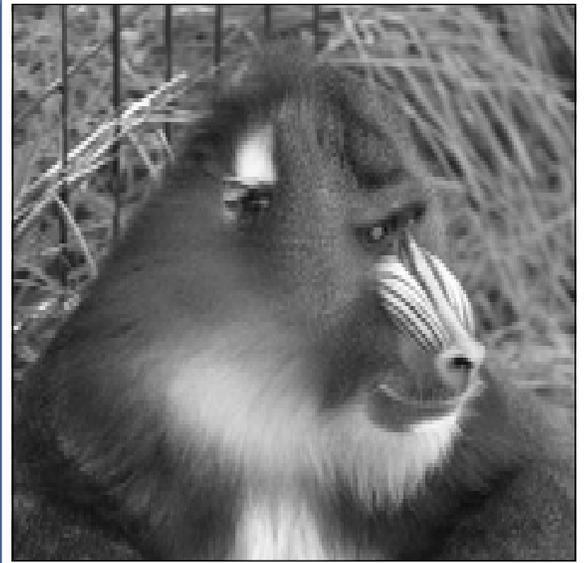
widely distributed they were in the northeast and midwest. We even found reports on these rare frogs from China.

This work led to my Ph.D. project, which I completed under the direction of William T. Keeton. Again, I did both a field and lab study, this time on the biology, distribution, and development of a common millipede. It was an obscure but fun project, and it landed me a senior-authored paper in *Science* before I even finished graduate school.

These fascinating little creatures (many of which are now threatened with extinction due to deforestation programs all over the world) come in all shapes and colors, but the one thing they have in common is lots and lots of legs and body segments. My task was to determine how they kept track of the number of legs and segments that emerge during development. And guess what? They can count! Even under adverse conditions, they still make the right number of legs; it just takes them twice as long, and they have to go through extra molts (shedding their hard outer skeleton for a bigger one).

A LASER-GUIDED CAREER PATH

This project became a study in evolution, adaptation, and survival of the species, and it allowed me to try a new "ray gun" called a "laser" to



Evolving Insight: New research into reproductive competition among monkey populations may ultimately provide significant insight into evolution.

perform delicate micro-surgical procedures through the microscope. The laser-surgery aspect of the study didn't work, but it launched my career in an entirely different direction once my Ph.D. work was completed, and it helps to explain the "evolution" of my current research.

Thanks to the generosity of the David and Lucille Packard Foundation, which has given approval to use earnings from the \$2 million Packard portion of the Institute's endowment, as well as the Arnold and Mabel Beckman Foundation's pledge to fund a new Center for the Reproduction of Endangered Species at the San Diego Zoological Society's Wild Animal Park, we are now embarking on a program to apply many of our BLI-developed technologies to the study

(see RESEARCH on p. 7)

Institute Spawns Laser-Assisted Hatching Studies

In its infancy, in vitro fertilization (IVF), the process by which eggs are removed from the ovarian follicles and introduced to sperm in a laboratory dish prior to re-implantation, was regarded by many as the stuff of science fiction. Fertility specialists have since turned that fiction into reality, and IVF is now common practice for couples who otherwise would be unable to have children.

More recently, researchers have employed micro-manipulation techniques to increase the chance of successful fertilization. Using glass pipettes (i.e., micro-needles) filled with specialized acids, fertility specialists have etched small trenches into the outer layers of the fertilized egg (*zona pellucida*), enabling it to cleave and “hatch” more successfully during the process of implantation.

Unfortunately, because this needle-based procedure lacks control and precision, it frequently damages the fertilized egg. Successful implantation rates have been relatively low, and IVF remains a costly, risky undertaking with no guarantee of success, especially for women over age 39.

All of this may be about to change. Studies are now underway to test the efficacy of a laser-assisted micromanipulation platform first developed in the laboratories of the Beckman Laser Institute.

EASIER AND SAFER IVF

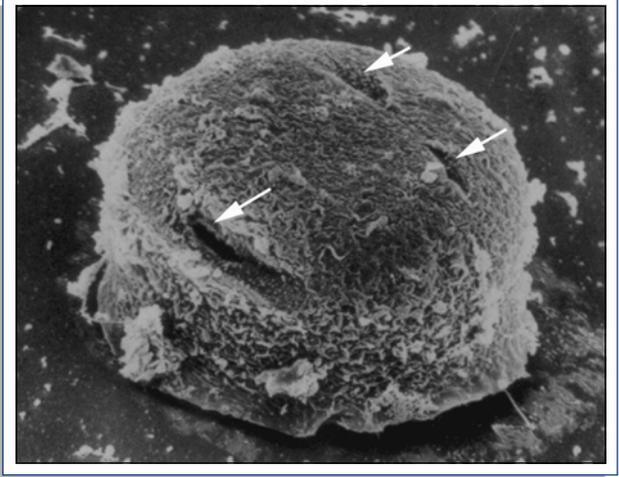
Yona Tadir, M.D., Professor of Surgery and Obstetrics and Gynecology, says breakthroughs in laser microscopy and micro-manipulation may

soon offer those who choose IVF dramatically improved pregnancy and delivery rates.

“This is far beyond what we imagined in 1988 when I first came to BLI,” says Dr. Tadir. “Back then, conventional micro-manipulation was still a novel technique, and nobody yet dreamed what the laser could offer in terms of ease, precision, and safety.” Zona drilling, as the technique is now called, creates patterned trenches on the outer layers of the fertilized egg, which then unfolds and “hatches” along these lines, allowing for better implantation in the uterine lining.

Zona drilling, which has not yet received approval from the FDA, has since migrated out of the BLI labs. Results of recent studies should help to move the technique through the approval process in the near future. It is currently practiced in human IVF clinics throughout Europe, Asia and Australia.

For Dr. Tadir, there is real satisfaction in pioneering a technique that offers so much promise. “Teams around the world now show the same positive results, says Tadir. “A handful of new studies indicate that we can achieve double the pregnancy rates and triple the delivery rates that conventional IVF has provided patients to this point.”



Ready to Hatch: Researchers can etch the outer layer of a fertilized egg with a laser for improved hatching. Here, a “smiley-face” has been created (see arrows).

FUTURE DIRECTIONS

In addition to the hope it offers for infertile couples, laser-assisted hatching has enormous commercial potential. Cell Robotics, Inc. (Albuquerque, NM) has sold the marketing rights for a laser-enabled IVF workstation to Hamilton Thorne Biosciences, Inc. (Beverly, MA), and sales are growing at a healthy clip. Three other companies sell a slightly modified system.

The same systems are also employed now in the rapidly developing field of pre-embryonic genetic diagnosis (PGD). Scientists can use the laser-microscope system to safely remove one of the dividing cells of the fertilized egg for disease screening and genetic testing.

“Seeing these systems on the market lets us know the research cycle works,” says Dr. Tadir. “It’s wonderful to see research and technology from the BLI ‘kitchen’ in the marketplace, making a real difference.” ■

A Desire to Give: One Man's Philanthropic Pledge

Editor's note: The Beckman Laser Institute wishes to thank John and Sylvia Michler for their generous commitment to the Children's Treatment Fund (CTF), which they seeded in 1989 to ensure that children with disfiguring birthmarks can receive appropriate treatment regardless of their family's income or ability to pay. I recently sat down with Mr. Michler to discuss his involvement with the CTF and to explore his commitment to local and global charities.

John Michler has made a personal pledge. After more than three decades in land planning and golf course design, Michler is fully committed to sharing his success with those who have been less fortunate in life. Philanthropy is now Michler's full-time passion, and he pursues his new venture with uncommon vigor.

"As my career developed and success came, I felt a desire to give," Michler explains while rummaging through the papers on his desk. He wants to share some pictures from a trip he made to Africa with Global Partners for Development, a rural development and hunger relief charity based in Santa Rosa, California.

Flipping through various snapshots (all of them featuring the smiling faces of those whose lives he has touched), Michler continues talking. "I hope the work I do inspires others to expand their own commitment to provide greater opportunities for all people."

What Michler does is nothing short of extraordinary. When he re-

tired at the end of 2000 from Hunsaker and Associates (Irvine, CA), he opened an independent consulting firm and earmarked all profits for charity. Michler's new venture donated over \$100,000 in 2001 alone.

Michler first became involved with the CTF ten years ago when he agreed to sponsor birthmark removal for a close friend's niece. "That was a wonderful gift for this little girl, but honestly I didn't think too much about it until recently. I was more focused on finding high-leverage charities — in other words, organizations which served a large population or promoted positive change in whole communities."

'A HIGH-LEVERAGE CHARITY'

Michler's attitude changed earlier this year when he was introduced to a young man with a disfiguring port wine stain on his face. "I could see that he lived behind a mask and that he wasn't comfortable around other people," says Michler. "I came to realize that birthmark removal is a high-leverage charity for those who live with these marks."

Michler immediately contacted BLI with an offer to sponsor the young man, who has subsequently begun treatment. More recently, Michler agreed to sponsor another patient, Cecile Inting, who had al-



Making A Difference: John Michler (center) will sponsor a birthmark removal procedure for Cecile Inting (right) through the Institute's Treatment Assistance Fund.

ready approached BLI with a request for assistance.

Michler recently had an opportunity to meet Ms. Inting and was encouraged by the results of her first treatment. "My involvement with the assistance fund and with young people like Cecile has been extremely rewarding. For me, it's always been fun to surprise people with a possibility that they didn't know existed or never dared to consider."

Michler hopes his philanthropic commitment will serve as an example to others: "I have always believed that people deprive themselves of a special joy when they shy away from opportunities to give."

If you would like more information about the CTF, or if you would like to make a donation directly to the program, please contact Erin Miller, BLI's Director of Development, at (949) 824-4111. ■

Reconstructive Surgery is a "Breeze" for Yellow Lab

Every so often, there comes along, through some glitch of nature, a dog whose bite is much worse than her bark. Luckily, doctors at the Beckman Laser Institute know just what to do in such cases.

When Meri Foreman, a kennel manager for Guide Dogs of America (Sylmar, CA), brought "Breezy" to the Institute for a consultation last year, the four month-old yellow lab was in poor shape. Born with a deformity affecting the tissue and bone on the roof of her mouth, Breezy had considerable difficulty eating and wasn't gaining weight. Not only was she unable to handle the rigors of the guide dog training program, her life was ultimately at risk. "With deformities of this severity, animals nor-

mally would not survive beyond a few months," explains BLI's Veterinary Director George M. Peavy, D.V.M. "It was clear right away that surgical intervention was Breezy's only hope."

Responding to Foreman's request for assistance, Dr. Peavy assembled a team of UCI surgeons, including Assistant Professor of Facial Plastic Surgery, Brian J.F. Wong, M.D., and Assistant Professor of Oral/Maxillo-facial Prosthodontics, Nelson Lowe, M.D., to begin the process of full palate reconstruction.

After four delicate surgeries, Peavy and his team managed to fuse Breezy's cleft palate and repair the gum and tissue deformities which had impaired her chewing and swal-



Sitting Pretty: Without surgical intervention at the Beckman Laser Institute, Breezy may not have survived to become a guide dog.

lowing. "Breezy was a model patient," says Peavy. "I expect she'll make a great guide dog." ■

Staff Profile: Diane Wilson, Analyst and Shutterbug

In her twenty-two years of university service, Diane Wilson has done "a little bit of everything." Before accepting a position at the Beckman Laser Institute in September of 1998, Diane worked in Central Purchasing and in Community and Environmental Medicine.

Originally hired at BLI as an Assistant Administrative Analyst, Diane was promoted to her current position as BLI's Financial Analyst one and a half years ago. The job suits her well. "I like numbers--of course, you really have to in this type of job--but I enjoy working with people, too," Diane says. "We're lucky to have a good

group in administration." Diane also enjoys the opportunity to contribute to a successful research program. "It's a challenge," she says, "but the cooperation is great, and the success rate we have in our grant funding is extremely gratifying."

Born in Queens, New York, Diane was raised in Southern California but still considers herself a "displaced Easterner." When she isn't traveling (recent trips include vacation ventures to London, the Grand Canyon, and Disneyworld), Diane can be found in the darkroom she has set up in her home. She currently serves as President of the South Coast Camera



Diane Wilson, BLI's Financial Analyst.

Club and has exhibited her work at the Orange County Fair and on the pages of a local travel magazine. ■

(cont'd from p. 3)

RESEARCH: HELPING TO PRESERVE ENDANGERED SPECIES

of rare and endangered species.

Two projects have already been initiated. The first of these employs the microscope-based optical tweezers that Dr. Yona Tadir and I pioneered to grasp and release single sperm cells in order to measure the force with which they swim. It turns out that female monkeys in several primate species mate with numerous males during estrous. As a result, their reproductive tracts will have sperm from different males which compete to fertilize the egg.

The theory is that sperm competition (dubbed "sperm wars") plays a crucial role in determining the direction of the "gene pool" and, ultimately, evolution. In other words, if a particular male has sperm that consistently out-compete the sperm from other males, that male's genetics will dominate the population. There is some evidence based on morphology of sperm that the mid-piece of the

sperm (which is the energy center for swimming) is larger in sperm from certain males. Therefore, their sperm should swim faster, and with more force, and should be more successful in fertilizing the egg.

This project is currently underway in San Diego and is a collaboration with the Director of CRES, Dr. Alan Dixson, and his post-doctoral fellow, Matthew Anderson, as well as myself and BLI's newly appointed Beckman Fellow, Elliot Botvinick. In two preliminary studies, we have shown that the laser tweezers can be used to "trap and release" monkey and mandrill sperm. More recently, we have begun to design another key series of studies on sperm competi-

We have begun to design another series of studies on sperm competition in rare and endangered primates.

tion in rare and endangered primates.

The second BLI-CRES project involves alligator sexing. Perhaps this is something we will report on in a future issue of the BLI newsletter. Suffice it to say we are excited about this new partnership and the promise it holds both for endangered species and for the "evolution" of the BLI research program.

Who would have thought that the basic and applied work that I have been involved with in my thirty-plus years of research would eventually return to my first passion — helping the animal kingdom? Of course, we have been doing this for years through the BLI veterinary program, but never before with the intention of preserving the planet's most precious and threatened species. ■

BLI NAMES SECOND BECKMAN FELLOW

Elliot Botvinick, Ph.D., has arrived as the Beckman Laser Institute's second Beckman Fellow. Botvinick joins the BLI research team having completed his doctoral work this past summer in the Department of Bioengineering at the University of California, San Diego.

Although his training at UCSD focused primarily on the development of biomedical instrumentation, Botvinick looks forward to delving more deeply into biological and medical research. "I have a lot to learn about the intricacies of cell biology," he says, "but I am enjoying the challenge, and the environment is great."

Botvinick is collaborating with In-

stitute Director Michael Berns, Ph.D., on two projects: the construction of a robotic laser-microscope and an investigation, co-sponsored by the San Diego Zoo, into sperm competition in monkeys (please see the "Research Update" on page 3).

Botvinick's fellowship is funded by the Arnold and Mabel Beckman Foundation as part of a \$1.1 million initiative to support young scientists in the field of optical biology. BLI's first Beckman Fellow, Anthony Durkin, Ph.D., is conducting research on analytical techniques to complement optical spectroscopy. A third fellow is expected to join Beckman Laser Institute in 2002. ■

(cont'd from p. 1)

DCD PATENT

we reduce the number of treatments that are necessary for these conditions by delivering higher light doses in a single session," Nelson says, "we can even adjust the cooling effect on an individual basis to optimize results for patients with different skin types." The end result is safer and better treatment for a variety of common dermatological conditions at a greatly reduced cost.

Nelson and his research team are currently working to develop a "second-generation" cooling device which would be coupled to an optical imaging sensor for real-time monitoring and thermal feedback. ■

NEWS BRIEFS

(cont'd from page 1)

"It's a wonderful honor to be recognized by your peers at a time when so much innovation is taking place in our field," says Tromberg.

MATH MODELING GRANT

Jerome Spanier, Ph.D., has been awarded a grant in the amount of \$192,621 by the Los Alamos National Laboratory to support his work on "Advanced Monte Carlo Transport Methods." The 12-month grant is administered as a subcontract to UCI and represents a continuation of work Spanier began in 1997 at the Claremont Graduate University.

Funding will be used to bring together on a single, dedicated computer a set of algorithms that Spanier and his colleagues have developed over the past five years. These algo-

rithms will be used to determine material properties in specific medical applications. The improved Monte Carlo methods may eventually be incorporated into the Los Alamos computer program, MCNP.

WILDER-SMITH UPDATE

The Cancer Research Foundation of America has awarded a one-year, \$35,000 grant to Dr. Petra



Wilder-Smith, Director of Dental Programs at the Beckman Laser Institute. The grant will support her work in optimizing early cancer detection.

Dr. Wilder-Smith recently con-

ducted a lecture at The Annenberg Foundation in Rancho Mirage, CA. Speaking at a forum for continuing education, Dr. Wilder-Smith's lecture detailed how new dentistry-related discoveries at the Beckman Laser Institute and elsewhere can apply to surgery, detection, prevention and diagnostics.

RESEARCH STUDENT GRANTS

Research students Sirintra Charoenbanpachon and Sheri Fago have been awarded American Society for Laser Medicine and Surgery (ASMLS) travel grants. The students will use the funds to present their work on non-invasive oral cancer detection at the 2002 ASMLS Meeting in Atlanta, GA.

Charoenbanpachon and another research student, Armen Boghosian, were awarded UC Irvine Undergraduate Research Opportunities Program grants.



BECKMAN LASER INSTITUTE

1002 Health Sciences Road East

Irvine, California 92612

<http://www.bli.uci.edu>

Nonprofit
Organization
U.S. Postage
P A I D
Santa Ana, CA
Permit No. 1202

Address Service Requested