LASER
BECKMAN LASER INSTITUTE

IN THE NEWS

Winter 2000-2001

Institute Launches New Fellows Program

With fresh funding in the amount of $1.1 million from the Arnold and Mabel Beckman Foundation, the Beckman Laser Institute is set to launch a five-year postdoctoral fellowship program for young scientists in the field of optical biology.

"This gift allows us to recruit the nation's brightest young scientists and place them in an interdisciplinary environment with access to the most sophisticated scientific and medical technologies," explains Institute Director Michael Berns.

Beckman Fellows will conduct research on the use of lasers to study biological and chemical processes in molecules, cells, and tissues, as well as applications of this knowledge to the development of biomedical engineering systems for optical diagnostics and the treatment of disease. At the end of their appointments, the Beckman Fellows are expected to assume tenure-track positions at major universities in the United States.

"Optical medicine holds enormous promise in fields like cancer treatment, cellular analysis, and non-invasive physiological imaging, and the Beckman Fellows will be part of our effort to put these exciting technologies in research and medical facilities in this country and around the world," says Berns.

The Beckman Foundation will fund additional research fellowships at four other Beckman Centers across the country. ■

Alexander Karn (left), Senior Writer for Development, accepts the Disneyland Community Service Award for Health Services on behalf of the Institute (see newsbrief below).

Newsbriefs

MAGIC KINGDOM AWARD

The Beckman Laser Institute was honored at the 43rd Annual Disneyland Community Service Awards ceremony, held Thursday, September 14, 2000, in the Disneyland Magic Kingdom.

BLI was one of six Orange County non-profit organizations to earn a distinction in the category of Health Services. In addition to a $5,000 check, the Disney Awards Committee presented BLI with a limited edition lithograph depicting Disneyland's Fantasyland castle (see photo above).

The cash award will help to support the Children's Treatment Fund (CTF), an indigent care program established in 1989 for the treatment of

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Is Technology Transfer Steaming on the Right Track?

by Michael Berns, Ph.D.
Arnold and Mabel Beckman Professor
President and Director

Two of my mentors, Arnold Beckman and David Packard, were among the pioneers in the transfer of ideas from academia to the real world. Their efforts have left an unmistakable imprint on society, academia, and the business world. But have these shining examples of industry and innovation become relics of the 20th century? Is the 21st century academic-turned-entrepreneur a reflection of these 20th century prototypes, or are they and the rapidly proliferating academic "tech transfer" programs horses of an entirely different color?

My concern stems from my own experiences and observations. Over the years, I have watched repeatedly as inventors squabbled over ownership rights and royalty percentages. I have seen faculty struggle with allocation of their time to potential royalty-yielding research projects at the expense of innovative basic research. I have seen students, collaborators, and post-docs excluded from lab discussions because of proprietary issues surrounding their projects. I have seen colleagues who could benefit from close collaboration keep their distance instead because one or the other principal just doesn't want to share inventorship. I have heard stories of scientists supplying their "competitors" with incorrect information at meetings so as to send rivals down some "blind alley." I have seen universities (not UCI) approach commercialization of intellectual property so aggressively that science "for the sake of the idea" has all but disappeared. I have seen education and the academic process corrupted.

One of my colleagues from a prestigious east coast university recently told me about an incident I could hardly believe. A scientist from a biotech firm was giving a widely publicized lecture at my colleague's campus. Just before the seminar started, a university official announced that (1) individuals not employed by the university would have to sign a secrecy agreement and (2) university employees in attendance were bound by the secrecy agreement which the university had already signed with their guest lecturer's biotech firm. Attendees were basically prohibited from discussing details of the seminar with people from outside institutions. I forgot to ask whether students in attendance were asked to leave as many probably were not employees of the university. Is this really what academia stands for: secrecy and inhibition of the free exchange of information and ideas?

I'm also concerned that this kind of atmosphere will help to accelerate academic "brain drain." How many of our best students no longer even

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Getting to the Root of Laser Dentistry

For those who want the facts on laser dentistry, there is an old adage worth remembering: things are never quite as bad as you imagine them to be, nor quite as good as you hope they are. "Whenever a new tool like the laser comes along, we see a kind of pendulum-effect within the profession," says Petra Wilder-Smith, D.D.S., Ph.D., Associate Adjunct Professor of Surgery and Director of the Dental Research Program at the Beckman Laser Institute.

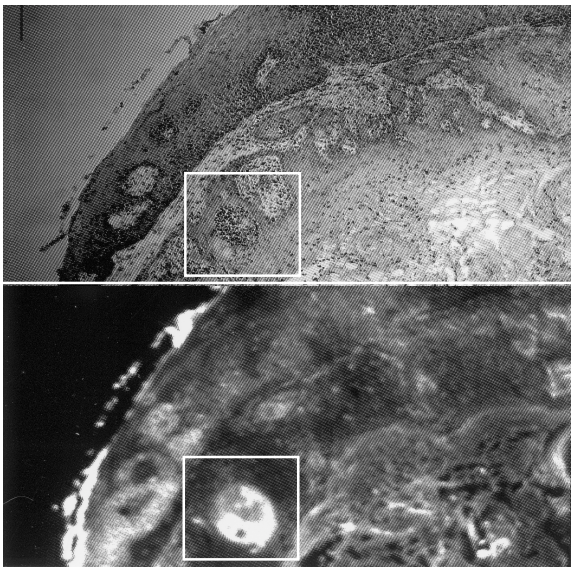
"At first, there is a sense of euphoria built on premature assertions that the perfect tool has finally arrived. Later, there is a sense of deep disappointment and even despair, as clinicians face the limitations of this new tool. Finally, the pendulum swings back to the middle where we can make a realistic assessment of what can and cannot be accomplished." So what promises and potentials does laser dentistry hold for the future?

Laser Diagnostics

As a therapeutic tool, lasers play a limited, albeit effective, role in the dentist's office. On the other hand, lasers offer excellent potential for a range of dental diagnostics. In fact, Wilder-Smith has secured more than $900,000 in new funding this year from the California Cancer Research Program, the Cancer Research Foundation of America, and the National Institutes of Health to develop "optical biopsy" techniques for the early detection of oral cancer.

Wilder-Smith and Diana Messadi, D.D.S., Ph.D., Associate Adjunct Professor of Oral Biology at UCLA, have already demonstrated in newly published studies that cancerous and pre-cancerous lesions in the mouth will fluoresce (i.e., glow) when they are treated with certain photosensitive compounds and subsequently exposed to the harmless red light that is emitted by diode lasers.

"This technique should allow us to make definitive diagnoses without surgical biopsy and, in addition, should help us to catch potentially deadly malignancies in their early stages when they still respond well to treatment," says Wilder-Smith.



Dental diagnostics: oral cancer is nearly invisible (top) under a conventional microscope, but the malignant cells glow when illuminated with a laser (bottom).

Lasers could also play a major role in the early detection and treatment of gum disease. Wilder-Smith is collaborating with Intelligent Optical Systems (Torrance, CA) to develop fiber-optic probes which can detect the biological agents responsible for gingivitis and gum disease. "If we can identify problem areas before there is significant damage, then there is a good chance we can selectively target and destroy the bacteria responsible for gum disease," explains Wilder-Smith. This would be a major development since conventional methods cannot detect the "bugs" which cause gum disease until irreversible damage has already occurred in the periodontic tissues which support our teeth.

Modeling the Mouth

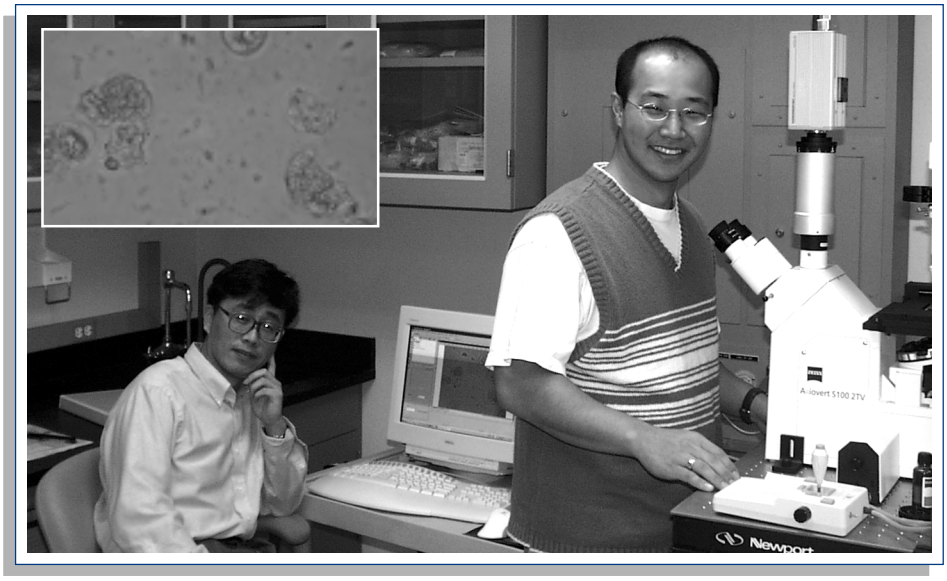
Another area where lasers might make a significant contribution is optical imaging and measurement of dental and orofacial structures. Wilder-Smith is working in conjunction with researchers at MetroLaser (Irvine, CA) to develop a device which could quickly and accurately construct "optical impressions" of a patient's teeth and mouth.

"Laser holography provides us precise measurement and representation," says Wilder-Smith. "With a three-dimensional image of the mouth, we could eliminate the need for plaster molds altogether." These digital images could even be moved over the Internet to labs where appliances and prosthetics could be tailor-made for the patient. Indeed, the future is bright for laser dentistry. ■

Gene Targeting and Inactivation Via Laser Microscope

For researchers at the Beckman Laser Institute, two photons really are better than one. Not only has multi-photon (two-photon) laser microscopy revolutionized the field of microscopic biological imaging, but it now seems likely that two-photon techniques will open new frontiers for cellular surgery, including gene targeting and gene inactivation.

"We've come to a point where we can target individual genes and, without otherwise damaging the cell, shut down active sites on single chromosomes," says Michael W. Berns, Ph.D., Director of the Beckman Laser Institute and senior investigator on the "gene inactivation" project. "A good deal of work remains before this can be applied practically, but the initial results have been extremely encouraging."



Zifu Wang, Ph.D., (left) and Joon You have equipped the Institute's two-photon microscope with remote capabilities, making it possible to perform experiments from off-site locations and transmit "live" data streams (inset) across the Internet.

Adjusting Our Focal Points

Lasers have been used to "knock out" the genetic components of chromosomes for close to thirty years. Berns' early single photon experiments with low power visible and ultraviolet lasers demonstrated that irradiation of nuclear material inside living cells could inactivate parts of chromosomes which had been "labeled" with photosensitive compounds.

Unfortunately, in these early studies, thermal and secondary damage produced by the laser was sufficiently severe to reduce cell survival. "It was like throwing the baby out with the bath water," says Berns. "We switched off the genes, but the cell couldn't endure the associated stress."

In the past decade, two-photon techniques, which deliver two light parcels of lower energy rather than a single photon with twice the energy, have allowed scientists to better pinpoint targets inside the cell. By relying upon focal point specificity, two-photon microscopy provides the capability to image and probe objects in extremely precise focal planes with little or no excitation or effect at other points surrounding the target.

"Whereas before we had to blast our way down to these structures, regardless of what was in our way, now we can deliver light beams which only produce their effects at fixed depths within the cell," explains Berns. "The upshot of this is that we can reduce or possibly even eliminate collateral damage to the cell's other organelles and structures."

In a recent study published in the *Proceedings of the National Academy of Science*, Berns and Beckman Laser Institute collaborators, Zifu Wang, Ph.D., Andrew Dunn, Ph.D., Vincent Wallace, Ph.D., and Vasan Venugopalan, Sc.D., report that two-photon gene inactivation is now possible with nearly 100% cell survival.

"In photomedicine, specificity and survival make all the difference," says Berns. "I think we've made big strides here in two respects: first, because we're able to introduce photosensitive molecules into the cell which localize where we want them and, second, because we're able to achieve the desired photochemical results in selectively targeted sites."

Scoping New Technologies

The preliminary success of two-photon gene targeting opens new possi-

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Loretta Sparks: Basking in the BLI 'Spotlight'

Loretta Sparks provided the show-stopper at last year's BLI Holiday Party. With microphone in hand and a twinkle in her eyes, Sparks, BLI's Personnel and Payroll Manager, treated faculty and staff to an earful of melodious talent.

"Karaoke has been a big part of our lives for about four years now," Loretta says a bit sheepishly. "My husband, Ted, is the real star, though. We just have fun with it."

Born in Indiana, but raised in Southern California, Loretta joined the BLI family in February 1998. After a temporary assignment as Office Manager for UCI's Palo Verde housing unit, Loretta made the switch to Human Resources. "I love to be around people, so the change was a good one for me." Loretta admits that "there are days" when juggling the demands of the job can be a challenge, but she is convinced that the rewards outweigh the stress. "I'm lucky to work in a diverse environment," she says. "I truly believe that we can learn something from everyone who crosses our path."

Outside the workplace, Loretta has plenty to keep her busy. She is actively involved with Beta Sigma Phi, a national women's service organization. Last year, Loretta and her fellow BSP members in California helped to raise over $100,000 for scholarship programs and charities. Loretta also became a grandmother this year. "Daniel is my joy. After a million kisses, he knows me." ■

Loretta Sparks, BLI's melodious Personnel Payroll Manager.

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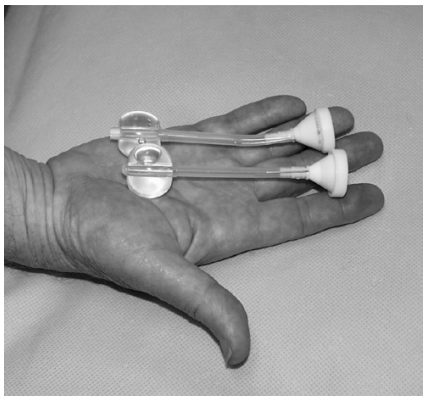
Implanted Therapy: Targeting Brain Cancer with Lasers

A new surgical device developed by visiting researcher Henry Hirschberg, M.D., Ph.D., could offer new hope to patients with migrating and regenerating brain cancer.

Hirschberg, who currently splits his time between the Beckman Laser Institute and the Department of Neurosurgery at University Hospital, Rikshospital (Oslo, Norway), has developed a balloon-tipped applicator for combined brachy-photodynamic therapy. The device, which will be used in patient trials in Norway, is implanted in the cranial cavity following routine surgical resection so that doctors can continue to deliver ionizing- and light-radiation to the tumor site on an ongoing basis. "By keeping the applicator inflated in the brain cavity, we can continue to treat the periphery of the tumor site where stray cancer cells might otherwise try to regenerate," explains Hirschberg.

Hirschberg is collaborating with Steen Madsen, Ph.D., Assistant Professor of Physics at the University of Las Vegas, and Chung-Ho Sun, Ph.D., on a series of dosimetry studies to determine what combination of drugs and laser light will be most effective in arresting tumor regeneration.

The device holds excellent commercial potential. Hirschberg has applied for a patent and is conducting talks with Proxima Therapeutics, Inc. (Atlanta, GA) to begin producing the device. Additional talks are underway with PhotoCure (Oslo, Norway) to develop new photosensitive compounds which will be tested for use with Hirschberg's novel applicator. "Ultimately, we hope the device will be available to hospitals around the world," says Hirschberg. ■



Implantable laser applicators allow physicians to provide post-operative treatment for patients with brain cancer.

Veterinary Outreach Director Collects Anthony Award

George M. Peavy, D.V.M., BLI's Veterinary Director, has received the Russell H. Anthony Award, given by the American Veterinary Medical Association (AVMA), in recognition of outstanding contributions to the veterinary profession in the area of governmental affairs.

Peavy was recognized at the AVMA's 137th Annual Conference held in Salt Lake City, Utah. The Anthony Award was presented at a luncheon attended by Utah Senator Orrin G. Hatch. The five-term senator thanked conference attendees for the contributions of veterinary research to the nation's biomedical research industry. "Human medicine can learn a lot from your dedication," Hatch said. "We'll continue to rely on veterinary research and biotechnologies as means to unlock the secrets of disease and for the development of appropriate [treatments]."

"I'm honored to be recognized," says Peavy. "I think it's important for individuals to be involved in the issues and political processes of their community."

Peavy served on the AVMA's Political Action Committee from 1982 to 1989 and the Council on Governmental Affairs between 1992 and 1999. He is credited with founding the legislative and political action programs of the California Veterinary Medical Association. Peavy also served on a health advisory committee to U.S. Senator Samuel I. Hayakawa. ■

George M. Peavy, D.V.M., received the Russell B. Anthony Award at this year's meeting of the AVMA in Salt Lake City.

(cont'd from p. 4)

GENE TARGETING AND INACTIVATION

bilities for both basic and applied research, and Berns expects BLI to be at the forefront of these efforts. "With the development of photosensitive probes that can target specific genes, it should be possible to offer an entirely new method for regulating genes and proteins," says Berns.

To this end, the BLI team is constructing a new microscope system designed specifically for multi-photon experimentation. Innovations to the two-photon microscope system include the addition of remote control capabilities. These enhanced capabilities, powered by broadband Internet technologies, enable remote experimentation which will facilitate studies that require long-term cell tracking and assessment.

"For experiments that take a long time, remote-control offers clear benefits," says Zifu Wang, Ph.D., who has taken the lead along with doctoral student Joon You in the effort to equip two-photon systems at BLI and the University of California, San Diego, with remote capabilities. "With gene inactivation and other cell manipulations we need to follow the progress of the cell for twenty-four hours or more," says Wang. "Now we can do that from any Internet terminal. There's no reason for us to stay locked in the lab, and we should even be able to conduct laser manipulation studies remotely."

Berns and his team envision a time when collaborators from around the world will "tune in" via the Internet to conduct experiments with a computer keyboard or joystick. "We're refining our software and addressing bandwidth limitations to make these things possible," says Berns. In recognition of the potential impact of multi-photon gene inactivation, the journal *Nature Biotechnology* selected this study for special recognition in their October 2000 issue. ■

(cont'd from p. 2)

DIRECTOR: TECH TRANSFER TALES

consider an academic career because of the attraction of wealth and opportunity in the private sector? How many faculty are "spinning off" their own companies and leaving academia when conflicts of interest and time commitment become overwhelming? And how many of those who do stay compromise and corrupt the academic process by doing so?

I don't know what the precise figures are. My observations represent only a small sample, and they shouldn't lead to hasty conclusions. Clearly, there are many positive examples of technology transfer to consider as well as faculty who leave academia for the private sector. Certainly one of the missions of the university is to provide well-trained and talented people for the private sector. This is the backbone of our free-enterprise economy after all.

But perhaps it is time to assess the impact of the aggressive marketing and licensing of university-derived (often with public funds) intellectual property. Of course, the income to universities from royalties as well as future philanthropic gifts from grateful "company founders" may make these questions seem rhetorical or even moot. Still, there is a question worth posing: how can we get the most from academia without undermining the academic mission? ■

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Newsbriefs

children with disfiguring birthmarks. Since 1989, the CTF has assisted 72 children by providing more than $330,000 in partial and full treatment subsidies.

"The need, unfortunately, never seems to diminish or go away," says Institute Director Michael Berns. "I feel strongly about our obligation to continue offering this program to children in need, and we're certainly honored to have been recognized by Disneyland, whose own record of philanthropy in the community is so admirable."

The CTF Review Board receives requests for assistance from an average of five patients every month and considers all referrals on an individual basis. Physicians provide *pro bono* treatment, and facility and administrative costs for the management of the CTF are incurred by UCI rather than by patients, their families, or donors.

If you would like more information about birthmark removal or the Children's Treatment Fund, please call (949) 824-7980.

OPTICAL BIOPSY FUNDING

Zhongping Chen, Ph.D., Assistant Professor of Surgery, has received new funding from the National Science Foundation (NSF) to develop micro-electric mechanical systems (MEMS) technology for optical biopsy devices.

The three-year NSF grant, worth $450,00, will support collaborative research involving Cornell University and the Integrated Nanosystems Research Facility at the University of California, Irvine (UCI). NSF provides these funds as part of its initiative on biophotonics partnerships.

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NEWSBRIEFS

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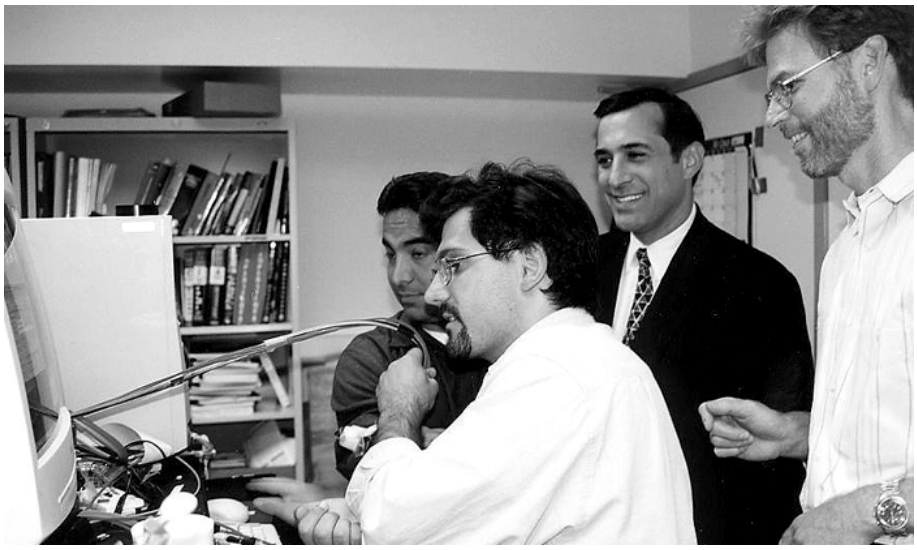
CONGRESSIONAL 'FINDINGS'

A stream of congressional representatives and staffers have made their way to the UC Irvine campus this year to review the unique research and "tech-transfer" programs which help to keep the Beckman Laser Institute on the biomedical fast-track. Institute Director Michael Berns isn't surprised: "With so many major government-funded programs operating at our facility, it makes sense that our elected officials want to have a look at the breadth and depth of our research."



Congressman-Elect Darrell Issa (South Orange County) visited the Beckman Laser Institute on August 11, 2000. Issa (second from right) reviewed BLI's unique research and tech transfer programs. For more on Issa's "findings," please see story at left.

Congressman-Elect Darrell Issa (48th district) became the latest member of the House to learn more about new technologies in the field of photomedicine when he paid a visit to BLI on August 11, 2000. Staff members for Christopher Cox (47th district), Loretta Sanchez (46th district), and Jerry Lewis (40th district) toured BLI earlier in the year.

Issa, founder and CEO of Directed Electronics (Vista, CA), replaces long-standing BLI supporter Ron Packard, who is retiring from his seat in Congress after nine terms. "It's an honor to have Mr. Issa visit us," says Berns. "I think he got a very good taste of the innovative work we do here." ■

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