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Spring 2001

Sanchez Pays Institute Congressional Visit

Congresswoman Loretta Sanchez (CA, 46th District) paid the Beckman Laser Institute a visit in December to learn more about the Institute's federally funded research programs as well as BLI's unique "tech-transfer" program which continues to cultivate partnerships between the public and private sectors.

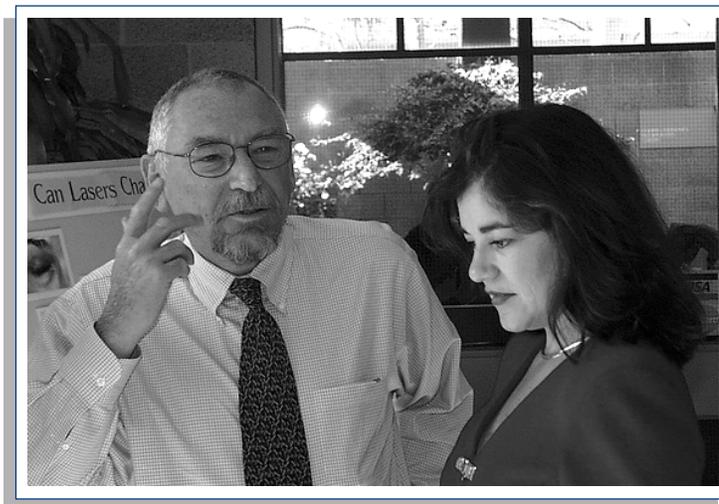
During her tour of the Institute, Ms. Sanchez had an opportunity to

view several research demonstrations, including "hands-on" work in the Institute's clinical research wing and in the Photonic Incubator.

"I am very impressed with the Beckman Laser Institute's vision and knowledge of how laser biotechnology will change our future," said Sanchez. "Only through public-private partnerships can we prepare to be competitive in the 21st century. I am proud that the federal government is investing in Beckman's work."

Ms. Sanchez is the latest in a stream of elected officials to visit the Institute. Congressman Darrell Issa (CA, 48th District) toured the BLI facilities last fall.

"Naturally, we're eager to keep our elected officials informed about the promise of biophotonics and the federally-funded core programs which help to keep our research running," explains Institute Director Michael Berns. "Ms. Sanchez serves on the House Appropriations Committee, so it's especially nice to see her take an interest in us." ■



Congresswoman Loretta Sanchez (CA, 46th District) discusses the Institute's newest research programs with Institute Director Michael Berns, Ph.D., during her recent visit to BLI.

Newsbriefs

TROMBERG HONORED

Associate Professor Bruce J. Tromberg, Ph.D., Director of BLI's Laser Microbeam and Medical Program (LAMMP), has received a Young Investigator's Award in Biomedical Optics from the Coherent Laser Group.

Tromberg was honored in a special awards ceremony at the Photonics

West Conference in January. University of Pennsylvania Professor Britton Chance, Ph.D., was also honored at the ceremony with an award for Lifetime Achievement. "To be honored alongside Brit was very special," says Tromberg. Drs. Tromberg and Chance each received \$25,000 of equipment from the Coherent Laser Group.

(newsbriefs continued on p. 7)

For Years of Dedication and Service: Thank You

by **Michael Berns, Ph.D.**

Arnold and Mabel Beckman Professor
President and Director

Recently, two people who have lent the Institute and me personally an enormous amount of time, expertise, and friendship have stepped down from the BLI Board of Directors. Brian Demsey and Linda Cahill cannot be thanked enough for the valuable imprint which they have left on the Institute and its operations.

Brian was one of the major architects behind the original business plan that was presented to Dr. Arnold Beckman back in 1980. He served as one of the original BLI Board mem-

bers, and most importantly, he was always there for me when I needed advice and guidance.

Brian never missed a single Board meeting in over 16 years! He served on many of the Board's executive committees, and he truly embraced the philosophy and the original BLI "vision" that he, himself, helped to shape so expertly.

Brian and his wife, Susie, have been "true" supporters of BLI in every way, and they are both wonderful friends who will be with BLI forever. I am excited about Brian's new endeavor with RemoteNet (already a leader in the computer networking and desktop management

services arena), and I know that it will be a successful venture which will make a significant impact in the technology sector.

Linda Cahill has served on the BLI Board for over nine years. I first met Linda while she was Vice-President for New Business at Johnson and Johnson. Linda brought to BLI an energy, astuteness, and personal interest that long epitomized what a Board member and friend can be.

Linda was there for me in tough personal times, and when it came time to deal with the reorganization and redefinition of BLI's clinical activities, Linda responded extraordinarily, with patience and acumen. Linda could always be counted on to express her opinion directly and without ambiguity--a quality which, sadly, is often lacking in today's business and academic worlds.

I thank Linda for her dedication, time, and sense of humor. These are the things that often make a grim situation more bearable. I wish Linda my sincere and best wishes as she embarks on her new venture with Signal Analytics, a company with real potential to revolutionize the field of biotechnology.

In twenty years of operation, we have been fortunate to benefit from excellent leadership, and I have been fortunate to work alongside those who have helped to nurture BLI.

Brian and Linda, all of us at BLI, and especially myself, are truly excited about your new ventures. We look forward to future visits and interactions with both of you. ■

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Women's Health: Understanding Cervical Cancer

Since the 1960s, the incidence and mortality rate for cervical cancer have steadily declined in the United States as well as in most other industrialized countries. Health care professionals attribute this to the introduction of Pap smear screening.

Unfortunately, this positive trend seems to have tapered off over the last decade. According to the National Cancer Institute, an estimated 12,800 cases of invasive cervical cancer occurred in the U.S. in 1999, while the disease proved to be deadly for nearly 5,000 of these women.

Even more alarming, however, are the statistics for the world's poorer countries: cervical neoplasia is now the leading cause of cancer-related death for women in underdeveloped nations. Worldwide, between 400,000 and 500,000 new cases of cervical cancer are diagnosed each year. Most of these women can be classified as economically disadvantaged.

Taking a Molecular Approach

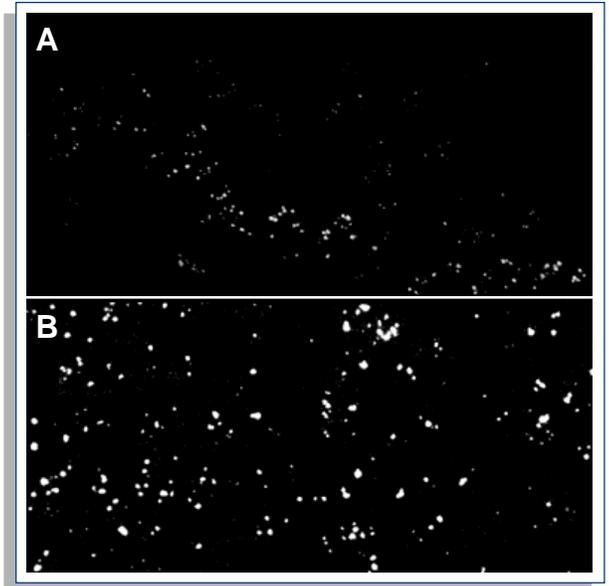
In response to these grim statistics, researchers at the Beckman Laser Institute have been working to develop a new technique which will complement existing diagnostic modalities that primarily examine morphology (i.e., cell shape). "A biopsy significantly improves our diagnostic capabilities," says Vickie LaMorte, Ph.D., Assistant Professor of Surgery, "but there are limitations with this technique also." Diagnoses based on morphology are subjective such that two pathologists may "grade" the same sample differently. "Our approach

has been different," LaMorte explains. "We are looking at the molecular level to identify markers which change their expression or pattern throughout the progression of the disease." According to LaMorte, this sort of molecular approach could significantly aid pathologists in making definitive diagnoses.

"We have to evaluate what's happening at a sub-cellular level if we really want to understand what triggers the growth and spread of cancer," says project co-investigator Melinda Szendefi, M.D.

"Molecular mechanisms provide information that simple morphology cannot." Dr. Szendefi has worked alongside LaMorte since she arrived at BLI as a Swiss National Science Foundation Fellow in September 1999. The work is co-sponsored by the Laser Microbeam and Medical Program (LAMMP), a National Institutes of Health user facility located within the Beckman Laser Institute.

Initial studies conducted by LaMorte and Szendefi suggest that a special protein, known as PML, plays a key role in the progression of cervical cancer. By assessing the profusion and dispersion of PML in cervical tissue samples, researchers may soon have a clearer understanding of the biochemistry of cervical cancer. "With better knowledge about the biochemistry, we take the first steps toward



Biochemical markers: Normal (A) and cancerous (B) cervical tissue samples. Note diffusion of PML bodies (indicated by glowing dots) in sample B.

better diagnostics and intervention," says LaMorte.

PML Protein Expression

By labeling PML proteins with a fluorescent marker, Szendefi and LaMorte have been able to monitor protein expression at different stages of cervical disease. So far, their findings have been instructive.

In healthy cervical tissue samples, PML is found in well-ordered, discrete bodies within individual cells. These subcellular bodies are distributed evenly in a homogenous, dotted pattern. In dysplastic (abnormal) samples, these bodies become larger and more numerous. By following this altered pattern, researchers hope to better understand the cancerous changes taking place within the tis-

(continued on p. 7)

Cartilage Reshaping: High-Tech Facial Plastic Surgery

In the hands of a surgeon, the laser becomes an extremely precise tool for cutting and ablation--an optical scalpel of sorts. But the laser's unique properties make it an extraordinarily versatile instrument also.

Current research at the Beckman Laser Institute suggests that lasers may soon play a different kind of role in the operating room. A team of researchers and clinicians led by Brian J.F. Wong, M.D., Assistant Professor of Facial Plastic Surgery in UCI's Department of Head and Neck Surgery, are working to perfect a new technique for laser-mediated cartilage reshaping.

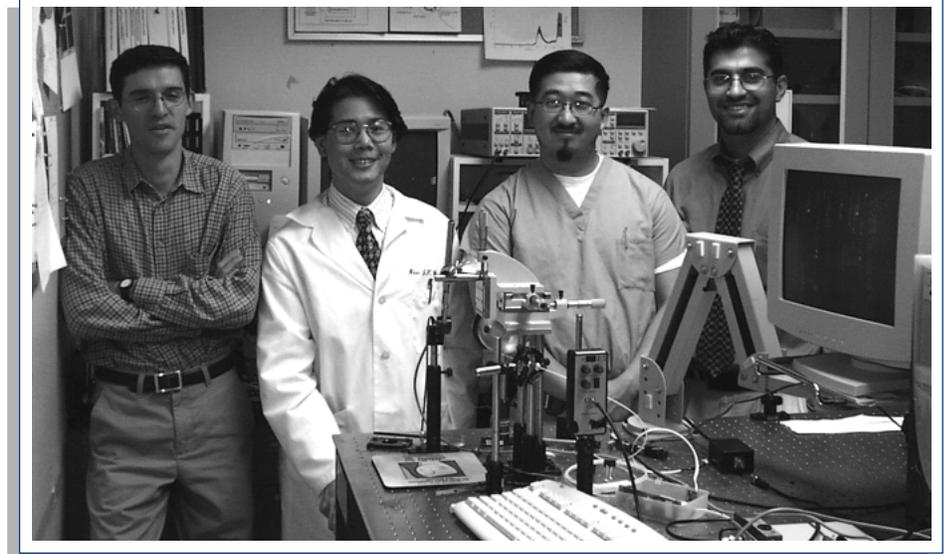
By heating cartilage samples with a laser, clinicians can bend and mold the tissue in order to create grafts and prosthetics for reconstructive surgeries.

"It's important not to raise expectations irresponsibly, but the work we're doing could, ultimately, revolutionize the way we approach facial reconstructions and cosmetic surgeries," says Wong.

Plastic Possibilities

Cartilage has unique molecular properties which make it suitable for reshaping. When heated to sixty degrees centigrade, cartilage enters a plastic state and can be molded into new shapes which harden as the sample cools. Reheated, the tissue can be remolded and set once again. Tissue viability appears to be the sole limit to unlimited malleability.

"We have to work within a 'sweet spot,'" explains Wong. "The energy produced by the laser must be suffi-



In the lab: (l-r) Sergio Diaz, Ph.D., Brian Wong, M.D., John Chang, M.D., and Amir Karamzadeh (medical student) pose in the laboratory. Wong and his multi-disciplinary team are working to perfect a new technique for laser-mediated cartilage reshaping.

cient to achieve malleability, however, too much heat jeopardizes the health of the tissue."

Dr. Wong is collaborating with colleagues at the Russian Academy of Science and the University of Texas to establish the exact parameters of the so-called 'sweet spot.' Dr. Wong's team, which also includes a handful of UCI researchers (J. Stuart Nelson, M.D., Ph.D., Enrique Lavernia, Ph.D., Sergio Diaz, Ph.D., and graduate student Yong Seok Chae), are working to develop an automated control system which regulates the amount of energy delivered by the laser to optimize the results of reshaping.

"In order to produce a viable graft, we need to ensure that a suitable percentage of the tissue structure survives after being heated and molded," says Wong. "One of the associated projects that we're working on with

the help of [UCI medical student] Alex Rasouli is the development of an assay to determine what percentage of the cartilage cells have withstood the heat." By taking a biological survey of the remolded tissue before implantation, clinicians improve the chances of a successful graft.

Looking to the Future

Wong's research is currently funded by the Department of Defense and the National Institutes of Health. His joint-appointment at BLI and the UCI Department of Head and Neck Surgery allows him to keep one foot in the operating suite and another in the laboratory. "I've been fortunate to have the support of [Institute Director] Michael Berns and [Chairman of Head and Neck Surgery] Roger Crumley so that I can integrate my

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Anthony Durkin: First Beckman Fellow

When he applied to become the Institute's first Beckman Fellow, Anthony (Tony) Durkin, Ph.D., worried that his research skills were a bit rusty. "I had been working in the corporate sector for two and a half years and found myself craving a more hands-on environment."

Tony had already spent a week at BLI in 1997 while working with the Food and Drug Administration as a National Research Council Fellow, and he remembered that stint--spent in close collaboration with Vasan Venugopalan, Sc.D., and graduate student Tuan Pham--as particularly productive. "When I heard about the Beckman Fellowship at last summer's

Gordon Conference, I jumped at the opportunity to return."

Tony, who completed his doctoral work in 1995 at the University of Texas in the Department of Electrical and Computer Engineering, joins the BLI research staff as the first Beckman Fellow. This three-year fellowship program was launched last year with a \$1.1 million gift from the Arnold and Mabel Beckman Foundation.

Tony describes the Fellowship as a welcome opportunity. "This is a unique opportunity to rejuvenate my research skills, learn some new things, and begin to establish my own research program." In addition to salary, the fellowship includes start-



Tony Durkin, Ph.D., has been selected as the Institute's first Beckman Fellow.

up funds for lab equipment. Tony plans to focus his work on analytical techniques to complement optical spectroscopy technologies. ■

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Laser Vet Program “Lionized” in Long Beach

Veterinary Director George M. Peavy, D.V.M., paid a very special “house call” to the Long Beach Aquarium of the Pacific on March 25, 2001. Peavy carted a portable laser unit to the Aquarium in order to treat a geriatric California Sea Lion suffering from serious nasal and respiratory blockages.

“Any time a critter needs help, and our lasers and expertise might be part of the answer, we’re willing to get involved,” says Dr. Peavy of the unusual visit.

Peavy and veterinary endoscopic specialist Mark Kopit, D.V.M., worked alongside Aquarium of the Pacific staff veterinarian, Johanna Sherrill, D.V.M., M.S., in a four-hour procedure to remove an inflammatory membrane and polyps obstructing the nasal passageway of a female sea lion dubbed “Kai” by her handlers in Long Beach.

Kai’s Journey

Now tipping the scales at more than 175 pounds, Kai was rescued from the wild as a pup and shipped to Sea World, San Diego after having lost her mother. When cataracts developed in her eyes two years ago, she was deemed “unreleasable” and relocated to the Aquarium of the Pacific’s newly opened facilities.

More recently, Kai developed growths in her nasal passageway--the secondary effect of a parasitic infection that she likely contracted in the wild--which made ordinary activities and even normal breathing difficult. Recognizing that her condition was



Dr. Johanna Sherrill, D.V.M., M.S., prepares Kai, a female California Sea Lion for laser surgery at the Long Beach Aquarium of the Pacific. BLI’s Veterinary Director, George Peavy, D.V.M., performed a procedure to remove abnormal growths from Kai’s nasal passageway.

life-threatening, Dr. Sherrill put out a call for help. The Aquarium’s head veterinarian knew that her options would be somewhat limited.

“To our knowledge, this is the first time a procedure like this has been performed on a sea lion,” notes Sherrill. “Certainly, it’s a first for the experts that attended.”

Kai did extremely well during the four-hour procedure, although the extent to which her breathing has been improved cannot be determined until the swelling goes down. “We managed to remove a significant portion of the blockages,” explains Peavy. “The thermal effects of the laser should ensure that any abnormal tissue left behind sluffs off naturally like an ordinary scab would.”

For her part, Dr. Sherrill believes that Kai’s prognosis is excellent.

“She’ll have a sore nose for a few days, but she’s eating well, which is a very good sign,” says Dr. Sherrill. “We provided her with state-of-the-art treatment. If anything can help her, this is it.”

The VOP Mission

Kai’s surgery falls under the auspices of the Institute’s Veterinary Outreach Program (VOP). The VOP extends the resources of the Institute to area veterinarians and offers treatment modalities for veterinary cases which do not respond suitably to conventional therapies.

“The VOP helps to create win-win situations,” explains Peavy. “The Aquarium gets assistance for an animal with a naturally occurring problem, and we get to refine a technique which can also benefit humans.” ■

(cont'd from p. 3)

UNDERSTANDING CERVICAL CANCER

sue. For instance, as dysplasia increases, a second protein, SUMO, is recruited to the PML bodies. Finally, as the disease progresses to carcinoma, the “partnership” between PML and SUMO is lost, and PML bodies are down-regulated. The key for researchers and clinicians is that this biochemical progression may be visible in the early stages of dysplasia *before* any definite changes in morphology have taken place.

“Basically, the expression of the PML protein gives us a marker for each stage of the progression from dysplasia to cancer,” explains LaMorte. “We get a view of the disease which pathologists right now do not see.”

“What’s interesting,” says Szendefi, “is that PML levels appear to drop off in more advanced tumors, especially in poorly differentiated tumors.” This makes sense, according to Szendefi, because PML is thought to be a tumor suppressor. Early proliferation of

PML would seem to indicate that a cell is attempting to regulate its growth. As PML dissipates, this could be a sign that the battle is lost. “Genetic and environmental risk factors for this variety of cancer are well documented,” says LaMorte. “We’re working on unraveling the exact progression of the disease to enable better and earlier detection and, hopefully, more effective treatment.”

What Lies Ahead?

LaMorte and Szendefi have filed a disclosure and are preparing their results for publication. Szendefi will return to Switzerland where she will oversee a new round of clinical trials to further study the role of PML in cervical cancer at the Pap smear level. “An annual Pap smear is still an important weapon in our arsenal,” says Szendefi. “Hopefully, our research can provide one more tool for physicians and pathologists.” ■

(cont'd from p. 4)

LASER CARTILAGE RESHAPING

clinical and research interests. I don’t think this kind of arrangement would have been possible anywhere else.”

Dr. Wong is set to begin a series of studies to test the long-term durability of remolded cartilage grafts in a laboratory setting. Assuming the results are positive, a first round of patient studies could begin within twelve months. “My Russian colleague, Dr. Emil Sobol, has already been involved with patient studies sponsored by the Russian Academy of Science,” notes Wong. “Our own studies are moving along nicely now, given the requirements of the American research environment.”

Wong is optimistic about the fu-

ture and the potential applications of cartilage reshaping. In addition to facial reconstruction and cosmetic surgeries, the technique could have a major impact on other bone and joint surgeries as well as corneal reshaping procedures. Patents have been submitted for this work.

In the meantime, Wong believes that cartilage reshaping holds immediate benefits for patients who respond poorly to conventional facial reconstruction. “Hopefully, this technique will become standard practice for septal surgeries and rhinoplasty,” says Wong. “Laser reshaping is cheaper and safer than conventional surgery, and that bodes well.” ■

(cont'd from page 1)

Newsbriefs

NEW PATENT AWARDED

Associate Professor J. Stuart Nelson, M.D., Ph.D., is among the inventors credited on a new patent award for a novel approach to optical coherence tomography (OCT). Nelson and former BLI researchers Johannes de Boer (Harvard University) and Tom Milner (University of Texas) are listed as the principal inventors for U.S. Patent 6,208,415: Birefringence imaging in biological tissue using polarization sensitive optical coherent tomography.

Polarization sensitive OCT is a novel optical imaging technique which detects changes in the electrical state of reflected photons. Since the structure and composition of biological tissues alters the electrical state of photons as they penetrate and backscatter, PS-OCT enables rapid, non-contact tissue imaging for a variety of medical procedures.

“PS-OCT allows us to chart and interpret changes in tissue properties which result from disease or trauma,” explains de Boer. “This gives us a better window for medical intervention.”

NEW BME APPOINTEES

The UCI Center for Biomedical Engineering has made a number of new appointments. Joining the BME Center are: James Brody, Ph.D., Noo Li Jeon, Ph.D., Lubomir Bic, Ph.D., Ranjan Gupta, M.D., Enrique Lavernia, Ph.D., Thay Lee, Ph.D., Brian Wong, M.D., and Fan-Gang Zeng, Ph.D.

The BME Center, now under the directorship of Steve George, M.D., Ph.D., was established in 1998 and is sponsored by a \$3 million Development Award from the Whitaker Foundation (Rosslyn, VA).

(newsbriefs continued on p. 8)

NEWSBRIEFS

(cont'd from page 7)

BLI HOSTS OC LEADERS

The Beckman Laser Institute opened its doors on January 26, 2001 to members of the Orange County Business Council who attended a Legislative Advocacy Workshop. The purpose of the workshop was to brief attendees on issues which are on the agenda at the OCBC's upcoming bi-annual legislative session. Representatives from a host of Orange County's largest and most dynamic business ventures were present, including: the Disneyland Resort, Irvine Community Development Company, the Orange County Transit Authority, Conexant, Pacific Bell, and Pacific Life Insurance.

DIPLOMAT VISITS INSTITUTE

Mr. Tsuneo Nishida, Consul-General at the Japanese Consulate's office in



Another Milestone: Institute Director Michael Berns, Ph.D., (left) and newly appointed Beckman Fellow Anthony Durkin, Ph.D., (right) pose alongside Dr. Arnold O. Beckman at the latter's 101st birthday celebration held at the Institute on April 9, 2001.

Los Angeles, visited the Beckman Laser Institute on November 17, 2000. Mr. Nishida was escorted on a tour of the Institute by longtime BLI staff member Elaine Kato and visiting researcher Arata Ebihara, D.D.S,

Ph.D., who is currently working on a series of collaborative projects with BLI's Dental Research Director, Petra Wilder-Smith, D.D.S, Ph.D., thanks to funding from The Tokyo Medical and Dental University in Japan. ■



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