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Fall 1996

Construction Grant Awarded

The Institute has been awarded a \$1 million federal grant to establish a public-private consortium to facilitate the conversion of defense technologies to medical uses.

The Economic Development Administration (EDA), of the U.S. Department of Commerce, has approved the grant to build a facility housing a Photonic-Based Defense Technology Incubator

for military purposes to the diagnosis and treatment of disease.

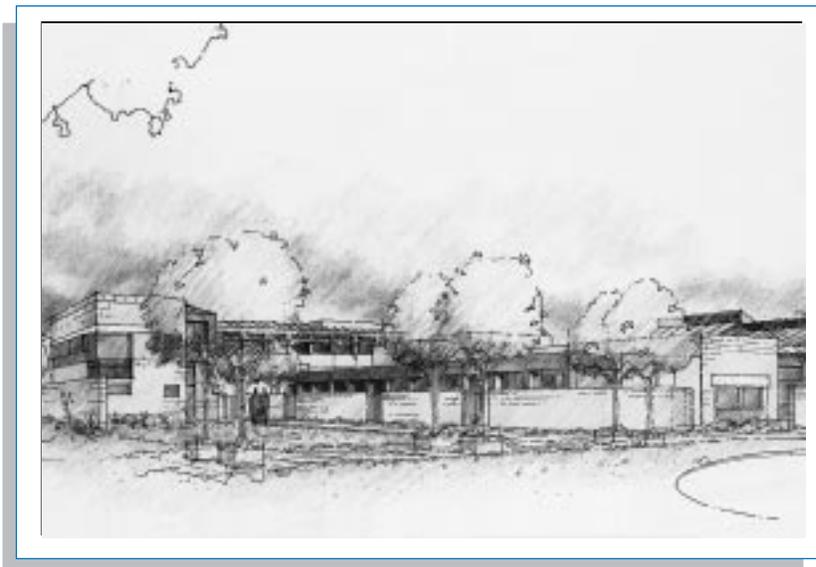
This consortium should encourage start-ups and nurture new businesses in biotechnology, enabling the creation of new products and jobs, while benefiting Southern California with its extensive defense company infrastructure. At the same time, it will support the defense industry by providing new uses for military technology.

The Photonic Incubator will be housed at the Institute in a 10,000 square-foot building expansion, which will include engineering development and testing labs, a clinical applications suite, and program office space.

“Placing research and development operations in close proximity to our clinical treatment facilities,” explains Institute Director Michael W. Berns, “will create a unique environment attractive to corporate medical device developers. This means the physicians who will be testing the new medical technology will be able to interact with the people who developed it.”

In addition to the grant from the EDA (which is providing approximately 50% of the construction funds), this project is receiving operational funding from the State of California (Office of Strategic Technology), UC Irvine, and the Beckman Laser Institute.

Dr. Arnold Beckman (The Beckman Family Trust) has issued a challenge grant to provide construction funds. ■

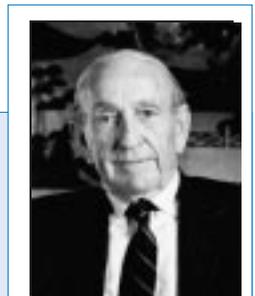


Architectural rendering of the new Photonic Incubator Wing.

for Biomedical Devices and Systems. This incubator (or think tank) will provide an opportunity for medical device entrepreneurs and biotechnology firms to work with university biomedical researchers and clinicians to apply lasers, optics, and detectors developed for mil-

Tribute to David Packard

This issue is dedicated to a leader in American industry and a friend of the Institute. The Director shares his memories of David on page 2, and Institute friends remember him on page 6.



David Packard: In Every Sense A Philanthropist

by Michael W. Berns, Ph.D.

Arnold and Mabel Beckman Professor
President and CEO

There are a few people in life that we meet that we can honestly say “It was a privilege to know.” For me, such a person was David Packard. It was with great sadness that I learned of his passing.

Following so closely on the loss of Charley Hester, David’s death was especially felt by those at the Institute who had the privilege to work with him.

Big Picture Philanthropy

In the conventional understanding of philanthropy—targeting financial support to various causes and organizations—David Packard was clearly one of the greatest philanthropists this country has ever had.

He supported projects ranging from the Monterey Bay Aquarium to the Packard Children’s Hospital at Stanford University.

The foundation he started with his wife Lucile has become one of the largest in the country and has been especially important in promoting children’s welfare.

In 1989, he created the David and Lucile Packard Center for the Future of Children at his charitable foundation in Los Altos to target the health and social problems of young minority children.

As a final act of generosity, David left all of his personal Hewlett Packard stock, some 9% of the company worth about \$4.4 billion, to the Packard Foundation.

For us at the Beckman Laser Institute, David Packard’s philanthropy has ensured permanent support for the Children’s Treatment Fund and related research projects. To help further extend the benefits of this treatment, the Packard gift includes a two million dollar endowment gift to support port wine stain research and clinical treatment.

In addition to funding research to

make this treatment more effective, this fund continues to support the laser removal of disfiguring birthmarks in young children whose families cannot meet the costs of this treatment. And this treatment continues to make a big difference in the self-esteem and happiness of children at a crucial stage of their development.

Another lasting legacy to us was opening the door to Hewlett-Packard. Now, HP is a major supporter of our research programs and a valued collaborator. We are confident that the relationship David began between the Institute and the company will continue to flourish for years to come. *(Please see the related story, our corporate profile of Hewlett-Packard, on page 4).*

Philanthropy and Friendship

There is no doubt that David Packard’s place of honor in the pantheon of American philanthropists is assured. Yet, I like to think of David as a philanthropist in a more personal sense, too.

As a deeply humane man with a bent to make things better wherever he happened to be, David was also very much a philanthropist to his friends.

I am personally grateful for the opportunities to experience David’s philanthropy that went way beyond his financial support.

This was a philanthropy of humor at the lake at Tetachuk in Canada when he read poetry to us; it was a philanthropy of his teaching Robbie, my wife, and me how to tie our first flies on a fishing line; and it was a philanthropy of his time to convey a sense of integrity in whatever endeavors we undertook together.

David was a philanthropist in every imaginable sense of the word. With his passing, the lives of those he knew are diminished because we can no longer share in his friendship, but his legacy of experiences is rich and sustaining. ■

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Beckman Laser Institute News

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Experimental PDT to Prevent Esophageal Cancer

This Spring, the Institute became the first site on the West Coast to perform a new laser treatment for an increasingly common malady of the esophagus.

Dr. Kenneth Chang of UC Irvine's Chao Family Clinical Cancer Research Center used an experimental application of photodynamic therapy (PDT) to treat a patient suffering from Barrett's Esophagus. This was the first procedure in a series of clinical trials to be conducted jointly between the Institute and the Cancer Center.

Affecting approximately 70,000 people in California and between 800,000 and two million nationwide, Barrett's Esophagus is a disease caused by long-standing acid reflux that converts the esophageal lining into stomach-type tissue.

When stomach acid splashes up into the esophagus, it causes heartburn. If this condition persists over time, the acid can severely damage or destroy the normal lining of the lower esophagus.

Stomach- or intestine-like cells then grow into the esophagus to replace the acid-damaged lining there. These abnormal cells can develop a dysplasia that may be a prelude to cancer.

Heartburn and Cancer

About 24 percent of all cancer deaths in the United States are due to cancers of the gastrointestinal tract. Barrett's Esophagus is a major cause of these cancers, and the likelihood of Barrett's patients developing esophageal cancer is 30 to 40 times that of the normal population. Between 1976 and 1990, the annual incidence of Barrett's-associated cancer tripled, making it one of the fastest growing cancers in the country.

Diagnosis a Challenge

Heartburn is the most common symptom of acid reflux. Patients with long-standing heartburn are at risk for Barrett's Esophagus and should con-

sult their physician about possible testing for the condition. Those patients diagnosed with the condition may need to undergo endoscopy on a routine basis. Any suspicious areas can then be examined through biopsy for signs of pre-cancerous dysplasia or cancer itself.

"Early diagnosis is key," Dr. Chang notes. "In general, 95% of patients with advanced esophageal cancer die within 5 years. Early diagnosis of potentially pre-cancerous dysplasia can allow us to prevent the cancer from ever starting."

Treatment Options

Most patients with severe dysplasia must undergo surgery for the removal of part of the esophagus to eliminate the Barrett's mucosa. This surgical procedure, called esophagectomy, is a major cutting operation requiring full anesthetic and long hospitalization.

Patients can suffer prolonged pain during recovery. Afterwards, patients will have to make major lifestyle changes and may have to endure continuing medical problems. Esophagectomy also carries a relatively high mortality rate.

In contrast, PDT can be considered an office procedure because it requires no cutting and only a local anesthetic. A minimally invasive procedure, PDT is also very cost effective and offers encouraging results to eliminate Barrett's tissue without lingering side effects.

PDT to treat Barrett's Esophagus involves the use of the photosensitizing drug Photofrin (manufactured by QLT Phototherapeutics, Inc., in Vancouver, and distributed in the U.S. by Sanofi-Winthrop) in combination with an argon dye laser. The drug is administered systemically, but it concentrates mainly



Dr. Kenneth Chang performs photodynamic therapy to treat Barrett's Esophagus.

in abnormal tissue, in this case, located in the esophagus.

When the laser light shines on the photosensitized diseased tissue, the drug produces a chemical reaction that kills only the target cells, leaving healthy tissue relatively unaffected.

Although PDT is less invasive than esophagectomy, complications can occur, including stricture formation. PDT patients must also bear with the inconvenience of staying out of the sun for thirty days.

So far the results are promising. The patient returned for a follow up treatment a couple weeks after the initial PDT. "Now," Dr. Chang explains, "he is recovering nicely. We expect his condition to return from almost malignant to nearly normal."

Institute Clinical Research Director Dr. Yona Tadir, himself a minimally invasive surgery specialist, is enthusiastic about the project. "Esophageal PDT," he feels, "is a promising new application of a laser treatment that we have studied to treat conditions ranging from dysfunctional uterine bleeding to skin cancer. This project could result in great medical benefit." ■

Lasers Shine in Canine Dentistry

Institute researchers, in collaboration with veterinarian Dr. David Nielsen of Manhattan Beach, are investigating a new laser dental treatment that has shown much promise in repairing fractured teeth in dogs. Dr. Petra Wilder-Smith, the Institute's Director of Dentistry, and Veterinary Director Dr. George Peavy have been working with Dr. Nielsen to apply the carbon dioxide (CO₂) laser to treat dogs' teeth.

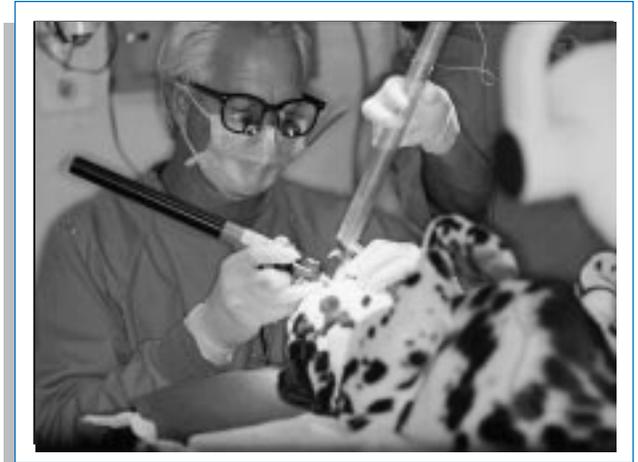
When a tooth is fractured, the pulp inside is exposed, allowing it to become infected. If the infection becomes acute, the tooth must be extracted. This can create a serious problem for dogs. "Many of these cases involve a fractured eye tooth," Dr. Nielsen explains. "Loss of this tooth severely reduces a dog's ability to chew its food."

Pulpotomy is a procedure in which inflamed dental pulp is removed before infection can set in, leaving healthy tissue intact and thus preserving the tooth. For the last two years, Dr. Nielsen has offered CO₂ laser pulpotomy to every patient who comes to his office with a recently fractured tooth. So far, the results have been excellent, and all nine-

teen teeth that have been documented remain healthy and fully functional.

The challenge in developing this procedure for wide-spread application in veterinary dentistry, and then for use in human dentistry, is controlling the laser's heat. "Heat from the laser during pulpotomy," explains Dr. Wilder-Smith, "can damage surrounding healthy tissue. Since pulpal tissue is so sensitive to heat—a five degree Celsius rise in temperature can kill it—we have been working to reduce collateral laser thermal damage to a minimal level."

Once the problem of thermal damage has been solved, Dr. Wilder-Smith feels that laser pulpotomy could replace millions of root canals performed annually. The root canal is a highly imperfect treatment that, aside from its pain and expense, leaves teeth dry,



Dr. David B. Nielsen performs a CO₂ laser dental pulpotomy on a Dalmatian.

discolored, easily breakable and with a reduced life-span. She feels that "a laser method to drain infected soft dental tissue without killing the tooth would be a major boon to patients."

Dr. Peavy is enthusiastic about the project. "This work is an example of how new treatments for naturally occurring conditions in animals can advance both human and veterinary medicine." ■

Industrial Associate Profile: Hewlett-Packard

Established to provide corporations with a window into the evolving world of laser biotechnology, the Beckman Laser Institute's corporate relations program offers companies a formal affiliation with the Institute which allows these firms to conduct joint research projects and tap into the Institute's expertise in biomedecine.

In 1992, the Industrial Associates Program (IAP) was founded to offer small companies or divisions of larger corporations the opportunity to collaborate formally with the Institute. Hewlett Packard joined the IAP in 1994.

Hewlett-Packard (HP) specializes in the design, manufacturing, and servicing of electronic products and systems for measurement and computation. HP, one of the 19 largest industrial companies in the U.S., was founded in 1939, by William Hewlett and David Packard, as an electronics company in a garage in Palo Alto, California.

Still headquartered in Palo Alto, HP has become a pioneering influence in the electronics industry and on company management practices during the last half-century.

Collaborative projects with the Institute focus on the development and use of Optical Low Coherence Reflectometry in the diagnosis and treatment of disfiguring portwine stain birthmarks in children.

"Our collaboration with HP has been really valuable," states Associate Director J. Stuart Nelson, M.D., Ph.D. The engineers (Wayne Sorin and Steve Newton) we work with at HP Labs are very knowledgeable and easy to work with. They have helped us to make important advances in our work imaging vascular skin lesions." ■

The Importance of Chromosome Tips

Chromosomes are the cell structures that contain all genetic information. Currently a major effort of the science establishment is to map the location of all the known human genes, and also determine the DNA sequences of all these genes. From this information are likely to come the cures and treatments for many serious diseases and illnesses.

In addition, however, to the massive push to map and sequence the human genome is a lesser known but probably equally as important effort to understand how the chromosome is structurally composed and how different distinct regions of the chromosome control specific cellular processes.

For example, every chromosome has a region called the centromere which is the point that the chromosome attaches to the apparatus in the cell called the spindle. The spindle is what exerts forces to equally separate chromosomes into daughter cells when the cells reproduce. But the mechanisms by which the centromere region interacts with the spindle is still not well known.

Within the LAMMP facility, Institute researchers have previously used a laser microsurgery microscope ("laser scissors") to destroy the centromere on single chromosomes in order to study how the chromosome separation process was disrupted.

However, more recently the very ends of the chromosome have been attracting much attention with respect to the control of cell reproduction. For example, it has been hypothesized that these tips, which are called telomeres, somehow control whether or not the cell can reproduce itself and become immortal.

This is of particular relevance to the problem of cancer, because cancer cells grow unchecked: in other words, they reproduce in an uncontrolled fashion.

There is a body of evidence that suggests that the telomeres of chromosomes

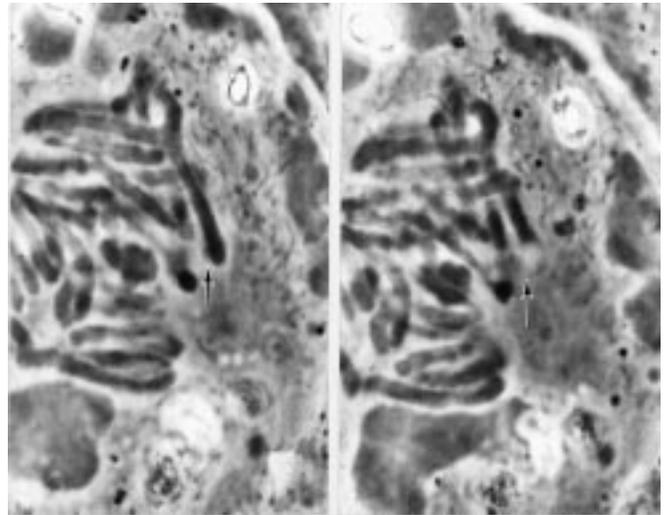
are controlling elements in this process. For example, researchers have hypothesized that if the telomeres maintain a certain molecular structure and activity (through a specific enzyme called telomerase) the cells can become immortal and literally reproduce forever.

If these cells are in a human body, this could result in a cancer that eventually kills the person. On the other hand, if the telomere is damaged or destroyed, the cell might lose its immortality (i.e., be blocked from going through the reproduction process).

A new exciting project that Institute researchers have undertaken in collaboration with Professor Harald Biessman's laboratory at the UC Irvine Developmental Biology Center is to test this hypothesis using the laser scissors. One of Dr. Biessman's students, Hung Tran, has just initiated a joint project between Dr. Biessman's lab and Dr. Berns' lab at the Institute.

The goal of the project is to directly test this hypothesis using a finely focused laser beam through the microscope to damage/destroy different numbers of telomeres and chromosomes of reproducing cells in a tissue culture. The cells that will be first used are rat kangaroo kidney cells.

These cells have been grown at the Institute for more than 10 years: thus, they are very immortal. In addition, they have only a small number of chromosomes (13 instead of the 46 that humans have) and they remain very



The figures above shows a dividing rat kangaroo cell with the chromosomes clearly visible.

flat under the microscope, allowing Institute researchers to easily visualize individual chromosomes and target the laser to the telomere.

The figures (above) shows a dividing rat kangaroo cell with the chromosomes clearly visible. The region that has been selectively destroyed with the laser beam is indicated by the arrow (figure 2). This region is less than 1 micron (1/1000 of a millimeter). In future experiments, researchers will destroy the telomere and then follow the cell for several days to see if destruction of that region, as compared to the destruction of another non-telomere region, causes the cell to lose its ability to reproduce.

"If this is the case," states Dr. Berns, "then we will have learned a very important fact about the role of the telomere in cell reproduction. More importantly, this will provide us with a cell model system to study the mechanism by which the telomere controls cell reproduction and, consequently, the role that this chromosome region may play in the control of cancer cells." ■

David Packard: A Life of Vision and Innovation

David Packard, co-founder of Hewlett Packard, leading figure in American business, and member of the Institute's Board of Directors passed away at the age of 83.

An Institute board member since 1992, Packard became involved with the Beckman Laser Institute through his friendship with founder Arnold Beckman, a long time personal friend.

Born in 1912 in Pueblo, Colorado, Packard took an early interest in engineering. With Stanford classmate Bill Hewlett he founded HP in 1939 in a garage in Palo Alto. Walt Disney Studios used the new company's first product, an audio oscillator, in developing the soundtrack for the film "Fantasia."

HP went on to become the second largest computer manufacturer in the United States, essentially creating Silicon Valley. Packard's management philosophy, "the HP Way," was ahead of its time in challenging boundaries between employees and managers.

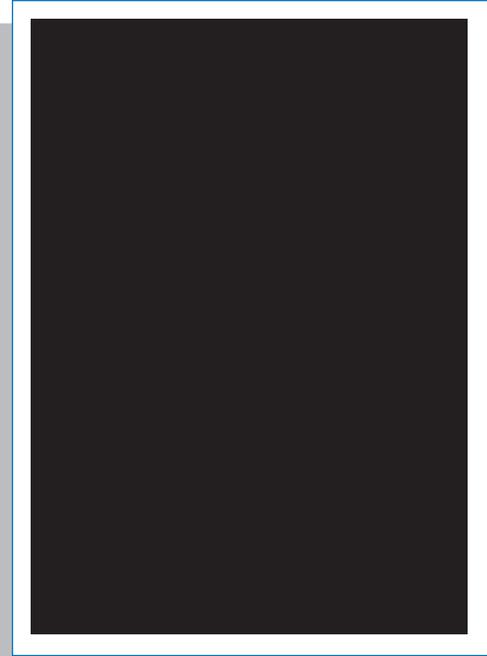
With wife Lucile, Packard became a major supporter of charitable causes. In 1964, they formed the David and Lucile Packard Foundation.

To date, the foundation has donated \$461 million for scientific research, community organizations, education, health care, conservation, population projects, and the arts.

His philanthropy extended to the Institute, which received an endowment gift to support research and treatment of young children with disfiguring birthmarks.

"David was a good friend to me," comments Dr. Beckman, "and to the Institute. He was a truly humane and generous person."

Lucile Packard died in 1987. Packard is survived by his four children, David Woodley Packard, Nancy Ann Packard, Susan Packard Orr, and Julie Elizabeth Packard. ■



David Packard.

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PRESENTATIONS

J. Stuart Nelson, M.D., Ph.D., spoke on "Initial Space-Dependent Temperature Distribution in Human Skin After Pulsed Laser Exposure" at the Symposium on Laser Diagnostics in Photomedicine. He also gave a presentation entitled "Lasers: in Photomedicine" at the Surgical Applications of Energy Sources meeting in Estes Park, Colorado.

Bruce Tromberg, Ph.D., spoke on "Frequency-Domain Photon Migration (FDPM) Measurements of Normal and Malignant Cell and Tissue Optical Properties" at the Optical Society of America in Orlando. He also gave the Rank Prize Funds Lecture on "Diagnostic and Therapeutic Applications of Tissue Optical Properties" at the Mini-Symposium on PDT in Grasmere England, and served as Chairman of the Microscopy Session at the 1996 Gordon Conference on Lasers and Medicine in Biology held at the Kimball Union Academy in Meriden, NH.

Dr. Petra Wilder-Smith made two presentations at the American Society for Laser Medicine and Surgery (ASLMS) annual meeting: "A SEM and CLSM Evaluation of the Effects of a 532 nm Laser on the Pulp Chamber and Root Canal," and "Effects of Ho:YAG Laser Irradiation on Pulp and Pulp Models," a presentation awarded the Research Poster Prize at the conference.

Attila Major, M.D., spoke on "In Vivo Fluorescence Detection of Ovarian Cancer in the Nutu-19 Epithelial Ovarian Cancer Animal Model Using 5-Aminolevulinic Acid (ALA)" at the Western Association of Gynecologic Oncologists in San Diego, CA.

Tatiana Krasieva, Ph.D., presented "Confocal Ablation Trapping System at BLI" at the Optical Biology Users Group Meeting sponsored by the UC Irvine Optical Biology Shared Resource.

Bahman Anvari, Ph.D., spoke on "Cryogen Spray Cooling in Conjunction with Laser Treatment of Selected Dermatoses" at the ASLMS meeting.

Zhongping Chen, Ph.D., gave a presentation on "Low-Coherence Doppler Tomographic Image of Flow in Highly Scattering Media" at the Gordon Conference.

PUBLICATIONS

J. Stuart Nelson, M.D., Ph.D., published three articles: "Space Dependent Temperature Increase in Human Skin Subsurface Chromophores Immediately Following Pulsed Laser Exposure" and "Epidermal Cooling During Pulsed Laser Treatment of Selected Dermatoses" in *SPIE*, as well as "Dynamic Epidermal Cooling in Conjunction with Laser-Induced Photothermalysis of Port Wine Stain Blood Vessels" in *Lasers in Surgery and Medicine*.

Bruce Achauer, M.D., and **Victoria VanderKam, R.N.**, published "Traumatic Tattooing: Treatment with the Q-Switched Ruby Laser: A Case Study" in *Annals of Plastic Surgery*.

Bruce Tromberg, Ph.D., published "Frequency-Domain Photon Migration (FDPM) Measurements of Normal and Malignant Cell and Tissue Optical Properties," in the *Proceedings of the Optical Society of America, Topical Meeting on Biomedical Optical Spectroscopy and Diagnostics*.

Tatiana Krasieva, Ph.D., published "Fluorescence Imaging Studies for the Disposition of Daunorubicin Liposomes (DaunoXome) within Tumor Tissue" in *Cancer Research*.

Bahman Anvari, Ph.D., published "Spatially Selective Photocoagulation of Biological Tissues: A Feasibility Study Utilizing Cryogen Spray Cooling" in *Applied Optics*.

NOTABLES

Pamela D. Aufhammer, R.N., joins the staff of the Surgery Laser Clinic as a per diem nurse. Previously, she worked at the Aesthetic Surgery Center in San Juan Capistrano, CA.

Sheryl Cherrison, has joined the staff as Administrative Assistant to Dr. Michael Berns. Prior to joining the Institute, she worked for Enterprise School District in Redding, CA.

Marguerite Critelli, M.D., joins the staff of the Surgery Laser Clinic as a Dermatologist. She completed her residency at UC Irvine and earned her medical degree at University of Colorado Medical School.

Janet Dickson, R.N., joins the Institute staff as a per diem nurse. She comes to us from Freedom Village in El Toro, CA, a subacute health care facility.

Jeffrey D. Gross, M.D., joins the Institute staff on a research sabbatical from the UC Irvine Medical Center Department of Neurological Surgery. He is performing clinical and basic studies on tissue optical properties.

Vickie LaMorte, Ph.D., has joined the Institute as Senior Scientist. She uses laser and molecular techniques to study gene expression. She received her doctorate from UC San Diego and served as a postdoctoral researcher (for Dr. Ron Evans) at the Salk Institute.

Stan Lowenberg, M.D., is Associate Clinical Professor of Surgery and Otolaryngology. He performs LAUP for snoring and Laser Turbinectomy to treat severe allergic rhinitis.

Vasan Vanugopalan, Ph.D., is a Harvey Mudd Fellow who is studying photon migration and laser microscopy. He received his Ph.D. from MIT/Wellman Labs (Harvard University) and was a postdoctoral researcher at Princeton.

NEWSBRIEFS

NEW CHAIRMAN OF THE BOARD

Gavin S. Herbert has been chosen to succeed Charles "Charley" Hester as chairman of the Institute's Board of Directors. Mr. Herbert is Chairman Emeritus of Allergan, Inc., headquartered in Irvine.

Allergan is a global provider of specialty therapeutic products. He helped found the company in 1950, served as its Chairman from 1977 to 1995 and as CEO from 1961 to 1991. He was Executive Vice President of SmithKline Beckman Corporation from 1986 to 1989.

Mr. Herbert is also Chairman and Owner of Roger's Gardens, a large retail nursery in Newport Beach, and Chairman of Regenesys Bioremediation Products in San Juan Capistrano.

Mr. Herbert has served on the board since the Institute opened its doors in 1986. He also is a trustee of the University of Southern California and serves on the boards of Research to Prevent Blindness, the California Healthcare Institute, and Beckman Instruments.

"We are honored to have Gavin Herbert as our Chairman," states Institute Director Michael W. Berns. "He continues a strong tradition as only our third Chairman."



Michael Berns, Patricia Beckman, Gavin Herbert (l-r) and Arnold Beckman (seated)

NEW BOARD MEMBER

Patricia Beckman, daughter of Institute co-founder Arnold O. Beckman, Ph.D., has joined the Institute's Board of Directors.

Ms. Beckman was educated at Mills College. She worked in Occupational Therapy before returning to school to pursue her interest in medicine. She became a registered nurse and worked at a number of hospitals, including Canyon General Hospital in Anaheim, California.

Her interests include traveling, hiking and reading.

"We are pleased by Pat Beckman's commitment," stated Institute Director Michael W. Berns, "to continuing her family's involvement with the Institute."

INSTITUTE CELEBRATES 10 YEARS

The Beckman Laser Institute recently celebrated its 10 year anniversary at an evening event attended by the Institute's Board of Directors, supporters, and current and former employees. A ceremonial groundbreaking for the new Photonic Incubator Wing was also celebrated. (Please see cover story, "Construction Grant Awarded," page 1).



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