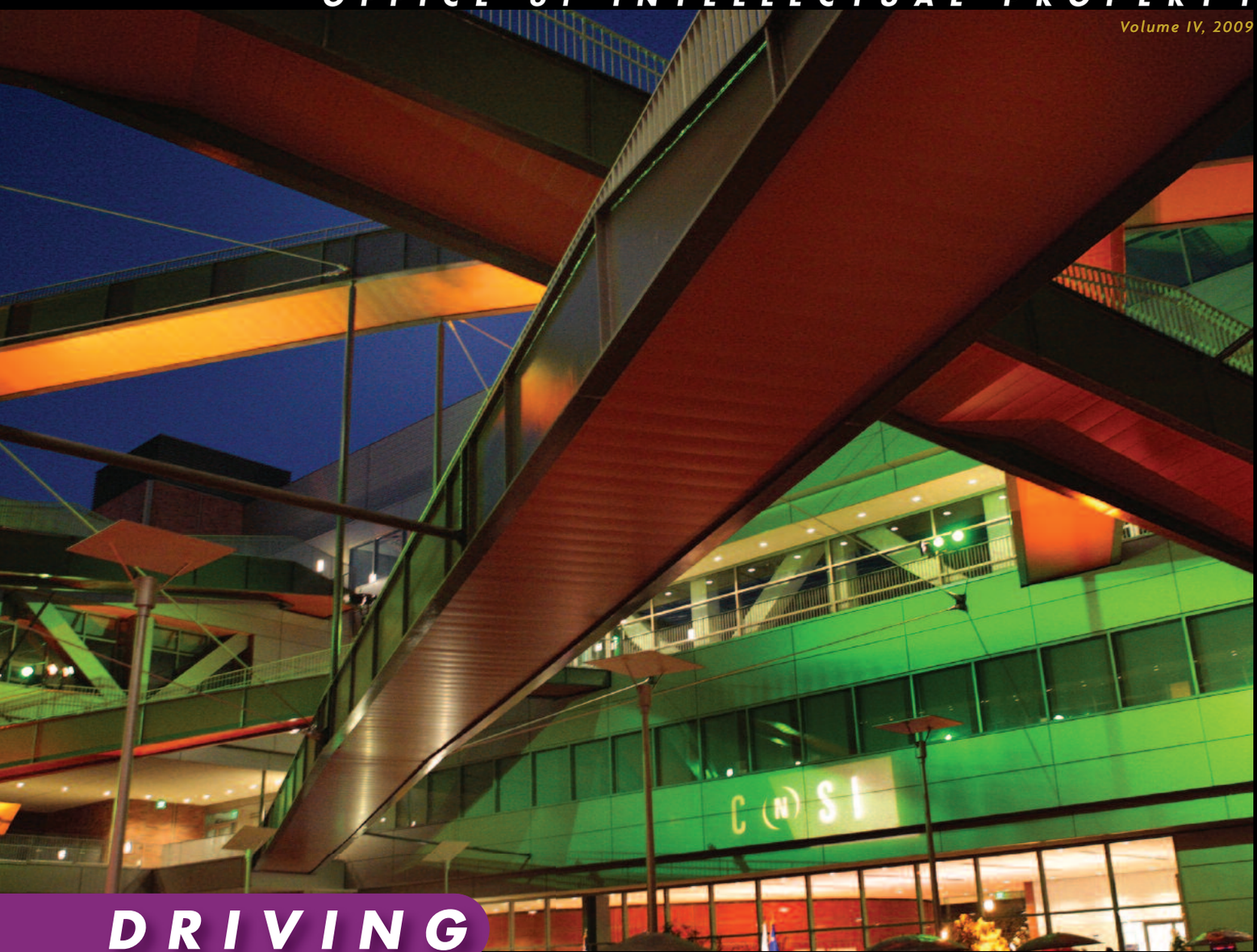
UCLA INVENTS

OFFICE of INTELLECTUAL PROPERTY

Volume IV, 2009



DRIVING iNNOVATiON TO MARKET

CONTENTS

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"They do more than pass out knowledge around here. They create it."

LETTER FROM THE VICE PROVOST

Driving Innovation to Market

Welcome to our fourth volume of *UCLAInvents*. As we go to press, the U.S. faces the deepest recession in 80 years. There is no more important time to focus on invention. The return of a vibrant economy for California, the U.S. and indeed the world depends on talented people who produce novel ideas — and have the capacity to transform those inventions into products and services with benefit to the public.

This *UCLAInvents* highlights some extraordinary faculty members and the novel ideas they produce. The potential impact of these ideas is great. Ultimately, they may help people in the areas of health, the environment, even home design.

We also highlight the synergistic relationship between our gifted faculty and students. Every year, undergraduate and graduate students and postdoctoral scholars are active participants in UCLA's inventive process. Age is no bar to innovation: the youngest inventor on record for the U.S. is Julian Pavone, age 4, who invented the "Abracadabra" Stain Cover-Up. Our inventive students add another dimension to faculty efforts.

Like a published manuscript, a patent application can be the first step in disseminating new knowledge. But a novel idea cannot stand alone. Innovation must be encouraged and nurtured to fruition. So *UCLAInvents* also spotlights experiments in incubation, including startups that share lab space to reduce overhead and to cross-pollinate different disciplines and technologies.

I hope you enjoy reading this issue as much as we've enjoyed preparing it. For more stories, technology and ideas on how to manage your intellectual property, check out our website at www.oip.ucla.edu.

Kathryn Atchison, *D.D.S., M.P.H.*

ECONOMIC

Nurturing New Ideas

Michael Phelps, Ph.D.

When Michael Phelps considers a map of the United States, he sees a problem. The largest concentration of biotech companies in the nation is in the Boston area. And the next highest are in the greater San Diego and San Francisco areas. In fact, there is a match between the location of the top 20 universities in America and the density of biotech companies, with one exception: the Los Angeles area.

Hoping to help change this situation, Phelps and a number of colleagues at UCLA and Caltech joined forces in 2007 to create Momentum Biosciences, a business incubator located in Culver City.

"Part of our goal," says Phelps, "is to retain and attract creative people to help rebuild our local economy in new ways. Universities throughout California must all take the initiative to invigorate the pioneering spirit that historically made California an innovative leader in areas ranging from agriculture to microcircuit electronics and information technology. The second part of our mission is to create an environment where faculty members themselves are owners of these companies. Ownership builds pride and drive. The faculty are also a creative force in redefining the relationship between the academic and commercial worlds at the entrepreneurial level, where new experiments can be performed in science and technology, along with new business models developed under criteria of the very different world ahead."

The Momentum portfolio has reached a peak of six startups based on technology primarily licensed from UCLA. They share laboratory facilities and office space, and also have access to a variety of essential services ranging from personnel, accounting and insurance to finance and license agreement negotiation. This approach reduces costs, allowing startups to focus the bulk of their attention and resources on product development.

"A typical biotech company will spend approximately $1.5 million in the first year," says Phelps. "About a million will be spent on all the services and activities necessary to operate a business, and only half a million on product development. Momentum established high-quality, low-cost services shared across the startups such that they spend about two-thirds of their funds on product development and only one-third on operations. The intent of Momentum is to incubate startups for 12 to 18 months to build value sufficient for them to be capitalized on their own or close them."

To date, three companies have been spun out, one has been put in hibernation while further research is pursued within the university, and two more are being added. Momentum was established after a proposal was submitted for review by university administration.

While the major focus is on biomedical sciences, primarily molecular diagnostics and therapeutics, other promising areas are also being pursued. For example, Richard Kaner, a professor in UCLA's Department of Chemistry & Biochemistry, has a research focus on polymers — or plastics — that conduct electricity. Using recent advances in nanotechnology, Kaner and his colleagues have been able to overcome two problems that have prevented industry from exploiting the considerable promise of these unique materials.

"Conducting polymers don't dissolve, and they don't melt," Kaner explains. "But we found that if you make nano forms of these polymers, they will disperse in water. And once you have water-based conducting polymers, you can spray coat them, spin coat them, and use them like paint."

This opens the door to many possible applications, including flexible electronic sensors and even conducting fibers that could be woven into clothing, potentially turning everyday apparel into portable — and fashionable — electronic devices, as

DEVELOPMENT

well as anti-static coatings and electromagnetic shielding materials for computers and other electronic components.

Kaner recalls that Momentum approached him with the idea of starting a company in the incubator. "The Momentum people were looking at UCLA technology that hadn't yet been licensed, and they noticed a lot of patents from my group involved with conducting polymers, and they saw an interesting fit. That's what got us started."

Fibron Technologies, the company that emerged with Kaner and Chris Behrenbruch as founders, is one of the startups that recently exited Momentum with an investment from a Korean company, Kolon Glotech. Fibron, and the other companies that exited Momentum, remain in the Culver City area.

Kaner appreciates the many business services that Momentum provides. But, he notes, working in the same building with five other startups involving cutting-edge scientists translating their research into products is the big plus. "With the close proximity of these other companies, the scientists involved are constantly talking to each other, so ideas come up that would not normally happen."

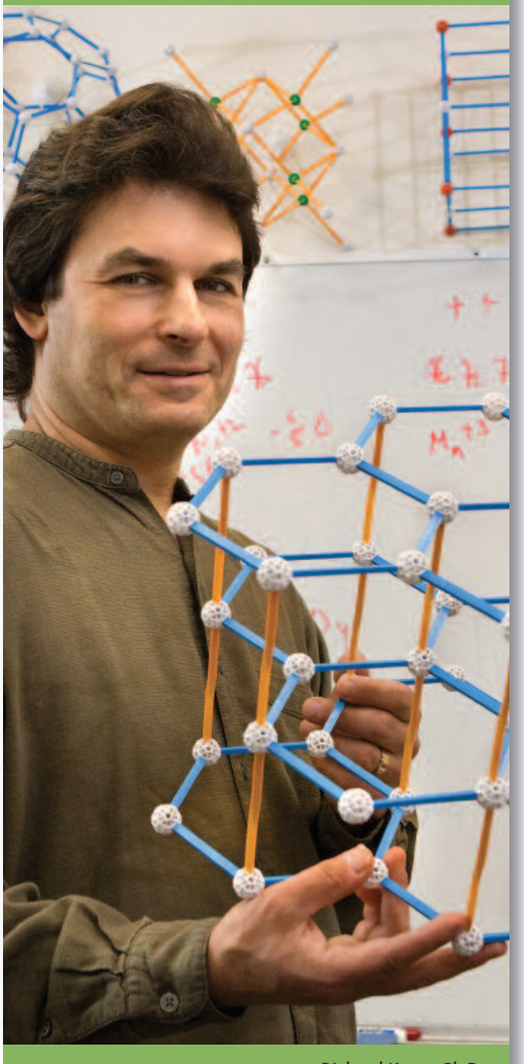
This commitment to moving innovative ideas out of the laboratory and into the marketplace is shared by UCLA's Office of Intellectual Property. As a land-grant institution, The University of California is not only responsible for providing a quality education to the students enrolled here, it is responsible for giving something back to the state of California. The extent of OIP's commitment to this mission is clearly demonstrated in the new on-campus teaching incubator that UCLA has established at the facility that also houses the California NanoSystems Institute (CNSI).

With 2,000 square feet of state-of-the-art laboratory and office space, the incubator offers not only a place for product development, it offers a place where research-oriented faculty members can learn about — and meet — the challenges of the business world.

"We are working to connect the new companies to MBA students who want to work with them on business plan writing or market plan assessment," explains Kathryn Atchison, vice provost, Intellectual Property and Industry Relations. "And we are also introducing them to law students who would like to learn about IP management and commercialization. We're probably going to have six to eight little companies in there, and they will have access to the core facilities, as well as interns and fellows who are interested in learning more about the commercialization of intellectual property."

Atchison says that "16 or 17" faculty members have approached her thus far, expressing an interest in becoming part of the incubator. But because space is limited, a faculty advisory committee has been established to evaluate the various proposals that have crossed her desk. Members of the committee are drawn from the CNSI, the School of Medicine, the Henry Samueli School of Engineering and Applied Science, the School of Public Health, the College of Letters and Science, the Anderson School and the School of Law — a roster that reflects the truly multi-disciplinary nature of the incubator.

"We believe that the obligations for a land-grant institution for 2009, and moving forward, have more to do with economic development," says Atchison. "It's more about things like business incubators and commercialization than trying to teach farmers about pest control."

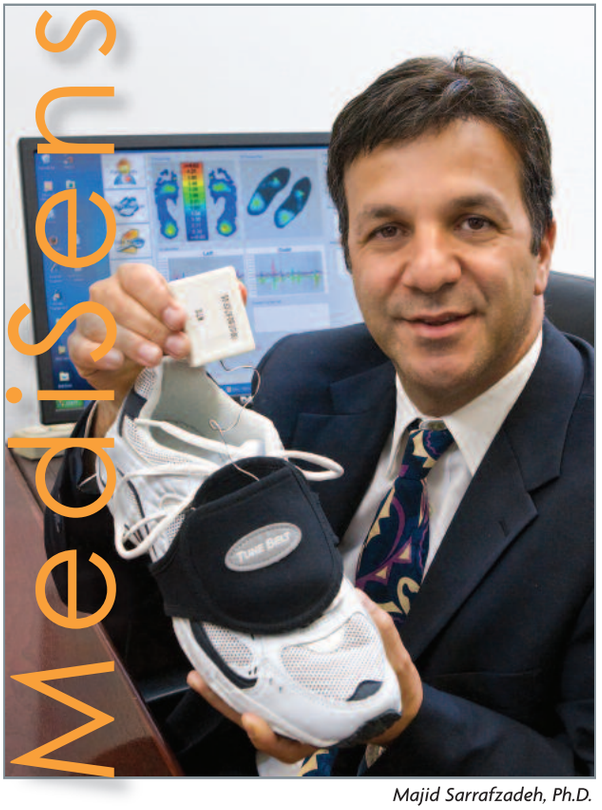


Richard Kaner, Ph.D.

The roots of the teaching incubator may well stretch back to UC's origins as a land-grant college. But in facilitating the commercialization of the UCLA faculty's cutting-edge research, the incubator brings the original concept in line with the realities of the 21st century. ♦

STARTUPS

If the e-Shoe Fits



Majid Sarrafzadeh, Ph.D.

When Majid Sarrafzadeh and his wife brought their newborn daughter home from the hospital, they were confronted with a problem that all too many parents face. The child was born prematurely and required round-the-clock monitoring. While this had not presented a significant problem in the hospital, at home the couple now faced the daunting challenge of having to maintain a constant vigil over the infant.

"That was truly nerve-wracking for us as parents," Sarrafzadeh recalls. "But having some background in technology, I thought, 'Gee, it would be so easy to build a very small device to monitor her breathing and all that at home instead of us watching her 24/7.'"

Having "some background" in technology is perhaps something of an understatement. Sarrafzadeh currently serves as the director of The Embedded and Reconfigurable Computing Lab at UCLA's Computer Science Department, and in large part because of his experience with his daughter, he was a driving force in the creation of the UCLA Wireless Health Community some seven years ago. The community's vision is a multidisciplinary approach to the challenges facing the healthcare system, and it includes researchers from the university's Schools of Engineering, Law, Management, Medicine, Nursing, Public Health, and Theater, Film, and Television.

The multidisciplinary approach is essential, says Sarrafzadeh, because technology is important, but technology alone won't solve the problem of spiraling healthcare costs. "It's not that you will be designing a faster computer or building a better gadget. You're solving real problems, so you have got to be looking at end-to-end systems. You have to go all the way from design to medicine to public use, and find a way to provide feedback to the doctor. It involves designing an entire system. And this has its own interesting challenges."

Sarrafzadeh and his colleagues have been working on a variety of projects ranging from smart canes to body sensor networks to personalized systems that monitor exposure to ultraviolet radiation. But the device that is now on the verge of making the transition from laboratory to the marketplace is a sophisticated electronic shoe that will allow healthcare professionals to monitor and assess patients who are experiencing balance problems.

Traditionally, Sarrafzadeh explains, physicians have had to rely on patients themselves to report difficulties with keeping their balance after starting a new medication, say, or if they are in the early stages of a diabetic condition. With patients perhaps reluctant to report the problem, or not even realizing the problem exists, this has left many of them susceptible to falls. And with falls costing the healthcare system an estimated $20 billion annually, Sarrafzadeh and several colleagues concluded that there might well be a market for a product that could give physicians the ability to monitor their patients' balance problems remotely.

Working with the Office of Intellectual Property (OIP), they assembled a group of investors, drafted a licensing agreement with the university and formed MediSens, a company that will bring this "smart shoe" platform to market and explore the feasibility of commercializing other wireless medical solutions.

"There are many horror stories I have heard from colleagues in other universities," says Sarrafzadeh. "But the people in the OIP office here were extremely helpful and extremely encouraging in our first meetings."

Maintaining this vital connection to the university and its resources, MediSens will open an office in the business incubator that has been established at the California NanoSystems Institute on the UCLA campus. There, the company will continue to focus on developing products that enhance the physician's ability to continuously monitor a patient's medical condition.

"This is the future," says Sarrafzadeh, "being able to continuously monitor people and create a personalized health system that is tailored to the individual. We don't envision that any of these devices will replace doctors. We envision them as helping the doctors make better and more informed decisions. And this is going to reduce healthcare costs tremendously as we move forward." ♦

A Common Language

For Jack Judy, the most interesting place in all of science and engineering is the interface between seemingly unrelated fields of research. Hence, it is not surprising that shortly after taking an appointment in UCLA's Department of Electrical Engineering in 1997, Prof. Judy extended a hand across disciplines, reaching out to his colleagues in the university's medical school. A specialist in MEMS — Micro-Electro-Mechanical Systems — Judy believed that, working together, researchers from such different disciplines could effectively address a wide range of vexing healthcare issues.

"After speaking to many people in the health and life sciences, the ones that seemed the most keen and desperate for a technology injection in their field were those associated with the nervous system and the brain," Judy recalls. "And frankly, as an electrical engineer who makes circuits and microsystems, I felt a certain affinity with my colleagues who were studying neural circuits. Together we quickly recognized the huge opportunities that existed in the combination of the technologies I worked on and the kinds of problems they were trying to solve."

With this spirit of cooperation in mind, Judy was instrumental in co-founding the world's first formal graduate program in neuroengineering. The goal of the program is to bring students together in an environment where the boundaries between engineering and neuroscience begin to blur. It is here, Judy believes, that students can learn a common language and recognize mutual interests.

"When you have a neuroscientist talking to an engineer, you often speak past each other," he says. "We sometimes use the same words and mean completely different things. When I say the word 'vector,' for example, I mean a mathematical construct with a direction and magnitude. A doctor or biologist, though, is thinking of a plasmid or ring of DNA. Another problem is that engineers with new technologies typically won't consider pursuing neural applications because they don't know they exist. Neuroscientists are also stymied because they don't know the new technologies exist. Graduates from the NeuroEngineering Program are trained to traverse this disciplinary chasm with ease."

One of Judy's students, Alejandro Covalin, has turned out to be particularly adept at thinking across disciplines. Covalin earned his undergraduate degree in physics engineering at Universidad Iberoamericana, in Mexico City. He began his professional life working as a new projects engineer in the forestry industry in his native Mexico. But after overseeing the design and construction of a new sawmill facility, Covalin recalls that he felt the need to move on. He came to UCLA in 2000, and, with Judy as his advisor, he decided to study the role of feedback mechanisms in the autonomic nervous system.

He researched various options, and after discussing them with UCLA neurosurgeon Antonio De Salles, he turned his attention to obesity and the role the autonomous nervous system plays in determining metabolic rates. Covalin and Judy found that there is in fact a region in the brain that controls metabolic activity, and that by introducing an electric current, it is possible to regulate the metabolic rate.

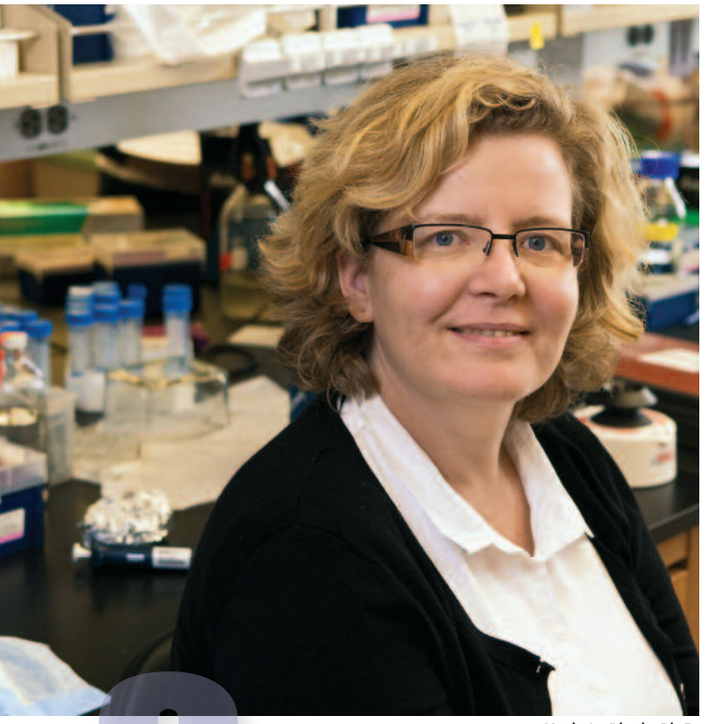
Having successfully demonstrated the technology on small animals, Covalin and Judy, together with De Salles and Los Angeles-based entrepreneur Leon Ekchian, founded NeuroSigma, Inc., in 2008. NeuroSigma exclusively licensed the patent application from UCLA, is currently taking steps to obtain FDA approval for human clinical trials, and is moving forward with plans to commercialize the technology.

Alejandro Covalin, Ph.D., post-doctoral student, and Jack Judy, Ph.D.

"Without Alejandro's work as a graduate student," observes Judy, "NeuroSigma wouldn't be where it is. Without the neuroengineeing training program, Alejandro wouldn't be where he is. UCLA is extremely fortunate to have a top-notch medical school immediately adjacent to a top-notch engineering school. This is another thing that makes UCLA such a fantastic institution." ♦

TRANSFER AGREEMENTS

Stem Cells **Simplified**



Kathrin Plath, Ph.D.

Over the past decade, stem cells have emerged as one of the most promising tools in the world of medical science. But despite their considerable potential for treating disease, stem cells are controversial because of moral questions surrounding the use of stem cells taken from embryos. UCLA researcher Kathrin Plath notes that even before one deals with the socio-political ramifications of research on embryonic stem cells, however, there is a more fundamental medical problem.

"That problem is rejection by the immune system," says Plath, who is an assistant professor of biological chemistry at UCLA's David Geffen School of Medicine. "It's like when you do a liver transplant from one person to another person. There's often an immune rejection because the transplanted organ is not recognized as self by the body."

Plath and her colleagues are currently working on research that could address this problem. The process they have developed uses retroviruses to introduce a set of four special genes into normal adult skin cells. These genes effectively reprogram the skin cells, causing them to revert to a primitive state. Known as induced pluripotent stem cells (iPSCs), these cells – like embryonic stem cells – have the capacity to turn into any type of cell in the body.

"These four genes basically decide which genes are turned on and turned off in this cell type," Plath elaborates. "The genes that we put in are highly expressed normally in embryonic stem cells and regulate which genes are expressed in these cells. So the idea is that by over-expressing them, you can force the embryonic state onto an adult cell."

Plath notes that the process of reprogramming the adult cells, however, is both inefficient and time-consuming. Because not all laboratories are yet equipped to do this work, researchers who want to experiment with iPSCs often turn to Plath's lab with requests for both the cells themselves and the retroviruses that are used to carry the four genes to their targets.

Plath is committed to sharing these valuable cells with other scientists, and she regularly sends cells grown in her lab to universities and research institutions around the world. As requests for iPSCs come in, the Office of Intellectual Property arranges for the material transfer agreements, and the requested cells are shipped directly to the lab or institution. Requests for the retroviruses, originally obtained from the University of Tokyo, are routed through ADDGENE, an organization that stocks UCLA's retroviral vectors and sends them to researchers who place orders for them. UCLA has entered into an agreement with ADDGENE to permit the distribution of these retroviral vectors to other researchers.

The hope among lay people and many researchers is that healthy tissues grown from stem cells may one day be used to replace diseased tissues. Plath acknowledges that this may indeed be possible and even inevitable – some day. In the meantime, she believes that the real promise of stem cell research is in disease modeling.

"There are many, many diseases out there that nobody knows how they develop or what goes wrong," she says. "So now you can take skin cells from these patients, turn them into iPSCs and then differentiate them into the cell type of interest. Then see if you can model the disease in the culture dish."

Plath cites Parkinson's Disease as a good example. "Often you cannot get to the neurons that are of interest," she explains. "You can't just drill into the brain and get the neurons out. But with the iPSCs, you can differentiate the iPSCs into neurons and see if anything goes wrong during the differentiation."

Once the disease has been modeled, researchers might come to understand the underlying mechanism that triggers the disease, and this in turn could point them in the direction of methods for either preventing or treating it. "It is," says Plath, "a very good study system." ♦

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The Art of **Survival**

With ongoing improvements in our understanding of human biology and the delivery of quality medical care, a growing number of formerly fatal diseases have been largely vanquished in recent years. And that is very good news. But for many individuals with cancer, the transition from patient to survivor can be an awkward period of anxiety and confusion. The healthcare professionals who were once so much a part of their lives have moved on to new patients. The survivors are forced to embark on this new phase of their journey alone.

Patricia Ganz, professor of health services at the UCLA School of Public Health, has long been interested in the outcomes of these survivors. So early in her 30-year career as an oncologist, she began to research the effects of cancer treatment, with an eye toward improving the patient's quality of life after treatment. This interest led to a groundbreaking study of breast cancer survivors that was funded by the National Cancer Institute.

"We tested three different strategies to see if we could improve recovery after breast cancer treatment," Ganz explains. "The control group received a general informational booklet from the National Cancer Institute that was focused on survivors. The second group got a specially developed video, which had several women who were survivors talking about their experience recovering, role modeling and talking about the common areas in which it took time to recover and get their lives back together. The third group had an in-person visit with a cancer health educator and mental health specialist, focusing on the specific issues or problems that were most difficult for them at the time when they finished treatment. They also received the same video, as well as a much more detailed book that included information on breast cancer-specific issues in recovery. Two weeks later they received a follow-up phone call from the health educator."

Somewhat surprisingly, the researchers found that the second method — the video alone — resulted in the best outcomes for the cancer survivors.

Having demonstrated that she had created an effective tool for helping breast cancer survivors recover from the course of treatment they had just come through, Ganz decided to make the video available to the public.

"I'm a very practical and applied person," says Ganz. "My thought had been that if either of the two interventions that we used were effective, we would want to see them used in clinical practice. So I partnered with the National Cancer Institute, with funding from the Susan G. Komen Breast Cancer Foundation, to transform this video into a product that could be distributed through the resource center at the National Cancer Institute."

Before long, Ganz found that she had a hit movie on her hands. Institutions like the Cleveland Clinic and other hospitals approached her, seeking permission to show the video — now titled "Moving Beyond Breast Cancer" — to patients on their own internal video networks. Ganz turned to the Office of Intellectual Property to arrange the licensing agreements, and OIP responded by creating a "ready-to-sign licensing agreement" that interested parties can complete and sign directly on the Internet.

Patricia Ganz, M.D.

"I'm a very practical and applied person. My thought had been that if either of the two interventions that we used were effective, we would want to see them used in clinical practice."

Ganz says that she has no interest in pursuing a new career in video production. Still, she is happy that she was able to participate in the creation of a video that has helped so many women come to terms with life after breast cancer.

"This was a great opportunity to translate something from the laboratory out into the population," she says. "I think that is one of my responsibilities and missions." ♦

WATER FRONTIER

"As far back as the 1940s, faculty and researchers here were writing pro

ON THE WA

WATER IS THE PARADOX. To the west, the Pacific Ocean stretches as far as the eye can see. Wet. Blue. And inviting. But turn around and you are immediately confronted with the reality on the ground. Much of California is little more than scrub desert. Harsh. Hostile to life. Given this paradox, it is not surprising that water has been a defining issue in the history of the Golden State.

UCLA has long been at the forefront of the struggle to secure adequate supplies of fresh water for California's ever-growing population. That, in fact, has been one of the school's primary missions, says Yoram Cohen, the founding director of UCLA's Water Technology Research Center.

"The School of Engineering and Applied Science was founded on four pillars: energy, transportation, air pollution and water," he elaborates. "As far back as the 1940s, faculty and researchers here were writing proposals and doing research on novel technologies for fresh water production."

Yoram Cohen, Ph.D.

UCLA patented the first commercially viable reverse-osmosis (RO) membrane in 1960. And although the original UCLA membrane was replaced with more efficient membranes developed in industry, the UCLA team has been globally credited with giving birth to modern RO membrane technology. Carrying this proud tradition on into the 21st century, Cohen and fellow researchers Eric Hoek and Julius "Bud" Glater founded the UCLA WaTeR Center in 2005. And using the WaTeR Center as their base of operations, they and their colleagues have embarked on a mission to advance our understanding of water use and production around the globe in order to develop technologies for new and economical alternative sources of potable, irrigation and consumptive water uses.

"Given the severe water shortage problems we face in this state," says Cohen, "we have had to accelerate our efforts to develop and improve technologies for water reclamation and recycling, while exploring the utilization of water sources that are not currently used for potable water. This technology has moved very quickly from traditional technologies that utilize large treatment basins to membrane-based technology."

This approach has resulted in the development of revolutionary, UCLA-patented, surface nano-structuring technology for synthesizing another class of membranes for water desalination. With their high resistance to fouling and mineral scaling, these membranes represent a significant improvement over the technology that is currently available commercially. WaTeR Center students and faculty have also developed patented desalination technology that integrates RO desalination with chemical demineralization. And using this technology, an unprecedented 95-percent product-water recovery in desalting of brackish water has been achieved.

"Effective operation of RO plants, specifically for inland water desalting, requires monitoring of the onset of mineral scaling and fouling," adds Cohen. "And to that end, WaTer Center faculty and students have also developed a patented online monitor that interfaces with the RO plant control system to enable advanced scaling and fouling mitigation."

With membrane-based technology, Cohen notes, processes occur at a much shorter time scale, and this in turn requires expertise in process control, in material science, in hydrodynamics, in fluid mechanics, in the area of membrane bioreactors, in the area of desalination, in the area of transport phenomena, in chemistry, and in polymer science. "So when you combine all those together," he says, "you realize that the only way to achieve that is a team approach."

Thus, the research and development work at the WaTeR Center necessarily reaches across departmental lines. But Cohen points out that the WaTeR Center also works with partners in industry, state and municipal water agencies, and a number of international partners such as Victoria and RMIT Universities in Australia, the Universitat Rovira i Virgili (Catalunya, Spain) and Ben Gurion University in Israel. He counts 20 affiliates in all and notes that one thing they all have in common is an interest in making better use of the planet's dwindling reserves of fresh water.

posals and doing research on novel technologies for fresh water production."

TER FRONT

"Water is a local resource," he says, "There is not much competition in terms of the mining of that resource for import or export. So it's easier to share knowledge."

With this focus on finding solutions to real-world problems, technology transfer is a natural outgrowth of the WaTeR Center's day-to-day activities. Cohen notes, for example, that students from the WaTeR Center have tested UCLA's water desalination technology in the field both in California and in collaborations with foreign partners.

This pays dividends not only for the WaTeR Center's affiliates; it also advances UCLA's mission as an institution of higher learning.

"It's incredibly exciting not just for the faculty researchers but for the students when they get the opportunity to put the science and engineering that they developed to use during the course of their thesis research," says Cohen. "This gives them an incredible opportunity, and it also gets them very excited. They interact with professionals, and they see that they can make a difference in the world."

TECHNOLOGY TRANSFER: *THE ESSENTIAL CONNECTION*

WaTeR Center co-founder Eric Hoek, an assistant professor of civil and environmental engineering, understands the importance of bringing innovation out of the laboratory and turning it into commercially viable technologies. His story, in fact, tells a lot about the way the WaTeR Center is meeting its responsibilities to both the University of California and the community that supports it.

Working with his students and colleagues at the WaTeR Center, Hoek has pioneered a new approach to making reverse osmosis membranes. This technology produces energy-efficient and fouling-resistant membranes by combining nanoparticles with conventional membrane polymers.

Eric Hoek, Ph.D.

"About six years ago," he explains, "we started synthesizing nanoparticles that, when integrated into standard membrane polymers, produce very high water productivity and improve the functionality of the membranes so they don't foul as quickly. We expect our 'thin film nanocomposite' membranes to open up new process engineering opportunities for more cost-effective and environmentally friendly desalination plant designs.

"Our initial research was funded by the UCLA engineering school, but later we received additional support to further explore nanocomposite RO membranes from a private company — NanoH_2O Inc. — and the California NanoSystems Institute (CNSI)."

As a private company, NanoH_2O is in business to turn a profit, of course. But as Hoek points out, the ongoing efforts to commercialize his nanocomposite membrane technology serve to inspire and educate his students as well.

"It's infectious as far as the students go," he says. "It seems that every student in the group wants to do something that is going to lead to a new company. Obviously, every student is not going to accomplish that. But it does add a certain amount of excitement to what we do and inspires a sense of what is possible. We have also learned a lot about more practical issues related to membrane formation and application, which informs our larger research efforts on nanotechnology, membranes and water treatment."

Although he is a bit more circumspect on the importance of commercializing the technology he and his colleagues develop, this more or less echoes Yoram Cohen's guiding philosophy when it comes to setting a long-term course for the WaTeR Center. "I don't consider technology transfer to be the act of making money or having a commercial entity that will develop a process. I consider it to be a success when the process or intellectual property can be put to good use, and we can demonstrate that it can." ♦

WATER CENTER

PROMETHEUS

Diagnoses Done Right

Jonathan Braun, M.D.

Dr. Jonathan Braun describes inflammatory bowel disease (IBD) as being a "mosaic of diseases." And although this might seem an oddly charming way to describe a condition that most of us would rather not think about at all, research that Braun conducted for the National Institutes of Health in the mid-to-late-1990s demonstrated that "mosaic" is indeed an apt description. Working with Dr. Stephan Targan of the Cedars-Sinai Medical Center, Braun tested the hypothesis that IBD is not one disease, but rather a condition caused by a spectrum of inappropriate immune responses to bacteria that normally live in the human digestive system.

"We all have bacteria that live in our gut," Braun explains. "The reason that most of us are okay is because we let them live there. We need them to digest our food. In IBD, however, there is an immune response against these bacteria, so the patient is undergoing constant warfare."

The nature of this warfare, unfortunately, varies from patient to patient. And, without knowing the precise terms of the engagement, physicians have been forced to use something of a trial-and-error method when treating IBD patients. This is both costly and time consuming. But based on their understanding of IBD as a mosaic of diseases, Braun and Targan developed a set of serologies, or blood tests, that allow physicians to quickly identify the exact nature of the patient's immune reaction.

"These serologies provide a way to read out the details of the inappropriate immune response to the bacteria," says Braun. "And these different markers — the details of these markers — allow you to validate whether somebody actually has the disease, and it allows you to predict the course of the disease and then guide strategies for treatment. None of that was possible before."

Understanding the breakthrough nature of their discovery, Braun and Targan decided to form a company to bring this diagnostic test to market. They approached a number of venture capitalists, wrote business plans, and worked closely with both Cedars-Sinai and UCLA to hammer out licensing agreements and avoid conflict-of-interest issues.

Prometheus Laboratories emerged from the negotiations, and on the strength of Braun and Targan's discovery — marketed today as Prometheus IBD Serology 7 — the company has become a major force in the diagnosis and treatment of gastrointestinal disorders. Having achieved profitability in 2004 and 2005, the company reported net sales of $278.1 million in 2008, a figure that represents a 32.7 percent compounded annual growth rate since 2004.

Braun currently chairs the Department of Pathology and Laboratory Medicine at UCLA's David Geffen School of Medicine and is no longer involved in Prometheus' day-to-day operations. He notes, however, that bringing Serology 7 to market was a transformational experience, one that has helped define his current research interests.

"Prometheus was my first major link to clinical translation," he says. "Because of what I learned from that — understanding the whole pipeline that goes from a very basic finding, all the way to something that is used clinically, in addition to understanding the business issues that determine whether or not something makes it there — it has really affected the choices I've made about my areas of research. You need to make it possible for companies to find financial value in what you're doing and bring it out into the community. There's a real excitement and real gratification in seeing research that actually affects the community directly." ♦

Brain Watch

The human brain is one of the most complex and remarkable objects known to man. And when it is healthy, it is capable of performing feats that still leave medical researchers scratching their heads in amazement. Unfortunately, when problems arise, this very complexity leaves researchers and clinicians equally baffled. Functional MRI, a new technology that actually shows which parts of the brain are engaged when people perform cognitive or behavioral tasks, is making it possible for us to unravel many of the brain's secrets. But as researcher Mark Cohen, Ph.D., notes, useful as it is, this technology has several limitations.

"What it does is follow blood flow changes in the brain, and those changes can take seven to 10 seconds to appear," explains the UCLA brain mapping specialist. This time lag makes it difficult to determine exactly when events in the brain occur. A much older technology, the EEG, skirts this problem because it records electrical impulses, which can be seen as they occur. But, as Cohen notes, the EEG relies on electrodes that are attached to the scalp. It can tell a physician or researcher what is happening in the brain, but not where.

The ideal solution, then, would be to use functional MRI and EEGs in tandem — a solution, unfortunately, that comes with its own set of problems.

"There are two sets of problems in combining EEG and MRI," Cohen explains. "One set of problems is how the EEG equipment interacts with the MRI and causes trouble in the images. That has to do with the introduction of electrical conductors inside the MRI device. And there is also a safety issue. The MRI device uses a relatively high power radio transmitter, and that can be coupled to the head through the physical electrodes. So in rare cases, people have suffered skin lesions when EEGs have been done in combination with MRIs."

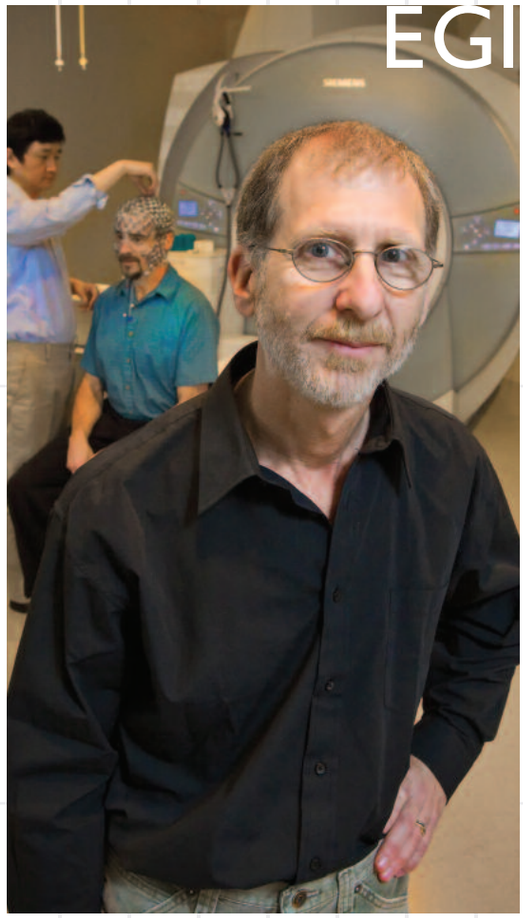
Cohen and his colleagues spent a decade of federally funded research trying to solve this problem, and the solution required a complete rethinking of the standard EEG hardware, from the electrodes themselves all the way to the display screens.

The new technology, Cohen believes, will be particularly useful in clinical settings. Patients with severe cases of epilepsy, for example, often undergo brain surgery that removes the part of the brain that is believed to be causing the patients' seizures. One of the major drawbacks to this approach, however, is the difficulty of determining exactly where in the brain the problem lies. Cohen believes his new technology addresses this concern.

"During the periods when people are not having seizures, most persons with epilepsy have abnormal brain signals," he says. "So we can pick up events in the brain which you, as a normal person, would be very unlikely to have. By trying to associate the timing of these intermittent events with changes in the blood flow signal in the brain, we can have a window into trying to identify brain regions that are candidates for resection."

Cohen speculates that the technology could also be used in the diagnosis and treatment of other central nervous system diseases, such as Parkinson's disease, depression and obsessive-compulsive disease. He also believes that the method this invention uses to remove EEG artifacts in scanning could have very broad impacts in digital noise reduction in telecommunications, audio and video. He hopes to find additional partners to license the technology in those domains.

The technology has been licensed to EGI, a company based in Eugene, Oregon, that hopes to market commercial applications in the near future. Cohen currently serves as a professor in the departments of Neurology; Radiological Sciences; Psychiatry & Biobehavioral Sciences; and Biomedical Physics at UCLA's David Geffen School of Medicine. ♦

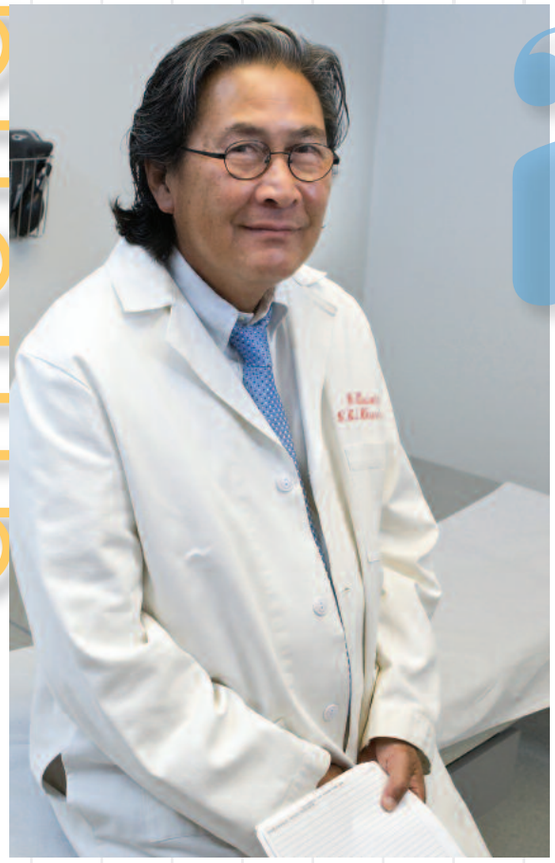


Mark Cohen, Ph.D.

"By trying to associate the timing of these intermittent events with changes in the blood flow signal in the brain, we can have a window into trying to identify brain regions that are candidates for resection."

athena

Taking the **Uncertainty** out of **Epilepsy**



Antonio Delgado-Escueta, M.D.

Although it can take many forms, one of the most familiar types of epilepsy is the condition known as juvenile myoclonic epilepsy, or JME. This condition usually manifests itself in adolescence, and it is commonly associated with the dramatic "grand mal" seizures that typically afflict its victims.

Antonio Delgado-Escueta has spent the last two decades of his life studying epilepsy, and he has seen the devastating effects of JME firsthand. "Grand mal epilepsy is the most horrible form of seizure to witness," he says. "Patients fall and lose consciousness, and get stiff and convulse, and the eyes roll up. It scares the hell out of parents."

Fortunately for the victims and their families, JME is usually non-fatal. And when diagnosed early and accurately, it does respond to treatment. Making an accurate diagnosis is not easy, however. Twenty different forms of epilepsy have been identified thus far, and when the disease starts manifesting itself in adolescent patients, it is virtually indistinguishable from other debilitating forms, as well as fatal forms, of epilepsy.

Delgado-Escueta, who serves as professor-in-residence and attending neurologist at UCLA's David Geffen School of Medicine, has developed a tool that greatly simplifies the process of diagnosing JME. The technology is an outgrowth of Delgado-Escueta's ongoing search for a cure for JME, which he has been conducting in collaboration with research organizations in Honduras, Mexico and Japan. In the course of their research on the genetic basis for the disease, Delgado-Escueta — whose own work is funded by the National Institutes of Health — and his colleagues isolated a single mutated gene that is associated with the onset of JME. When this gene is detected through a simple blood test, it is possible to make a definitive diagnosis of JME and eliminate the possibility that the patient is suffering from another variant of the disease.

"It's very important that you know exactly what you're dealing with," says Delgado-Escueta. "If you can separate it from the fatal forms of epilepsy, that means a lot to the families, especially when you can reassure them that the prognosis is good because you can control the seizures."

UCLA's Office of Intellectual Property (OIP) has entered into an agreement with the three foreign co-owners, so that it can be the leading party in licensing the technology to Worcester, Massachusetts-based Athena Diagnostics. Athena specializes in the development and commercialization of diagnostic testing for neurological disorders.

Delgado-Escueta is happy to let OIP and Athena handle the details of commercializing his test. His focus, he says, is on finding cures for epilepsy, and that quest commands his full attention. Working with his students, he has already identified three genes that are associated with various epileptic conditions. But while isolating the genes is important, his real challenge is defining the mechanism of action by which the mutated genes cause JME. Once this mechanism is understood, he believes it might well be possible to find a cure.

With more than 2 million Americans suffering from epileptic conditions, Delgado-Escueta believes this is the best use of his time. ♦

profiles

PET Snoop Boys

As remarkable as the human immune system is, it doesn't always work as well as one might hope it would. Cancer and infectious diseases can overwhelm it. And in some cases, the immune system itself goes rogue, attacking the very body it is supposed to protect.

UCLA researchers Owen Witte and Caius Radu share an interest in the immune system that stretches back across the arc of the two men's careers. "Years and years ago, when I was a medical student, I had worked on and developed an interest in cancer immunotherapy," recalls Witte, who serves as a professor of molecular and medical pharmacology at UCLA's David Geffen School of Medicine. "I wanted to see how we could use the immune system to treat cancer."

Radu, who once worked as a fellow in Witte's lab and describes the older scientist as his mentor, notes that being interested in the immune system is one thing; understanding how it functions is quite another matter. "You face roadblocks," he explains. "And one of those roadblocks, which is very significant, is the fact that the immune system is so complex, we cannot model it outside of the body. You have to see it at work in a living organism."

The key to breaking through this roadblock turned out to be Positron Emission Tomography (PET), an imaging technology developed by UCLA's own Dr. Michael Phelps.

Using PET, it is possible for physicians and medical researchers to monitor biological processes as they happen. The challenge for Witte, Radu and their colleagues was to find a method that would allow the PET scanner to focus on activities within an organism's immune system. By observing the immune system at work, they reasoned, it would be possible to determine the effect of various drugs on immune system function.

The key to making the secrets of the immune system visible to PET scanners was the development of molecular probes that would target the immune system after having been injected into the bloodstream. Since these probes are labeled with radioisotopes, it is possible for PET scanners to detect them and show what is happening in the immune system.

"The radioisotope decays by emitting positrons, which are electrons with a positive charge," Radu explains. "It's like antimatter. Positrons encounter electrons in surrounding tissues where these probes accumulate. Then you have matter interacting with antimatter, and when that happens both particles are completely annihilated. Their mass is converted into energy, and this can be detected by special detectors."

"The idea is that it is an enabling technology," Witte elaborates. "It helps make a diagnosis, and it helps as well to evaluate the response to therapy. With this technology we should be able to see where immune cells are. Are they in the right places? Are they moving to the right places? And we should be able to quantify the numbers of cells, which might change up or down, depending on the therapeutic intent. For example, in cancer you might want to amplify the immune system, but in an autoimmune disease you might want to inhibit it."

Believing strongly in the promise of this technology, Witte and Radu — along with Drs. Phelps, Johannes Czernin, Nagichettiar Satyamurthy and several other colleagues — have formed the company Sofie Biosciences. Currently headquartered in the Momentum Biosciences business incubator (see page 2), Sofie has licensed the probe technology from the UCLA Office of Intellectual Property and is hoping to develop commercial applications that it can bring to market — a process that is no less daunting than the technical challenges the group has had to overcome.

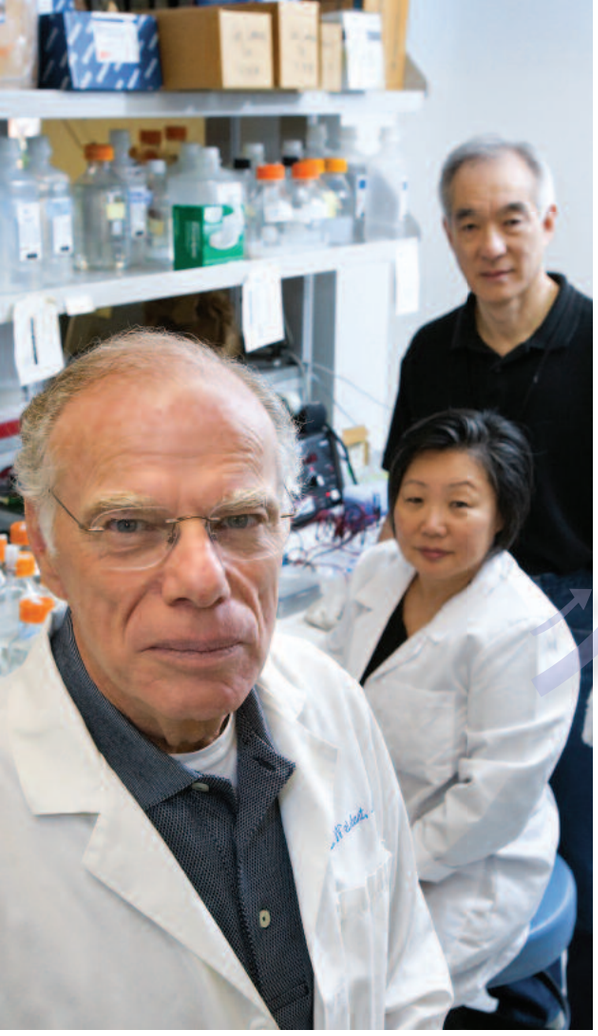
"We have a company," says Witte. "But that part's easy. Making it a successful company is where we need to go next." ♦

Caius Radu, M.D., and Owen Witte, M.D.

"You face roadblocks, and one of those roadblocks, which is very significant, is the fact that the immune system is so complex, we cannot model it outside of the body. You have to see it at work in a living organism."

profiles

My Antibody, Myself



Richard Weisbart, M.D.
Grace Chan, M.D., and Robert Nishimura, M.D.

"Once the cell-penetrating antibody delivers its payload into the cell, the cell destroys the antibody within a period of time, so there's nothing left over to be harmful."

With recent advances in micro- and nanotechnology, medical researchers are increasingly turning their attention to the cell itself as the key to treating and curing a host of diseases. By manipulating our very genes and the proteins they regulate, researchers believe they might well be able to restore health to patients suffering from diseases ranging from Parkinson's and Alzheimer's to lupus and arthritis to various forms of cancer.

Most of the current research in this area focuses on a technique known as gene therapy. In practice, this involves introducing new or altered genes into the nucleus of the target cell. These genes, in turn, are delivered to the nucleus by means of cell-specific viruses.

Unfortunately, as promising as this line of research is, altering biological processes at the cellular level brings risks of its own.

"When a virus is delivered into a cell, the virus integrates into the DNA and remains there forever," says Richard Weisbart, professor emeritus at the UCLA David Geffen School of Medicine. "A virus can integrate into a wrong place, resulting in potential problems, including the development of leukemia and cancer. Some day these problems will be solved, but in the meantime, alternative therapies are needed. Antibody-mediated intracellular delivery of proteins is one possibility."

Weisbart — whose own work is funded by federal grants — believes, however, that he has discovered a safer alternative to gene therapy. A rheumatologist by trade, Weisbart has spent most of his career studying autoimmune diseases and the antibodies associated with them. Some 14 years ago, he and his colleagues Robert Nishimura and Grace Chan first observed an autoantibody in patients suffering from lupus. This autoantibody, they discovered, has the unique ability to penetrate living cells and enter the cells' nuclei without causing harm.

Intrigued by their discovery, the researchers embarked on a series of experiments in which they mutated these autoantibodies one amino acid at a time.

"And when we did that," recalls Weisbart, "we ended up with an antibody that could penetrate into living cells 50 times better than the native antibody. And, remarkably, it didn't cause any harm to cells. So it occurred to me when we were doing this work 14 years ago that this antibody could be developed into a therapeutic intracellular- and intranuclear-delivery system."

Using such an autoantibody to deliver therapeutic proteins to the nucleus, Weisbart explains, is potentially far safer than gene therapy, because it not only eliminates the introduction of new genes into the target DNA, it eliminates the viruses that are now used to deliver them.

"Once the cell-penetrating antibody delivers its payload into the cell, the cell destroys the antibody within a period of time," says Weisbart, "so there's nothing left over to be harmful."

Now retired from UCLA and conducting his research largely as a labor of love, Weisbart explains that this technology appeals to him because of his career-long interest in finding therapies that minimize the side effects and create a minimal amount of discomfort and disruption in his patients' lives.

Weisbart believes that this technology could be commercialized soon and acknowledges that at least one company has discussed the possibility of licensing his discovery from UCLA. "It takes a company to develop products for commercial use. However, my interest is in working fulltime in my laboratory to continue perfecting this technology so that it can be applied to the treatment of many different human diseases. This is a platform technology that has many potential applications, so there is a great deal of work that still needs to be done." ♦

profiles

After the Flood

Thom Mayne and his graduate students, (top left to right) Ryan Whitacre, Ian Ream, Erin Smith, Monica Ream, and Saji Matuk. (not pictured) Linda Fu and Jeanne Legier Stahl.

In the aftermath of Hurricane Katrina in 2005, the residents of New Orleans were confronted with a series of difficult and potentially painful decisions. The most contentious of all, perhaps, was the question of whether or not it was even worth rebuilding a city that is inherently prone to natural disasters of this nature.

Thom Mayne, though himself a resident of Southern California, was faced with a similar decision.

"Right after Katrina, we were asked by the Netherlands Architectural Institute to do a project," recalls Mayne, who is a professor in the Department of Architecture and Urban Design and the founder and design director at Morphosis, an interdisciplinary and collective practice involved in experimental design and research. "They wanted a symbolic, iconic building to initiate the rebuilding of New Orleans."

Despite the prestigious nature of the commission, Mayne and his associates believed that an iconic building was inappropriate. According to their assessment, what New Orleans really needed was an urban plan that would relocate and restore wetlands to the 32 square miles of Crescent City property that is at risk when storms as violent as Katrina hit the Louisiana coast. The two concepts appeared to be irreconcilable, and Mayne's involvement in the rebuilding of New Orleans might have ended there. But then Brad Pitt and his Make It Right Foundation approached the architect. Pitt wanted to know if Morphosis would be interested in designing a prototype for a low-income house that could be built in the largely devastated Lower Ninth Ward.

"Right after Katrina, we were asked by the Netherlands Architectural Institute to do a project. They wanted a symbolic, iconic building to initiate the rebuilding of New Orleans."

"We thought, 'Uh-oh, it doesn't seem like we can do this, because we're basically violating our own recommendation'," Mayne recalls. "But we sat on it for two or three weeks, and we came up with another idea. Maybe there's a middle ground. What if we develop a residence that deals with the reality of the flooding but represents a more rural kind of lifestyle? It wouldn't mean reurbanizing this area, but some people would remain, and they'd be living in an estuary restored to its natural condition."

After agreeing to take on the project, Mayne decided that instead of running it exclusively through Morphosis, he would open the problem to students in UCLA's Department of Architecture and Urban Design. The department offered the course, and seven graduate students took up the challenge. Working with Mayne, they set about designing a new kind of house — a house that could sustain its own water and power needs, a house that could survive the floodwaters generated by a storm the size of Hurricane Katrina and, perhaps most importantly, a house that could be manufactured cheaply enough to function as low-income housing.

"We came up with this idea of building a chassis," explains Mayne. "It comes with everything — kitchen, bathroom, everything is attached to the chassis. You just have to put a body on it and you're done."

After they deliver the prototype to New Orleans, Mayne hopes that he and his students will be able to interest some appropriate public agency or commercial enterprise in helping to mass-produce their design ideas.

For Mayne, though, the real payoff has been the learning experience the project has given his students. From studying the site in New Orleans, through the design and building process, all the way through to figuring out how to ship the 8,000-pound concrete chassis and the prefabricated house panels from Los Angeles to New Orleans, the students have been involved at every step along the way.

"My assessment is that we've done some things that are quite interesting," says Mayne. "And since it's real, the students are involved at a completely different level." ♦

Spirit of Invention

Robert LeMoyne, doctoral candidate

"I have applications for patents for water purification and applications for advanced propulsion systems, but my favorite is for virtual proprioception. It's like a breakthrough concept for biofeedback in gait and step detection."

Robert LeMoyne is more than a promising UCLA doctoral candidate. He is also a prolific inventor. So prolific, in fact, that at this stage of his career he has a hard time remembering just how many invention disclosures for patents he currently holds. As of the summer of 2009, however, LeMoyne could confirm that he had 30 invention disclosures to his credit.

That LeMoyne is alive at all, let alone applying for invention disclosures for patents at such a prodigious clip, is something of a miracle. At the age of 12, while playing football with a youth group near his hometown of Livonia, Michigan, he was struck on the side of his head. The injury went untreated for six to seven hours, and in the aftermath — even though LeMoyne survived the internal hemorrhaging — it was widely assumed that the brain damage would be both catastrophic and irreversible.

Fortunately, that grim prognosis was wrong. LeMoyne awoke from a comatose state, mute and quadriplegic, but he miraculously emerged with his mental faculties intact. LeMoyne went on to earn master's degrees in both aerospace and mechanical engineering from the University of Michigan, while graduating summa cum laude. He took a job with Boeing's Rocketdyne division in the San Fernando Valley.

After working in the aerospace industry for several years, LeMoyne decided to leave Boeing in the early 2000s and strike out in a new direction. He is currently wrapping up the research, funded in part by federal money. The work will earn him a Ph.D. in neural engineering a subfield of biomedical engineering. The focus of his work is reflex quantification systems, an area of research that has meaning for him personally.

"I remember once going through a neurological battery examination," explains the 35-year-old inventor. "And there were two young residents evaluating me. I saw that the nature of quantifying reflexes was highly qualitative in nature. So I'm trying to make it more precise, quantifying it with objective accelerometers."

Even as he works on his doctoral degree, LeMoyne has somehow found time to file disclosures for inventions in fields as diverse as aerospace, biomedicine and mechanical engineering. The range of his interests is almost dizzying.

"I have applications for patents for water purification and applications for advanced propulsion systems," he says. "But my favorite is for virtual proprioception. It's like a breakthrough concept for biofeedback in gait and step detection. It could be very useful for soldiers coming back from Iraq with prosthetics or brain injuries like myself. People with brain injuries and prosthetics have disparate perception of the motion of the affected limb. So I'm using accelerometers to provide biofeedback."

When he wraps up work on his doctorate, LeMoyne hopes to make a career in either academia or private industry. The determining factor, he says, will be the degree of intellectual freedom that is accorded him.

"I want to do something where I can grow and innovate," he explains. And given the range of his interests and achievements, one can easily understand why. ♦

OIP @ A GLANCE

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TOP 10 REVENUE-PRODUCING TECHNOLOGIES FOR FY2008

1. Medical coil device for aneurysm treatment
2. Biodegradable medical coil device for aneurysm treatment
3. Nicotine patch — smoking cessation
4. Diagnostic test for gastrointenstinal diseases (Crohn's and IBD)
5. Connective tissue stem cell
6. Embolism Retrieval Device
7. Treatment and diagnosis of cardiovascular disease
8. Human monoclonal antibody targeting prostate stem cell antigen
9. Human monoclonal antibodies therapeutically effective against cancer
10. Granulocyte colony stimulating factor used for the treatment of neutropenia

IP PROTECTION, TECHNOLOGY TRANSFER AND RESEARCH ACTIVITIES FOR FY2008

Gross sales from UCLA licenses	$156,146,062
Invention disclosures	314
New U.S. patent filings	142
Secondary filings	112
Issued U.S. patents	42
First foreign filings	73
License and option agreements	38
Amendments with new IP matter	10
Confidentiality agreements	171
Letter agreements	49
Inter-institutional agreements	14
Material transfer agreement (case related)	37
Material transfer agreement (non-case related)	980

OIP OVERVIEW

TOTAL INVENTION PORTFOLIO	1,560
TOTAL ACTIVE U.S. PATENTS	535
TOTAL ACTIVE FOREIGN PATENTS	537
TOTAL ACTIVE LICENSE AGREEMENTS	227

"Many of my most valued colleagues have been graduate students and post-doctoral fellows with educated imaginations, fresh perspectives and questions no one had ever thought to ask."

— Dr. Paul Boyer
1997 Nobel Prize for Chemistry

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