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California Institute for Telecommunications and Information Technology

Calit2

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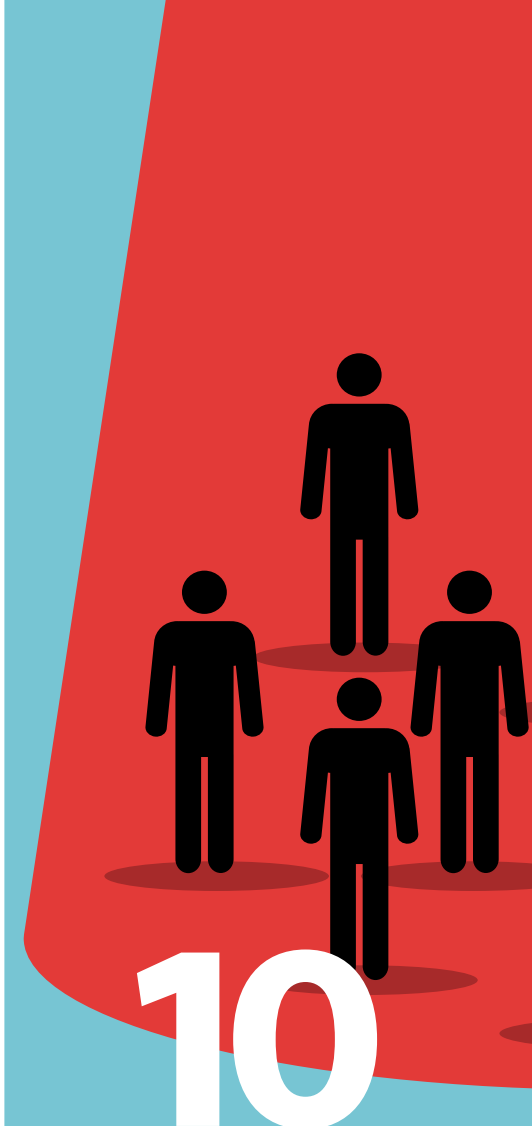
University of California, Irvine

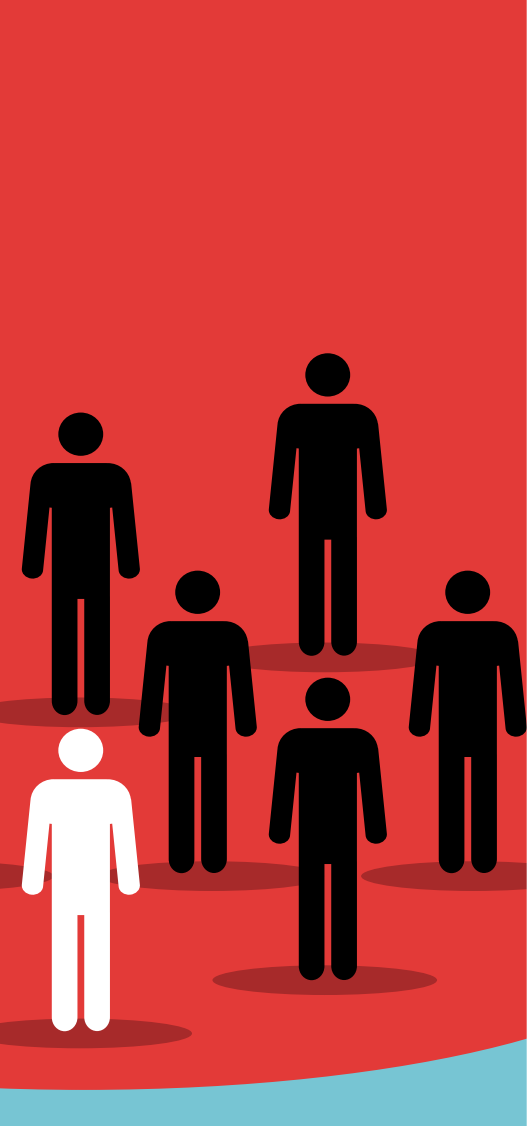
DiseaseDetector



features:

On the cover: *A droplet microfluidic device being developed with the help of Calit2's BiON clean room aims to identify individual cancer cells in blood samples. The technology could one day help doctors diagnose tumors earlier. Story, page 10. (Photo: Steve Zylius)*

departments:



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Executive Editor: Shellie Nazarenus
Managing Editor: Anna Lynn Spitzer
Contributing Writers: Lori Brandt, Christine Byrd, Shari Roan, Stuart Ross
Art Director: Michael Marcheschi, m2design group
Publisher: Mike Delaney, Meridian Graphics

Calit2
University of California, Irvine
4100 Calit2 Building
Irvine, CA 92697-2800
(949) 824-6900
www.calit2.uci.edu
info@calit2.uci.edu

2

Students' exposure to global health challenges influences biomedical device designs

life changing

by Lori Brandt

Left: A local health worker checks a villager for fever, which can indicate malaria.

Right: Bill Tang (middle), with students who traveled to Thailand: from left, Abdullah Siddiqui, Amanda Ngo, Tracey Tien and Reaz Rahman

(Photos courtesy of Bill Tang)

Malaria kills a child somewhere in the world every minute. This life-threatening disease, caused by parasites transmitted through infected mosquitoes, can be prevented and cured if detected and treated early.

But malaria afflicts primarily the poor, who often do not have ready access to healthcare and who tend to live in malaria-prone rural areas in dwellings that offer few barriers against mosquitoes.

This type of global health challenge inspired students at UC Irvine who participated in Calit2's Multidisciplinary Design Program.

The program engages undergraduates campuswide in research teams co-mentored by at least two faculty members from different schools. Under the guidance of biomedical engineering professor BIll Tang and public health professor Dele Ogunseitan, two student teams designed portable, low-cost, rapid-diagnostic devices using microfluidic technology. One team's device detects malaria; the other's, HIV.

A few students from each team were selected to travel abroad to the very places grappling with these diseases. The expeditions, supported by a $25,000 gift from Edwards Lifesciences, provided the ultimate field research experience.

Myanmar (formerly known as Burma) accounts for the vast majority of malaria cases and deaths in Southeast Asia. The country's poverty impels its residents to move back and forth into neighboring countries looking for work and seeking adequate healthcare. This migration spreads the disease, increases reinfection and leads to inconsistent treatment.

Reaz Rahman was one of four biomedical engineering students who went to the Thailand-Myanmar border to observe the spread, diagnosis and treatment of malaria. Working through the NIH's International Centers of Excellence for Malaria Research and with public health professor Guiyun Yan, Rahman witnessed the impact malaria has on the lives of Thai villagers and Burmese refugees.

The students accompanied local health workers as they screened villagers for fever, a symptom of malaria. If fever is identified, the health worker takes a finger prick blood sample and transports it back to the clinic to test for infection.

The team's project is a portable, low-cost, microfluidic diagnostic device, which uses saliva instead of blood to test for malaria. (Microfluidics involves extremely small volumes of liquid, nano or micro liters, to detect antigens or reactions to a virus or disease.)

The approach targets a specific enzyme reaction present in the saliva of a person with the disease. If the reaction occurs, the enzyme acts as a catalyst, lighting up an LED connected to an electric circuit in the device, indicating the presence of malaria.

"The experience I gained from doing [this] field research is unlike any education I have ever received before," says Rahman. "It was something I

could never have learned from a book. Seeing the diagnostic process helped me understand the need for better and more advanced diagnostics that would improve lives."

Ogunseitan, chair of UCI's Program in Public Health, says developing nations present many challenges in the collection of blood for diagnosing both malaria and HIV. "We see issues with storage, adequate refrigeration and cross-contamination. People who have malaria, particularly chronic malaria, are often anemic as well, so you don't want to take too much blood from them. And in places where HIV/HPV are endemic, there is also a lot of stigma associated with the disease, so there is a need for discreet, rapid testing that uses a small amount of fluid."

Physics major Vladimir Satchouk's team designed a rapid HIV test, the size of a credit card. The microfluidic device contains test reagents and a place to add a blood sample. The reagents and blood are held at atmospheric pressure in wells etched into the plastic, while the rest of the card is sealed below atmospheric pressure.

The user simply pricks his or her finger, places a small drop of blood in the collection site, and pulls an adhesive strip. This breaks the hermetic seal between the reagents and the reaction area, creating a difference in pressure between the two sides that drives the fluid flow. The flow of reagents is controlled by varying lengths and widths of the fluid channels so each reagent reaches the test site at precisely the right time. If the patient is HIV positive, the reaction site turns black, giving a clear yes-or-no diagnosis.

Under the guidance of lecturer Brandon Brown from UCI's Program in Public Health, Satchouk and Nigel Fernandez traveled to Lima, Peru, to visit HIV/STD clinics serving the region's gay and transgender sex workers. "The issues marginalized groups such as sex workers face in developing nations was a motivating reason behind the genesis of our project," Satchouk says.

They returned from the expedition with a new appreciation of the struggles faced by the LGBT community in a conservative Catholic society. Group members ultimately determined that their diagnostic device should include testing for STDs as well.

"From a holistic perspective, the exposure to other cultures, customs and socioeconomic classes was of incalculable educational and personal value," he says.

"I was extremely excited with the outcomes from these expeditions," says Tang, who initiated the trips in an effort to enhance students' senior design experience. "Even though traveling to these areas was strenuous and taxing, in the end, all the students came back transformed in their ideas about biomedical engineering. They were fired up and excited about continuing in this line, almost as a life calling or mission."

Top: Epicentro is a men's community health clinic on the outskirts of Lima, Peru.

Center: Vladimir Satchouk (right) talks with a health worker at Socios En Salud, a community-based health program in Lima's Carabayllo District.

Bottom: Carabayllo is one of the oldest and poorest districts in Lima.

(Photos courtesy of Nigel Fernandez)

Entrepreneurial Spirit

The first TechPortal company to advance into its own

headquarters is improving your online search experience

by Christine Byrd

UC Irvine professor Chen Li jots equations directly on the windows of his new office overlooking a busy intersection near Orange County's John Wayne Airport.

The view just outside is loaded with information, he says, which he wants to make easier for you to search.

Li is the founder of SRCH2, the inaugural startup housed in Calit2's TechPortal business incubator, and now the first to generate enough capital to move from the incubator to its own offices.

In a world with so much readily available information, search tools can be either limiting or empowering. Li's proprietary algorithm provides instantaneous, "search-as-you-type," error-tolerant results for large amounts of data. CEO Dev Bhatia describes SRCH2 as a disruptive search technology because it takes advantage of the recently decreased cost and increased availability of computer memory.

They're not trying to replace Google – although Google cofounder Sergey Brin was Li's lab mate at Stanford University. Instead, SRCH2 aims to dramatically improve your experience in the search box of any given website – from medical journals to retail outlets.

In fact, you may already be using SRCH2's technology on your mobile phone, social networks or cable boxes without realizing it.

"SRCH2 is the only technology that can support instant/forward search same time with the kind of performance consumers have come to expect

Visitors to last summer's Edinburgh Fringe Festival searched shows throughout the city with GiggleMaps, powered by SRCH2. "SRCH2 is the only technology that can support instant/forward search and geolocation at the same time with the kind of performance consumers have come to expect from their smartphones," says Karl Hampson, group board director at Realise, the Edinburgh-based agency that developed GiggleMaps. "It was a perfect fit.

"We've been working on search for 14 years and when I first saw SRCH2 doing that, I realized I was seeing something new."

Li first applied this technology at UCI in 2008, when he created Psearch to help search for people in the campus directory even with incomplete or misspelled information. Start typing "Wil" in the search box, and instantaneously a list of names matching Wilson, William, Williams, Bill and so on, starts appearing.

Ever since graduating from Stanford, surrounded by friends who became wildly successful Silicon Valley entrepreneurs, Li had dreamed of an opportunity to turn his academic research into a practical technology. He finally found it.

"Psearch is really the seed of this company," he says. "Then we thought about how to scale it up, and asked, can this work on other data sets?"

Initial funding to create SRCH2 (originally called BiMaple) in 2010 came from Li's personal finances. It was a turning point. "There is a psychological change when your company becomes a real legal entity," he says. "You have to decide it's time to stop thinking and start doing."

He hired two UCI information and computer sciences students and was seriously considering following Steve Jobs' and Steve Wozniak's lead by running the company in his garage.

But when Li learned Calit2 director G.P. Li was looking for startups to house in the building's new incubator, he jumped at the chance.

SRCH2 resided in TechPortal for its first three years, and Li says he benefited from the knowledge, ideas and creativity on campus, especially from those outside of his field. "One thing I learned is to work with more people I don't usually interact with – outside of computer sciences – to make connections, learn and grow."

Li says he appreciates the services TechPortal provided, and found they far exceeded the discounted space, security and networks. The institute generated publicity and the opportunity to meet high-profile university visitors who toured the incubator – all important benefits for a startup business.

and geolocation at the from their smartphones."

In 2012, ready to move to the next level, Li landed Dev Bhatia as CEO. Bhatia has managed four previous startups, including one acquired by Yahoo!.

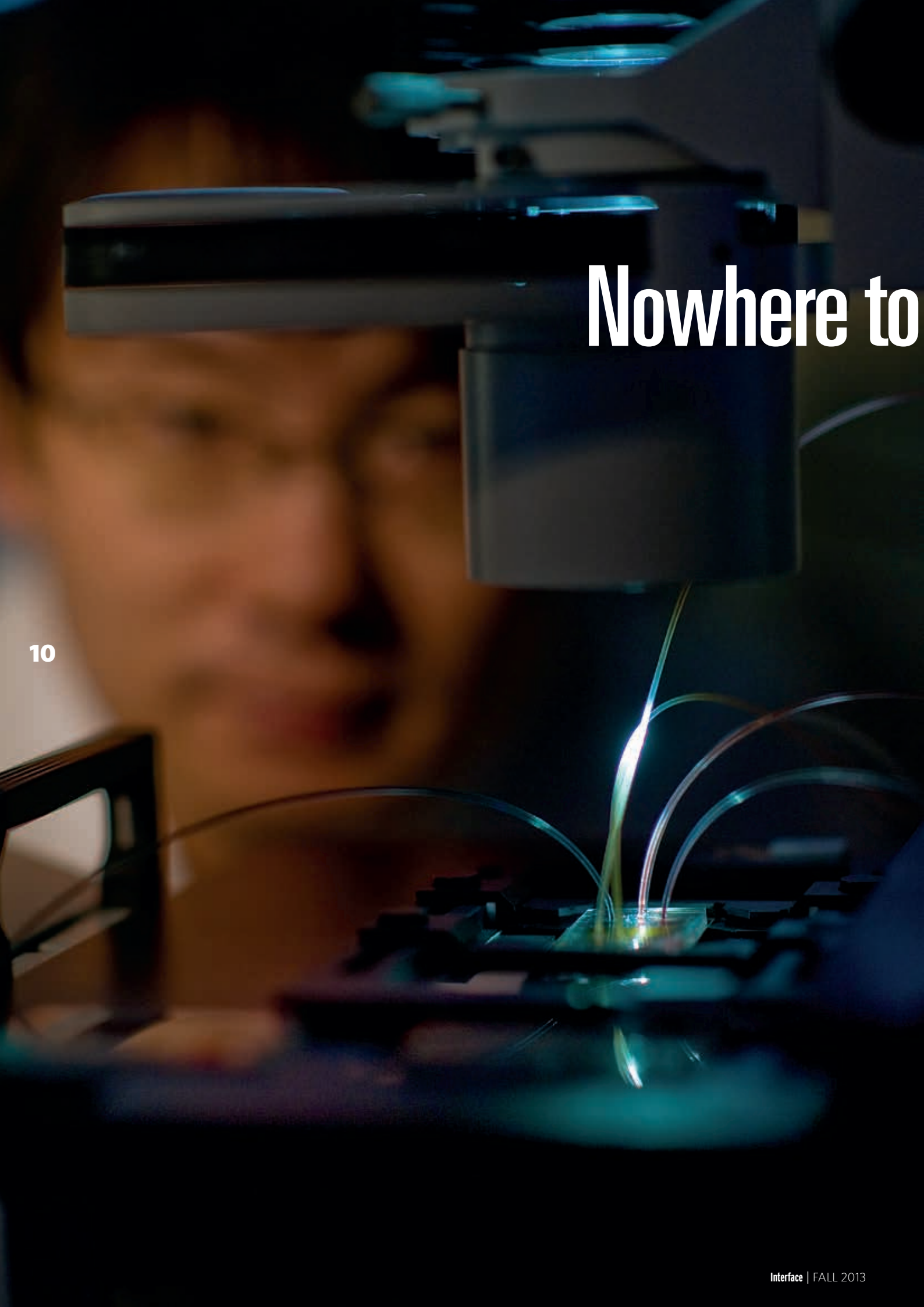
"The thing that excited me about SRCH2 is that the asset was in place. It's one thing to pitch a venture capitalist with an idea, and it's another to go in with Chen and a product," says Bhatia.

Bhatia was also impressed with Li's entrepreneurial spirit, which he thinks came from Li's experiences in the Silicon Valley and working for technology companies prior to arriving at UCI. "He's got the goods and he's got the right appetite for risk."

All the best search companies, Bhatia explains, had a long incubation period and came out of a university.

This is not the only way SRCH2 fits what Bhatia describes as the template for successful search company startups. "In nine years, there have been nine exits in search software on the enterprise side – all over $100 million and three over $1 billion," he says. He predicts SRCH2 will be the 10th.

"We had some hard times, some ups and downs," says Li. "But when I look back, it's worth it." And when he looks forward, he sees continuing innovation, including introducing version 4.0 of their enterprise search software, with a new round of improvements this fall – driven by those algorithms on Li's window. They compute an exciting future for search, and for SRCH2.



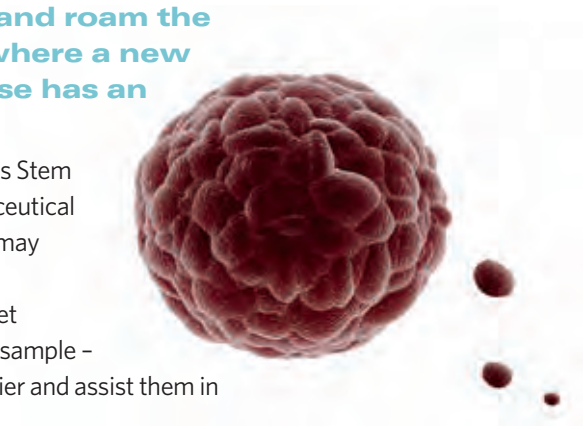
Nowhere to

HIDE

Using droplet technology, researchers shine a spotlight on runaway cancer cells

by Shari Roan

Among the many disturbing aspects of cancer is the fact that single cells can detach from a tumor and roam the bloodstream, perhaps settling in a place where a new tumor forms. And, just like that, the disease has an opening to spread or recur.



In his busy laboratory on the third floor of the Sue and Bill Gross Stem Cell Research Center, Weian Zhao, assistant professor of pharmaceutical sciences, holds a miniaturized device in the palm of his hand that may someday outfox those tiny cancer cells as they make a run to new destinations in the human body. Zhao's technology, dubbed droplet microfluidics, is designed to detect solitary cancer cells in a blood sample – information that could help doctors diagnose primary tumors earlier and assist them in monitoring patient treatment and prognosis.

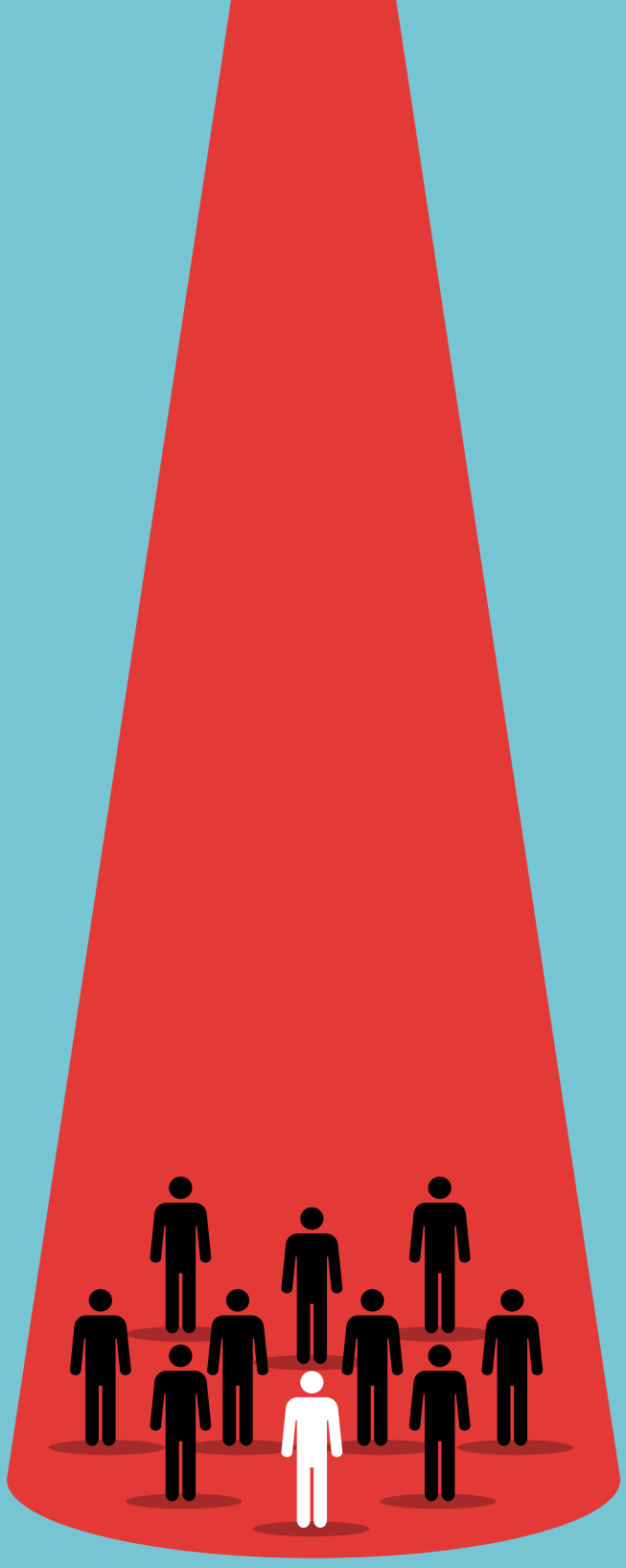
The technology, developed with the help of Calit2's BiON clean room facilities and staff, uses DNA-based sensors to bind to a wide range of cancer biomarkers, including cancer cells found in whole blood.

Zhao was well-prepped for the project when he arrived at UC Irvine. He studied chemistry at Shandong University in China before earning his doctorate in chemistry at McMaster University in Canada. As a postdoctoral fellow at Harvard Medical School, he worked on micro- and nano-engineered tools to support cancer diagnostics.

When cancer develops, even before symptoms appear, cells are shed from the primary tumor and circulate in the bloodstream. These cells have the potential to settle in the brain, liver, lung or other places and cause a recurrence of the disease. Existing diagnostic technologies, such as conventional blood tests or imaging devices, can't spot these micro-metastases.

But Zhao is hot on the trail of these runaway cancer cells.

Photo: Steve Zylius



It's as if a police searchlight settled its bright beam on a group of 10 people standing in a crowd of 1 million. Among those 10 people, the police can now spot the guy on their most-wanted list.

"People argue that if you can detect the cancer early enough, even before a person feels any symptoms, the chances that you can cure the cancer are much higher," says Zhao, a perpetually cheerful man who exudes enthusiasm about his work.

His droplet microfluidics device aims to detect those circulating tumor cells in order to diagnose patients earlier and to help monitor them after treatment to ensure there are no residual tumor cells that could lead to a relapse. That's a huge challenge, he says.

"These circulating tumor cells are rare," Zhao explains. "We're talking about just a few tumor cells in every microliter of whole blood. That's why there are few current technologies that robustly detect that."

His sensor makes use of a library of short pieces of DNA that can selectively bind to almost any type of molecule, such as cancer biomarkers and cells that circulate in whole blood. Fluorescent dyes can be attached to the DNA, and that package reports the activity of a cancer cell.

Zhao and his collaborators have created two channels in their microfluidic device: one carries the blood sample and the other carries the sensor solution. The two solutions are mixed and an oil-based solution is applied to break the merged stream into millions of tiny droplets 10 to 100 microns in size. Breaking the stream into droplets is the key step, because rare tumor cells are encapsulated where they can be recognized. It's as if a police searchlight settled its bright beam on a group of 10 people standing in a crowd of 1 million. Among those 10 people, the police can now spot the guy on their most-wanted list.

A high-speed, high-throughput processor is able to see which droplet contains a tumor cell. The encapsulated sensors allow researchers to detect markers inside the cell and on the cell membrane. Zhao and his colleagues were the first researchers to show, via the droplet technology, that molecular biomarkers could also be detected in the extracellular space.

"Everything is super concentrated, so you can really see what's in the cell," Zhao says.

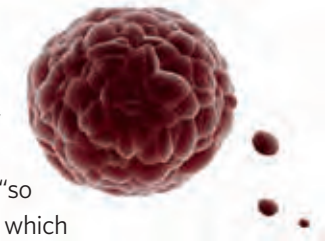
By using an enormous library of DNA, the process can also overcome the problem

of having to identify specific biomarkers that might be involved for a particular tumor. Once the sensors encounter the targeted cancer cells, the fluorescent dye lights up to make the droplet visible.

"We fish out the molecules that are specific to cancer," he explains, "so we can avoid any of the genome sequencing, the proteomics approach, which takes so much money and time to develop."

The process is also fast, says Dong-Ku Kang, assistant project scientist.

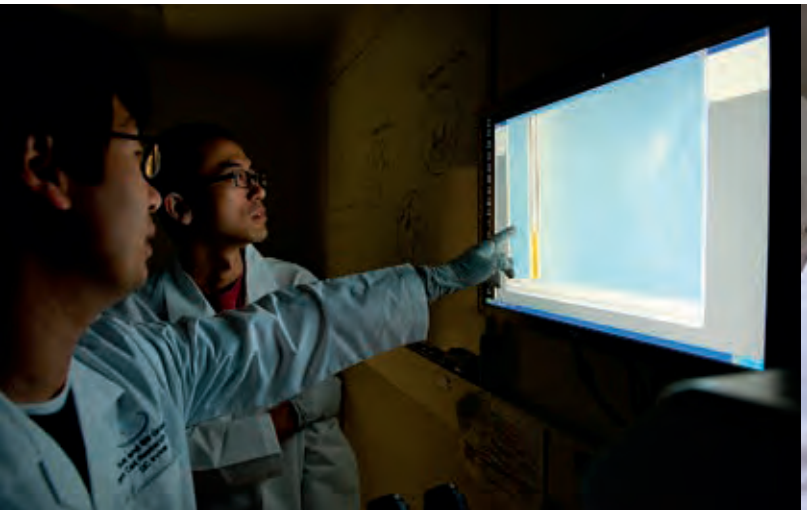
"Screening these droplets in a high-throughput manner using our cancer cells-specific sensor will easily find that droplet within a few hours," he notes. The next major challenge, Kang adds, is to develop a smaller and lower-cost microscope system to pick up the fluorescent signal.

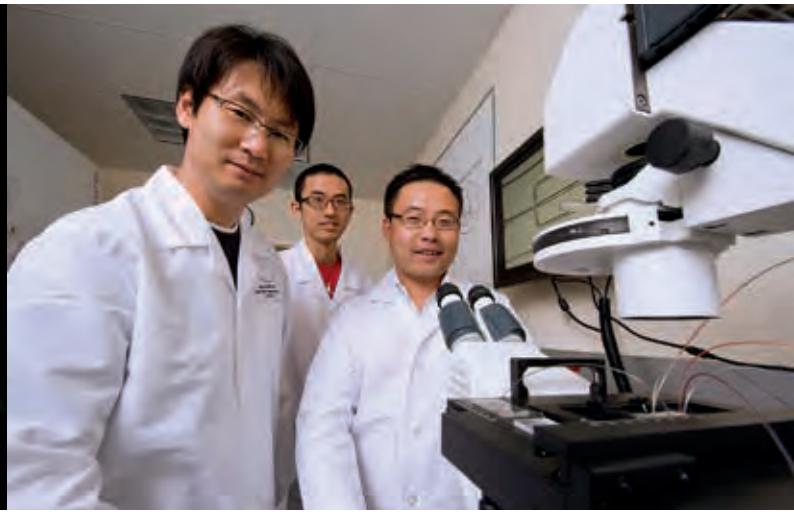


Left: Dong-Ku Kang, project scientist (left) and graduate student Kaixiang Zhang examine a blood sample with a confocal fluorescent microscope connected to a wall-mounted monitor.

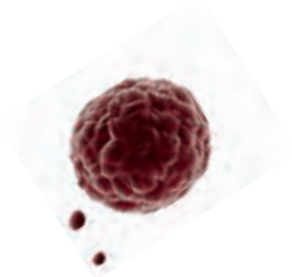
Right: (From left) Kang, Zhang and Zhao – their microdevice employs a DNA sensor that targets specific DNA, protein or cells, allowing researchers to identify cancer cells in whole blood.

(Photos: Steve Zylius)





Besides cancer, droplet microfluidics could be used to detect bacteria and viruses in the blood. Zhao is collaborating with Ellena M. Peterson, associate director of medical microbiology in the School of Medicine, on a project to detect bacteria in blood. If successful, such technology could allow doctors to diagnose bacterial infections like pneumonia or septicemia in minutes rather than 24 hours.



"Technology that will allow us to detect very low amounts of pathogens in a rapid manner has great promise in diagnostics," Peterson says. "We don't have anything like that in medicine right now."

Zhao, who last year was named to the MIT Technology Review's list of "35 Innovators Under 35," has many collaborators interested in droplet microfluidics, including physicians at UCI Medical Center who plan to test the concept in a clinical trial.

"Dr. Zhao is vibrant, energetic and a go-getter," Peterson notes. "That's the type of person you want to work with."

Zhao credits strong support from UCI in the form of state-of-the-art facilities, strong mentorship and a collaborative spirit for his success.

"The research here is so strong," he says. "For nano- and micro-fabrication, Calit2's BiON facility is just one of the best. I so appreciate their help and the facility they offer. Otherwise none of this would be possible."

The SURF-IT Formula for Unequaled SUCCESS

7 inquisitive undergraduates + = 10 weeks of diverse summer

—compiled by Shellie Nazarenus

Top to bottom: Eriberto Vargas, Taylor Kisor-Smith, Timothy Vu, Gary Chang, Payum Noshiravan, Sandy Pham and Helena Do

Gary Chang + Prof. Bill Tang = strain gauges for soft tissues
Helena Do + Dr. Shahram Lotfipour = computerized alcohol consumption assessment
Payum Noshiravan + Dr. Shahram Lotfipour + Dr. Phyllis Agran = "Clinic in the Park" evaluation
Sandy Pham + Prof. Gillian Hayes = mobile apps for individuals with autism
Taylor Kisor-Smith + Prof. Debra Richardson = networked computers energy data usage analysis
Eriberto Vargas + Prof. Alon Gorodetsky = n-type organic semiconductors synthesis
Timothy Vu + Dr. Leif Havton = spinal cord injury research supported by MATLAB

8 dedicated faculty mentors research project experiences

Project + (Goal x Outcome) =

- The ultimate goal of my project was to steer at-risk alcoholic individuals toward making better decisions about their well-being and lower their intake. I found that the computerized screening had a high success rate, with over half of the study participants decreasing their alcohol consumption from the time they took the survey. —*Helena*
- My project's goal was to develop a fully functional energy consolidator that would be able to be deployed on a network of devices. We found our tool, Joulery, is capable of collecting energy consumption data at a rate of approximately 250 MB per day per computer. —*Taylor*
- Nobody wants to use an unattractive mobile application! Our research is still a work in progress, but we have definitely redesigned and are further developing an existing app that is more modern and appealing to the target audience with the potential to personalize it. —*Sandy*

Research x Significance =

- Many community-based programs have good intentions, but being able to evaluate and prove the effectiveness of the model of disease prevention and health promotion was really powerful. In the future, this could be a permanent fixture in the healthcare system, especially with the contemporary changes in healthcare delivery in this country. —*Payum*
- This research will help increase the understanding of the biomechanical behaviors of bones and tissues to help with prostheses and rehabilitation. —*Gary*
- Spinal cord injuries at the cauda equina site affect motor, sensory and autonomic functions in the lower body. If our research shows positive results, we could translate our surgical model to clinical studies. —*Timothy*

Rewards ≥ Challenges

- One of the most rewarding aspects is finding connections in places not normally found. Every week, I listened to a different presentation and I realized that my research and future career don't have to follow narrow paths but need to constantly cross over into other disciplines. —*Eriberto*
- The most difficult aspect was the problems I ran into when I was programming, getting stuck on a problem for hours. Despite several times of frustration, I learned not to get discouraged and keep working. —*Sandy*
- Many researchers do not get the opportunity to see the impact their work has on individuals. I was able to become familiar with people who were receiving real health services that they otherwise had no access to – that level of fulfillment is impossible to quantify! —*Payum*
- Getting used to talking in front of audiences has been the most difficult aspect. —*Gary*
- The challenge is learning the background needed for this project and applying the tools I learn in class to a real research topic. —*Timothy*
- The most rewarding part of the program has to be the people and the amazing mentors! —*Helena*

Vargas' two sisters celebrate the program's completion with him.

(Eureka!)^2 =

- That moment came when it took me more than three hours to figure out what was wrong with my code, and finally discovering a tiny error, which, of course, took one second to fix. —*Timothy*
- I would say when the client computers on the test network first talked and shared data with our Joulery server. —*Taylor*
- It was more of: "Why isn't this doing what I want!" —*Gary*
- I found that research is punctuated by several of these moments; every new approach brings its own set of difficulties and unexpected results. —*Eriberto*

Chang, Pham and Vu: different projects, same satisfaction.

(Program x Participation) + (Benefit x Future) =

- The experience I have gained and the connections I have made will be very useful, and I am excited to think of all the new ways in which I can apply my training as a chemist and my studies as an engineer. —*Eriberto*
- Apart from the overwhelming empowerment I have gained from my research team and mentors, I have developed skills applicable in all types of research: I participated in IRB protocol submission, abstract and presentation production, research team collaboration, grant-writing, and valuable data analysis and processing experience. —*Payum*
- Not many people are given the opportunity to participate in a project at this level, or are given the same resources as I was. I learned many important lessons that will take me far. —*Sandy*

f(x)=7x + 10 (Sage Advice) find f =

- I would tell next year's participants: Don't be afraid to speak your mind and ask questions; that's how you learn. —*Gary*
- You'll receive help and constructive criticism that you might never receive in the classroom, so take advantage of it. —*Sandy*
- Begin your project with clear, attainable goals and objectives. —*Payum*
- Don't be afraid to disagree with those you work with. If you have a better idea and justification, go for it. —*Taylor*
- Take time to reflect on how your specific project fits into the larger scheme of things. —*Eriberto*
- Definitely keep in touch with your mentor throughout the project and even after! —*Helena*
- Ten weeks isn't very long, so you have to make it count. P.S. don't spend all of your stipend when you get that check. —*Timothy*

SURF-IT mentors and fellows gather at the conclusion of final presentations.

A Perfect bala

by Anna Lynn Spitzer

nce

An ambitious engineer finds a second home at Calit2

Won first place in the nationwide Hellenic Olympiads in Mathematics at age 14

Received 2008 NSF CAREER award

Awarded $2-million NSF Cyber-enabled Discovery and Innovation grant in 2010

In 2006, soon after arriving at UC Irvine, a new assistant professor was introduced to an engineering school administrator who asked what her major was.

Raised $5.2 million as PI or co-PI

Received a $150,000 Phase 1 SBIR grant for startup Shoelace Wireless

Won NSF Innovation Corps grant in 2012

"I'm not an undergrad," the new hire said politely.

"Oh, you're here for the graduate program?" inquired the woman.

"No," answered Athina Markopoulou.

Was she a postdoc, then? Markopoulou explained that she was joining the electrical engineering and computer science faculty.

As the embarrassed administrator learned, appearances can be deceiving. Markopoulou, who still can pass for a grad student, is now a highly regarded EECS associate professor, well-funded researcher, entrepreneur, wife and mother, and an ardent and active Calit2 affiliate.

"In the beginning, it bothered me," Markopoulou recalls of being mistaken repeatedly for a student. "But now I am used to it and I think it's fun. It can be a good ice-breaker."

Born in Athens, Greece, to high school math teachers, she won first place in the nationwide Hellenic Olympiads in Mathematics at age 14. The motivated student entered National Technical University of Athens in the top 1 percent of her class, choosing electrical engineering and computer science over math.

"Technology can make a difference; you can build things," she says. "I started university when the Internet started booming. Engineering felt like a more happening place to be than in a math department."

That prescient decision was a game changer. She graduated in 1996, still in the top 1 percent of her class, and set out halfway across the world to Stanford, where she earned master's and doctoral degrees in electrical engineering.

"I started university when the Internet started booming. Engineering felt like a more happening place to be than in a math department."

Her first year of graduate school was an eye-opening experience. Markopoulou, ever the achiever, was surprised after receiving a 97 percent on her first programming assignment to learn that the score was just average. "I had never met so many smart, ambitious people together in one place. It was humbling and incredibly motivating at the same time," she says. "We were from so many different countries and different backgrounds but we all had in common our love for science."

Silicon Valley was also entrée into the world of high-tech, dot-com entrepreneurship and successful academic-industry collaboration. She remembers the launch party for Google, which took place on campus. "I was chatting with other students: 'What

kind of name is Google? And what new remains to be done in the area of search?'" she recalls, laughing at the memory.

With doctorate in hand, she did a short stint in a large research lab; then she returned to Stanford for a postdoctoral fellowship, followed by six months in a Bay-area startup company. The experiences taught her a new lesson: her heart belongs to academia. "I tried a big lab and a startup, and they were both very interesting. But they weren't the right places for me in the long run," she says.

"If Calit2 were a person, he/she would be ambitious, professional and fun to be around."

She landed at UCI, where she immersed herself at Calit2, attending workshops, collaborating on grants and setting up an office in the building.

She felt at home immediately. "Calit2 has been love at first sight for me ... it is a happening place, with activity and collaborative projects, diverse groups of researchers, modern space and friendly staff," Markopoulou says. "If Calit2 were a person, he/she would be ambitious, professional and fun to be around."

Above: (From left) Markopoulou, Le and Matijasevic explored the marketability of the Microcast project through an I-Corps grant; the project later was spun off into Shoelace Wireless.

Opposite Page: Markopoulou credits her team with much of her funding success. "After we built critical mass in the group, things just seemed to happen on their own."

(Photos courtesy of Athina Markopoulou)

"Athina exemplifies Calit2's approach to research," says Stu Ross, the institute's assistant director for research development, who has overseen several of Markopoulou's grants. These include a prestigious 2008 CAREER award and a $2-million NSF Cyber-enabled Discovery and Innovation (CDI) award she and two colleagues won in 2010 for a collaboration spanning computer engineering, biology and sociology.

"She is interdisciplinary and she addresses basic theoretical problems as well as their practical implications," Ross says. "She's hardworking, she writes extremely well, she's willing to work with private companies, and she gives priority to finding funding for her research group in addition to funding for her own research."

The numbers speak volumes – she has raised $5.2 million as PI or co-PI, $3 million of which was for her own research. "I have been lucky with fundraising so far; fingers crossed, I don't want to jinx it," she laughs. "But it's not all me. There are co-PIs on those grants. And a lot of credit goes to my students. After we built critical mass in the group, things just seemed to happen on their own."

One of those students was Hulya Seferoglu, Markopoulou's first Ph.D. candidate. Seferoglu attributes, at least in part, her new faculty position at the University of Illinois, Chicago, to her advisor's influence. "Athina supported and guided me," she says, encouraging her to attend conferences, workshops and funding meetings, and secure relevant summer internships. "These were important steps ... I had a chance to present my work in different venues and learn different research aspects."

Markopoulou's own research focuses on designing, analyzing and optimizing computer networks, including network coding, online social and mobile networks, measurement and security. "I got interested in this field because it has a good mixture of theory and practice," she says.

Last year, she won an NSF Innovation Corps (I-Corps) grant that helped her explore the marketability of one of her recent projects. "Microcast," which grew from her NSF CAREER award and an Air Force MURI (Multidisciplinary University Research Initiative) award, is an application that enables mobile devices

that are near each other to automatically share their network connections; this allows them to aggregate their bandwidth and download content much faster.

Assistant Vice Chancellor for Alumni and Constituent Relations Goran Matijasevic, who also is the executive director of the UCI Chief Executive Roundtable, mentored the Microcast team during its intensive six-week I-Corps training program. "I admire Athina's technical brilliance and entrepreneurial spirit, but also her willingness to learn new things," he says. "These characteristics have contributed to her success so far and will make her even more successful in the future."

After determining that the project did indeed have market potential, the Microcast team took the next step and launched Shoelace Wireless – named for its ability to tie mobile devices together. The team includes Anh Le (a former postdoc in Markopoulou's group) and Christina Fragouli, a longtime friend and collaborator, who is currently at UCLA. The startup received a $150,000 Phase 1 SBIR (Small Business Innovation Research) grant and recently moved into Calit2's TechPortal incubator.

"Athina has great research vision, execution and delivery. She is very good at identifying great collaborators and giving them the best environment and support to perform," says Le, the company's chief technology officer.

Fragouli concurs. "Athina is an extremely smart and creative researcher. She is very organized, motivated and determined in her pursuit of excellence."

The high-energy dynamo says she is learning to delegate. "I understand we can get more from a team than we can get from a single person," she says. "But I still spend more time than I should on all kinds of things."

Carter Butts, a key collaborator and member of the CDI team, calls her "tough, sharp and no-nonsense," but also cites her generosity and strong sense of fun. "I think Athina embodies the spirit of Calit2," says Butts, UCI sociology professor. "She combines creative and rigorous science with an engineer's pragmatism, creating technologies that address important real-world problems."

"A colleague once said that in academia, you have the flexibility to work any 80 hours of the week you like."

That pragmatism has benefits outside of academia, too. Markopoulou and husband Kristian Jessen are parents to 4-year-old Hector *(pictured, page 18)*, born when both were striving to earn tenure (Jessen in chemical engineering at the University of Southern California). "It was a pretty stressful period for our household," she recalls.

The family returned recently from a sabbatical year in Denmark – Jessen's birthplace – where both worked as visiting professors at Danish universities. "A colleague once said that in academia, you have the flexibility to work any 80 hours of the week you like," Markopoulou grins. But the commitment came with a bonus – their son got to spend time with both sides of his international family this year. "That was important for us."

What is next on Markopoulou's agenda? At the top of her list is expanding her research efforts. "At this stage, I hope I can afford to take some risks with the topics I choose and think bigger than I could while I was trying to attain tenure," she says. "My favorite part of the job continues to be working with my group. Seeing them do well is very, very rewarding."

DOWN WITH

UP WITH LEARNING

by Anna Lynn Spitzer

A student team digests some unexpected challenges with surprisingly satisfying results

When a group of UC Irvine students began creating a mobile game to teach children the mechanisms of human digestion, they never imagined how much the kids would ultimately teach them.

They also had no way of knowing the widespread reverberations their experiences would generate.

Dubbed "Down with Food," the project was created under the auspices of the Multidisciplinary Design Program. Offered by UCI's Calit2 and Undergraduate Research Opportunities Program, MDP brings together students and faculty mentors from multiple disciplines to create and design a project.

The effort began in 2011, during MDP's inaugural year. Cathy Tran, a graduate student in the School of Education, was registering for winter quarter and decided to include a drawing class as a creative outlet. Her somewhat skeptical graduate advisor, AnneMarie Conley, forwarded the MDP call for projects to Tran: "How about instead of taking an art class, you develop a mobile app?" Conley asked.

With a master's degree in educational technology from Harvard, as well as several years of experience in educational television and software, Tran is interested in understanding how kids choose what they want to learn – "bringing the way kids approach games – whatever motivates them – into teaching them more serious topics like science and math."

She jumped at Conley's offer, seeing an opportunity to delve deeper into her research, while simultaneously indulging her craving to "make something."

So she and fellow grad student Katerina Schenke – both are in the School of Education's Learning, Cognition and Development program – assembled a multidisciplinary team that included undergraduate students majoring in digital art, English, global cultures, psychology, informatics and computer science. The goal: to design an educational game that would be fun to play.

"We bounced around a few different game topics, and the group storyboarded a few things," says Conley, education assistant professor and one of the group's faculty mentors. "But 'Down with Food' was a perfect example of what was good about games and what was hard to learn about science, and putting the two together. I think that's why this one worked."

The team decided to structure its effort as a series of mini-games, one for each organ involved in the digestion process. They began with the small intestine, and from the start, the process was fraught with challenge. Ideas put forth by the game designers often elicited groans from those in education and psychology. Educational concepts proffered to the group were sometimes dismissed by the designers.

"Researchers on the one side are interested in making sure all the facts are correct, while some of the designers are saying, 'No, the game design is more important so children will want to play,'" says Christine Bediones, an undergraduate majoring in

Above: (From left) Macalinao, Tran and Bediones are all smiles after the "Down with Food" presentation at the Games+Learning+Society conference last summer.

Below: Artists, designers and researchers brought different – sometimes conflicting – points of view to the game's storyboards.

English and global cultures who has been on the team since the start. "Our project is trying to reconcile the two different, often opposing views between education and fun."

But it was after a prototype for the fledgling game finally was designed and tested on its target audience – children ages 7-12 – that the real dilemmas began to surface.

In an effort to make learning fun, the team employed what's known in game parlance as a "tower defense" approach. This schema involves building and defending towers by "shooting" at waves of oncoming enemies.

From interviewing children prior to the design phase, the team knew that tower defense games were extremely popular; because kids were already familiar with the strategies, they decided it was a good fit for their effort.

In the "Down with Food" prototype, players build towers with nutrients – fats, proteins and carbohydrates, for example – and "shoot" different-colored enzymes at the food particles to break them down as they travel through the small intestine. The goal is to teach children that particular enzymes break down particular types of food, and once broken down, the nutrients are absorbed into the fingerlike projections of the small intestine called villi.

"We wanted to create a game that was fun, challenging and educational, but we realized we were assuming a certain level of knowledge. So we went directly to the experts – the kids themselves – to see whether the desired outcomes were actually occurring," Bediones says.

Unfortunately, they weren't. Instead of understanding the process of shooting enzymes into the food particles as a positive action that aids digestion, the kids saw the food as an "enemy" that the body was attacking.

More alarming to the developers, some of the children equated the blasting enzymes with buckets of water dousing the food. One child characterized it as "washing poop."

"We thought, 'Oh no, this is a disaster!'" Bediones recalls.

"It's ironic," she sighs. "We chose this way of playing because it's popular, but because it's popular, the kids ended up having preconceived notions."

The student researchers set about revisions. They began developing an enzyme mini-game that they hope will further clarify the process for the children. They are working on sound effects that will convey a positive tone as the enzymes break down food. They are adding tower upgrades, additional difficulty levels and unlockable features to keep the kids interested in learning.

And in a classic case of turning lemons into lemonade, they wrote and submitted a paper about their eye-opening experiences, which was accepted at a major research and design conference. Authors Bediones and Camille Macalinao presented "Are We Washing Poop? Unintended Consequences in Educational Game Design," in June at the Games+Learning+Society 9.0 conference in Madison, Wis.

They brought down the house, according to Conley, who flew to Madison to hear her charges. "There were 30 rows behind me, packed," she says. "People were standing along the walls, sitting on the floor; there was no room left.

"These girls were phenomenal. The team had more people [rooting for them] than the academics who have been at this for a couple of decades."

Moreover, two of the three lead authors were undergraduates, a rare feat in the world of academia. "It's almost unheard of for undergraduates to have papers accepted at this conference," Conley says. They even snagged one of the most competitive slots: the conference's "Hall of Failure," described as a place for "ideas that should have worked but didn't, presented by the forward-thinking people who dared to try."

Now in its third year as an MDP project, "Down with Food" continues its upward evolution. New faces replace those who have graduated, progress on the game continues at a steady pace and the team's enthusiasm for its work is palpable.

Future plans include more user testing, formation of a children's advisory board, expansion from iPad to Android and Web platforms, and applications for additional funding to conduct more game-based research.

And, like enzymes after a food fest, success stories are multiplying.

Project participants Katerina Schenke and Neil Young presented the research in August at the European Association for Research on Learning and Instruction conference in Munich, Germany. A demonstration session attracted overwhelming attention, says Schenke. "Lots and lots of people were interested in the game and some even asked if it was available on the App Store. I am still shocked at how many people showed interest in what we are doing!"

workingexamples.org, a well-known website at the intersection of education and technology, wrote a feature article about the team. And several of the students have parlayed their experiences into paid internships and jobs in mobile apps, education and game design.

Recent graduate Camille Macalinao is a paid intern at Calaborate, Inc., a startup mobile app company in Santa Monica, where she is responsible for quality assurance testing, market and application research, and competitive analysis.

"The opportunities I experienced and skills I learned have helped me grow as a researcher and given me the inspiration to continue working in a similar environment, one that is fun and motivating," she says.

Computer science alumnus James Gamboa graduated in 2012 and immediately went to work for the MIND Research Institute as a software engineer. "He had a full-time offer before he left school; he's just that good," Conley raves. Gamboa, who is developing iPad versions of an educational math game, says of "Down with Food": "This project created an environment that encourages its members to become innovators. It challenged us to create a solution to [a] problem with the resources we had available."

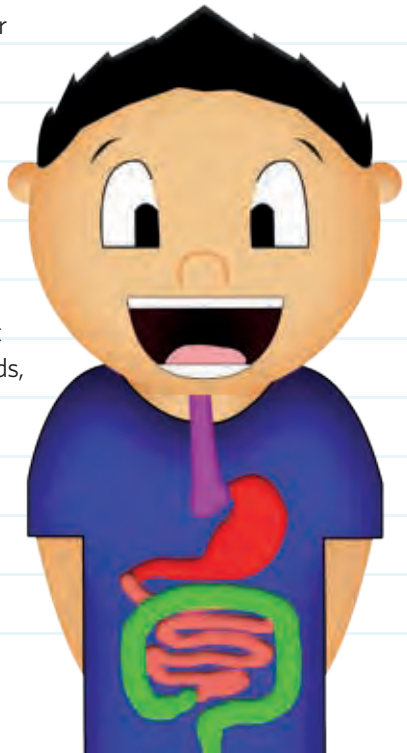
Kenny Fernandez was part of the original "Down with Food" team, designing the game's main character and most of the layout. He graduated in June and worked over the summer for public broadcast station WGBH in Boston as an intern on the Next Generation Preschool Math project, where he won rave reviews from his supervisor.

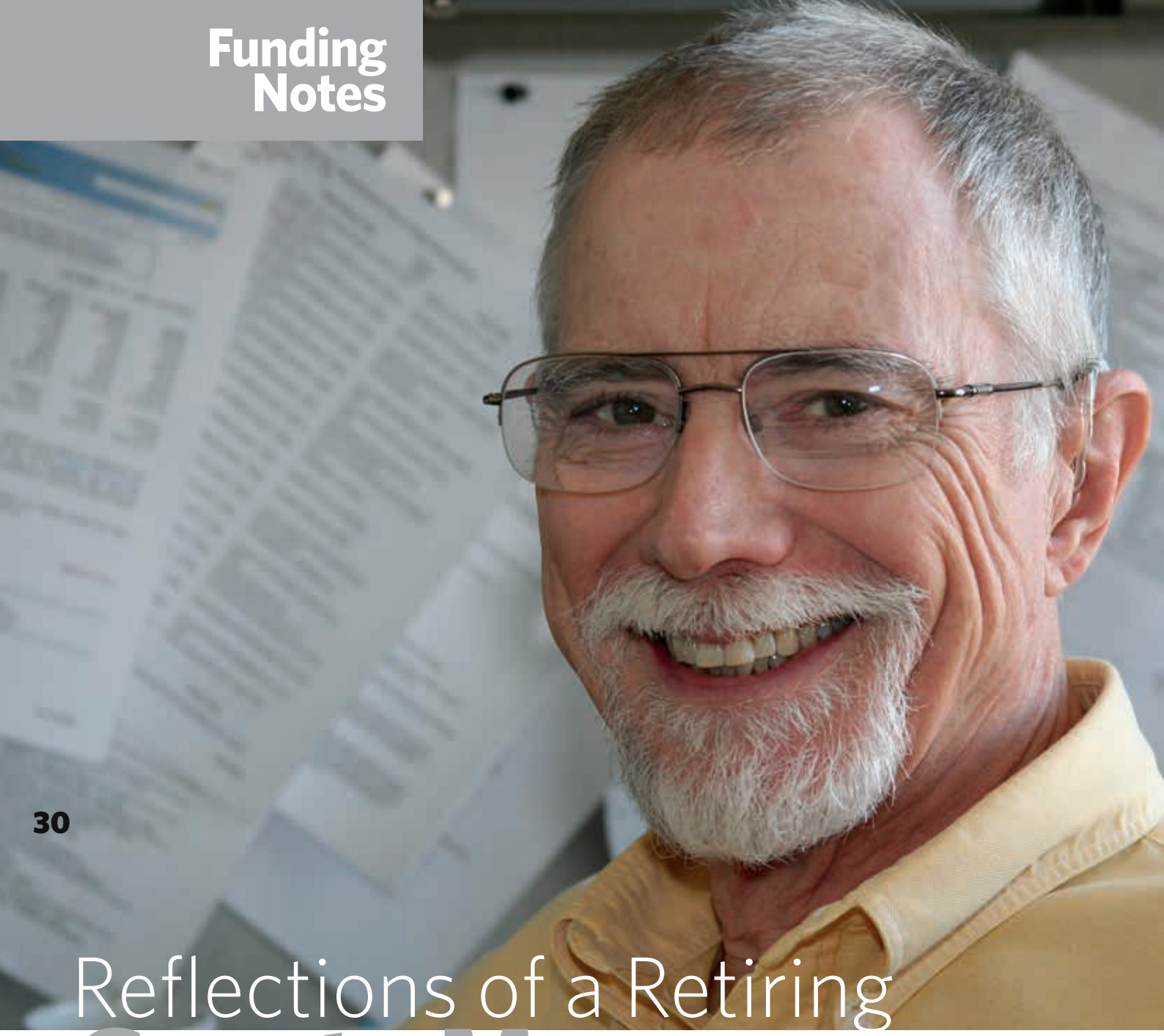
"He is like a miracle worker," Jillian Orr wrote in an email to Cathy Tran in early August. "One of the best interns I've ever had (and I've had superb interns)…. Thank you so much for passing him my way!"

Conley says these achievements are no coincidence. "These kids, from their experience working together on this team, know how to talk to people and they know what matters. They work hard and they are committed," she says. "That's what college is supposed to be about; it's rare to see it as clearly as I do with these MDP kids, and it's phenomenal."

Above: Undergraduate Katherine Chung observes a young test subject as he navigates the game.

Below: Fernandez designed the game's main character as well as most of its layout.





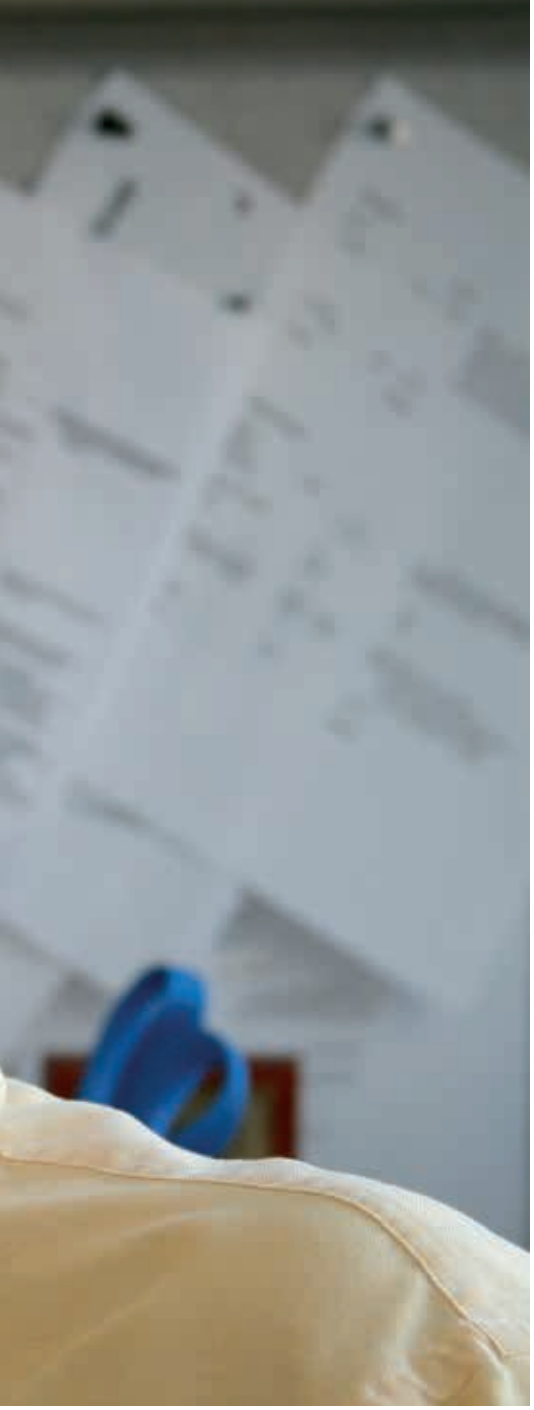
Reflections of a Retiring Grants Manager

by Stuart Ross

I have spent more than 30 years – the major part of my career – preparing grant proposals; 12 of those years were with Calit2. I've worked on proposals from $3,000 to more than $20 million, from arts education to fisheries to semiconductors. That level of experience is hardly unique; many of my fellow grants officers have similar resumes – but it does entitle me to reflect on my experiences and on the profession in general.

Few of those in my generation planned on a career in research administration. The need for research administrators grew with the increase in government funding for research and the concomitant accountability measures, and recruits came from varied places – some were academics who got off the tenure track and chose research administration instead (like me); some were administrative assistants or accountants who inherited unfinished paperwork when the previous grants person moved on; some were non-university folks who applied for a research management job merely because it was in a preferred location.

Trends in research accountability and



in the scale of research, however, have required ever more professionalization, and now, people two generations behind me are earning accredited degrees in research administration. The field currently includes many specializations and "silos," as do academic schools and departments, especially in large research universities. Grant writers often don't know what's in the proposal budgets, budget folks don't touch the patent issues, and patent experts never interfere with animal-care matters.

Of course, most grant proposals require the cooperation of two or more of these experts. This usually occurs in a smooth handoff for standard proposals, but it can be awkward and ad hoc for more unusual ones. Managing many proposals for a group of several faculty, as I have done at Calit2 and others do for academic departments, therefore is a job of integration and coordination.

UC Irvine now has a computer system that puts all the pieces in one package for review, with tabs and forms for everything, and that is a huge advantage for paperwork efficiency, but it does not actually integrate the parts. Using the terminology we have all learned from Professor Dan Stokols, grants management is usually multidisciplinary, occasionally interdisciplinary and rarely transdisciplinary.

Most research administrators enjoy their jobs, even though outsiders may perceive only the deadlines and the paperwork. This enjoyment takes many forms, depending on one's silo, personality and background. Often, the pleasure comes from helping others – assisting a junior faculty member win her first grant or patent, or helping a group of strangers come together as a team of friends in the course of a week. For those who stay with it for several years, there is the satisfaction of seeing a program or department grow.

Then there is the professional pleasure of doing the job right, and quickly, when called upon – for example, completing three government forms and a cover letter in 20 minutes and knowing what exceptions will work in this case. It's the pleasure of turning a deadline problem into a nice job, almost like executing a clean double play.

Because we live on deadlines, some take secret pride in the long work hours, the desperate decisions, the amazing saves – what has been termed "exhaustion chic."

Finally, some of us also enjoy learning the many research topics, perhaps because like me, they never could settle on just one.



I've been privileged to experience all these pleasures. I helped Athina Markopoulou apply for her first major NSF grant. I was on the team for large proposal efforts by Roxane Silver, Sharad Mehrotra, Marc Madou, John Hemminger and others, and in each case the feeling of teamwork had lasting good effects even if the proposal was not successful.

I watched and helped as Calit2 transformed itself from an idea into an exemplar of interdisciplinary and intercampus cooperation, as the HIPerWall grew from idea to grant project to successful company, and as the California Plug Load Research Center was born within Calit2 and became a recognized player on the California energy scene. I had personal tutoring from the nation's best scholars about the many aspects of IT: from power factors to telemedicine, from networks to nanotubes.

The environment within Calit2 has been a blessing as well – wonderful facilities, good friendships, a spirit of teamwork, laughter in staff meetings, special events. It's been fun – I give thanks to all the people I have worked with.

So now I am at that stage of ripeness in which broad experience feels like enough to carry the day, and occasionally it still is – perhaps like Bruce Willis in the movies, but probably more like most other people past normal retirement age. I will take up new activities in retirement (including the newly discovered joys of being a grandparent), but I will still hover around Calit2, helping when appropriate and always cheering.

This will be my last Funding Notes update, but certainly not the last for Calit2.

UCI recently won a **$500,000** award for 'cyberinfrastructure' from the **National Science Foundation** to build out the fiber optic network on campus. This project will be a big step forward for the whole campus, because several research groups with great need for data exchanges work in the oldest buildings with the weakest Internet links. This effort required building a team quickly and pushing across ordinary boundaries to express real commonalities. UCI's Vice Chancellor of Research **John Hemminger** is the project's Principal Investigator; co-investigators include the director of IT and faculty members from chemistry and physics. The project plans were drawn up by campus IT staff; letters of support were written by two biologists and an aerospace engineer. Another grants officer and I contributed different grant skills and backgrounds – chemistry (her) and political science (me).

Calit2 Irvine Director **G.P. Li** recently received two awards for the California Plug Load Research Center. One award was for **$100,000-plus** from **Southern California Edison** to develop and demonstrate an innovative way for consumers to display information about their electricity consumption on their existing set-top boxes, without other special equipment. For this award, getting through the many silo boundaries did take time, as multiple department managers and writers on both sides frustrated each other for months. I created some of the delays myself.

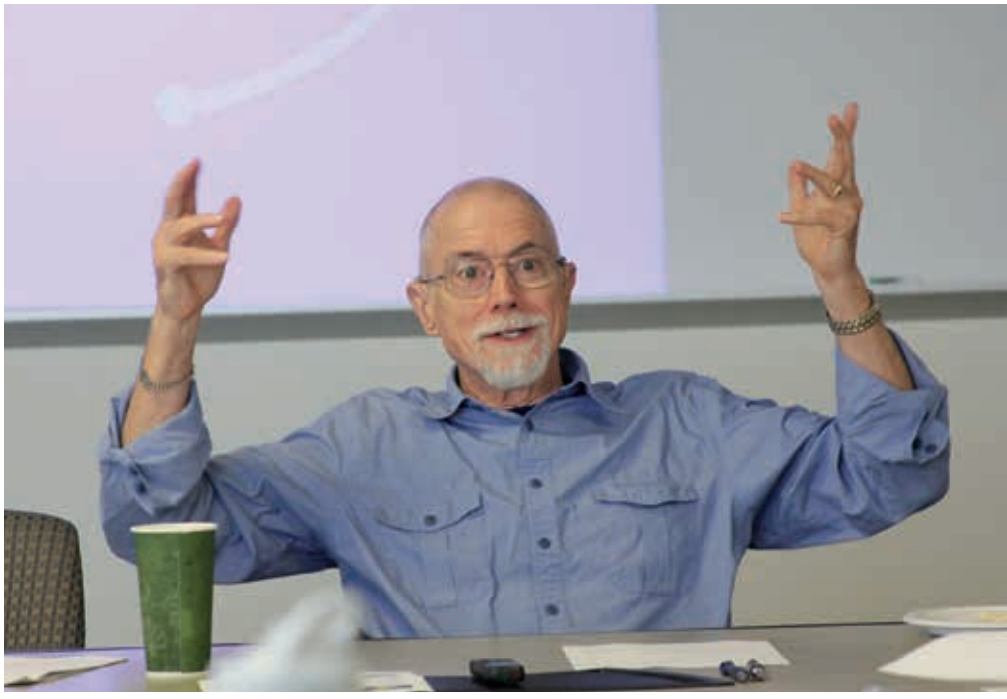
Li's second award was **$25,000** over nine months from a grant program designed specifically for **new trial efforts** that could eventually make huge advances in energy efficiency. This program is called "Max Tech" and is funded by the U.S. Department of Energy. Li and Calit2's technology manager, **Arthur Zhang,** proposed a new system for controlling the energy consumption of a home entertainment center by adapting to the consumer's usage patterns. The results of the small award will enable much bigger steps in the near future, beyond the home entertainment center to the adaptive management of the entire home.

Philip Sheu, professor of electrical engineering and computer science, recently won a first step toward a huge accomplishment – a **$15,000 planning grant** from the **National Science Foundation.** He will begin work toward establishing a university-industry consortium on semantic computing. (Roughly speaking, "semantic computing" means enabling computers to understand and react to the content of the material). Sheu has secured partnerships with UCLA and USC; with UCI in the lead, they will attend and conduct planning workshops and attend NSF meetings to prepare a full proposal. The goal is to develop a team of corporations as paid members, sharing research results and responsibilities to advance the industry as a whole over several years.







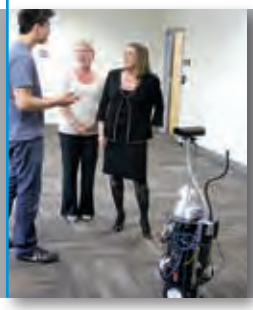
Twelve years of funding, friendship and unflagging devotion

BITS AND BYTES

A timeline of select Calit2 activities

APRIL

3 U.S. Rep. Loretta Sanchez gives RoboCam a test run during a CalPlug visit.



11 Engineer Jean-luc Doumont offers lessons on effective communication for rational minds.

MAY

6 CalPlug Advisory Board holds its annual meeting and tours the center's latest activities.

7 More than 50 invited participants exchange ideas during CalPlug's third semiannual workshop.

JUNE

1 Teams of students from different disciplines present their program-ending research design results.

6 The semiannual Igniting Technology program features an expert panel sharing its startup know-how.

12 Young researchers receive training on Calit2's new Xradia nano CT machine in the Nano-Bio Metrology Lab.

19 Students in the Multidisciplinary Design Program give midterm presentations.

14 A science and technology delegation from Myanmar's Yangon Technological University visits Calit2.

31 UCI Vice Chancellor for Research John Hemminger addresses the Calit2 Advisory Board during its annual meeting.

14 A group of Taiwanese researchers learns more about CalPlug's energy-efficiency technology solutions.

27 A fresh crop of undergraduates happily joins the CalPlug 199 research team.

25 An orientation, complete with paperwork, kicks off a summer of research for seven SURF-IT Fellows.

BITS AND BYTES

A timeline of select Calit2 activities

JULY

8 Representatives from Intel's Logic Technology Development group check out the microscopy center.

10 Ken Lowe, Vizio co-founder, presents eHealth Collaboratory manager Mark Bachman with an equipment donation.

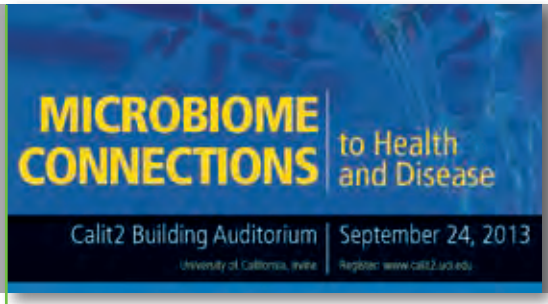
AUGUST

7 High school students participating in COSMOS-UCI learn about scanning electron microscopy in the LEXI facility.

14 Jessica Fernandez, legislative analyst to Rep. Loretta Sanchez, discusses funding support with eHealth researchers.

SEPTEMBER

23 Representatives from a Japanese lens manufacturing company tour the BiON cleanroom facilities.



24 A symposium features various perspectives on microbiome research, a relatively new field of study.

15 Middle-school students participating in UCI's FabCamp experience the 1KW Hour Challenge.

19 David Jacot, LADWP's director of energy efficiency, examines a CalPlug thermal characterization project.

29 Members of the National Assembly of Korea include Calit2 in their multi-stop visit to UCI.

16 UCI graduate students in Chemical and Materials Physics program spent time sharpening their skills in microscopy.

19 Incoming students participating in UCI's summer-session early start program spend an afternoon at Calit2.

29 A summer of undergraduate research experiences culminates with final presentations and awards.

25 On his first visit to Calit2, UCI's new Provost Howard Gillman experiments with the music glove.

25 CalPlug member company Toshiba America's V.P. Chris Harrington checks up on project progress.

26 Thought leaders in technology and education convene a two-day "Reclaim Open Learning" symposium at Calit2.

Under the direction of Professor G.P. Li, Calit2@UCI develops information technology-based innovations in a multidisciplinary research environment. By integrating academic research with industry experience, the institute seeks to benefit society, incubate new technology companies and ignite economic development. Calit2 focuses on the digital transformation of healthcare, energy, the environment and culture.

University of California, Irvine
California Institute for
Telecommunications and
Information Technology
4100 Calit2 Building
Irvine, CA 92697-2800

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Calit2 at your R&D Service

For more than 10 years, Calit2 has been a campus hub for multidisciplinary, IT-enabled research projects. In an effort to bring these "value-added" collaborations to the next level, Calit2 recently announced expanded services for its academic and industry partners working in the areas of healthcare, energy, the environment and culture. Our new capabilities which will be **showcased November 14**, include proof-of-concept support, studies and surveys, fast prototyping, system-integration assistance and standard electronics testing.

An expanded staff with expertise in hardware and software design, development and integration can assist faculty and industry partners with the following services:

- Software development and cross-platform applications
- Electronics system development and fabrication
- Micro-system integration: micro sensors and actuators, rigid/flexible printed circuits
- IT services: server access, software/hardware system integration, system maintenance and upgrades

"Our goal is to provide a tailored technical solution to fit the short-term and long-term needs of our collaborators," said Calit2 Irvine Director G.P. Li. "We're doing more than just prototyping. We're seeding projects by developing and shepherding them through the research process."

More information: Arthur Zhang, Calit2/CalPlug technology manager, 949-824-7866, *yzhang@calit2.uci.edu.*

For a list of completed projects as well as those in progress, please go to: *http://bit.ly/17KrMkx.*