Young Scientists & New Faculty

Joining the fight against cancer

Maie St. John

Dr. Maie St. John vividly recalls her childhood visits to Egypt — annual trips that shaped her calling as a doctor and scientist. Each summer she would travel halfway around the world from her home in Texas, and later Altadena, Calif., to visit her mother's family. Her grandfather, the chief doctor in Zagazig, would take his bright, inquisitive granddaughter on house calls through the dusty streets of the bustling town.

"The village was quite undeveloped when I was young. We saw anything and everything," said St. John, now a head and neck surgeon and a researcher at UCLA's Jonsson Comprehensive Cancer Center. "We saw lots of people in the later stages of cancer."

She can still picture one patient in particular, a new mother who called complaining of tooth pain. When the doctor and his granddaughter arrived, the gravity of the situation was painfully apparent, even to young Maie. A tumor had overtaken a majority of the woman's face. Infection had set in.

"I can still see this young woman with a baby in her arms, dying of this disease. It was a very moving experience for me," said St. John, who also is an assistant professor of surgery. "Cancer became my calling. I never really considered anything else."

Head and neck cancer is the sixth most common cancer in the world. Nearly 70,000 new cases of head and neck cancer will be diagnosed this year alone. About 85 percent of these cases are directly linked to tobacco use.

Despite new and more effective therapies, the survival rate for patients with advanced stages of disease remains poor. The major cause of death in these patients is the spread of the cancer, known as metastasis.

The process of metastasis has emerged as St. John's primary research interest.

Working in the lab of Dr. Steven Dubinett, director of the UCLA Lung Cancer Research Program and the Specialized Program of Research Excellence in lung cancer, St. John and her colleagues are working to better understand a molecule called E-cadherin.

E-cadherin is the "glue" that keeps cells stuck together. When E-cadherin in tumor cells is lost, cells can break apart and are free to spread throughout the body. Tumor cells that lose E-cadherin become very dangerous, and patients with these tumors frequently die of metastatic cancer. Additionally, when E-cadherin is present, the cells are more sensitive to cancer therapies.

"We are focusing our work on understanding what controls the presence of E-cadherin, so we can come up with ways to prevent tumors from breaking apart and spreading," St. John said. "Studying E-cadherin will allow us to gain a better understanding of how cancer spreads. This will then enable us to increase the survival of patients with head and neck cancer."

St. John received her doctorate in cell biology and her medical degree from Yale University in 1999. During her surgical residency at UCLA, she was recognized for both her surgical and research prowess. After finishing her residency in 2005, she was invited to join the UCLA faculty.

Finding joy and fulfillment in both patient care and research, she pursues a vertically integrated approach to medicine. Her clinic and surgical workload cover the full range of head and neck disease, including cancer, endocrine disorders, pediatrics and trauma. At the same time, St. John spends long, productive hours in the lab in pursuit of discoveries that will improve diagnosis, treatment and prognosis for her patients.

"My husband, Rick, says I'm in the business of putting myself out of business. If that happens in my lifetime, I would be thrilled," she said.

Taking a cue from her grandfather, the mother of two young boys has already introduced the oldest, Zane, 3, to her lab and the hospital.

"He knows Mom's a doctor and feels that hospitals are a place where good things happen," St. John said. "My boys can pursue whatever career path they choose, but I do want them to learn compassion. I want both my boys to have a desire to help people."

Kathrin Plath

Kathrin Plath appreciates the basics. She grew up on the east side of the Berlin Wall but can't recall going without. In her spare time she enjoys a good book, classical music and a game of tennis. At UCLA, her focus is basic science — the foundation upon which life-changing discovery is built.

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By Dan Page

answers," said Plath, a stem cell scientist, a member of UCLA's Jonsson Cancer Center and assistant professor of biological chemistry. "You find the answer, and that leads to more questions and even more answers. It's a very dynamic, exhilarating process."

Basic science researchers typically toil in obscurity. The discoveries built on the foundations of basic science—those with an immediate impact on the world—typically attract the headlines rather than the basic science discoveries themselves.

Yet Plath and colleagues at UCLA and Harvard recently achieved a degree of international renown when they took normal adult tissue cells and reprogrammed them into cells with the same unlimited properties as embryonic stem cells—those that can give rise to every cell type found in the body.

The work, done with mouse models, appears in the inaugural June 2007 issue of *Cell Stem Cell*. Plath and colleagues took mouse fibroblasts, easily obtainable skin cells, and added four genes that bind to special sites on the DNA. Using this process, they turned the fibroblasts into pluripotent cells that proved nearly identical to embryonic stem cells.

The implications for disease treatment could be staggering. Reprogramming adult stem cells into embryonic stem cells could generate a potentially limitless source of immune-compatible cells for tissue engineering and transplantation medicine.

"If we can recreate this in human cells, it will have significant implications for regenerative therapies," said Plath. "Our reprogrammed cells were virtually indistinguishable from embryonic stem cells. We could find no evidence that they were different in any way. We were rather surprised at how well this reprogramming worked."

The level of collaboration that makes these kinds of discoveries possible attracted Plath to UCLA. The daughter of two East German scholars, she experienced the power of scientific collaboration first hand when she left Berlin's Humboldt University to study under the guidance of Tom Rapoport, a renowned East German scientist who had become a professor of cell biology at Harvard.

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"I like the way he thinks about science. He knows all the details and enjoys discussing them," Plath said. "He has many scientists in his lab, yet he's really involved in the research. His approach allows him to push his science quite far."

Her other adviser, Rudolf Jaenisch at the Massachusetts Institute of Technology, influenced Plath dramatically as well.

"He is able to envision each important step in his field and then takes the risk to move into the new direction long before others," she said.

Since her arrival at UCLA in 2006, Plath has been developing relationships with her new mentors, Larry Zipursky, chair of biological chemistry, and Geraldine Weinmaster, a professor of biological chemistry. Both help Plath with everything from grants to managing people to scientific questions.

"The depth and variety of research interests at UCLA opens doors to all kinds of collaborative opportunities," Plath said. "I enjoy interacting with scientists across the campus. It's very special to have colleagues that are supportive and want to share and help. UCLA offers a very open atmosphere."

Plath cites a conversation over coffee at UCLA with colleague Amander Clark, an expert on human embryonic stem cells,

"That conversation led to a fruitful collaboration aimed at understanding the basis of human stem cell self-renewal and differentiation," Plath said.

With Clark and other researchers at UCLA, Plath is now trying to reprogram adult human stem cells back to an embryonic state.

She never imagined such an opportunity when she entered Humboldt University in East Germany only weeks before the Berlin wall was toppled.

"The day the wall came down was exciting," said Plath. "Rumors were going on for a long time that something would happen. Then one night you could go over to West Berlin, go to West Germany, travel in Western Europe, the U.S.—it was amazing."

Today, the larger impact on her life is more apparent.

"Looking back at what I've been able to accomplish since coming to America," Plath said. "I doubt I would have been able to do that if I'd stayed in Germany."

Bill Lowry

Discovery is only skin deep for scientist William E. Lowry. Trained in epidermal biology, the UCLA assistant professor of molecular, cell and developmental biology spends much of his laboratory time isolating stem cells in skin and studying the signals that instruct them to grow or differentiate.

"The anatomy of skin has been studied for a hundred years. It's an accessible and well-described system," said Lowry, a researcher at UCLA's Institute for Stem Cell Biology and Medicine and the Jonsson Comprehensive Cancer Center. "The broad, basic questions about the organ and system have been answered. We can get into the more detailed, nitty-gritty questions."

And it's the quest to understand the nitty-gritty that drives Lowry's scientific pursuits.

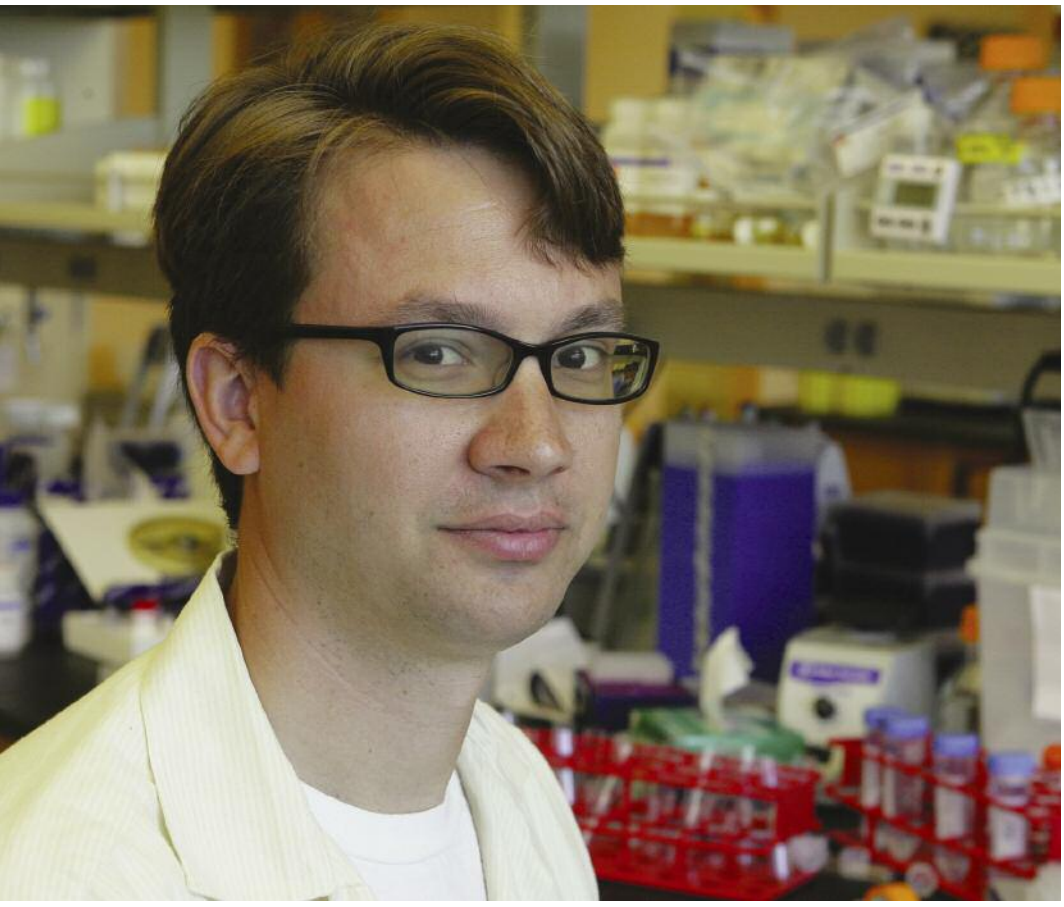
"When you deal with clinical questions involving the whole tissue or system, you have many more variables," Lowry said. "If you study questions at a molecular level, you discover the underlying mechanisms that make tissues and systems work. Data are much more precise."

Found in most major organ systems, adult stem cells provide a source for replenishing tissue lost to damage or simple wear and tear. Stem cells have the ability to both self-renew and differentiate into specific types of cells.

Lowry and his UCLA team are interested in whether stem cells found in different tissues and organs use similar mechanisms to undergo self-renewal and differentiation. By understanding these processes, Lowry hopes to bring new insight to the "cancer stem cell" hypothesis.

"That's the idea that malignant tumors, and maybe tumors in general, may be a derivative of a stem cell gone haywire as opposed to a regular cell," Lowry explained. "While many scientists are interested in how to stop the spread of tumors, I'm interested in what initiates tumors."

Lowry thought he wanted to be a physician when he entered his freshman year at the University of Washington, but his experiences in the lab as an undergraduate sent him down a different career path. Lowry subsequently studied cell signaling as a graduate student at Cornell Medical College and sharpened that focus to stem cells while conducting postdoctoral work at Rockefeller University.



"The field wasn't as developed at that point as it is now," Lowry said. "It took a while to characterize a system and sort of figure out stem cells. We didn't actually study signaling until the latter part of my postdoctoral training."

As stem cell knowledge has increased exponentially in recent years, the potential for using stem cells to heal and regenerate entire systems and organs has captured the imaginations of both the public and politicians.

"The public perception can be a little distracting, but it's nice people are interested," Lowry said. "The whole stem cell frenzy has brought attention and new money to the field. The interest is helpful not only for research like mine but for the biological research community in general."

California's support for the field through its stem cell initiative, Proposition 71, and UCLA's success at developing the infrastructure necessary to support this kind of work was a drawing card for Lowry to join the faculty, as was the university's collegial atmosphere.

"I really like the atmosphere," said Lowry, who came to UCLA in July 2006. "It's scientifically rigorous but at the same time pretty friendly and laid back. UCLA had their act together in terms of the kinds of things I was interested in studying. It made it very easy to decide to come here."

As he sets up his UCLA lab and gets to know the graduate students and colleagues who will be working with him, Lowry recalls lessons learned from his former boss, the late Harold M. Weintraub, a researcher at the Fred Hutchinson Cancer Research Center in Seattle, Wash.

"I got the feeling from working in his lab and from his reputation among his assistants and peers that he was someone special to work with, not only because he was super smart but because he was generous scientifically," Lowry said. "He wasn't paranoid about sharing his work, and he helped people develop their ideas. I've always tried to live up to that ideal, if not scientifically then at least to his generosity of ideas. ✶