

Four Young Scientists

Genhong Cheng: an incredible journey in search of new ways to fight cancer.

As a child, Genhong Cheng labored alongside his parents in communal rice fields outside the tiny village of Pingdu in southeast China. “It was hard work, for not much money,” Cheng recalls.

The family ate a lot of rice. To bathe, they heated water over a wood fire. Entertainment was mostly “running around the countryside,” Cheng says. “We led a simple life. But it was a good one.”

No one from Pingdu, population 750, had ever gone to college.

Today, Genhong Cheng, Ph.D., runs a sophisticated, modern laboratory at UCLA’s Jonsson Comprehensive Cancer Center.

The 38-year-old assistant professor lives with his wife and two children among upper middle class neighbors in a contemporary home in Calabasas, Calif., an ocean and some 6,500 miles east of the mud and brick house without running water where he grew up.

Cheng teaches at UCLA, a remarkable contrast to the two-room school house he remembers from his youth.

The cellular and molecular biologist supervises 10 doctoral and post-doctoral students in his lab. They treat him with great respect and admiration approaching adoration.

“Genhong is the boss without barriers,” says one student. “He interacts a lot. He’s honest and frank. He listens. He advises. He is a brilliant, creative, adaptive scientist.”

Two projects move forward in Cheng’s lab.

One quest involves finding the difference between the normal immune response and the inflammatory response that causes rejection of organ transplants and many diseases, including Alzheimer’s and atherosclerosis.

The second project centers on Cheng’s discovery that, while some chemotherapy drugs kill cancer cells, they also activate “pathways” that protect cancer cells. “That is one reason that chemotherapy is often pretty efficient at first, but then the

cancer relapses and is very hard to treat,” Cheng says.

So Cheng believes chemotherapy leads to “chemo resistance,” and he’s working to:

- ❖ Find existing chemotherapeutic drugs that do not induce “chemo resistance.”
- ❖ Improve existing drugs to eliminate that resistance.
- ❖ Discover the mechanism of “chemo resistance,” thereby enabling physicians to prescribe the most effective drugs.
- ❖ Find a way to block the pathways that enable cancer cells to become resistant to chemotherapy.

Cheng says he is making excellent progress in his lab. He also emphasizes that his work is a long way from clinical use.

As a child, Cheng wanted to be a physician. But in 1980, when he entered Wuhan University, professors selected students’ majors. They told Cheng he was a biology major. “I wasn’t sure what the biology department did,” he says.

He found out. And he liked what he found. After Wuhan came research at Albert Einstein College of Medicine and Rockefeller University in New York, then MIT in Cambridge, Mass., and then, in 1996, UCLA, where Cheng has won the prestigious Scholar Award for original research from the Leukemia and Lymphoma Society and the Research and Career Development Award from the STOP CANCER organization.

“Now I’m a researcher, not a physician, and I love it,” Cheng says. “I’d much rather find something new than fix something old.”

Linda Liau: a scientist and brain surgeon with a hero.

Linda Liau wants to write the great American novel and to save people from dying of brain cancer.

She hasn’t started the novel. But she’s definitely on the road toward saving brain cancer patients.

Brain surgeon, brain cancer researcher, magna cum laude graduate of Brown

University, high honors graduate of Stanford School of Medicine, Assistant Professor Linda Liau, M.D., Ph.D., 34, performs brain surgery twice a week and heads the Malignant Brain Tumor Program at UCLA School of Medicine.

When not in the O.R., Liau can most often be found in her lab working on one of two projects: developing ways for the human immune system to battle brain cancer, and seeking the function of genes that she’s discovered to be more active or more prevalent in brain cancer patients than in healthy people.

Or she will be busy writing grants (she’s particularly good at that), editing (she is primary editor of a new, 18-chapter textbook, “Brain Tumor Immunotherapy”) or at home relaxing with her husband (also a brain surgeon) and their two-year-old son.

“I tend to keep busy,” Liau says.

Liau grew up in Cerritos, Calif., the daughter of a real estate broker and a homemaker. She attended public schools and never got a grade below A. The list of upper echelon colleges that accepted her: Brown, Columbia, Harvard, Johns Hopkins, UC Berkeley and Yale.

She picked Brown, majored in political science, found medicine more appealing than politics or law school, and entered Stanford School of Medicine, where she got heavily involved in research.

In 1991, Liau graduated from medical school and came to UCLA as a neurosurgery intern and then resident, focusing on clinical medicine as opposed to research.

During her fifth year of residency, Liau’s mother died of breast cancer that spread to her brain. She was 51. “If I have a hero in life, it is my mother,” Liau says. “I was very close to her. If it were not for my mom, I would not be where I am today. I would probably be a housewife. She was the only person throughout my life who told me, ‘You can be whatever you want to be.’ I am very proud of her for that, and I love her very much.”

Her mother’s death led Liau back into research.

“Even with aggressive neurosurgery,

chemotherapy and radiation, a brain cancer patient's life expectancy is only about a year," Liau says. "When my mother died, I decided to find a way to make things better than that."

In 1995 Liau entered UCLA's neuroscience doctoral program. Four years later, she added Ph.D. to her name.

Given surgery, research, grants, editing, teaching and her husband, child and home, will Liau get to that great American novel?

"It's not a question of *will* I," Liau says, "It's a question of *when* will I. The longer I wait, the more I have to write about."

Luisa Iruela-Arispe: a woman at war.

Luisa Iruela-Arispe's mother told her, "Be a physician, because they are the *real* doctors."

Arispe tried the M.D. route, but says she detoured to her Ph.D. "because my passion is to meet the challenges of puzzles I find every day in my laboratory."

When she talks about her work, Arispe sounds happy, excited, respectful, even somewhat in awe. It's as if she's struck gold.

She may have found a greater treasure than that.

The 37-year-old vascular biologist discovered two proteins that inhibit the growth of blood vessels.

Everyone naturally produces these proteins, called METH-1 and METH-2, and they appear to be cancer fighters.

"Tumors produce more than normal amounts of METH-1 and METH-2," Arispe says. "Both those proteins cause blood vessels to shrink. So it looks as if their increased production in tumors is a natural attack by the body against the network of blood vessels that tumors develop to nourish themselves."

Arispe's strategy in her battle against cancer approximates scientific warfare. Military tactics often include cutting off an enemy's supply lines. Tumors build their own supply lines: the blood vessels that deliver essential oxygen and nutrients required for tumor growth. In sufficient quantities, METH-1 and METH-2 deprive new tumors of their blood supplies, so the tumors cannot grow bigger than pinheads, and remain harmless. Older, larger tumors deprived of new blood ves-

sels by METH-1 and METH-2 shrink and become dormant, Arispe says.

"METH-1 and METH-2 are the body's soldiers, the guys who attack the enemy's (tumors') supply lines," Arispe says. "There are just not enough of them, so they can't win the battle. We have good guys and bad guys. We need more good guys."

The body makes blood vessels in many subtly different ways. No one fully understands the unique method tumors use to build their blood vessels.

In her lab, Arispe and the 15 scientists who work for her, strive to gain that understanding, which could lead to developing a way to deliver METH-1 and METH-2 directly to tumors, thereby destroying their ability to build the blood vessels they need.

"When we can do that," Arispe says, "perhaps we will be able to treat some or all cancers with a pill. Of course, that's still a dream. I'm working hard to make my dream come true."

Mark Pegram: his choice was music or medicine.

What's a kid to do with his life after performing at the Kennedy Center in Washington, D.C. as a percussionist with the North Carolina Symphony at age 16? Become a famous musician, of course.

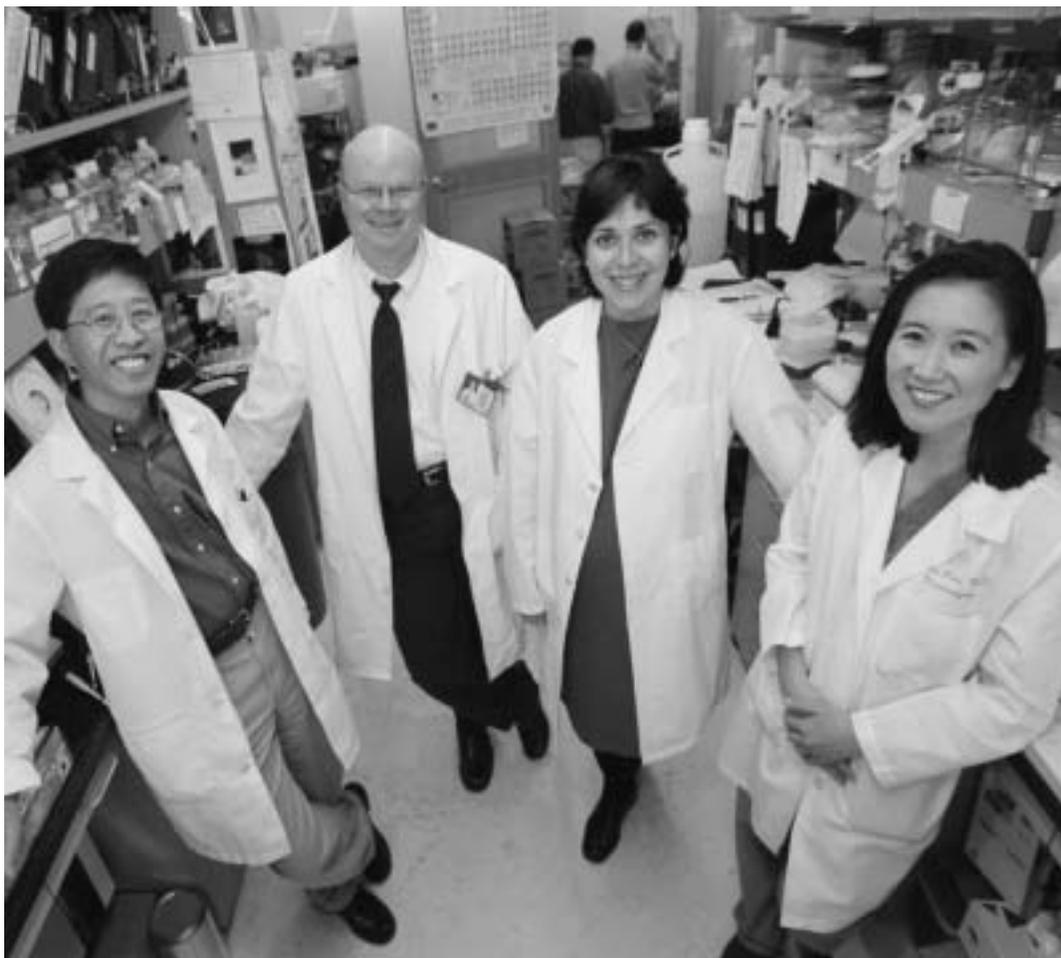
Wrong.

Become a cancer researcher and physician. That's more like it.

Mark Pegram, M.D., still loves to talk about the role of percussion in music. He's probably the only doctor at UCLA's Jonsson Comprehensive Cancer Center who can expound on the intricacies of playing every percussion instrument from the kettle drum to the triangle. "Yes," he says, "There are intricacies to playing the triangle."

But Pegram put down his sticks a long time ago. These days the 41-year-old associate professor concentrates on moving cancer therapies from his lab to his patients.

Pegram's two current lab projects involve:



Left to right: Drs. Genhong Cheng, Mark Pegram, Luisa Iruela-Arispe, Linda Liau

- ❖ Tricking an enzyme that resists chemotherapy in colon cancer patients. Pegram combines that enzyme with a drug that becomes toxic on contact with the enzyme and kills the cancer cells that had been resisting chemotherapy. He succeeded in doing this in his lab and is preparing a Phase I clinical trial. (Experimental therapy typically goes through three phases of clinical trials before it can be approved by the FDA.)
- ❖ Seeking ways to make the cancer drug, Herceptin, effective for women with newly diagnosed breast cancer. Currently, Herceptin is only approved for women with advanced disease. Pegram is co-investigator for a Herceptin clinical trial for women with early stage breast cancer.

When not in his lab, Pegram can most often be found with his patients or lecturing about his research. Occasionally, he's even home in San Pedro, relaxing with his wife, Nora (also an oncologist) and his two politically adversarial dogs, Nixon and Clinton.

As a youth, growing up in Buffalo Grove, Ill., Pegram had two passions: music and chemistry. "I played drums in my high school band, orchestra, marching band and jazz band," he recalls. "But I knew that, no matter how talented a musician is, it's a stressful life and you have to be lucky to make a living at it."

So he turned to his other love, and by his junior year at the University of North Carolina he was taking graduate school courses in chemistry.

When he finished college in 1982, Pegram had two choices: pursue a doctorate in chemistry at CalTech or a medical degree at UNC. He chose the latter, and for two years regretted it.

"I hated the trivia and minutiae I had to memorize," Pegram says. "I missed the need to think, to derive facts." Between his second and third years of medical school, Pegram worked in a molecular biology lab. "That turned me around," he says. "It gave me the chance to do basic science and apply it to medicine. I loved combining the two fields. I still do, and I expect to for many years." ☆