

New Faculty: **Joining the fight against cancer**



Christina Jamieson wants to know why some cells die and others survive and how that life and death drama plays into the development of cancer.

To do that, Jamieson studies genes and steroid hormones—key players that either turn off or turn on cells. For Jamieson, timing is everything and she’s trying to figure out why some cells turn on and why others turn off.

“I’m looking at normal cells and cancer cells for differences in the gene regulation. I study hormones that lead to the difference in cell death or survival,” she said.

Jamieson joined UCLA’s Jonsson Cancer Center in early 2002 and is an assistant professor of urology and human genetics.

“I’m really interested in exploring how the life versus death signal is regulated and why steroid hormones can do both,” she said. “For instance, in normal prostate cell growth, the cells are totally dependent on androgens, such as testosterone. But if you remove androgens, the cells of the prostate will degenerate and die. They really are dependent on the hormone. In prostate cancer, however, the cells often lose this dependence on androgens and grow well without it.”

Jamieson uses DNA microarrays to study the activity of genes in normal and cancer cells exposed to steroid hormones. A DNA microarray, about the size of a postage stamp, allows her to survey the activity of tens of thousands of genes all at once in a small sample.

She currently has two projects underway in her lab. One is a prostate cancer project that uses DNA microarrays to study the genes that regulate certain events

in metastasis of cancer to bone. The goal is to understand how prostate cancer exerts its unique destructive effects when it gets to the bone.

The other project is looking at how another class of steroid hormones called glucocorticoids, such as cortisol, regulate T-lymphocyte survival. Glucocorticoids are used to treat lymphoma and have the ability to induce normal and cancerous T-cells to die. Strikingly, other signals from the environment can reverse the death signal.

“We are identifying the genes that carry out the death using microarrays and studying how their activity is blocked by these rescuing signals,” she said.

Jamieson chose to come to UCLA because its research communities offer the full spectrum of research: From the most fundamental questions of how life works to applied clinical research.

“This enormous scientific breadth allows me to pursue both my basic science and to develop research in the clinically-related implications of my work,” Jamieson said.

“My five year goal is to find pathways of genes that are regulating cell death and to understand how that pathway is being regulated by a steroid hormone. That’s interesting in itself as basic science, but I’m also interested in learning to apply it since steroid hormones are a major target of chemotherapy. These drugs are very effective in killing cancer cells. However, the cancer cells can learn to convert the death signal to a survival and growth signal,” she said. “In understanding how you get a specific response in what are generally widely shared regulatory factors, we are going to be able to target drugs to a specific factor where the pathway has gone wrong.”

Jamieson was born in Scotland and spent her early life in Chile. Then her family moved to a small town in the Canadian Rocky Mountains and then to Ottawa and Vancouver. She received her bachelor’s degree in microbiology from the University of British Columbia and her doctorate in molecular immunology from Brandeis University. Prior to joining the cancer center, she was a postdoctoral fellow at the University of California, San Francisco.



Clifford Ko joined UCLA’s Jonsson Cancer Center in early 2003 as a surgeon and researcher who works with patients who have colon and rectal cancer.

When he’s not in the operating room, Ko is conducting research about quality of life and quality of care issues as they relate to patients with colon cancer.

“We measure and evaluate their quality of life so we can improve patient care. We also look at the use of appropriate cancer care for patients,” Ko said. “For example, if we determine that people who should be getting chemotherapy are not receiving it, we look at the reasons why—whether it’s a problem of a doctor not offering it to them, or a patient not understanding they need it or the patient refusing. Studying these things helps us evaluate and improve the quality of cancer care. Chemotherapy is just one area of study. Surgery is another that I am very interested in because there may be some important improvements that can be made.”

Typically, Ko splits his time between surgery and research.

“For me, it’s just a great combination because what I research is exactly what I operate on clinically. For example, being involved in day-to-day patient care affords me the opportunity to see where clinical care may be improved. This helps to set a research agenda and prioritize issues in terms of clinical relevance and importance. But it also works the other way around. Studying what constitutes high quality of care and the quality of life these patients have has made me a better clinician for my patients, and also helps me to teach better.”

Growing up, Ko wanted to be a teacher. “I took all the classes in college to

become a science teacher but unfortunately, or fortunately depending upon how you look at it, they were also the same classes that the pre-meds took. My college advisor said I might as well apply to medical school—and that’s how I got here,” he said.

Now Ko teaches colon and rectal surgery to medical students, residents, and practicing surgeons. He is the recipient of UCLA’s Golden Scalpel award for best teacher of 2003.

One of Ko’s two master’s degrees is in ethics, which helps him navigate the often-complicated terrain of practicing

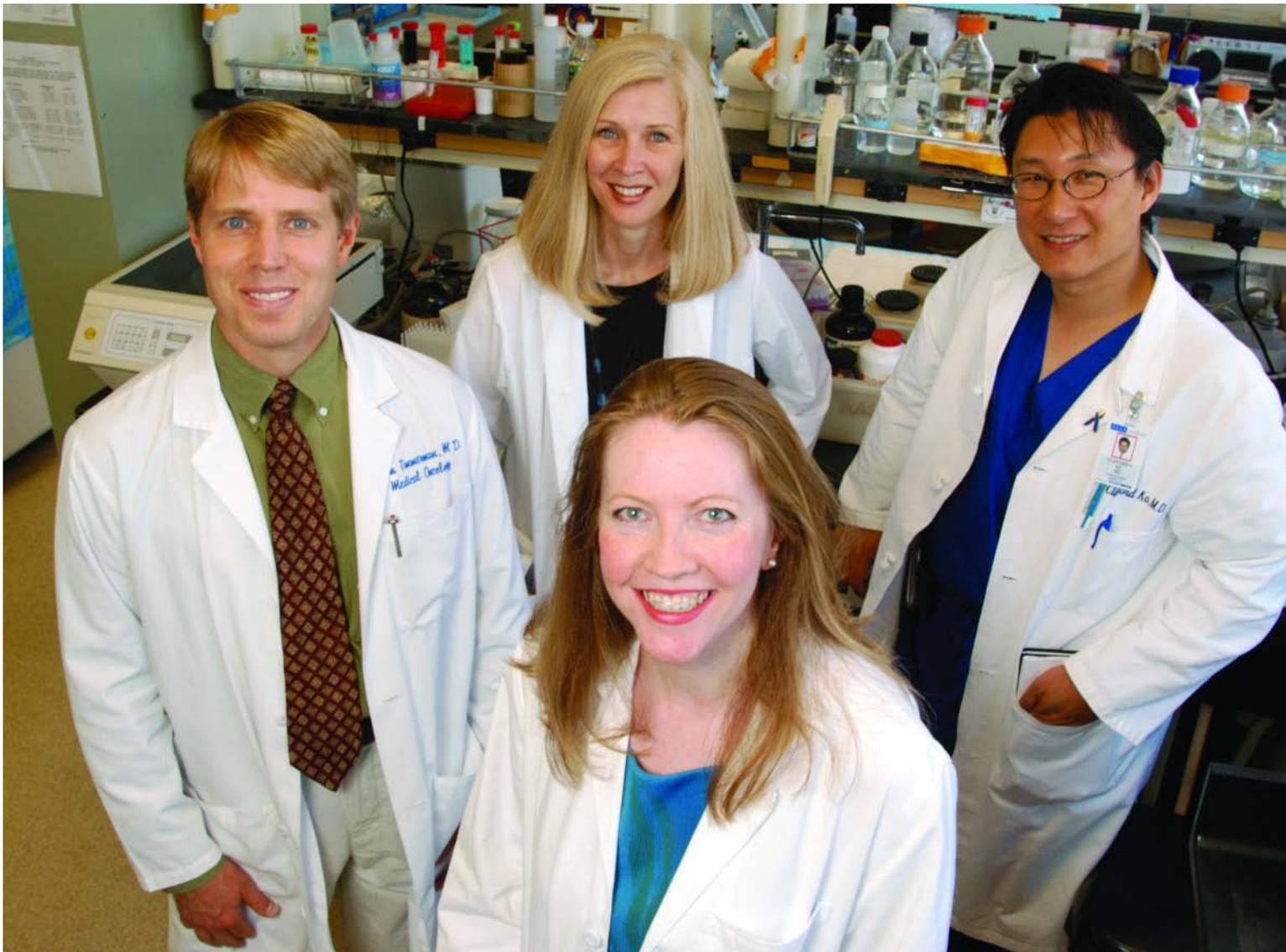
medicine today.

“Medicine and particularly surgery is much less paternalistic now. We don’t just tell patients ‘You should get this because I said so,’” Ko said. “Although medical science is achieving more and more, very little is black or white. Everything seems to be shades of gray. I don’t think anyone thinks it’s right that the doctor puts his or her own priorities and values into the decision for the patient.

“This shared decision-making is important, especially in cancer care where making choices can become very complicated,” he

added. “There are clinical factors that come into play—the extent of the cancer as well as the extent of surgery. And there are patient issues regarding such things as their age and their own values and priorities. People feel differently when given the choice of quality of life versus quantity of life. Helping to make an individualized decision is not only important for the patient, but to me, constitutes appropriate and high quality care.”

Besides being involved in a National Cancer Institute project looking at the quality of care in colorectal cancer, Ko also



Clockwise from left: John Timmerman, Annette Stanton, Clifford Ko, Christina Jamieson.

is working with surgeons across the country to develop quality indicators for colorectal cancer surgery. This project will identify the important processes of care that all surgeons should perform when operating on a patient. Another research project examines the disparities in colon cancer care throughout California.

“Achieving high quality of cancer care regardless of demographic characteristics is important for improving the overall level of care,” said Ko, who received his bachelor’s, master’s and medical degrees from the University of Chicago. “Hopefully, all of these projects together will contribute to improving such care.”

Ko said he picked UCLA because the campus has so much to offer in his areas of interest—surgery, the cancer center and health services research.

“I also work on projects at RAND, so between the two facilities we have the top experts in the world,” he said. “This is a great place.”



Annette Stanton, a national leader in the field of health psychology, is fascinated by the way people cope with life-threatening illness.

“People often are amazingly resilient, even though cancer can create significant life disruption,” said Stanton, who in January joined the faculty of UCLA’s Jonsson Cancer Center to work in the division of cancer prevention and control research. “I was drawn specifically to health psychology through observing the marked individual variability in responses to the diagnosis of life-threatening illness. I became fascinated with attempting to specify factors that help and hinder individuals as they face health-related adversity.”

A professor of psychology and psychiatry

and biobehavioral sciences, Stanton’s research focuses primarily on the psychological consequences of serious illness, particularly cancer, and on contributors to psychological and physical recovery.

“Knowing the psychological consequences of cancer can aid professionals in providing the best patient care,” Stanton said. “Identifying the factors that make patients vulnerable to negative psychological consequences and those that bolster positive adjustment can help us design the most effective interventions.”

Her research also helps patients cope as well, she said.

“Learning about common psychological concerns can help individuals with cancer understand that they are not alone or abnormal,” Stanton said. “For example, some people are surprised and dismayed when they don’t recover quickly, both physically and psychologically, once their treatments are over. Learning about the challenges that many people face at this time can help ‘normalize’ the experience.”

Stanton’s research is exploring new ground in studying how the mind and body are connected.

“I’m trying to identify effective strategies for promoting psychological and physical health during the experience of cancer and other illnesses. When people are diagnosed with a life-threatening illness, they face many challenges, including managing a range of strong emotions,” she said. “In our research, we have found repeatedly that individuals who attempt to avoid cancer-related emotions and thoughts are at risk for poor adjustment across the first year after diagnosis. People who try to push it out of their minds, try to push it away, tend to do more poorly in the long run.”

By contrast, Stanton has found that the use of more approach-oriented coping strategies predicts more favorable outcomes.

“Having strong social support, being an active information seeker, actively expressing emotions and identifying the benefits of the experience—those strategies predict better adjustment over the long run,” she said.

For example, Stanton recently randomly assigned women with breast cancer to write in a journal over several sessions. One

group wrote about their deepest thoughts and feelings about breast cancer, and another wrote about the benefits of their cancer experience. Other women wrote only about the facts of their experience. Stanton discovered that participants who wrote about their emotions or about the benefits surrounding their experience had fewer medical appointments for cancer-related problems and reported better health over the next three months than did women who wrote about the facts.

Once a music major, Stanton put down her flute and switched to psychology after a particularly intriguing undergraduate class.

“I can’t think of anything more fascinating than trying to understand how humans work,” she said. “It is really heartening to know that most people are resilient, and their approach can teach us something about how to help people who are more challenged.”

Stanton became interested in cancer when her father was diagnosed with prostate cancer.

“I come from a very stoic, Midwestern family so I went through the experience of our family trying to deal with his cancer. That got me interested on a personal level,” she said. “Then, during my clinical internship, I began to work with patients diagnosed with life threatening illness, some of whom were cancer patients. I was struck by the variability in their responses and began to be really curious about how it is that some people do well and some people do poorly.”

Born in France and raised in a small Kansas town, Stanton earned a bachelor’s degree at the University of Kansas and completed an internship at Los Angeles County-USC Medical Center. She received master’s and doctorate degrees from the University of Connecticut. Prior to joining the Jonsson Cancer Center, Stanton was a professor at the University of Kansas.

In 2002, Stanton won the Senior Investigator Award from the American Psychological Association for outstanding contributions to health psychology. She is co-author of the book “Psychology of Women’s Health: Progress and Challenges in Research and Application.”



John Timmerman is determined to stop the immune systems of people with lymphoma from slacking off. “My job as a translational investigator is to build new programs and the most exciting part of it for me is developing new therapies for lymphomas,” said Timmerman, who recently joined UCLA’s Jonsson Cancer Center as an immunology researcher for lymphoma.

Timmerman and his group make custom-made vaccines for people with lymphoma. The vaccines are designed to stimulate the immune system and make it do the work it should be doing—killing cancer cells.

“My study right now is a dendritic cell vaccine. When I was at Stanford we treated 35 patients with this tumor marker called idiotype that’s loaded into these special antigen presenting cells called dendritic cells,” Timmerman explained. “When we vaccinated patients with these special white blood cells, the tumors shrank in a portion of those patients, so we were very excited about those results.”

Timmerman’s new study will start with 20 volunteers and UCLA is the only site in the world where this study is being done.

“Our goal is to treat patients who have relapsed lymphoma and we are going to try to get the tumors to shrink,” he said.

He hopes to answer some questions about the secrets of the immune system.

“Our focus really is to delve into the biology and the immunology of how the vaccine works. So when a tumor shrinks, I want to know how it’s working. What mechanisms does the body use to kill those cancer cells? Your immune system has two arms—antibodies and T-cells—does it use antibodies, does it use T-cells, does it use both? One or the other,

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—Dr. John Timmerman

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Timmerman said he chose UCLA because of its long history of research into immunotherapy.

“One of the big attractions of coming here is that we have what we call a good manufacturing practices suite. This suite allows us to grow dendritic cells for use in patients,” he said. “This facility was specifically designed by Dr. James Economou and his colleagues for growing dendritic cells. That’s something we didn’t have at Stanford, so that was a big attraction to come here. All the ingredients were in place to do these types of very labor intensive, cumbersome trials.”

Timmerman’s interest in immunotherapy stems from a desire to decrease debilitating side effects of cancer treatment.

“As long as I’ve know about immunology I’ve always been fascinated by the ability of the immune system to fight cancer,” he said. “What drove my interest in cancer was probably just a curiosity about the biology of this strange and frightening disorder. I also had a friend in college who had lymphoma and was treated at Stanford. There I was holding her hand while she was getting chemotherapy and vomiting, and that experience told me that was not the answer, this was not the

way to treat cancer.”

At one point in graduate school, Timmerman wasn’t sure if he wanted to get his doctorate degree so he could do laboratory research or his medical degree so he could work with patients.

“I decided I really wanted to do clinical medicine because I wanted to bring new treatment approaches to patients. This job really is a dream come true,” he said.

“Now I’m doing translational research, which is developing new therapies based on existing knowledge and translating that from the laboratory to the clinic and back again. It’s a lot more trouble to be a human doctor than it is to be mouse doctor when you are doing cancer research, but the rewards are so much greater. A lot of people can cure cancer in mice, but to do it humans is really, really exciting. We’ve gotten to the point now where we’ve seen some spectacular tumor shrinkages in some of our patients, yet we don’t really understand why.”

Timmerman spends about 80 percent of his time in the lab and about 20 percent of his time on patient care. He is a recent recipient of a \$225,000 Clinical Investigator Award from the Lymphoma Research Foundation.

He grew up in San Rafael, Calif., and earned his bachelor’s degree at the University of California, Berkeley, and his medical degree from Boston University. ★