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Searching for a Cure for Cancer

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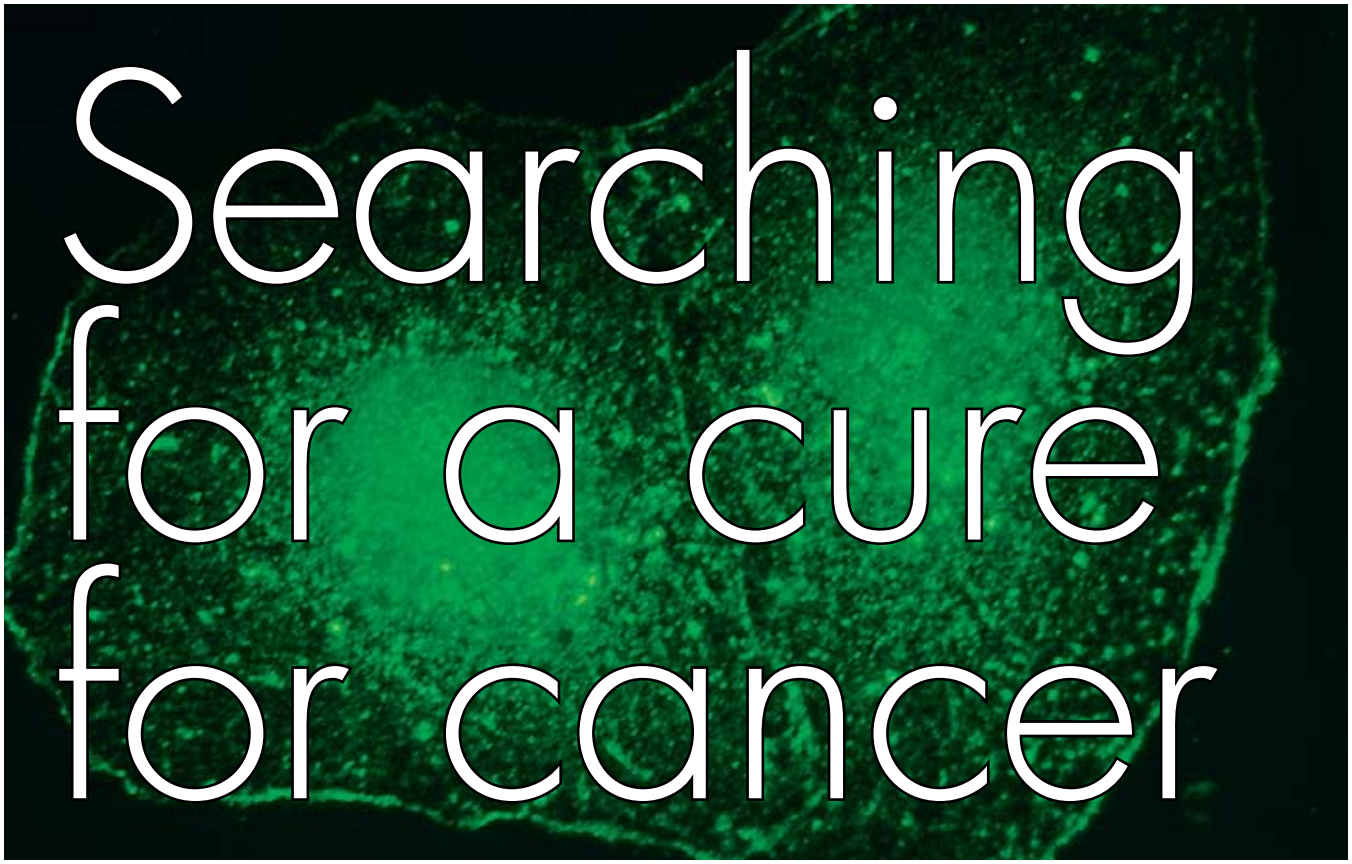


Searching for a cure for cancer

Cancer is more than a disease to Anne Kruchten.

She considers it from an analytical, clinical and scientific perspective, but at the end of the day, it is personal. What drives her is the need to understand why her brother died in his early 20s of a rare and deadly form of bone cancer and what can be done to stop it. Her research has become an integral part of her classroom as well as an important component in the lives of students who work by her side in Linfield laboratories.

At 18, Kruchten took a summer job washing dishes in a laboratory at Indiana University in her hometown of Indianapolis. Her future was planned. She would attend Transylvania University (home of the Pioneers, not the vampires, she notes with a laugh) in Lexington, Ky., and then head to medical school.

But that summer her focus slowly began to shift. The lab became more than just another summer job and she took her first tentative steps into research, which started as a challenge from the lab director.

"He gave me two pieces of paper and said I needed to learn every piece of equipment listed," she said. "I think it was a sink or swim test, but within a week I finished everything and I started to do research."

It's a lesson she has not forgotten and she follows the same philosophy with her Linfield students. "I start out with some hand holding to get them used to the process, but in the end, they are on their own," she said.

After four summers in the lab at Indiana, medical school was set aside and she headed to graduate school. Five years later, Ph.D. in hand, she began a postdoctoral program at the Mayo Clinic in Rochester, Minn., where she switched her research focus from obesity and diabetes to cancer.

Kruchten, an assistant professor of biology at Linfield for three years, is tall with a head of brown, curly hair that bounces around her face. She is quick to laugh,

Cortactin, highlighted in bright green masses along the edges of the cells, is suspected to play a role in how malignant cells move throughout the body.

has a good arm in softball and a knack for explaining complicated research. She can be intense, demanding and funny, and students love her.

Jeneva Foster '09 is pursuing a Ph.D. program in biochemistry, molecular and cell biology at the University of Oregon. Her work with Kruchten helped her learn how to think like a researcher and define her goals. She not only worked in Kruchten's Linfield lab, she also learned about writing research papers and grants, which also helped prepare her for graduate school.

"Working in a research lab is different than the labs you do for class," she said. "You don't blindly follow the protocol the professor printed out; you have to really think about and understand what you are doing and why you are doing it.

"Before I started working with Anne, I didn't know what I wanted to do and I doubted myself all the time," Foster added. "She is one of the biggest reasons I'm [at UO]. She always challenges you, but never discourages you. She helps you find the answers without telling you what they are."

Understanding cortactin

A nanometer-sized protein called cortactin lies at the center of Kruchten's work, research that began during her post-doctoral studies at the Mayo Clinic. She and her students are trying to determine the role cortactin plays in how cancer metastasizes, when malignant cells break off from a primary tumor and travel through blood vessels.

"People die from cancer because tumor cells migrate to other places in the body and disrupt organ function," she said. Understanding this movement, or metastasis, is at the heart of her research.

Some cancers are far more metastatic than others. For example, skin cancer can be relatively metastatic. Some forms of breast cancer can be much more so and pancreatic and bone cancer are highly metastatic. Cort-

Cancer and heart disease

Cancer is the second leading cause of death in the United States, after heart disease.

Headway has been made to address heart disease, but similar advances have not been made in reducing cancer deaths.

There are reasons for that, according to Anne Kruchten. Heart disease is not just one disease, but it's a few things affecting one organ. Once you figure out what's going on with the heart, it is easier to determine how to treat it.

In contrast, there are many types of cancer all working in different ways. For example, in one tumor, every cell can be different. Research has been segmented to address different aspects of cancer. There is a move to create consortia so that information on, for example, cell migration, is funneled into one website so no one is working in isolation.

Discussion at a conference Kruchten attended focused on how small colleges fit into the consortia.

"We can't be the front runners, but we can do the little bits big labs don't care about, but which are important parts of the puzzle," she said. "That's how small schools and undergraduate researchers can be effective. It involves little things that are key components to finding out the answers."

Anne Kruchten, assistant professor of biology, completed her Ph.D. in biochemistry, molecular biology and biophysics. Her broad training is helpful at Linfield because she has experience in everything from very fine molecular biology all the way to intensive crystallography and biophysics.

On choosing a major

Anne Kruchten understands being uncertain about a major.

When she enrolled in Transylvania University, she was a premed major. Then she changed to biology and spent a week as a chemistry major, before giving up on the hard sciences. She was a psychology major for a semester, then a Spanish major before completing the circle and earning her bachelor's in biology.

When it came time to apply to graduate schools, she was looking for a mentor who would allow her to be independent. She chose the University of Minnesota, where her research focused on obesity and diabetes.

When she was investigating postdoctoral programs, she wanted to conduct cancer research and needed skills that she hadn't picked up in her graduate program. The Mayo Clinic offered the opportunity to work in an intensive cell biology and microscopy cancer lab – the best of both worlds.

"Minnesota is very much an academic institution, so you get to see the academic side of laboratory work," she said. "Mayo is extremely medical, very clinical and the lab space is more focused on clinical studies."

Looking for evidence

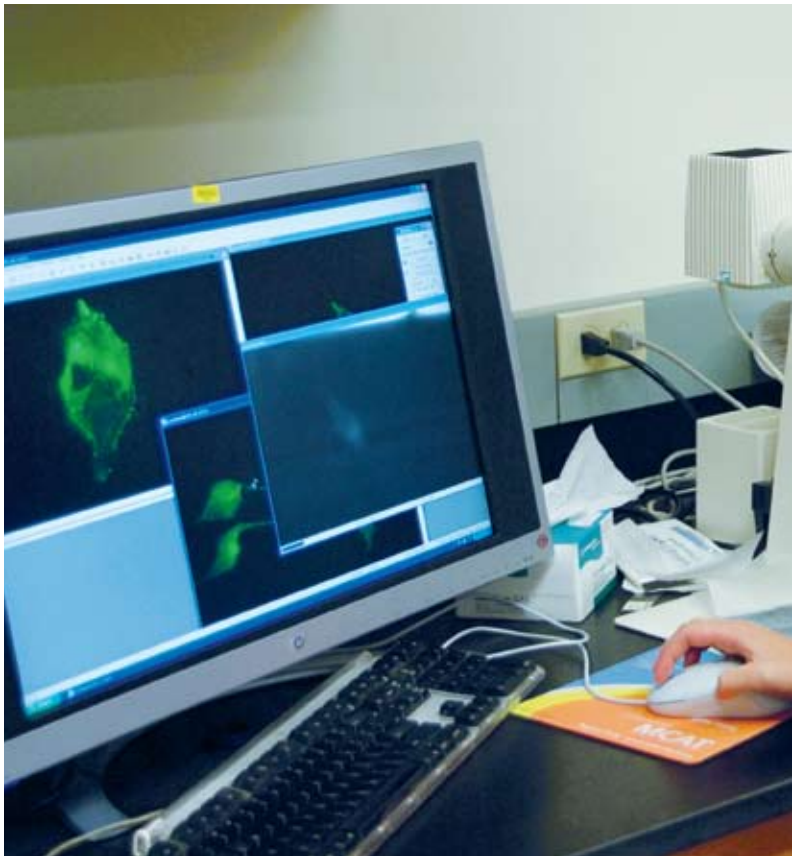
Sarah Click '11 hunches over a microscope with a built-in camera.

She inserts slides of cells and takes photos that magnify the cells 100 times. Click is trying to determine whether cells that are highly metastatic show an elevated concentration of cortactin. If it plays a role in helping malignant cells move, there should be high levels of the protein along the edges of cells.

Once she has the photos of the new cells, she shifts to the computer, pulls up the shots and begins isolating the cells that best illustrate her project. She spent hours in a biology lab, shooting hundreds of photos, then sharpening the images.

Click's research with Anne Kruchten will determine her future – either medical school or graduate school. She calls Kruchten patient and approachable.

"She took the time to make sure I understood all the science and the significance of what I was doing in the laboratory and answered my questions thoroughly," Click said. "It was a really positive learning experience and a way for me to work toward some of my career goals."



actin is involved in trafficking proteins in normal cells, making sure that cells get where they are supposed to be. Kruchten's hypothesis is that a modified form of cortactin is also involved in moving malignant cells to different parts of the body.

Kruchten made some progress during her research at the Mayo Clinic, showing that one pool of modified cortactin might push the cell forward, and a second, different pool helps to retract it, much as an inchworm moves forward – when the front moves ahead, the rear has to retract. Now her students are following up on that work.

In her second day in the lab last summer, Katherine Arns '11 made the unexpected discovery that she could isolate pools of cortactin using a simple separation method. She spent the summer working to make sense of this finding.

"It was very exciting, and it changed my entire summer project for the better," said Arns, who learned valuable laboratory techniques and became well versed in a protein she'd never heard of before.

Learning the structure of cortactin is essential in trying to understand how it might react. The structure of the protein cannot be photographed because, unlike some proteins which form a repeating pattern, cortactin doesn't form the same shape every time.

"If I could get a picture of the structure, it would help me understand what it will do," Kruchten said. "Without an understanding of the structure, it's harder to predict how it will function."

She and Brian Gilbert, associate professor of chemistry, are hoping to collaborate on a project that could help determine the structure of the protein.

"Ultimately, we don't want the cell to metastasize," Kruchten said. "If we can figure out the structure of cortactin, we might also figure out how to change that structure and prevent metastasis. That's the long-term goal."

Research complements teaching

As passionate as Kruchten is about her research, she's also a committed teacher. She brings research into all of her classes, whether it's an advanced biochemistry class with four students, or an introductory principles of biology class.

"I firmly believe that research should be part of teaching, I don't see them as separate entities," she said. "Biology is an experimental science, it's not just observation. And, I like explaining scientific things to people who don't do science."

Kruchten, who also hopes to someday be a science writer on the side, is a voracious reader, who is constantly reading articles and researching subjects on the Internet. She uses textbooks, but augments her classes with articles and projects to keep students engaged, involved and asking questions. In January, she's leading her first off-campus course, "Biogenesis in Italy and France: A Historical Perspective on Microbiology Discoveries."

Kruchten's brief window for focused research – 10 weeks in the summer – can be frustratingly short, but the fact that she and her students continue to make progress keeps her going.

"I don't think the students really believe when they first come in that they are going to do anything worthwhile," she said. "They might have grand ideas that they are going to cure cancer, but I don't think they understand they really can have a part in that."

Her students have consistently made headway, collected data and presented findings at national conferences each of the three years she's been at Linfield.

"When they make these presentations they have an opportunity to talk to post-doctoral researchers and graduate students and they have to defend what they did and explain why it contributes to the field," she added.

Combining teaching and research, mentoring students and keeping her work fun are all important.

"The nice thing about working with undergraduates is that they have a lot of enthusiasm," she said. "It can be monotonous working in the lab, but for students, finding their first data is very exciting."

The mystery that drives investigative research continues to intrigue her.

"You have to figure out how all these different pieces fit together," she said. "Because you are working in a test tube, you have to figure out what's real and what happened because you took the protein out of the cell. And the hardest part is 'does this really mean anything?' How do you actually relate this to what happens to someone who has cancer? Can it be related? That's the hard part." ■

– Mardi Mileham

Sarah Click '11 examines a batch of slides she photographed to determine whether high levels of the protein cortactin indicate that it plays a role in how cancer cells metastasize. Sometimes the results are almost artistic – the bright green cortactin is highlighted on the black background. One slide, with hundreds of cells sprinkled across it, suggests city lights seen from a plane at night.