Dream

Promises of the future
A farewell from Rick Borch

Director, Purdue Cancer Center

Ten years ago, with the encouragement of Dr. William Baird, I assumed the role as director of the Purdue Cancer Center. Dr. Baird served as director for 11 years and created a lasting impression on faculty, staff, and students — this, too, is the precedent I hope I set during my time as director.

Within my first year as director, the center secured significant support from the administration at Purdue and the Walther Cancer Institute. This has continued to help the center become a more prominent figure at the University and around the country. Since 1997, we have hired 42 new faculty members at the Purdue Cancer Center. These developments have enabled us to promote inter-programmatic collaborations on and off campus, to sponsor a partnership with the Indiana University Cancer Center to work on joint grants that have a high potential for clinical benefits, and to undergo our seventh competitive review by the National Cancer Institute. We are pleased that our standing has been renewed through 2008, and we have high expectations we will be renewed again next year.

As I step down, I am pleased with the accomplishments and successes that we have achieved together and am excited about the promise of the center’s future. It is with great pleasure that I welcome Prof. Timothy Ratliff as the new director of the Purdue Cancer Center. Tim joined us for several meetings and events even before his tenure began on July 1, 2007. Along with his duties as the PCC director, he also has an appointment as professor of comparative pathobiology in the School of Veterinary Medicine. He has studied at the University of Texas, Arlington; Texas A&M, Commerce; and the University of Arkansas. From 1997 to 2007, Prof. Ratliff was at the University of Iowa, most recently serving as the vice chair in the Department of Urology.

Timothy J. Ratliff, PhD
Richard F. Borch, MD, PhD
Director, 1998 – 2007

Statistics

Purdue Cancer Center Faculty by college*

<table>
<thead>
<tr>
<th>College</th>
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<td>College of Agriculture</td>
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*One professor is listed in two colleges.

Our faculty published 297 publications last year.
About the Purdue Cancer Center

When President Richard Nixon declared war on cancer in the early 1970s, he mobilized various entities of the U.S. government against the nation’s second largest killer. Hundreds of miles west of Washington, DC, researchers at Purdue University were dreaming BIG as well. In 1975, with the aid of a two-year planning grant from the National Cancer Institute (NCI), a University Cancer Research Committee was established and in December 1976, the Purdue Cancer Center was created as a separate administrative unit within the University.

In April 1978, the center was awarded its first NCI Cancer Center Support Grant, which has been renewed continuously ever since. The Center also received NCI construction grants and financial support from the University to establish the Hansen Life Sciences Research Building as the permanent home for the Purdue Cancer Center. Our efforts have been overseen by excellent leaders, Prof. D. James Morré; Prof. William Baird; Dr. Richard Borch; and newly appointed director, Prof. Timothy Ratliff, who began July 1, 2007.

Today, with expanded research staff, scientific partnerships, and sources of funding, the Purdue Cancer Center strides even more vigorously alongside our fellow researchers worldwide to eliminate the suffering and death due to cancer. By collaborating within and among disciplines, we are discovering new ways of making cancer more manageable.

On the development front

The finale to the $1.5 billion Campaign for Purdue was officially celebrated on June 30, but even prior to the start of 2007, the University had surpassed its monetary goal. The Purdue Cancer Center also exceeded our goal as well; funds totaling more than $5.3 million will help provide new opportunities for faculty and program support.

The center says farewell to Marilyn Hines

Unbeknownst to Marilyn Hines, assistant to the director, a special surprise ceremony was held on April 27 thanking Marilyn for her 21 years of dedication to the center. Andrea Gregory-Kreps was hired as operations manager for the Purdue Cancer Center beginning June 25th.

Marilyn has been the administrator for the Cancer Center’s National Institutes of Health (NIH) Core Grant, NIH Training Grant, the American Cancer Society Institutional Research Grant (ACS-IRG) and five internal grant programs. Her wealth of knowledge about the Center is unsurpassed – faculty, staff, and students relied on Marilyn as the chief communication guru and key-keeper for over 21 years. Marilyn’s last day was May 31, 2007. We wish Marilyn well as she takes time to enjoy retirement.
Oncological Sciences Center

When Discovery Park was formed to create an interdisciplinary hub for the study of complex societal issues, cancer research was a natural fit. Here, in the sunlight-filled buildings of glass and steel, researchers affiliated with the Oncological Sciences Center (OSC) can discuss issues ranging from cancer prevention to the delivery of cancer care in Indiana.

As the longest standing interdisciplinary system at Purdue, the PCC boasts an extensive track record of collaborative breakthroughs. The Oncological Sciences Center is the Discovery Park arm of the PCC and was created to explore cancer-related issues that are not directly funded by the National Cancer Institute grant that supports the PCC.

"The OSC is the mechanism to harness some of that untapped analytical potential," says Julie Nagel, managing director of the OSC. "We bring people together that have expertise outside the four focused scientific programs of the PCC."

One of those areas is cancer prevention, now an OSC flagship program that Prof. Dorothy Teegarden directs. "Nutrition, engineering, veterinary medicine, psychology, and other disciplines all across campus are looking at different problems — how to help people stop smoking, how to determine cancer when you only have a few malignant cells, and how to create devices that detect ovarian cancer with a single drop of blood," says Nagel.

Cancer care engineering is another initiative. Collaborating with oncologists at the Indiana University School of Medicine, Purdue researchers are studying colorectal cancer in Indiana. By examining blood samples of cancer patients and their healthy caregivers, the professors hope to define molecular signatures for the disease.

They’re also looking at the bigger picture — even if you know the role diet plays in the development of colorectal cancer, and the best protocols for treating different stages of the disease, how can you ensure adequate prevention and treatment programs in areas farthest away from large medical centers? "We are researching and documenting rural counties to see where we can make a real difference by dedicating resources," says Prof. Marietta Harrison, interim OSC director and associate PCC director.

By looking at these systemic issues, faculty are doing exactly what they hoped for when they created the OSC — spawning new partnerships, new discussions, and new perspectives for dealing with a complex social problem.

About our National Cancer Institute (NCI) Accreditation

The National Cancer Institute (NCI) is a component of the National Institutes of Health (NIH), one of eight agencies that comprise the Public Health Service in the Department of Health and Human Services. Established under the National Cancer Act of 1937, the NCI is the federal government’s principal agency for cancer research and training.

The National Cancer Act of 1971 created the National Cancer Program, broadening NCI’s scope and responsibilities. Today, the National Cancer Program conducts and supports research, training, health information dissemination, and other programs concerning the cause, diagnosis, prevention, and treatment of cancer, along with the continuing care of cancer survivors and their families.

Through a competitive federal grant program, the NCI recognizes only the best cancer institutes in the United States as official NCI cancer centers. Currently there are 63 NCI-designated cancer centers nationwide, including the Purdue Cancer Center. The PCC also has the added distinction of being one of only seven NCI-designated basic research cancer centers in the country. Since we were awarded our first competitive grant in 1978, we have received continuous support from the NCI.
For many years now, researchers have blamed the deadliest form of pancreatic cancer on the duct cells that transport digestive enzymes to our intestines. Last year, Prof. Stephen Konieczny put a big question mark on that assumption.

Studying pancreatic cancer in mice, the biological sciences professor and his team of researchers discovered that another main cell type — the acinar cell, which produces the enzymes that make digestion possible — is really the culprit in pancreatic ductal adenocarcinoma. Because more than 90% of pancreatic cancers are discovered in the late stages of the disease when medical intervention is largely ineffective, the findings could spell big changes down the road.

“Diagnosis is still going to be a huge problem for us to deal with, but we now know that we’ve been looking at the wrong cell type,” Konieczny says.

Konieczny is one of 24 professors comprising the Cell Growth and Differentiation signature area, which, among other endeavors, seeks to identify the earliest events in cancer. Now that he’s implicated the acinar cells in the initiation events of pancreatic cancer, Konieczny and his collaborators at Johns Hopkins University and the Cancer Research Institute in Cambridge, England are narrowing in on specific pancreatic cancer markers. “If we can identify cells that develop mutations at the earliest stages of cancer, we can design better tests to diagnose patients before the disease progresses, giving them a higher chance for a successful outcome,” he says.

Another researcher making headway with mouse models is Prof. Susan Mendrysa. Recruited to Purdue in 2005, Mendrysa has been testing the long-held belief that a protein found naturally in cells has the devastating effect of premature aging and death when it’s used as a tumor suppressor.

Last year, the veterinary medicine professor and her collaborators published the results of their research, which demonstrates that at least in mice, p53 suppresses tumors without leading to a significant decline in life expectancy. “This groundbreaking work has renewed interest in the p53 pathway as a target for anti-cancer therapeutics,” says Prof. Elizabeth Taparowsky, who leads the Cell Growth and Differentiation signature area.

Now, researchers are looking for ways to harness the agent’s power.
Drug Delivery and Molecular Sensing

The wars on cancer and terrorism are being fought on different fronts, but the very technology that could help protect our country from terrorism may also be a weapon against one of the nation’s deadliest natural killers. Last October, Purdue Cancer Center researchers unveiled a new portable mass spectrometry technique that rapidly detects compounds produced by cancer cells nearly invisible to the naked eye.

The technology, known as desorption electrospray ionization (DESI), was developed in the laboratory of Prof. Graham Cooks, Henry B. Hass Distinguished Professor of Analytical Chemistry. Using a machine roughly the size of a shoebox, researchers can distinguish between diseased and non-diseased regions of tissue samples.

While DESI initially was designed to detect explosives during security checks, the probe also holds enormous potential for cancer care. Currently, pathologists must prepare biopsies — and frequently with some ambiguity try to identify aberrant cells — to help surgeons determine how much tissue to remove.

“This changes the paradigm entirely, because the instrument is very small but precise,” says Prof. Don Bergstrom, Walther Professor of Medicinal Chemistry and head of the Purdue Cancer Center’s Drug Delivery and Molecular Sensing program. “In the future, you could just carry the machine around with you, lay the sample down, and read the result. That is an enormous shift in ability.”

Another impressive development in this signature area last year took place in the field of nanomedicine. Prof. Peixuan Guo, professor of molecular virology and biomedical engineering, re-engineered a nanomotor component of bacterial virus phi29 to facilitate drug and gene delivery into cells. An NIH-supported nanomedicine center has grown up around this technology to develop a new generation of nanomaterials for sensing and therapeutics.

Every person’s cancer is a unique combination of genetic variabilities, similar to the distinctive mix of numbers on a combination lock. “That’s the reason that so many drugs don’t work — because of the individual biochemistry of cancer,” says Bergstrom.

Tiny instruments that study individual cell markers, however, could lead to the development of highly specific drugs, which could be precisely compounded to unlock each person’s cancer. “That’s the pharmacy of the future,” Bergstrom says.
In the last few decades, fundamental and technical advances in chemistry, biochemistry, and structural and molecular biology have provided unprecedented opportunities to probe the molecular systems involved in cancer. By collaborating among and beyond these disciplines, researchers are now determining more targeted methods of diagnosing and treating tumors.

Take, for instance, the team of Prof. Cynthia Stauffacher, a structural biologist; Prof. Debbie Knapp, a veterinary oncologist; and Profs. Mark Hall and Andy Tao, both biochemists who specialize in mass spectrometry studies. These four researchers are applying their different backgrounds to an interdisciplinary examination of the role that the cell surface receptor EphA2 plays in tumors.

“This particular protein seems to be involved in regulating the metastatic nature of some epithelial tumors, such as the most frequent kind of breast cancer,” says Stauffacher, who leads the Chemical and Structural Biology program of the Purdue Cancer Center. The team is attempting to identify the EphA2 phosphorylation signature and associate it with the aggressiveness of the disease.

“Nowadays, the National Cancer Institute is promoting the discovery of better biomarkers for cancers that can be correlated to specific chemotherapeutic treatments. In other words, can you do a quick biomarker scan and know what will work?” Stauffacher explains.

Currently, when breast tumors are removed, pathologists will study the biopsies for estrogen or progesterone receptors; the presence or absence of these hormones will drive the patient’s care. Despite this logical protocol, some tumors don’t respond to their correlated treatment. “Those unresponsive tumors are our target,” Stauffacher says. “We want to see if we can correlate those particular tumors with new biomarkers. This will ultimately allow physicians to know which tumors will respond to a particular treatment and which tumors should be treated differently.”

These discoveries would not be possible without partnerships within and beyond the Chemical and Structural Biology program. In fact, Knapp, the Dolores L. McCall Professor of Veterinary Medicine, is not a member of this signature area. Instead, her home base at the Purdue Cancer Center is the Drug Design and Discovery program. By lending her clinical veterinary expertise to the problem of breast cancer, Knapp is helping to develop new molecular sensing tools and inhibitors for future use in humans based on her colleagues’ increased understanding of biological systems.
Drug Design and Discovery

Certain tumors develop when cells begin dividing uncontrollably, so oncologists must suppress their growth to halt the spread of cancer. While a few medications are already targeting these abnormal divisions, many more such compounds are on the horizon. Some of these are being developed at the Purdue Cancer Center, where researchers are targeting a group of proteins implicated in certain pancreatic, ovarian, colon, and lung cancers.

Prof. Richard Gibbs is focusing his drug-design efforts on Ras, a group of proteins that are ordinarily beneficial to us. Like a light switch that turns on and off, Ras signals the cells to divide and also controls their development. When Ras is damaged in cancer cells, however, the protein gets stuck in the “on” position, and the cells begin dividing without end.

Gibbs, a professor of medicinal chemistry and molecular pharmacology, is collaborating with Profs. Marietta Harrison and Christine Hrycyna to develop agents that could stop the Icmt, an enzyme that is needed for Ras activity. Gibbs creates the compounds, Hrycyna tests them against Icmt, and then Harrison studies them in cells to see if they’re working as planned.

“We expect that these compounds are cytostatic, meaning they block tumor growth, rather than cytotoxic, meaning they kill cancer cells,” Gibbs explains. While it’s too early to say, his discoveries eventually could lead to more drugs that keep cancer from returning, like Tamoxifen does with estrogen-positive breast cancer.

On another front, medical chemistry and molecular pharmacology scientist Prof. Mark Cushman has developed a class of potential cytotoxic compounds. In vitro tests have already proved promising, and now Cushman is working with biologists at the National Cancer Institute on human clinical trials.

Along with Gibbs’ work, Cushman’s research falls under the realm of the newly created Drug Design and Discovery signature area of the Purdue Cancer Center. Members of the group use a variety of chemical, biochemical, cellular, and animal approaches.

“The idea here is just as the name says,” explains Gibbs, who leads this area. “We wanted to bring together a group of people who are all working on either synthesizing new molecules with anticancer capability or testing existing molecules. Collaborating with members of other areas of the Cancer Center, such as Profs. Harrison and Hrycyna, helps us focus these efforts.”
Traditional cancer treatments have focused on therapies that attack cancer cells but cause collateral damage to innocent tissue. In a few years, that scenario could be a thing of the past. Major pharmaceutical companies are aiming to rapidly phase out these non-targeted therapies, and Prof. Philip Low is one of the researchers leading the way.

The Ralph C. Corley Distinguished Professor of Chemistry and founder and chief science officer of Endocyte Inc., Low is using folate acid as a Trojan horse to deliver anticancer drugs only to cancer cells.

Cancer cells have many receptors to capture folate, which helps them grow and divide. Normal cells, however, have few of these receptors. When folate acid is linked to an anticancer agent, the compound targets the cancer cells while leaving the healthy ones alone.

Right now, Low and his team are testing some of their compounds in clinical trials. “These processes usually take some time, but that may accelerate because we have a lot of the preclinical processes in place to move drugs into and through the clinic quickly,” he explains. Once the FDA has approved each compound, then Endocyte will either manufacture it or sell the patent to another drug manufacturer. Within the next few years, some of these drugs could be available for regular prescription use.

Pharmaceutical companies, of course, have their own in-house researchers, but they also rely on the pioneering work taking place at institutions like the Purdue Cancer Center. In fact, many of the larger manufacturers are focusing on creating new compounds that specifically target the unique properties of cancer cells. In contrast, low is developing ways to bind existing compounds with ligands like folate. Both methods hold great promise for a future of cancer care without collateral toxicity.

“Chemotherapy as it currently exists generally kills any rapidly dividing cell,” he says. That’s what leads to miserable side effects like hair loss and nausea, along with more devastating consequences like nerve damage and suppression of the immune system. “The new therapies that are being developed will hopefully just kill the cancer cells.”

Because chemotherapy kills healthy as well as cancerous cells, it creates short- and long-term side effects like hair loss and nerve damage. Philip Low hopes that within a few years, his more targeted cancer treatments will eliminate much of that collateral damage.
June 30, 2006 marked the end of the seven-year fundraising effort at Purdue by celebrating The Campaign for Purdue. Thanks to the generous donors to the Purdue Cancer Center we are able to maintain a leadership position in cancer research and create awareness about all that is happening at the Purdue Cancer Center. Thank you for all that you have done to help the Purdue Cancer Center lead these successful efforts!

Due to space restrictions, we are unable to list every gift to the center. Below are the donors who contributed gifts in excess of $100 for the 2006–2007 fiscal year.

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