Purdue University
Center for Cancer Research

Annual Report • 2008–09

Science for Life
The Purdue University Center for Cancer Research is making a difference for people in Indiana and around the world.

As you will read throughout our 2008–09 annual report, our scientists are making great strides in cancer research. As one of only seven basic science cancer centers designated by the National Cancer Institute (NCI), we are distinguished for our scientific excellence and diverse base of cancer research programs.

Because of our focus on science, we officially changed our name on July 1 to the Purdue University Center for Cancer Research. The name differentiates us from clinical cancer centers that treat patients. In fact, our research — often conducted in collaboration with NCI-sponsored clinical cancer centers — helps make it possible for clinicians to diagnose and treat cancer.

This past academic year, we submitted our renewal application to the National Cancer Institute. Every five years, we must complete a comprehensive process to justify our continued funding from the NCI. In late September, NCI officials performed a site visit as part of our evaluation. By mid-October, we should know the official outcome of this lengthy process.

NCI sponsorship not only provides national recognition that helps us attract some of the best and brightest minds in cancer research today, but also provides necessary funding for discovery of life-enhancing treatments. Contributions from individual donors make a difference as well; your support helps further our efforts toward earlier diagnosis, more effective treatments, and, ultimately, brighter futures for people diagnosed with cancer. Thank you for your continued support.

Timothy L. Ratliff, PhD
Robert Wallace Miller Director,
Purdue University Center for Cancer Research
The NCI currently has designated and funded 65 cancer centers. Only seven of those — including the Purdue University Center for Cancer Research — are basic cancer centers. We are honored not only to have this prestigious designation but also to have such dedicated and talented researchers, faculty, and staff members working here to help the center continually grow.

Over the past three decades, thanks to NCI and other funding, our researchers have made continuing advances in genetic engineering, computerized imaging, immunotherapy, chemotherapy, and much more. Their efforts have been led by four directors: Professor D. James Morré, who served as founding director until 1986; Professor William Baird, who served from 1986 to 1997; Dr. Richard Borch, who served from 1998 to 2006; and our current director, Professor Timothy Ratliff, who began in 2007.

Membership
Currently, the Purdue University Center for Cancer Research has members from 15 departments and 6 colleges and schools: agriculture; consumer and family sciences; engineering; pharmacy, nursing and health sciences; science; and veterinary medicine.

Grants
Key grants for the year include:
- **Purdue Cancer Center Challenge grant**, $30,000 (Professor Julia Kirshner)
- **Indiana Elks**, $110,000 (Professors Ourania Andrisani, Richard Borch, Scott Briggs, David Colby, Chang-Deng Hu, Deborah Knapp, and David Thompson)
- **Sagamore Lions Club**, $500 (Professor Carol Post)
For the fourth consecutive year, the Purdue University Center for Cancer Research saw an upswing in donations. During the 2008–09 academic year, donors contributed $1,080,876.74.

As contributions have increased, we have been able to expand our research efforts. This year, we created discovery groups for breast, pancreatic, and prostate cancers. These organ-specific cancer groups are similar to our signature areas because they unite researchers from various disciplines. But instead of focusing on specific stages within the research process to tackle a variety of different cancers, each discovery group will concentrate on a single diagnosis, promoting collaborations around the world to spark new discoveries, diagnostic methods, and treatments. To learn more, visit our Web site at www.cancerresearch.purdue.edu.

To see a complete list of donors, visit: www.cancerresearch.purdue.edu

Darrell B. Sims Cancer Research Fund

Carlyle and Louann Sims are proud Boilermakers, as was their son Darrell. Darrell lost his battle to cancer in 1994, and as a tribute to him, the Sims family has committed $25,000 to establish the Darrell B. Sims Cancer Research Fund. To make the most of their contributions, they also have created a matching challenge for our donors.

If others contribute $100,000 to the fund, the Sims family will match the donations, bringing the total to $200,000. The fund will support unrestricted cancer research, allowing CRC administrators to apply the money where it’s most needed. Read more at www.cancerresearch.purdue.edu/donate_gift.
The second annual Purdue Cancer Center Challenge took place on April 18, 2009, on Purdue University’s West Lafayette campus. The 5K walk/run began and ended at Ross-Ade Stadium.

Danny Hope, Purdue head football coach and this year’s challenge spokesperson, started the race with a boom. Purdue President France A. Córdova won first place in her age division, giving everyone a run for his or her money.

The challenge raised more than $50,000 for cancer research, a $20,000 increase from the inaugural event in 2008. There also was an upswing in sponsorship and participation, with a total of 1,300 runners and walkers. Participants were treated to a free breakfast of pancakes and sausage courtesy of Bison Financial.

Organizers honored four teams with the Cuonzo Martin Student Participation Award; the women’s volleyball team, women’s golf team, men’s tennis team, and men’s basketball team all boasted 100% participation. The Purdue dance team, which also achieved 100 percent participation, was the first recipient of the new Coach Danny Hope Community Award.

Beth Saiki-Olsen and Paulette Moody, who helped launch the 2008 event, served as co-chairs again. “We passionately believe that the answer to the cancer puzzle lies in basic research, and we wanted to find a way to support our Purdue researchers in their efforts to find a cure,” says Saiki-Olsen. Co-chair Moody says, “We know we are raising awareness and much needed funds to help fight this disease.”

Professor Julia Kirshner received the first Purdue Cancer Center Challenge Research Award. Kirshner, assistant professor of biological sciences, was selected by the center’s executive committee and Professor Timothy Ratliff, the Robert Wallace Miller Director of the center.

Kirshner plans to use her $30,000 award to build a biological model to test new drugs on cancer cells that are resistant to current therapies. “I would like to thank everyone whose generous donations made it possible for me to receive the challenge award,” Kirshner says. “I would also like to thank the Purdue University Center for Cancer Research for awarding me this money and for having faith in my research.”
“We know we are raising awareness and much needed funds to help fight this disease.”
When patients are infected with hepatitis B virus, an oncogene called pX induces liver cells to replicate; eventually, this replication can become uncontrollable, leading to liver cancer. Five years ago, Andrisani established that pX also can program those infected liver cells to stop replicating, essentially halting liver cancer in its tracks.

Initially, Andrisani worked with liver tissue samples that were only a single layer of cells thick. To understand the complex conditions under which the X gene affects liver cells, however, she is now working with live animals and three-dimensional models.

Last year, her team discovered that under certain conditions some cells infected with HBV can survive long-term and continue to grow. Once they have a better understanding of how and when this happens, they could develop anti-cancer agents that only affect the X protein; that could mean more effective chemotherapy with less collateral damage.

Another group of researchers — Professors Chang-Deng Hu, Wallace Morrison, and Tim Ratliff — also are using animal models to investigate cancer treatment. Specifically, they’re studying the recurrence of prostate cancer after radiotherapy using tumors implanted under the skin of laboratory mice. And Julia Kirshner is examining treatment of multiple myeloma using three-dimensional models; she hypothesizes that different cancers share common underlying characteristics, which could mean that one drug or group of drugs can be used to treat multiple malignancies.

Traditionally, researchers in the Cell Growth and Differentiation signature area have focused their efforts on understanding the biochemistry of cancer cells using simple model systems for their experiments. Now, they are moving toward more complex study methods to more closely replicate cancer in its natural settings.

“Some of these researchers have accomplished this by moving into animal models; other people are using three-dimensional culture systems,” says Professor Elizabeth Taparowsky, signature area head. “That has led to major advances in developing model systems in which we can examine the behavior of cancer cells in a physiologically relevant environment or examine the behavior of cancer cells as they progress from a less malignant to a more malignant state.”
Earlier this year, Professor Ji-Xin Cheng and his colleagues — Professors Ignacio Carmarilo, Philip Low, Kinam Park, Paul Robinson, David Thompson, and Alexander Wei — announced that excessive dietary fat in laboratory animals led to a 300% increase in metastasizing tumor cells.

The researchers implanted cancerous lung tumors under the skin of laboratory mice, half of whom were fed a high-fat diet. Then, using an imaging method called Coherent Anti-stokes Raman Scattering (CARS), they documented how the increase of fat caused cancer cells to undergo changes necessary for metastasis. Afterward, they counted cancer cells in the bloodstream of the mice using intravital flow cytometry, which employed a laser to visualize cancer cells through the skin and blood vessels.

Along with documenting the role of fat in metastasis, the research could lead to new techniques for diagnosing cancer and for determining whether it is metastasizing.

Other researchers in the Drug Delivery and Molecular Sensing signature area also are making strides in biomarker discovery, cancer imaging, and nanotechnology. Professor Dan Raftery is investigating diagnostic procedures with nuclear magnetic resonance spectroscopy; since certain cancers alter the pattern of metabolites in blood and urine, he hopes to discover molecular signatures for cancer.

Professors David Nolte and Fred Ranier have developed a biological CD, which contains specific antibodies that target proteins over-expressed in cancer; the light bounces off the surface of the CD, creating specialized patterns. They are partnering with Professor Tim Ratliff to test the CD on prostate cancer antigens.

And Professor Graham Cooks is collaborating with Dr. Deborah Knapp to test DESI, a miniature version of a mass spectrometer, on canine cancers.

“Cook’s technique is revolutionary; he’s taken equipment that used to weigh thousands of pounds and miniaturized it to 11 pounds so that a person can carry it around with a notebook computer and obtain a diagnosis within several minutes,” says Professor Don Bergstrom, head of the signature area. “This is one of the many collaborative efforts in our area that is moving toward a groundbreaking clinical application.”
Traditionally, when breast tumors are removed, pathologists will study biopsies for estrogen or progesterone receptors, and the presence or absence of these hormones will drive the patient’s care. But because the tumors don’t always respond to their correlated treatment, some Purdue researchers believe that there must be a more precise way of planning cancer care.

For the past several years, Dr. Deborah Knapp and Professors Mark Hall, Cynthia Stauffacher, and Andy Tao have been working toward that end, trying to correlate unresponsive tumors with new biomarkers.

Specifically, they’re examining the role that the cell surface receptor EphA2 plays in tumors. EphA2 appears to regulate some epithelial tumors such as breast cancer, determining whether the cancer will metastasize or not.

Using mass spectrometry, the team members are analyzing EphA2 in both benign and malignant cell lines in breast, prostate, and bladder cancer. They are complementing these studies with high resolution X-rays and crystallization research. Ultimately, they hope to establish new biomarkers that will help physicians better predict which tumors will respond to a particular treatment and which tumors should be treated differently.

In another study being conducted by the Chemical and Structural Biology program, Professors Richard Gibbs, Christine Hrycyna, and David Thompson are investigating a group of membrane proteins called Ras. Normally beneficial to us, Ras works like a light switch that turns on and off, signaling the cells to divide and affecting their development. When Ras is damaged in cancer cells, however, the protein gets stuck in the “on” position, causing the cells to divide uncontrollably.

The researchers believe that a particular enzyme needed for Ras activity, ICMT, could be targeted by new therapeutic agents in cancer treatment. Ultimately, their discoveries could lead to the development of more drugs that keep cancer from returning.

“This is an excellent example of how our program provides researchers with powerful molecular approaches for examining the molecular details of systems involved in human cancer,” says Stauffacher, who co-directs the Chemical and Structural Biology program with Thompson. “By investigating the underlying mechanisms involved in cancer, identifying unique biological targets for cancer chemotherapy, and developing potential chemical approaches to cancer treatments, we are laying the foundation for better outcomes in the future.”
**Medicinal Chemistry**

Camptothecin is a chemotherapy drug often used as a measure of last resort. But it is unstable, doesn’t always reach the targeted cancer cells, and can cause serious side effects. Now, a synthetic compound created by Professor Mark Cushman may provide a more viable option in the future.

Topoisomerase I is a key enzyme for cancer cell growth, which is blocked by camptothecin and related anti-cancer drugs. Since discovering a new chemical compound that blocks the same enzyme Cushman has collaborated with the National Cancer Institute (NCI) to develop better versions of his compound. In particular, they have used X-ray crystallography to produce three-dimensional images of different variations of the compound together with Topoisomerase I.

After growing the crystals in the laboratory, the researchers bombarded them with X-rays, producing a two-dimensional pattern that was then converted to a three-dimensional model. Using these models along with computer-aided design, they have synthesized several compounds that show promising anti-cancer activity. If clinical trials bear out, the compounds may one day be used to combat difficult-to-treat solid tumors, such as ovarian and lung cancers.

Professor Philip Low has worked together with Professor Carol Post of the Chemical and Structural Biology signature area to design a DUPA-radiolabel conjugate, which targets a protein on the surface of prostate cancer cells.

Along with Professor Tim Ratliff (Cell Growth and Differentiation signature area), Low has used the conjugate to visualize prostate cancer cells on whole-body scans of experimental animals. They will soon collaborate on clinical trials with the Indiana University Melvin and Bren Simon Cancer Center.

Team studies between Purdue scientists, NCI internal researchers, and clinicians at other NCI-sponsored centers like the IU Simon Cancer Center represent a new wave of collaborations in the Medicinal Chemistry program.

“An overriding interest in cancer drug discovery techniques unifies all of us, which will promote interdisciplinary interactions vital to cancer discoveries in the future,” says Professor Richard Gibbs, signature area head.
Research Highlight

ABC transporter proteins are fundamental to our understanding and treatment of cancer, since they pump out toxic molecules and also allow nutrients into the cell. A promising young Purdue researcher has dedicated the early years of her career to examining the protein with the hopes of designing new, more effective chemotherapy agents.

Two years ago, Professor Jue Chen, a Purdue biological sciences researcher and a Howard Hughes Medical Institute investigator, announced that she and fellow cancer researcher Professor Amy Davidson had obtained an image of an ABC transporter protein at a midpoint in the transport of molecules through a cellular membrane.

One of the largest protein groups, ABC proteins serve many important biological purposes. One such purpose is providing a gateway for the protective membrane surrounding a cell. The gates close to prevent cell contents from escaping and toxins from entering. But in order to promote healthy cell life, the gates also open, allowing nutrients to enter and waste to be released.

Suppose that the cell is actually cancerous, however. If the gate does not allow anti-tumor drugs inside or forces them out before they have a chance to work, the chemotherapy will not be effective. By understanding each step of this process, researchers could design more effective treatments for certain kinds of cancer in which ABC proteins are overabundant.

That’s where Chen’s research comes into play. A structural biologist and an expert in X-ray crystallography, Chen likes to visualize the molecular-level details of cells. In her 2007 study with Davidson, she crystallized ABC proteins from an E. coli bacterium and fired X-rays at them, building three-dimensional computer models that showed the microscopic architecture of the proteins. That allowed them to capture an image of the ABC transporter protein as its gates opened, moving material through the cellular membrane.

Now that Chen has visualized how the gate opens to allow material to exit, she wants to see how the material is delivered into the cell. “By understanding the mechanisms of this entire process, I’m hoping to help us understand the reason we have drug resistance,” Chen says. “Hopefully, that knowledge will help people design new chemotherapy drugs that will work on ABC transporters.”
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Cell Growth and Differentiation
Program Leader: Elizabeth Taparowsky
Program Co-Leader: David Riese

Chemical and Structural Biology
Program Leader: Cynthia Stauffacher
Program Co-Leader: David Thompson

Drug Delivery and Molecular Sensing
Program Leader: Donald Bergstrom
Program Co-Leader: Alex Wei

Medicinal Chemistry
Program Leader: Richard Gibbs
Program Co-Leader: Debbie Knapp

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We can have the best minds, the best equipment and the best intentions in the world, but without funding, none of those matter. It is only through generous donations from individuals and organizations that we are able to continue our mission.

Thank you to the 4,957 donors who gave to the Purdue University Center for Cancer Research during the 2008–09 academic year. To see a complete list of contributors, visit www.cancerresearch.purdue.edu.

If you’d like to discuss supporting a research fund, or a personal cancer research goal, please contact our development office:

Tim Bobillo, Director of Development  
(765) 496-6374, bobillo@purdue.edu

Beth Steurer, Director of Donor Relations  
(765) 494-1109, steurered@purdue.edu

Or mail your contribution to:  
Hansen Life Sciences Research Building, Room 141  
201 S. University Street  
West Lafayette, Indiana 47907-2064
Purdue University Center for Cancer Research
Hansen Life Sciences Research Building
Purdue University
201 S. University Street
West Lafayette, IN 47907-2064
Phone: (765) 494-9129
Fax: (765) 494-9193
E-mail: pccinfo@purdue.edu
www.cancerresearch.purdue.edu

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