Purdue Cancer Center Annual Report | 2005-06

Dream

Stretching the Boundaries of Science and Imagination
As I reflect on this past year at the accomplishments that the Purdue Cancer Center has achieved, I am excited and energized for what 2006 is bringing our way. Soon we will be celebrating our 28th year as a National Cancer Institute (NCI)-designated cancer center.

In the past two years, the Purdue Cancer Center has added a staggering 15 new faculty members. They include Kinam Park, James Fleet, Kavita Shah, Sergey Savinov, Mark Hall, Jian Jian Li, Ji-Xin Cheng, Rashid Bashir, James Leary, Amy Davidson, Andy Tao, Claudio Aguilar, Arun Ghosh, Susan Mendrysa, and Tony Hazbun. Our new members bring expertise in a wide range of scientific interests, which include discovering new drug delivery systems for anti-cancer drugs, learning about dietary mechanisms for treatment and prevention of cancer, and engaging in anti-tumor therapeutic interventions.

Our faculty and administration continue their dedication to achieving our ultimate goal – finding a cure for cancer. We have made great breakthroughs this past year by emphasizing interdisciplinary research with our biologists, chemists, engineers, and veterinarians. Our partnerships with various academic departments on campus and our joint ventures with those outside the University continue to be a driving force in the fight against cancer. Purdue has also announced a new center in Discovery Park – the Oncological Sciences Center. This center’s initial focus is on applying portions of Purdue’s internationally recognized strengths in engineering to the prevention, treatment, and early detection of cancer.

I continue looking forward to the years to come, and there is little doubt that we will provide major advances in the successful diagnosis and treatment of cancer. The Purdue Cancer Center is proud to be a major part of the national cancer research effort, and we remain committed to the goal of rendering cancer a manageable and eventually curable disease.

Richard F. Borch
Director, Purdue Cancer Center
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“Universities are only able to make progress in research efforts thanks to partnerships that fund our efforts,” remarked President Jischke. “Purdue is very proud to be stepping up its cancer research at a time when the National Cancer Institute is recommitting our nation to fight against this disease.”

The Indiana Elks have been contributing to Purdue’s Cancer Center for several decades and have now passed the $2.7 million mark. The Indiana Elks ongoing support has raised more than $2.7 million for the Purdue Cancer Center.

Betty Lowe has given over $100,000 to establish the James R. Lowe Lung Cancer Research Fund in memory of her husband, who died of cancer in 2003. The first fund at the Purdue Cancer Center for a specific type of cancer, it has supported so far the development of a new line of lung cancer cells that will be used to conduct drug research.

Retired faculty member James E. “Jim” Robbers and his wife Diann are providing faculty research opportunities through a donation of $1.4 million in cash and deferred gifts. Their generosity also resulted in a $20,000 biennial grant award program — the “Jim and Diane Robbers Cancer Research Grant for New Investigators.”

Jim Robbers retired from the Department of Medicinal Chemistry and Molecular Pharmacology in 1997. “We wished to repay the University community with the same sort of opportunity that was extended to me at the outset of my career,” he said.

Dr. Charles Jordan has donated $250,000 in memory of his late wife, Joyce Fox Jordan, who died in 1993 from cancer. And in memory of Eva Bergstrom, the center has also received an anonymous $250,000 donation to support an endowed postdoctoral position in cancer research.

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Experimental Therapeutics & Diagnostics

Cancer treatment has traditionally been the domain of massive machinery. Now, nanotechnology – tiny machines unleashed inside human cells – holds great potential for diagnosing and treating tumors.

Last year, Purdue Cancer Center researchers Alexander Wei, Ji-Xin Cheng, and Philip Low unveiled their steps toward developing a medical imaging technique that can see individual cells. Gold nanorods, 200 times smaller than a red blood cell and detectable with a laser, are injected into the bloodstream, illuminating blood vessels and underlying tissues. Showing up at 60 times brighter than conventional fluorescent dyes, these nanorods could eliminate the obstacles associated with viewing tissue through light.

They likely could be used for therapeutic purposes as well. “Gold nanorods can be selectively heated in the area around a tumor; they can absorb energy and amplify it, so you wouldn’t be heating the surrounding tissue as much. The potential is to get high specificity for that area,” says Prof. Donald Bergstrom, leader of the Purdue Cancer Center’s Experimental Therapeutics and Diagnostics program.

The National Cancer Institute is aggressively supporting the development of nanotechnology in hopes of changing the very nature of cancer diagnosis and treatment. “For many years, researchers have been developing drugs that are very specific to cancer, but their progress has been incremental,” Bergstrom says. “All of these drugs work exceedingly well, but they also affect healthy cells.”

Nanoparticles, however, could unleash these same aggressive, toxic drugs – or new and better ones – with little damage beyond the tumors. “That would make a world of difference in cancer and chemotherapy,” he says.

Already, in fact, Purdue Cancer Center scientists have used nanoparticles constructed from three pieces of ribonucleic acid to halt the growth of cancer. The team, led by Prof. Peixuan Guo, has tested the nanoparticles in mice and lab-grown human cells.

Researchers have long known the therapeutic value of RNA, but until now, haven’t had a viable method for delivering several different forms simultaneously to specific cells. The team’s triangular-shaped devices are not only able to recognize the cancer cells and enter them, but also destroy them and mark their paths for later tracking. Once they ensure that the tiny RNA particles won’t damage healthy cells, the researchers plan to test the method in a clinical setting.
Bob Geahlen and Carol Post, professors of medical chemistry and molecular pharmacology, have teamed up to understand the structure and function of Syk in normal and cancerous cells. Their findings could potentially help researchers more clearly understand the molecular structures needed for the development of drugs to fight cancer.

“Our targets are molecules found inside cells that drive normal cells to become cancerous ones. Looking at those targets atom by atom adds a tremendous understanding for how those target molecules function to regulate cell growth,” says Prof. Cynthia Stauffacher, leader of the Purdue Cancer Center’s Structural Biology program.

For example, last year Drs. Carol Post and Bob Geahlen – both professors in the Department of Medicinal Chemistry and Molecular Pharmacology – teamed up to visualize the interaction of the molecular target Syk with its binding partner. While Syk is found in both normal and cancerous breast cells, as the cancer cells metastasize and become more aggressive, Syk disappears. “Seeing what Syk looks like helps to reveal the secrets of how it functions to prevent breast cells from metastasizing,” Stauffacher says.

The Structural Biology program consists of closely interrelated research groups that investigate the underlying molecular mechanisms for cancer treatment and prevention. The power to look at biological molecules and drugs atom by atom has greatly advanced investigators’ abilities to design new anti-cancer drugs. By visualizing how an anti-cancer drug grabs its target, researchers can design drugs that won’t let go.

The National Cancer Institute is particularly interested in this area because of the promise it holds for more selective treatment. In the past, scientists identified cancer based on the shape or size of a cell. Now, investigators are beginning to understand why cells are cancerous and how their inner workings differ from healthy cells.

To that end, researchers in Structural Biology are also investigating:

• the structures of cytoplasmic enzymes, which are potential targets for anti-cancer chemotherapy because of their importance in cell transformation;
• enzymatic bioremediation – how enzymes can negate the effects of aromatic carcinogens in the environment;
• multi-drug resistance and how cancer cells pump out drugs, reducing the effectiveness of chemotherapy; and
• membrane-coupled events associated with cancer, such as phosphotyrosine-linked transmembrane signaling.

All of these efforts will help researchers elucidate how inhibitors of molecular targets could work at a structural level to destroy cancer cells. “Those findings will provide the chemical framework for the design of potential new inhibitors,” Stauffacher says. Ultimately, the discoveries may lead to the development of clinically potent drugs.
Nearly 30 years ago, when J. Michael Bishop and Harold Varmus discovered that a normal gene could be mutated to cause cancer, their findings led to the groundbreaking idea that tumors are caused not by viruses, but by genetic alterations in normal cellular genes. Today, using many of the technologies developed for the Human Genome Project, researchers like Prof. Kavita Shah are pinpointing those mutations on a molecular level.

Shah, who was recruited through theWalther Cancer Institute as part of its commitment to advance basic research at the Purdue Cancer Center, has created a chemical-genetic approach for identifying how and when certain molecules act upon the gene c-Src. She reported her findings last year in the peer-reviewed journal *Molecular Biology of the Cell*. Along with explaining the biochemical processes of tumor development, such discoveries should assist applied researchers in developing new ways to diagnose cancer at an early stage and treat it more precisely.

“People want to design drugs to cancer targets, and most of these targets are going to be proteins that are misexpressed or misregulated in cancer cells,” says Prof. Elizabeth Taporowsky, leader of the Purdue Cancer Center’s Cell Growth and Differentiation program. “If you can identify these proteins and understand how their altered function impacts other processes in cells, new molecular targets for cancer drug design will be identified.”

The National Cancer Institute is supporting molecular research as part of its ambitious plan to systematically map genetic changes that occur in all kinds of cancer. “This approach toward cancer gene discovery cannot predict what will be found,” Taporowsky says. “However, this unpredictability is part of the excitement of basic cancer research, and the payoff will be the identification of novel ways in which we will be able to treat cancer in the future.”

The Sidney Kimmel Foundation also is aggressively supporting basic research in the fight against cancer. Since 2003, three members of the Purdue Cancer Center’s Cell Growth and Differentiation program have been awarded prestigious grants: Prof. Scott Briggs, who is studying the gene MMSET involved in multiple myeloma; Prof. Chang Kim, who is researching how cancer cells interact with immune-regulating T cells; and Prof. Ann Kirchmaier, who is investigating the Epstein-Barr virus, which causes infectious mononucleosis and is causally associated with such cancers as Burkitt’s Lymphoma and Hodgkin’s disease.
Over the last eight years, the institute has stimulated the recruitment of seven cancer-focused scientists to the Purdue Cancer Center. All told, its investment in Purdue totals more than $5 million.

“The strength of basic science programs that integrate chemical design and synthesis, protein structural analysis, and molecular mechanisms of cell growth lie at the heart of the Walther Cancer Institute’s support of the Purdue Cancer Center,” says Walther CEO Fred Haslam.

“We believe our investment in intellectual capital and the interdisciplinary approach Purdue takes to cancer research resonates well with a prime institute objective of fostering collaborative research within and among Indiana institutions. Purdue is a key partner in our quest to eliminate cancer as a cause of suffering and death, a partner that embraces the institute’s belief that collaboration can expedite discovery and the application of discoveries to benefit people.”

Since the late 1980s, the Purdue Cancer Center has partnered with the Walther Cancer Institute to enhance cancer research in Indiana. Located in Indianapolis, Indiana, the Walther Institute was established by Dr. Joseph Walther as a nonprofit research institute dedicated to benefiting people with cancer through basic research.

Last year, the Purdue Cancer Center and the Walther Cancer Institute said farewell to Joseph Walther. He passed away on December 10, 2005 at the age of 93. We also said goodbye to two other loyal and respected cancer supporters, Joseph S. and Ann Dawson, who staunchly supported the Walther Cancer Institute’s innovative research. The Dawsons established cancer research fellowships in the laboratories of Profs. Jack Dixon and Donald Bergstrom at the Purdue Cancer Center. Dixon is now at the University of California at San Diego. We will miss Dr. Walther and Mr. and Mrs. Dawson. The Purdue Cancer Center family extends its thoughts and prayers to both families.
In March 2004, the PCC and IUCC awarded three pilot projects aimed at furthering translational cancer research and collaboration among investigators. Dr. Rick Borch, Prof. Mark Kelley, and Prof. Millie Georgiadis are working on a project involving the design and synthesis of novel drugs that inhibit APE1, an enzyme crucial to the repair of DNA damage (and hence survival) in cancer cells. APE1 also regulates many important processes required for tumor growth. A selective inhibitor of this enzyme would have great potential as a novel kind of cancer drug. In August 2005, the PCC hosted a medical symposium, “Progress and Problems in Cancer Detection and Treatment,” in which clinical oncologists from the IUCC described the treatment problems they encounter in the clinic.

The two cancer centers are now undertaking a joint venture with Purdue engineers in Discovery Park to apply engineering principles to the cancer problem. Researchers are engaged in joint projects in cancer nanotechnology (see pages 14-15), and are also developing devices (“smart cameras”) to see very small numbers of cancer cells as they circulate in the blood from outside the body. The development of computer analyses will allow clinicians in the future to predict which patients will respond best to which drug, improving cancer care.
In 2002, scientists at Purdue University created the first protein “biochips,” mating silicon computer chips with biological proteins. Chips containing thousands of proteins could be organized into a device about the size of a handheld computer that could quickly diagnose cancer, test the efficacy of chemotherapy, and identify harmful or therapeutic chemicals.

Initial projects for the Oncological Sciences Center include:

Cancer Biomarkers: Diagnosing cancer before symptoms appear can dramatically improve long-term recovery and survival rates. But using molecular-level biomarkers within a clinical setting requires sophisticated tools and collaboration between materials scientists, engineers, chemists, biologists, and informatics scientists. A multidisciplinary team aims to develop new high-throughput technologies and devices that can rapidly analyze miniscule amounts of biofluids for early detection, risk prediction, and treatment.

Cancer Nanotechnology: Tiny machines could be the future of cancer diagnosis and treatment. Oncological Sciences Center researchers are using both bottom-up and top-down approaches to develop structures that can see tumors, detect biomarkers, and destroy malignant tissue.

Novel Engineered Diagnostic and Therapeutic Devices: Creating faster and more accurate devices for diagnosing and treating cancer requires the proficiency of both scientists and engineers. Interdisciplinary teams are using advanced engineering techniques to develop new optical detection methods, imaging systems, and biosprobes.
We sincerely thank all of the donors to the Purdue Cancer Center. Your gifts help us achieve our goals and make the dreams of so many become realities. Due to space restrictions, we are unable to list every gift to the center. Below are the donors who contributed in excess of $100 for the 2005 fiscal year.

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