Our Mission

Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, and Penn State Children’s Hospital are committed to enhancing the quality of life through improved health, the professional preparation of those who will serve the health needs of others, and the discovery of knowledge that will benefit all.

Education
We are committed to the education of medical and nursing students, basic science graduate students, medical residents and fellows, other students in health care related professions, and practicing health professionals. We seek to enroll students of exceptional quality, and their education will be based on the present and future health needs of the Commonwealth of Pennsylvania and the nation. Special recognition is given to the education of primary care providers.

Patient Care
Our objective is to provide a range of fully integrated patient care services for the people of central Pennsylvania and beyond. These services will extend from prevention of illness and maintenance of health through primary medical care to the highly sophisticated patient care expected at the nation’s premier academic medical centers.

Research
We strive to be a national leader in pursuing scientific investigation and developing programs to advance medical and scientific knowledge, which will ultimately contribute to the health of the public, the practice of medicine, and the education of health professionals.

Service
We will provide services to the public through health education, patient care, community activities, and applications of research.
The Research Annual Report for Penn State College of Medicine, Penn State Milton S. Hershey Medical Center is produced through the office of Strategic Services. It is intended to be an overview of the research accomplishments during Fiscal Year 2005, which ran from July 1, 2004 to June 30, 2005. The report captures the highlights of an expansive research enterprise and is not meant to be inclusive of all departments and specialty areas. Questions or comments may be directed to Megan Walde Manlove, Specialist for Science and Research Communications, using the contact information on the resources pages.

The Pennsylvania State University is committed to the policy that all persons shall have equal access to programs, facilities, admissions, and employment without regard to personal characteristics not related to ability, performance, or qualifications as determined by University policy or by state or federal authorities. It is the policy of the University to maintain an academic and work environment free of discrimination, including harassment. The Pennsylvania State University prohibits discrimination and harassment against any person because of age, ancestry, color, disability or handicap, national origin, race, religious creed, sex, sexual orientation, or veteran status. Discrimination or harassment against faculty, staff, or students will not be tolerated at The Pennsylvania State University. Direct all inquiries regarding the nondiscrimination policy to the Affirmative Action Director, The Pennsylvania State University, 328 Boucke Building, University Park, PA 16802-5901; Tel (814) 865-4700 / (814) 863-1160/TTY.
A greeting from the Vice Dean for Research

Research makes us better. As scientists, research lets us answer questions, confirm connections, and discover promising avenues for the development of new technology and treatments. As a medical institution, research means we can provide our patients the latest treatment options, improving health in some cases and increasing the quality of life in others.

As a community, research is a catalyst for economic growth, drawing interest from established companies and birthing new businesses. That growth translates to more funding potential for cutting edge research, development of innovative products and services, and the creation of the kind of high-caliber jobs that encourage our brightest young minds to stay in Pennsylvania.

That’s why research is a core focus of the Medical Center and the College of Medicine. That’s also why we continue to recruit clinicians and faculty who are among the best in their fields.

Grants awarded to our scientists this year topped a record $100 million—nearly double the total from just five years ago.

Those dollars make possible advanced biomedical research that leads to groundbreaking findings, such as the study by Craig Meyers, Ph.D., that showed a virus harmless to healthy cells can kill some cancer cells in just six days. In another promising study, Kyle Krady, Ph.D., found a common antibiotic used to treat acne may also slow or prevent diabetic retinopathy, which causes blindness in people with diabetes.

This spring, we were among a handful of institutions to participate in a national clinical trial of a blood substitute called PolyHeme®. We outfitted our ambulances and medical helicopters with the substance, which already has helped sustain the lives of the most critically ill patients while enroute to hospital emergency rooms.

Our General Clinical Research Center earned an $18.7 million program renewal through the National Institutes of Health. One of seventy-eight NIH-sponsored centers at institutions across the country, the center allows researchers to stretch precious dollars by sharing resources, such as lab space and support staff. The center also gives us a central location for physicians to meet with patients participating in the clinical trials that are critical to making new treatments available for widespread patient use.

No matter how top-notch our people and our facilities are, we can’t fulfill the promise of biomedical research alone. That’s why we helped organize the second Innoventure research and technology expo. Innoventure2005 brought together 600 representatives from universities, our academic center, healthcare institutions, and businesses. This biennial event inspires learning, collaboration, and investment, with its ultimate goal to help position central Pennsylvania as a region of enterprise and a community of scholarship.

While the research process is often an arduous and complicated one, it is the vehicle to our ultimate destination of excellence—in scholarship, in patient care, and in economic sustainability.

As scientists and students, as doctors, nurses and technicians, and as residents and employees of this community, we strive each day to show why research makes us better.

Jay Moskowitz, Ph.D.
Associate Vice President for Health Sciences Research, Penn State University
Vice Dean for Research and Graduate Studies, Penn State College of Medicine
Chief Scientific Officer, Penn State Milton S. Hershey Medical Center
In 2005, outside sources awarded researchers at Penn State Milton S. Hershey Medical Center and Penn State College of Medicine a record $100.8 million in grants. It is but one measure of how we are doing, yet a promising measure at that. More dollars mean one researcher can expand a study of a promising new use for a drug, while another can build on the findings of a colleague to develop a therapy that promotes greater patient healing.

"The joy of discovery is certainly the liveliest that the mind of man can ever feel."

Claude Bernard (1813-78)
French physiologist
Virus kills cancer, but leaves healthy cells alone

Six days is all it takes for a common, non-disease-causing virus to kill cervical, breast, prostate, and squamous cell cancer cells in laboratory cultures, according to recent research by Craig Meyers, Ph.D., professor of microbiology and immunology at Penn State College of Medicine.

“Our results suggest that adenovirus type 2 (AAV2), which infects the majority of the population with no known ill effects, kills multiple types of cancer cells, yet has no effect on healthy cells,” Meyers said. “We believe that AAV2 recognizes that the cancer cells are abnormal and destroys them. This suggests that AAV2 has great potential to be developed as an anti-cancer agent.”

Meyers’ study was presented at the 24th annual meeting of the American Society for Virology at the Penn State University Park campus. Though similar in design and effectiveness to some gene therapies, cancer cell treatment using AAV2 would not be classified as a gene therapy because Meyers’ team left AAV2 in its natural form rather than modifying it.

In general, AAV2 requires association with a helper virus to replicate. When it finds a helper virus, such as human papillomavirus (HPV-1), AAV2 disrupts the life cycle of the host and induces cell death. Building on its previous research on the ability of AAV2 to suppress cancer, Meyers’ team treated four types of epithelial cell cancers with AAV2. Epithelial cells are those that cover or line all internal and external parts of the body.

All cancer cells treated with the AAV2 were dead within six days. “So many cancer therapies are as poisonous to healthy cells as they are to cancer cells,” Meyers said. “A therapy that is able to distinguish between the two could be less difficult to endure for those with cancer.”

Future studies will investigate the precise mechanisms through which AAV2 causes cancer cell death and how the virus might be enhanced to more aggressively target and kill cancers.

Study team members included: Samina Alam, Ph.D., research associate, and Ellora Sen, Ph.D., Department of Microbiology and Immunology, Penn State College of Medicine.

Protein may be signal for ovarian cancer detection, treatment

More than 16,000 women die of ovarian cancer each year. It is one of the most difficult forms of cancer to diagnose, because symptoms often do not appear until the disease has progressed so far that treatment can do little to slow or halt it.

A team of Penn State scientists recently made a discovery that holds promise as a potential diagnostic tool, and possibly as a target for treating ovarian cancer.

The team, led by Kathleen Mulder, Ph.D., professor of pharmacology, and another investigator at the National Cancer Institute in Bethesda, Maryland, found a mutated form of a protein called “km23” that is present in the tumor tissue of at least 42 percent of ovarian cancer patients. Because the altered protein form is not present in healthy human tissue, the protein could be the linchpin to earlier detection and better survival rates for women diagnosed with the disease.

The findings were published in the journal, Cancer Research.

The possibility of her research leading to better therapies for cancer patients keeps Mulder—a certified private pilot who also occasionally breeds and raises black labrador puppies—motivated about the km23 project.

Her mother died of cancer last year, but Mulder says she was convinced of her role as a cancer researcher long before that.

“I decided that cancer was important to study since it affected so many people and was not near to being completely eradicated,” she said.

Mulder has been researching a cell growth factor called TGF-beta in relation to cancer since 1988. Her team’s latest study builds on a previous one that identified TGF-beta as the initiator of the process that signals km23 to attach a certain protein “cargo” to a “motor.”

In the cell, km23 acts sort of like a traffic cop for proteins as they move along highways called “microtubules.”

Imagine the proteins are the cargo, which must be moved to a specific cellular destination by a motor. The km23 protein, then, matches motors with cargo based on signals they give off. When km23 is mutated, however, it does not correctly identify those signals.

The “cargo” is not delivered to the right place at the right time. A cellular “traffic jam” occurs, causing chaos in the cell, or cancer.

When cells with the mutated km23 protein were placed in mice, the mice developed tumors. But when cells with healthy km23 were reintroduced, the tumors shrank and in some cases, disappeared.

There are still many unanswered questions about km23 and how it might lead to a screening test or treatments for ovarian cancer. But Mulder’s results are promising.

Now, studies can be done to see whether km23 alterations are also present in other forms of solid tumors, such as breast and colon cancer. If so, a screening test targeting the km23 protein will be an even more important tool to physicians and cancer patients.

“I decided that cancer was important to study since it affected so many people and was not near to being completely eradicated.”

Kathleen Mulder, Ph.D., look at the structure of their protein, km23, which may some day provide doctors with a screening for, or earlier treatment of, ovarian cancer.
Facility in State College.

of the Penn State Nanofabrication

Medical Center and College of

Tiny bundles seek and destroy breast
cancer cells

Although we’ve shown

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B

y developing improved methods of drug delivery that decrease negative
impacts on patients, Penn State researchers move medicine toward better
treatment of disease.

Penn State College of Medicine researcher Mark Kester, Ph.D., Distinguished
Professor of Pharmacology, has proven that ceramide, a naturally occurring
substance that prevents the growth of cells, can be administered through the
bloodstream to target and kill cancer cells. In his study, recently published in the
journal *Clinical Cancer Research*, Kester used mice as an animal model and an
interdisciplinary knowledge of nanotechnology to delivery ceramide directly to
tumor tissue.

Nanotechnology is a field of science that uses individual atoms and molecules to
create devices and materials thousands of times smaller than other technologies.
Nanoparticles as small as 1/1000th the size of a human hair change their characteris-
tics and offer scientists new functional possibilities.

Kester collaborated with James Adair, Ph.D., professor of mechanical engineering
at University Park, to adapt nanoparticle technology to his research.

Ceramide is the substance that accumulates in cancer tissue and helps to kill
cancer cells when patients undergo chemotherapy and radiation. But ceramide is
toxic if injected directly into the bloodstream. Kester bypassed this problem by
encapsulating the ceramide in tiny nanoparticle bundles called “liposomes.”
Ceramide is inherently attracted to tumor cells, though it is unknown why.
Liposomes are too small to be detected by the body’s defenses, so the liposome-
encased ceramide travels through the bloodstream to the tumor, where it dis-
rupts the mitochondria, or the energy producer of the cell.

This causes cell death. In the mice studied, ceramide bundles targeted and
destroyed only breast cancer cells, sparing the surrounding healthy tissue.

“Although we’ve shown that ceramide has an effect on breast tumor cells in mice,
breast cancer cells in humans may eventually resist the treatment, suggesting that
ceramide should be used in combination with more traditional cancer treatments as
a booster,” Kester said. “Our next step is to explore how additional chemotherapeutic
agents could be incorporated into the liposomes for a more lasting effect.”

Other study team members were: Thomas C. Stover, Ph.D., and Arati Sharma,
Ph.D., Department of Pharmacology, and Gavin P. Robertson, Ph.D., Departments
of Pharmacology, Pathology, and Dermatology.

An old drug shows a new trick

Research is not always about discovering a new substance or technique.
Sometimes, promising treatments come from a unique application of an
already successful therapy.

Such is the case with a study led by Kyle Krady, Ph.D., assistant professor of neural
and behavioral sciences.

Krady’s team found that minocycline, a common antibiotic often used to treat
acne, also may slow or prevent diabetic retinopathy, which is the leading cause of
blindness in people ages 20 to 74.

The team found that minocycline limits, by about 50 percent, the retinal damage
caused by microglia, cells that act as the “clean-up crew” for the central nervous
system. These microglia cells destroy damaged cells by releasing toxins, then
engulfing them, much like a Pac-Man™. Should the microglia become activated
and release their toxins in the retina, however, the toxins will kill healthy neurons
critical for normal vision.

The study was published in *Diabetes*, a journal of the American Diabetes Association.
Previous studies have shown that the changes in the body caused by diabetes lead
to increased production of cytokines, proteins that cause inflammation of the
nerves. This study goes a step further to show that in early diabetes, elevated lev-
el of cytokines activate microglia, which produce neurotoxins and kill nerve
cells. The neuron death causes the progressive vision loss characteristic of dia-
abetic retinopathy and results in 12,000 to 24,000 new cases of blindness each year
in the U.S.

“This study has shed more light on the processes that lead to vision loss in those
with diabetes,” said Steve Levison, Ph.D., professor of neural and behavioral sciences
at the College of Medicine. “We hope that these discoveries will lead to new treat-
ments for diabetic retinopathy, which remains a leading cause of blindness.”

In addition to Krady and Levison, the study team included: Anirban Basu, Ph.D.,
and Colleen M. Allen, Ph.D., Department of Neural and Behavioral Sciences; Yaping
Xu, M.D., M.S., Kathryn LaNoue, Ph.D., and Thomas W. Gardner, M.D., Department of
Cellular and Molecular Physiology.

“This study has shed more light on the processes that lead to vision loss in those
with diabetes. We hope that these discoveries will lead to new treatments for
diabetic retinopathy, which remains a leading cause of blindness.”
Melanoma is the most aggressive and deadly of skin cancers, and it is the seventh most common cancer in the United States, with nearly 60,000 cases diagnosed each year. That number increases by about 4 percent yearly. There are no successful treatments for advanced-stage melanoma, so research designed to understand the disease’s mechanisms and to identify possible therapeutic targets is crucial to improving health and quality of life for cancer patients.

College of Medicine researcher Gavin P. Robertson, Ph.D., assistant professor of pharmacology, pathology, and dermatology, studies melanoma cells and their operation. In 2005, he reported two promising findings in the journal Cancer Research.

In one study, Robertson identified the way v599EB-Raf, the most mutated gene in melanoma, aids tumor development. His work highlights the gene’s importance as a therapeutic target.

“Studies like this one could lead to the development of more effective long-term treatment options for melanoma patients,” Robertson said. “Studies that identify how inhibiting important melanoma-regulating proteins reduce melanoma growth will lead to a better understanding of the disease, and thus, better ways for treating it.”

The job of normal B-Raf is to relay signals from the cell membrane to the nucleus, which contains genetic material and controls many of the cell’s activities. B-Raf is one member of the chain that relays signals in cells. The protein is usually active only when needed to relay signals.

In contrast, mutant B-Raf is active all the time, which disrupts the chain’s normal function. Previous studies have shown B-Raf is present in about 60 percent of human melanomas. The role mutant B-Raf plays in causing melanoma tumors remained unknown.

Robertson used human melanoma cells—applying small interfering ribonucleic acids, or a general Raf inhibitor—to show that lowering mutant B-Raf protein reduced melanoma growth.

The study team also included Arati Sharma, Ph.D., Nishit R. Trivedi, M.S., Melissa Tran, B.A., and Charles D. Smith, Ph.D., Department of Pharmacology; and David A. Tuveson, University of Pennsylvania.

In a second study, Robertson found that wiping out a protein in skin cancer cells could significantly stall melanoma tumor development and increase the sensitivity of the cells to chemotherapy.

The protein, Akt3, appears to be responsible for promoting tumor cell survival and development in 43 to 60 percent of non-inherited melanomas.

Robertson used human melanoma cells—applying a general Akt inhibitor—to show that lowering Akt3 protein reduced melanoma growth.

Researchers used melanoma cells together with tumors taken directly from melanoma patients to show that as melanoma cells become more aggressive and begin spreading from the original site, the amount of active Akt3 protein in the cells increases. Akt3 is one of three Akt proteins, all of which have been implicated in various cancers.

For example, Akt2 activity has been found in cancers of the ovary, pancreas, stomach, and breast. Although all three forms of Akt are present in melanoma cells, this study found that in melanoma, Akt1 and Akt2 remain inactive and, therefore, have little if any role in melanoma development.

Ultimately, therapies targeted against Akt3 could be used with traditional chemotherapy to give those with melanoma more effective therapeutic options to fight the disease,” Robertson said.

In addition to Robertson, the study team included: Jill M. Stahl, M.S., Arati Sharma, Ph.D., Mitchell Cheung, Ph.D., Melissa Tran, B.A., Mark Kester, Ph.D., and Lakshman Sandirasegaran, Ph.D., Penn State College of Medicine; Jin Q. Cheng, Ph.D., University of South Florida College of Medicine; and Marcus W. Bosenberg, M.D., The University of Vermont.

The research was supported by the American Cancer Society and The Foreman Foundation for Melanoma Research.
Grant gives some researchers permanent space, study support

Researhers need not only monetary support to do their best work, but the space and time to apply newfound knowledge to patient care. The College of Medicine and Medical Center created the General Clinical Research Center (GCRC) in 1995 to fill this need. In 2005, the College of Medicine received an $18.7 million grant from the National Center for Research Resources, National Institutes of Health to help support research at the GCRC.

One of seventy-eight such NIH-sponsored research centers in the country, the GCRC provides physicians and researchers a centralized place to meet with patients who take part in clinical investigations. Researchers share staffing and specially equipped space, and they have access to facilities for sample and data processing. GCRC staff members help investigators with recruitment and provide other support for clinical studies.

“No NIH grant covers all research costs, and GCRCs allow groups at institutions to share core laboratory space, staffing, and other research needs to stretch those dollars farther than they might otherwise go,” said Lawrence Sinoway, M.D., GCRC program director, and professor of medicine at the College of Medicine. “Stretching those research dollars means that with every grant, we can get even closer to learning how the body works, how diseases change the body, and how to fight those diseases.”

In its evaluation of the Penn State GCRC, a visiting NIH review team noted program strong points, including: the well-organized minority recruitment program; outstanding physical facilities; outstanding program directorship; administrative and financial management; strong institutional support; and positive responses to previous critiques.

While the next funding renewal is five years off, Sinoway and his staff continue reaching up to the next level of excellence. They plan to add more junior investigators, increase use of GCRC core facilities, and bolster participation in the NIH-sponsored K23 program, which trains physicians in clinical research methods.

Among the College’s faculty who use the facilities and services of the GCRC are Edward Bixler, Ph.D., who studies patients with sleep disorders; Richard Legro, M.D., whose work focuses on women with polycystic ovary syndrome and the disease’s link to insulin resistance; Urs Leuenberger, M.D., who studies blood flow and hypoxia, a lower than normal blood oxygen level; Chester Ray, Ph.D., whose research includes the impact of aging, exercise, and simulated microgravity on nerve activity; and Diane Thiboutot, M.D., a recognized worldwide expert in sebaceous gland cell biology who studies acne.
Nursing research contributes to mission of improving health through innovation

Does a spoon full of sugar really make the medicine go down? A Medical Center nursing researcher recently accepted a grant to find an answer to this sweet question. Linda Hatfield, Ph.D., C.R.N.P., at Penn State, won a grant from the Children’s Miracle Network to study the effects of oral sucrose as treatment for pain during procedures in infants aged two to four months. Her work is one example of the contribution to research, and ultimately to improved patient care, that is made by nurses, who provide direct and in-depth care to hospital patients every day.

Many researchers have studied how oral sucrose, otherwise known as table sugar, affects pain during post-delivery procedures of pre-term infants. Hatfield’s is only the fifth study to look at the effects in older babies returning for vaccinations and other routine procedures. Her goal is to see whether there is a difference in the effectiveness of sugar as an analgesic depending upon the baby’s age.

“There’s an expanding body of evidence to show that a baby’s experience of pain early in life affects the way he responds to pain later in life,” Hatfield said. “Their nervous systems are still developing, and in response to the distress, they develop new pathways that are not normal.”

Studies of children and teens with disorders like attention deficit hyperactivity disorder (ADHD), anxiety disorders, depression, and others, show a history of pain and distress early in life. Many times, the distress came from routine vaccinations; children today receive more than twenty shots in the first two years of life, compared to five or six a generation ago.

Hatfield was an Aventis Pasteur/American Nurses Foundation scholar in 2003.

Other nursing research awards in 2004-2005

Lorri Phipps, R.N., M.S.N., C.P.N.P., of the Pediatric Critical Care Unit, for her study called “The Evaluation of Parental Presence During Bedside Medical Rounds in a Pediatric Intensive Care Unit,” which is funded by a Penn State University Families and Youth Consortium grant.

Susan E. Rzucidlo, R.N., M.S.N., of the Shock Trauma Center, for her study called “Early Traumatic Stress Symptoms and Their Effect in Psychosocial Impairment in Children After a Trauma,” which is funded by the Penn State University Families and Youth Consortium.
Generating a buzz about technology and medical research

Research in the life sciences can make us better as patients and a community only when investigators find a way to translate a discovery to everyday use. Often, that requires working across disciplines or navigating the unfamiliar territory of the business world.

But in the busy and competitive research environment today, it is not always easy to find opportunities for collaboration or to take a discovery to the next step—commercialization.

The biennial Innoventure technology exposition was created with these needs in mind.

Innoventure2005™ was the region’s second expo designed to showcase the role of regional partnerships in building the future of Central Pennsylvania.

By bringing innovators in research, education, and health care together with business leaders, the economic development community, and governmental representatives—more than 600—the expo facilitates a critical conversation about our region’s role in the technology-based economy, particularly in the life sciences and healthcare. Penn State Hershey Medical Center and Penn State College of Medicine played a key role in organizing the event.

For investigators performing translational or applied research, Innoventure is a chance to share their work and meet potential investors or licensees. Other researchers use the event as an opportunity to explain their work to a broad audience and explore collaboration.

Non-participating attendees get a glimpse of what’s next for central Pennsylvania.

“If the region has always been known for its strength in agriculture and manufacturing, but this is a chance to showcase the resources we can leverage to become a research development powerhouse as well,” said Jay Moskowitz, Ph.D., chair, Innoventure2005 and vice dean for research and graduate studies at the College of Medicine.

This year, more than 150 scientific and commercial exhibitors displayed their cutting-edge technologies in disciplines such as medicine, biotechnology, diagnostics and therapeutics, delivery of care, and education.

One of the region’s obstacles to sustaining a vibrant economy is the “brain drain” effect of recent college graduates leaving the state for other markets. Innoventure2005 included a specially designed program to enable high school students to explore the possibility of careers in research or entrepreneurship right here in central Pennsylvania.

“I appreciated the privilege of realizing that our discovery had become a benefit to mankind, not only through its great scientific importance, but also by its power of efficient action against human suffering and terrible disease. This was indeed a splendid reward for our years of hard toil.”

Marie Curie (1867-1934)
French chemist and pioneer in the early field of radiology
Part of the mission of the Medical Center and the College of Medicine is the education and improved health of our community. Some medically underserved populations need focused research and implementation efforts to achieve those goals.

In 2005, the National Cancer Institute awarded Penn State University a five-year, $1.3 million grant to continue its efforts to reduce cancer-related health disparities among residents of the rural communities of Pennsylvania and southern New York. The efforts are organized through the Northern Appalachian Cancer Network (NACN), a partnership of Penn State faculty, Penn State Cancer Institute, and community members. The network is designed to improve cancer outcomes for underserved residents through the development and testing of community interventions and the collection of data about their effectiveness. The grant will be used to continue the network’s efforts to bring medical education and programs to rural areas where cancer screenings are often unavailable, people are less likely to regularly visit physicians, and cancer mortality rates are higher.

“These efforts save lives, and we are grateful that we’ll be able to continue to help people who otherwise may not have access to medical care,” said Gene Lengerich, V.M.D., director of community outreach and education, Penn State Cancer Institute, and associate professor of health evaluation sciences.

Residents of Appalachia suffer from excess cancer occurrence, especially from cancer of the lung, colon, rectum, and cervix. They are also more likely to die from these diseases.

Tailoring this knowledge to the interests and resources of their local areas, community coalitions and partners of NACN’s parent organization, The Appalachian Community Cancer Network, have addressed a wide range of issues with grassroots efforts. The NACN also recently completed a community-based pilot study with the coalitions. The study found cancer education materials were more likely to be distributed in counties with cancer coalitions than in counties that were approached by staff of Penn State alone.

The study successfully demonstrated the effectiveness of community-academic partnerships in cancer prevention and control and highlights the strength of academic medical institutions like the Medical Center in serving their communities.

A key to that strength is collaboration with other top research institutions. The Medical Center and College of Medicine play a large role in several national studies aimed at understanding the nature of and finding therapies for specific diseases.

A College of Medicine team won a five-year grant renewal to continue as an anchor in one such study looking at childhood asthma.

In 1999, the National Heart, Lung, and Blood Institute created a federally sponsored clinical research program to study childhood asthma. The Childhood Asthma Research and Education (CARE) Network is comprised of five academic clinical centers, plus Penn State Hershey Medical Center, which serves as the CARE Network Data Coordinating Center. The CARE Network is funded through May 2009, and the Data Coordinating Center receives approximately $1.6 million a year for its activities in this project.

Asthma is a chronic disease that appears to be increasing among children in developed countries. It is estimated that between 6 and 10 percent of the children in the U.S. have some form of asthma. Pharmaceutical companies that develop and manufacture asthma medications do not regularly test them in children and do not attempt to determine optimal dose levels, the effectiveness and safety of combinations of therapies, and whether certain medications can prevent the onset of asthma in very young children.

The CARE Network conducts multiple clinical trials to investigate these various issues.

“Participating in the CARE Network project is one way Medical Center researchers can help improve the quality of life not only of children here, but of children nationwide who suffer from asthma,” said Vernon M. Chinchilli, Ph.D, chair, Department of Health Evaluation Sciences and project principal investigator.

The Medical Center’s role generally is to optimize the trials for accuracy, collect and analyze the data, conduct training, maintain the CARE Network computer network and Web site, and implement a quality assurance plan.

Other key College of Medicine personnel on the project include Susan Boehmer, M.A.; Loretta Doty, M.S.W.; Gavin R. Graff, M.D.; Wenlei Liu, Ph.D.; David T. Mauger, Ph.D.; Ian M. Paul, M.D.; and Brenda R. Phillips, M.S.
A favorite food back on the menu for some diabetics, thanks to Penn State researcher

It used to be pizza was off the menu for many people with diabetes. Its doughy, carbohydrate-dense crust and high fat content wreaks havoc in people with the disease. Now, a Penn State Diabetes Center study suggests a slow and steady insulin-dosing pattern may best combat the glucose-raising effects of that common favorite food.

Keeping glucose levels from jumping too high or dipping too low may help reduce the risk of cardiovascular disease, which has been connected to erratic glucose levels in those with diabetes.

“Our study shows that after a high carbohydrate, high fat meal like the pizza used in this study, spacing out insulin given by an insulin pump in two doses, one of which is over an eight-hour period, may keep glucose levels in a more favorable range than a single dose of insulin or a double dose taken over a shorter period,” said Robert Gabbay, M.D., Ph.D., associate professor of medicine, and co-director, Penn State Diabetes Center.

The study was initiated thanks to Susan M. Jones, M.S., C.R.N.P., C.D.E., a nurse practitioner, and Jill L. Quarry, M.S., R.D., L.D.N., C.D.E, a dietician, both of whom noted problems with their diabetes patients.

“We noticed that it was very difficult for those with diabetes who were using insulin pumps to maintain good glucose values when they ate pizza,” Jones said. “Because pizza is a favorite food for so many people and good quality of life is eating what you want every now and again, we suggested a study to see how best to help those with diabetes enjoy this common favorite food while maintaining good glucose levels.”

Volunteers were selected from the patient population at the Medical Center and were outfitted with a new glucose monitoring system that averages blood glucose levels every five minutes. For three days, volunteers ate an evening meal of plain cheese pizza with water. Each day, insulin was dosed differently and glucose levels monitored before and after eating.

The study was the first to look at the optimal timing of the dual-wave administration of insulin. Gabbay cautions that this method of insulin delivery may not be applicable to all high carbohydrate, high fat foods.

Future studies will investigate whether the method works with foods of other compositions.

In addition to Gabbay, Jones, and Quarry, the study team included Molly Caldwell-McMillan, M.D., Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, and David T. Mauger, Ph.D., Department of Health Evaluation Sciences. The study was funded in part by Medtronic Minimed, Northridge, California.

Latest therapies and technology offer hope for better outcomes

Another distinct advantage of academic medical institutions like Penn State Hershey Medical Center is that patients receive cutting-edge care. Not only are new technologies and promising therapies designed here, but our patients have the chance to participate in national studies of drugs and devices that have life-saving potential.

For example, the Medical Center was one of twenty-nine sites involved in a national clinical trial of the CorCap™ Cardiac Support Device, a proprietary mesh wrap that is implanted around the heart to relieve stress caused by an unhealthy increase in heart size.

The American Heart Association said the trial showed the CorCap device reversed heart failure progression and improved patients’ quality of life.

The Medical Center’s study team included John Boehner, M.D., cardiologist, and Walter E. Pae, Jr., M.D., cardiothoracic surgeon, Penn State Heart & Vascular Institute.

In March, the Medical Center’s Institutional Review Board approved the center’s participation in a national study of PolyHeme™, a universally compatible blood substitute, for the treatment of critically injured and bleeding patients.

The Medical Center is one of a few Level I trauma centers in the United States chosen to participate in the study.

Treatment begins before arrival at the hospital, either at the scene of injury or in the emergency treatment vehicle, and continues during a twelve-hour post-injury period in the hospital. Because blood is not carried in ambulances or helicopters, the use of PolyHeme in these settings could address an unmet medical need for an oxygen-carrying solution where blood in not available. Patients who have lost blood receive either PolyHeme or the current standard of treatment, saline solution.

Saline solution does not help supply the body with oxygen, buy PolyHeme can carry oxygen. The study will compare the survival rate of patients receiving PolyHeme to that of patients who receive the saline solution instead.

For information on Penn State clinical trials, visit: www.pennstateclinicaltrials.com.

The CorCap device is a mesh sleeve designed to fit around and support an enlarged heart.
One of the greatest achievements of an academic medical institution and of a medical researcher’s career is to see a lab discovery move toward widespread use by patients. In 2005, INNOVIVE Pharmaceuticals, Inc., a biopharmaceutical company headquartered in Manhattan, licensed worldwide use rights of opioid growth factor (OGF) for oncology.

OGF is a naturally occurring molecule found in the human body that has been shown to significantly reduce the growth of pancreatic cancer cells. The potential for OGF as an anti-cancer compound was discovered by Ian S. Zagon, Ph.D., Distinguished Professor of Neural and Behavioral Sciences at Penn State College of Medicine.

INNOVIVE is developing OGF under the name INNO-105.

OGF inhibits cell growth and division by interacting with OGFr, a receptor found on the nuclear membrane of a wide range of cells and tissues, including several types of malignant cells. OGFr has been found on pancreatic adenocarcinoma, head and neck squamous cell carcinoma, colon cancer, renal cell carcinoma, and neuroblastoma, among others.

After Zagon and his team found that mice given OGF with chemotherapy were healthier and survived longer than mice given chemotherapy alone, Penn State Professor of Medicine Jill Smith, M.D., did a small phase I clinical study in pancreatic cancer.

“Zagon and his team’s innovative work in the lab, followed by Smith’s shepherding of the work into the clinic and Innove’s efforts to expand clinical use, is a great example of how basic research can be translated to important new therapies,” said Alan Snyder, Ph.D., associate dean for technology development, College of Medicine.

INNOVIVE initiated a phase I trial of its own this year to confirm OGF’s maximum tolerated doses and its anti-tumor activity in pancreatic cancer. Smith is working on a separate phase II trial.
Michael Katzman, M.D., associate professor of medicine and microbiology and immunology, received a $120,000 grant from The W.W. Smith Charitable Trust to study how retroviruses like HIV, the virus that causes AIDS, infect cells. The one-year grant is titled "The Nuclease Activities of Retroviral Integrase." Katzman will focus on understanding the structure and function of an enzyme called integrase, which is responsible for incorporating the genetic information of a retrovirus into the DNA of an infected cell. The action of this enzyme makes retroviral infections permanent. In the case of the retrovirus HIV, the action of this enzyme leads to the development of AIDS and some cancers.

Thomas W. Uhde, M.D., chair, Department of Psychiatry, was appointed director of the Penn State Hershey Neuroscience Research Institute. The mission of the institute is to promote and support interdepartmental and translational brain research, as well as to direct pre-doctoral education and graduate neuroscience doctoral and fellowship training. Uhde earned his medical degree from the University of Louisville, then completed his psychiatry residency training at Yale University. He was the senior level scientist at the National Institute of Mental Health from 1981 to 1993, earning tenure there and serving as founding chief of the section on anxiety and mood disorders, Biological Psychology Branch. Uhde has published more than 300 scientific papers. His primary areas of research include fear, arousal and anxiety mechanisms in humans and animals. His published papers are widely cited, and he is recognized as a world leader in the treatment of anxiety disorders. He serves as editor-in-chief of the scientific journal, Depression and Anxiety.

Robert A. Gabbay, M.D., Ph.D., associate professor of medicine, was named the first recipient of the Laurence M. Demers Career Development Professorship in Medicine and Pathology. The endowed professorship provides $25,000 per year for three years to support Gabbay’s research on improving diabetes care in both inpatient and outpatient settings. Gabbay investigates ways to bridge the gap between clinical findings and implementation of those findings in the primary care setting, where most diabetic patients get their care.

In the award letter, Demers, a Distinguished Professor of Pathology and Medicine at the College of Medicine, said he hopes the award and its seed money will inspire Gabbay to continue his work and find innovative ways to approach diabetes care.
A fundamental awareness of the principles and practices of research is essential to the education of the next generation of outstanding scientists, even those who plan to focus primarily on the practice of medicine. That is why the College of Medicine’s M.D. curriculum includes the Medical Student Research Program (MSR).

Through this program, medical students have the opportunity to choose a research area of interest, design a study plan, and collaborate with veteran faculty and physicians. Students gain an understanding of the research process, limitations and variability of data, and application of research to clinical practice. The MSR program gives the Penn State medical student a distinct edge when applying for residency and other post graduate programs.

Each spring, the College of Medicine highlights some of the outstanding research of its medical students with the Medical Student Research Symposium. Here are a few of the studies presented in 2005:

• “Effects of Total Sleep Deprivation and Daytime Napping on Daytime Sleepiness, Performance, and Sleep-related Hormones in Men and Women”
  Student: Michael Prematta
  Sponsor: Alexandros Vgontzas, M.D., College of Medicine

• “Predictors of Opioid Variability in Postoperative Patients”
  Student: Carmella Shemansik
  Sponsor: Rosemary Polomano, Ph.D., R.N., University of Pennsylvania

• “Impact of an Animated Interactive Cranial Nerve Tutorial on Medical Student Learning in Human Gross Anatomy”
  Student: Amy Bridgeman
  Sponsor: Loren Evey, Ph.D., College of Medicine

• “Cardiac Health Status of New York Police Officers Following September 11, 2001”
  Student: Curtis Coley
  Sponsor: Rebecca Bascom, M.D., M.P.H., College of Medicine

• “Effect of Dextromethorphan, Diphenhydramine, and Placebo on Nocturnal Cough and Sleep Quality for Coughing Children and Their Parents”
  Student: Katharine Yoder
  Sponsor: Ian Paul, M.D., College of Medicine

Vernon M. Chinchilli, Ph.D., Distinguished Professor of Health Evaluation Sciences, was named chair of the Department of Health Evaluation Sciences (HES). Chinchilli has been a professor in HES for more than thirteen years and served as vice chair of the department from 1997 to 2002.

As interim chair, he helped grow the department’s new Health Services Research Group, which focuses on health economics and outcomes-based research.

Chinchilli led the effort to establish a Bioinformatics Consulting Center in collaboration with Penn State University Park, which opened in 2003. The cross-campus center, initiated under a grant from the Tobacco Settlement Funds, is a resource for researchers who use gene chips and other bioinformatics tools in their investigations.

The center provides expertise in study design, management, and analysis to ensure information that will generate valid conclusions.

He has published more than 140 articles on biostatistical and biomedical research and was appointed a Fellow of the American Statistical Association in 1997 for his contributions.

Judith S. Bond, Ph.D., chair of the Department of Biochemistry and Molecular Biology, is finishing her second and final year as president of the American Society for Biochemistry and Molecular Biology. Bond presides over the national organization during its 100th anniversary year. She had a hand in organizing the celebratory events and venues, which include the annual symposia. The event’s program includes ten Nobel Laureates, who will talk to aspiring scientists and students of the nation’s biochemistry and molecular biology programs.

The organization’s 12,000 members are dedicated to promoting understanding of the molecular nature of life processes. Bond says it is an honor to have served.

“In the 100 years of the organization, there have been twelve Nobel Laureates who have served as president, so I was very honored to be chosen,” she said.
Penn State medical and graduate students present their research at conferences and seminars across the country and around the world. The opportunity to share work with colleagues outside of the College of Medicine and to publish their work in recognized industry journals is essential to prepare clinicians and researchers for the requirements and challenges of the fields they are about to enter.

In 2005, students participated in conferences in Seattle, St. Louis, Denver, Washington, D.C., and many other cities.

- MD/PhD students Shane Quitier and Brian Blasiolo attended the 19th Annual National MD/PhD Student Conference in Keystone, Colo., where they presented posters of their work. Blasiolo’s work, entitled, “Knockdown of the Otopetin 1 Gene Results in Otolith Agensis and Ectopic Mineralization in the Developing Zebrafish Inner Ear,” was also accepted for publication in the journal Developmental Biology.

- Graduate student Ato Wright participated in the Fortieth Annual Student National Medical Association Conference in St. Louis. Wright is an active member and former officer of the student organization.

- Graduate student Christina Ryan attended the American Association of Immunologists annual conference in San Diego. She presented data from her own research in tumor immunology.

- Graduate student Subarna Hamid presented her work at the American Association of Cancer Research meeting in Anaheim. Her poster presentation was titled “Chemotherapeutic Nucleoside Analogues and DNA Polymerase Beta.”

Students published their work in a variety of journals, including:


- American Journal of the Physiological Cell, “MAP kinase and Calcium Signaling Mediate Fluid Flow-induced Human Mesenchymal Stem Cell Proliferation,” Ryan Riddle, a graduate student in cell and molecular biology.

Medical and graduate students in the College of Medicine are recognized nationally for their research, not only during presentations at national conferences, but also when it comes to awards and honors.

For example, physiology graduate students Brian J. Krawiec and Damian Dyckman represented the excellence of the College of Medicine by earning awards for their promise.

Krawiec won the Mead Johnson Award for Outstanding Research, given by the Endocrinology & Metabolism Section of the American Physiology Society at Experimental Biology 2005. Dyckman won the Environmental and Exercise Physiology Section Gravitational Physiology Predoctoral Award at the American Physiology Society.

A Note from Dr. Kirch

As I prepare to leave my position as leader of the Penn State Hershey campus, it is with great pride and admiration that I reflect upon the achievements of our scientists, medical students, and graduate students, not only in the last year, but during my entire time at Penn State.

Work in our laboratories and clinics has produced innovative discoveries with the potential for application across academic disciplines and clinical specialties.

We have merged clinical programs and research interest areas—both on our campus and with our affiliates and partners at University Park and other campuses—to encourage creative collaboration among physicians and scientists in complementary fields. These partnerships have led to growth in important areas such as nanotechnology and bioengineering.

Our physicians have earned top honors in national rankings several years running. Our researchers continue to publish and receive recognition for their work in the most well respected scientific journals and at international conferences. Our medical and graduate students accept positions at the finest hospitals and in competitive post-doctoral programs, ready to make their contributions to the next generation of medical advances.

We continue to attract the best men and women in their fields of study and practice.

Of course, there are still challenges ahead. In 2006, medical researchers will feel the effects of the first cut in National Institutes of Health funding in twenty years. Competition for other grant sources will grow ever stiffer, and researchers will have to reach out to other sources to help fund their studies.

A majority of the population feels that academic medical institutions like Penn State Hershey Medical Center are better than other community hospitals because they do research and train medical professionals. Yet many of those same people do not want to participate in clinical trials or be seen by a student or resident in training supported by a physician. If we are to succeed in our mission, we must bridge this gap. We must increase community awareness of our studies and trials and communicate the connection between medical research and quality of care. We must do our best to spread the message that the end goal of research is improved patient care through more prepared medical professionals and more promising treatments and therapies.

In short, better research means better health and a better quality of life for the community.

I feel fortunate to have spent the last six years among such caring and devoted professionals who do their best each day to demonstrate that philosophy. I have no doubt the years to come hold even greater promise for the College of Medicine and Medical Center community.

With best regards,

Darrell G. Kirch, M.D.
Senior Vice President for Health Affairs and
Dean of the College of Medicine, Penn State University
Chief Executive Officer, Penn State Milton S. Hershey Medical Center
“Research is to see what everybody else has seen, and to think what nobody else has thought.”

Albert Szent-Györgi (1893-1986)
U. S. biochemist