TO THAT END, the materials chemist is researching sugar-based polymers for biomedical uses—such as delivering nucleic-acid drugs that may prove valuable in treating cancer, or for imaging agents in MRI scans. Collaborating with Keith Jones in UC’s College of Medicine and Jeffrey Robbins at Cincinnati Children’s Hospital Medical Center, Reineke and her team have created novel polymers that, Reineke says, do a great job “delivering the goods.”

Reineke’s research is significantly adding to knowledge about making drugs work better in the body. Exciting work to her, and to others as well. The young scientist has received recognition from the American Chemical Society and the National Science Foundation and was selected an Alfred P. Sloan Research Fellow in February. And a major pharmaceutical company is screening compounds developed in her lab for commercial application.
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Numbers
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Genomics Tool Identifies Disease Susceptibility

UC and Cincinnati Children’s researchers have established a powerful new gene information resource that more effectively identifies human genome alterations associated with an individual’s susceptibility to disease.

The system, developed at the Computational Medicine Center and known as PolyDoms, integrates the results of multiple genetic computational analyses and protein functional modeling. It provides biomedical scientists with important information on the theoretical probability that changes in genomic sequence are disease-relevant and indicates whether they warrant further clinical investigation.

Funded by the National Institute of Environmental Health Sciences and the National Cancer Institute, PolyDoms is considered part of a new wave of informatics resources that the computational biology community is developing to expedite and advance research in personalized, predictive and preventive medicine.

A paper outlining PolyDoms’ design and application appeared in a winter issue of Nucleic Acids Research.

UC PARTNERS WITH INDUSTRY
IN METALS ANALYSIS CENTER

A new partnership between UC and Agilent Technologies Metallomics Center of the Americas will support research in all fields related to the analysis of metals and metal species and their interactions within biological and ecological systems.

UC and Agilent scientists, together with associates in Canada, Mexico, Argentina and Brazil, will use liquid chromatography, mass spectrometry and inductively coupled plasma mass spectrometry to research the role of metal compounds in predicting stroke damage, detecting chemical warfare agents, determining ultratrace-level organic compounds, monitoring the environment and other applications.

UC officials say the pairing is a perfect complement for UC|21 strategic vision goals of putting students at the center, growing research and academic excellence, and forging key relationships and partnerships.
Genetically Altered Cells May Be Infection Fighters

Cincinnati burn researchers have created genetically modified skin cells that, when added to cultured skin substitutes, may help fight off potentially lethal infections in patients with severe burns.

Dorothy Supp, PhD, and her team found that skin cells that were genetically altered to produce higher levels of the protein human beta defensin 4 (HBD4) killed more bacteria than normal skin cells.

HBD4 is one in a class of proteins that exist throughout the body’s natural defense system. Researchers have only recently begun targeting these tiny molecules as a way to combat infections.

Supp says defensins could become an effective alternative method for burn wound care and infection control. Used in cultured skin substitutes, she adds, they could also decrease a patient’s risk of infection, improve skin graft survival and reduce dependence on topical antibiotics.

UC researchers reported these findings in the Journal of Burn Care and Research.

UC Faculty Among the Nation’s Most Productive

A new annual report ranking doctoral programs at the nation’s research universities has the University of Cincinnati at the head of the class when it comes to the scholarly activity of faculty. UC’s doctoral programs in the College of Education, Criminal Justice, and Human Services and the College of Medicine are listed among the top 10 nationally in faculty scholarly productivity, according to the Faculty Scholarly Productivity (FSP) Index.

The FSP Index, produced by the for-profit company Academic Analytics, measures the productivity of 200,000 faculty members in nearly 7,300 doctoral programs across the United States from 2005 data. The index ranks programs on the basis of faculty publications and citations, as well as faculty financial and honorary awards.

The index, reported in the Chronicle of Higher Education, ranked UC’s criminal justice program sixth among the nation’s top 10 doctoral programs in criminology and justice studies. UC’s special education program was ranked ninth among the nation’s most productive doctoral programs in special education.

UC’s physiology program ranked sixth in the FSP Index, and toxicology ranked 10th.

UC HAS RECEIVED FULL ACCREDITATION from the Association for the Accreditation of Human Research Protection Programs. The accreditation follows a rigorous three-year process and ensures protections are built into every step of research—from study design and selection of research sites and investigators, to the actual conduct of research and collection and interpretation of data. It also signifies that systems are in place to verify that these protections are genuine and that they are backed by policies, procedures and practices that guarantee the highest standards.
A Good Eye for Research

Undergraduates hungry for an observational research opportunity can definitely chow down during assistant professor Charles Ginn’s Introduction to Psychology 101 class.

You’ll see them—300 have taken the course so far—watching shoppers at Cincinnati’s Over-the-Rhine Findlay Market. They’re observing such things as who wears what, who buys what (and is it organic?), and even who minds the kids amid the hustle and bustle of the state’s oldest municipal market. Their findings end up in research papers documenting shopping trends.

In its third year, the Findlay Market Research Effort, funded by the Freshman Experience Program, engages freshmen with professors in activities beyond the classroom. The initiative comes alive as students observe human behavior at the market—90 percent of the time not interviewing subjects, but simply watching them.

Most of his students, Ginn says, have never been to the famed multicultural market before they take the course.

And because the students often don’t get into research until they’re upper-classmen, Ginn explains, to them the research process is an abstraction. He works to walk them through the basics, from forming a hypothesis to observing human behavior in a systematic way.

Orthopedic Surgeons Honor UC Researchers

A multidisciplinary team of UC engineering researchers, orthopedic surgeons and pathologists was honored with the Kappa Delta Award—the highest award given by the American Academy of Orthopaedic Surgeons—for their research and subsequent manuscript on tissue engineering for tendon repair using a type of stem cell obtained from bone marrow. The team will use the $20,000 award to support undergraduate and graduate summer research fellowships and pilot projects in the biomedical engineering department.

Studying Genetic Causes of Metabolic Syndrome

UC researchers have received more than $1.6 million from the National Institute of Diabetes and Digestive and Kidney Diseases to study genetic causes of metabolic syndrome, a disorder that can lead to cardiovascular disease and diabetes.

This UC-led study aims to isolate the specific genes associated with metabolic syndrome so scientists can identify at-risk populations.

Ranjan Deka, PhD, the UC environmental health professor who will lead the international study, believes that genetic dispositions may be coming together with changed lifestyle—one of unhealthy food intake, little exercise and an overall sedentary existence—to cause metabolic syndrome.

Deka and his team will attempt to establish a genetic basis for metabolic syndrome by identifying chromosomal regions associated with it. They will collect data from a genetically isolated population of about 80 large families living in the islands of Croatia.
BUILDING CONNECTIONS
About 15 years ago, UC architecture professor Dennis Mann began working with a colleague to collect information for what would become the nation’s first-ever Directory of African-American Architects. Since then, Mann and fellow researcher Bradford Grant, chair of architecture at Hampton University, Virginia, have continuously worked on updated versions of the directory, translated it into an online version, tracked trends regarding African-American architects and surveyed those same architects. For instance, they recently noted that the number of African-American women practicing as licensed architects has quadrupled in the last 15 years.

The value of that research—which has created a presence and community for African-American architects—has now been recognized with the 2007 Institute Honor for Collaborative Achievements from the American Institute of Architects (AIA).

Health and the Family Tree
Knowing your family's history for certain diseases can make a big difference in your own health, says UC genetics expert Melanie Myers, PhD.

Myers was awarded a $100,000 grant from the National Human Genome Research Institute of the National Institutes of Health to develop ways to educate low-literacy populations, including the Appalachian population in the Greater Cincinnati and Dayton metropolitan areas, about the importance of family history.

She will lead a team that will conduct focus groups to determine current mindsets about the importance of family history. The team will include experts from the UC College of Allied Health Sciences and environmental health department, the human genetics division at Cincinnati Children's Hospital Medical Center, the area health literacy program at Ohio State University, the Appalachian outreach studies program at Sinclair College in Dayton and six other community organizations.

The team will research what tools already exist to educate low-literacy populations about their health and health history, and will then develop additional resources to improve education about this important topic.

New Biomarker Predicts Drug Effectiveness
A UC research team has identified a new way to predict when anti-estrogen drug therapies are inappropriate for patients with hormone-dependent breast cancer.

Team leader Erik Knudsen, PhD, says the findings could help physicians more accurately predict which tumors will respond to anti-estrogen therapy and improve long-term survival for breast cancer patients.

The UC researchers, who reported their results in the Journal of Clinical Investigation, found that when a cell-growth pathway control known as the retinoblastoma tumor suppressor is disrupted or shut off, the tumor resists anti-estrogen drugs and the cancer continues to grow.

Anti-estrogen drugs such as tamoxifen (Novaldex) are standard treatment for hormone-dependent breast cancer, says Knudsen. But although these drugs are initially effective, many patients eventually develop a resistance to them.

Knudsen says the research suggests that physicians should examine both estrogen receptor status and retinoblastoma suppressor activation during the initial diagnosis, in order to prescribe the most effective therapy for that specific patient’s cancer.

The study was supported by funding from the UC Barrett Cancer Center at University Hospital that was made possible by philanthropic support from General Electric Aviation and other community donations. Additional support came from the Department of Defense Breast Cancer Research Program.
Researchers Identify Mechanism for Rare Lung Disease

Nearly 20 percent of reported deaths in people with the rare lung disorder pulmonary alveolar proteinosis (PAP) are attributed to infections—particularly microbial infections.

Researchers at UC and Cincinnati Children’s Hospital Medical Center have now identified a molecular defect in people with PAP, explaining why they are so susceptible to these deadly infections.

The study, led by Bruce Trapnell, MD, and reported in the Feb. 8, 2007, issue of the New England Journal of Medicine, suggests a direction for development of new therapies for PAP patients.

PAP develops when surfactant—a protein- and lipid-based surface material that keeps the lung from collapsing—builds up inside the air sacs (pulmonary alveoli). When this happens, breathing becomes difficult and microbial infections are common.

In healthy people, infections are fought off by protective antibodies. Sometimes, however, the body produces autoantibodies—antibodies that actually attack “good” tissue instead of infection.

It has long been known that people with PAP have high levels of autoantibodies, which work against an important immune-system regulator known as granulocyte-macrophage colony-stimulating factor (GM-CSF).

In clinical and animal-based studies, the UC and Children’s researchers determined that other important infection fighters—white blood cells called neutrophils—were also impaired in PAP. They further found that this neutrophil impairment was caused by the autoantibodies against GM-CSF.

Knowing the mechanism for the development of infection in PAP patients, Trapnell says, could lead to therapies to stimulate immune defenses.

The study was supported by grants from the National Heart, Lung, and Blood Institute, the National Center for Research Resources and the National Institutes of Health Office of Rare Diseases.

Boot It and They Will Pursue It: An Adventure in Math Skills

Recent reports suggest the state of American student math skills has reached crisis levels. Could the solution to the problem be where so many kids prefer to spend their time—in a video game?

UC faculty member Janet Mannheimer Zydney has a $400,000, two-year grant from the U.S. Department of Education to look into that. She’s creating software called Math Pursuits, which employs digital video clips to take third-to-12th grade students on a “math adventure.”

Zydney, assistant professor of educational technology in the College of Education, Criminal Justice, and Human Services, says the software shows students how they’re using math every day in real-life situations and helps them to develop fluency in mathematical problem-solving.

For example, one of the videos in development features siblings planning a family vacation, using MapQuest to explore how to use mileage and time to find a destination that fits the number of hours their dad is willing to drive.

Zydney is collaborating on the project with educational software pioneer Ted Hasselbring of Vanderbilt University’s Peabody College.
Leading to a Brighter Future

A university is a place of great innovation. One of endless idea production. But during that process, the size of our operation and the nature of our work often results in the production of a lot of waste.

UC has taken big steps to reduce waste and make our campus a sustainable one.

Just this spring, UC president Nancy Zimpher signed the President’s Climate Commitment, a pledge to “address global warming by garnering institutional commitments to reduce and ultimately neutralize greenhouse gas emissions on campus and to accelerate the research and educational efforts of higher education to equip society to restabilize the earth’s climate.”

Around campus, engineering systems have been upgraded to reduce utility costs, and the university has partnered with the U.S. Environmental Protection Agency through its Energy Star programs to purchase equipment with superior energy efficiency.

Simple changes over the past year—like resetting thermostats, monitoring air exchange in research areas, retrofitting lights and windows, and negotiating better energy contracts—have resulted in cost savings for the university of $2.6 million.

And in 2006, UC recycled more than 4,600 tons of waste.

While these are major initiatives, smaller changes around campus also add up.

We at UC Research have decided to join in UC’s efforts. We want to decrease our footprint on the environment, so in the future this magazine will be printed on paper manufactured using biogas energy and containing 30 percent recycled post-consumer fiber.

In fact, by making the switch with this one edition, we’ve already saved about nine trees, 564 pounds of solid waste, 5,322 gallons of water (equal to about a day-long shower), 1,573 pounds of air emissions and 4,301 cubic feet of natural gas.

We are as proud of these efforts as we are of the great research going on here in Cincinnati.

So when you’re done reading, add this issue to your collection or pass it along to someone else. And when the pages begin wearing thin, you can feel secure in knowing that the recycle bin is exactly where it belongs.
WHAT HAPPENS WHEN
researchers who study cancer
in a lab join with the
clinicians who see the
people in the exam room?

At UC, the result is a fresh
approach to creating
positive patient outcomes.

making
the
CONNEC
The patient was running out of options. At 75, he had spent years battling prostate cancer. Doctors had already removed his prostate gland, treated him with radiation and placed him on long-term hormone therapy. Still, his cancer returned.

Looking for answers, the patient’s radiation oncologist, William Barrett, MD, offered his case for discussion at the monthly meeting of UC’s Prostate Cancer Working Group, a multidisciplinary team of genitourinary cancer experts and translational researchers. Acting on insight from prostate cancer cell biology expert Karen Knudsen, PhD, on the body’s mechanisms for responding to hormone therapy, the team came up with a more logical sequence of treatment for prolonging the effectiveness of the hormone therapy. Barrett, who is director of radiation oncology at UC, quickly changed the treatment regimen and, six months later, the therapy has effectively slowed the progression of this patient’s cancer.

This is just one example of how interdisciplinary cancer research groups are changing the approach to cancer care—and research to improve that care—at the University of Cincinnati.

Ask any scientist or oncologist to predict the future of cancer care, and most will say two things: it’s tailored to the patient’s specific tumor characteristics and it’s a collaborative effort by an entire medical team that includes not just clinicians, but basic and translational scientists as well.
Yes, it may take a village to cure cancer. And that “village” will include medical oncologists, surgeons, radiation oncologists, nurses, pathologists, radiologists, basic scientists and even patient advocates—all working toward the same goal: not only to cure cancer, but actually to eliminate it.

UC’s interdisciplinary cancer research groups bring clinicians and basic scientists together to carve out common “need” themes that, if investigated jointly, may improve overall cancer care.

About three years ago, the National Institutes of Health (NIH) announced a new roadmap to guide the future of American translational medical research. The intent was to improve the process of moving promising research concepts beyond the lab bench and into the clinic, so those discoveries can more quickly begin improving the lives of cancer patients.

The roadmap, as Knudsen puts it, “requires researchers to address the human implications” of a basic or translational research project from its very beginning.

“Today’s research model demands that even the most basic scientists be clinically oriented,” she explains.

For scientists to successfully secure grants from the NIH and Department of Defense—two of the primary funders of cancer research—they must be able to draw a line to a new therapeutic agent that the work might lead to.

“I work with cells and mice, and if I stopped there, I doubt my work would benefit anyone,” Knudsen says. “As basic scientists, we have to have the passion and wherewithal to push our ideas beyond test tubes, cells and mice and collaborate with clinicians to shepherd those ideas through the entire process of testing in human tissue and, ultimately, clinical trials.”

She praises the Prostate Cancer Working Group for starting to break down the silos of “clinicians” and “basic scientists” that existed in the past, and for bringing together the physical and intellectual resources from both arenas to work toward a common goal.

“It’s exciting to identify a potential biomarker,” she adds, “but if it doesn’t show up in a patient, what’s the point? I couldn’t go the next step without the Prostate Cancer Working Group.

“In the past it was all too easy to say ‘it’s the clinician’s responsibility to test my theory in the patient’ and move on, but that can’t be accepted anymore.”

Cancer has become the second leading cause of death in the United States, and although survival outcomes are improving for certain types of the disease, the American Cancer Society estimates that more than 559,000 Americans still die every year from some form of it.

The NIH believes interdisciplinary research programs are needed to address significant and complex health problems—like cancer—that have resisted traditional approaches.
“The cross-pollination of ideas between researchers and clinicians is the only feasible way to chart the course of future therapies,” says Alex Lentsch, PhD, vice chairman for research in UC’s department of surgery. “Researchers working in silos may generate new insights into the cellular or molecular basis of a certain type of cancer, but the scientists by themselves can’t translate that information into meaningful clinical therapies.

“Likewise, clinicians often know from firsthand experience what needs to be investigated,” he adds, “but are unable—by themselves—to address these problems scientifically. By working together, we can pursue the most promising areas of research and target new areas for therapeutic development.”

PROSTATE CANCER WORKING GROUP

Barrett started UC’s Prostate Cancer Working Group in 2002 in an effort to stimulate collaboration between cancer clinicians—surgeons, radiation oncologists, medical oncologists, urologists and nurses—and the basic and translational researchers working on projects related to genitourinary diseases.

The overriding objective, he says, was to give patients the very best care possible, while at the same time improving the quality of research conducted at UC.

He says patient advocates also play a critical role in this effort, because they keep the researchers grounded and focused on what is important to the patient.

“Science for the sake of asking the question is great, but at the end of the day, we all want to improve the patient’s quality of life,” says Barrett. “Scientists and clinicians need to work together to reach that goal. An idea is only valuable if it can help us better understand—and treat—cancer.”

As Barrett explains, clinicians don’t always have a good understanding of what is feasible to study in the laboratory and, conversely, scientists may not know what’s most important clinically in terms of improving a patient’s quality of life.

He founded the Prostate Cancer Working Group to bridge that gap, increasing communication and understanding between the worlds of clinical care and research so that the two groups could support one another and pursue the most logical avenues for improving patient care. The melding of minds would allow clinicians to better understand what was feasible to study, and scientists would understand what was important to study.

“We get both education and intellectual stimulation when clinicians come together with basic and translational scientists to share their expertise and ideas,” says Shuk-mei Ho, PhD, chair of UC’s environmental health department.

“It’s very important—both for me personally and for my trainees—to be embedded in this type of collaborative research environment,” she stresses, “where the laboratory scientists and clinicians are working in tandem every day to test scientific theories for significance in human prostate cancer. That ‘cross talk’ is the best way to make progress against the disease.”
**ALTHOUGH STILL IN THEIR INFANCY, the UC cancer working groups have already developed new research study concepts and helped refine research ideas.**

- In collaboration with urologists, radiation oncologists and biostatisticians from the Prostate Cancer Working Group, Alex Lentsch, PhD, submitted a $1.95 million grant to the NIH to further investigate a gene mutation found in 70 percent of African-Americans. Lentsch believes that genetic mutation may explain why African-American men appear to be more susceptible to prostate cancer and die from the disease at higher rates than Caucasian men. The mutation prevents expression of a protective red blood cell receptor—the Duffy antigen/receptor for chemokines—that would normally reduce tumor progression by binding to and removing its growth factors.

- Karen Knudsen, PhD, and William Barrett, MD, are currently conducting a retrospective trial looking at prostate cancer patients who failed to respond to hormone therapy. They believe a certain genetic alteration—known as the retino-blastoma tumor suppressor gene, RB—may cause hormone therapy to fail in a specific segment of patients.

- Another major effort is currently under way through the Prostate Cancer Working Group to form a prostate cancer tumor and tissue registry, which would give members of the group access to a large bank of prostate tumor tissue so promising basic science theories can be tested for human relevance. The registry protocol—written cooperatively by members of this group—is being evaluated by UC’s Institutional Review Board.

- As part of the still-evolving Lung Cancer Working Group, environmental health researcher Michael Borchers, PhD, secured a $2.4 million grant from the National Institute of Environmental Health Sciences to study how environmental toxicants can stimulate the body’s natural defense system to cause additional damage in people with chronic lung diseases. The study is aided by Borchers’ access to biological samples from the Lung Cancer Working Group’s tumor registry and corresponding tissue bank.

**THE TYPE OF COLLABORATION that these working groups make possible** is key for UC to become a premier national cancer research institution, according to Erik Knudsen, PhD.

“We need to bolster our ability to perform translational research and provide a clinical outlet for our basic researchers,” says Knudsen, scientific director.
for the cancer center. “No investigator has experience in all areas. By interacting with our clinical colleagues, we can bring together individual expertise and facilitate the development of innovative approaches in the treatment of cancer.”

To support this collaborative spirit, Sohaib Khan, PhD, and Knudsen secured more than $900,000 in training grants from the National Cancer Institute in 2006 to help support the next generation of cancer researchers. Knudsen says such collaborative activities will help lay the groundwork for additional multi-investigator projects involving various disciplines.

Echoing Knudsen is Alex Lentsch. By interacting with clinicians and other cancer-oriented researchers, Lentsch says he continually gains insight into what he should be investigating to make the biggest impact clinically.

“I work primarily with cells and animals, so I can feel disconnected from the clinical course of this disease and its impact on individuals and families,” he explains. “I’ve learned a great deal about the disease from a diagnostic, treatment and outcomes perspective by being part of the Prostate Cancer Working Group—and that makes me a better scientist.”

The UC cancer working groups have also taken an active role in cancer education and prevention screenings in the community.

- The first successful initiative, the Mobile Prostate Cancer Screening Program, was started by Barrett and patient advocate/cancer survivor Herschel Chalk. The program aims to raise awareness of prostate cancer among men living in traditionally low-income, urban neighborhoods who may not have access to regular health care. “The important thing,” says Barrett, “is that this population is getting the message that they are at high risk for developing prostate cancer. We hope that once they get screened, they’ll encourage their friends and family to do the same.”

The group has also organized four Greater Cincinnati Prostate Cancer Forums for the general public, drawing up to 600 attendees for some.

- On the lung cancer side, Jane Pruemer, PharmD, is leading a smoking-cessation program—called Win by Quitting—that provides free medication and counseling to smokers who want to kick the habit for good. She says of the 600 people who’ve enrolled in the program, about 350 people have completed more than one visit in the past year, and 56 percent of those who have completed four visits have successfully stopped smoking long-term. Those numbers are substantially better than the national average—public health officials estimate that only 20 to 30 percent of smokers who enroll in a quit program will be successful long-term.
It’s a time of growth and change for cancer care and research at UC, but David Stern, MD, dean of UC’s College of Medicine and interim director of the UC Barrett Cancer Center at University Hospital, has a clear vision of what the program will become in the next 10 years.

It’s a tall order: “... to be a preeminent cancer care resource in the region by delivering the highest quality patient- and family-centered care in a collaborative environment, while continuing to produce outstanding research and emphasize education and outreach.”

“We want to transform cancer care in our region by providing the most advanced and compassionate care possible,” explains Stern. “And we’ll do that by building upon a foundation of innovative research and quality education that exists right now.”

To expedite progress toward these goals, last year Stern created a community cancer advisory board for the Barrett Cancer Center. He hopes this core group of community leaders will serve as the voice of Greater Cincinnati and help guide the development of new cancer services that will lead to improved health outcomes in the Tristate region.

He’s also refocusing and reorganizing the way UC approaches cancer research, which will be the cornerstone for becoming a National Cancer Institute–designated cancer center. The new model reflects what the Prostate Cancer Working Group is already beginning to achieve: disease-based, multidisciplinary research programs that will include basic, translational and clinical researchers.

“These specialized programs will give rise to the scientific interactions that promote clinical trial development and other activities that directly help cancer patients,” adds Stern. “Team that with strong relationships with community providers, and you create a cancer center that can impact the community in a very positive way.”
LEADERSHIP: Erik Knudsen, PhD, associate professor of cancer and cell biology, serves as scientific director for the cancer center. UC College of Medicine dean David Stern, MD, currently serves as interim director while the Academic Health Center completes a national search for an appropriate candidate. William Barrett, MD, is associate director for education and community outreach and Peter Stambrook, PhD, acts as associate director of the Barrett Cancer Center.

PEOPLE: The cancer center has about 100 research faculty members from multiple clinical and basic research departments at UC and Cincinnati Children's Hospital and more than 300 supporting staff members who work in scientific laboratories.

GRANTS: Cincinnati Children's and UC together have nearly $30 million in cancer-related grants from the National Institutes of Health and $15 million from the National Cancer Institute.

KEY BUILDINGS: The Barrett Cancer Center has both research and patient care facilities, including the Vontz Center for Molecular Studies (cancer and cell biology research), the Genome Research Institute (cancer research), the Barrett Center building (cancer outpatient care), Cincinnati Children's Hospital Medical Center (cancer care and research) and University Hospital (in-patient cancer care)

INSTITUTIONAL INVESTMENT: In the past five years, UC has invested about $60 million in cancer—this number includes building, faculty recruitment and other costs associated with creating a world-class cancer center.

“A SNAPSHOT OF CANCER AT UC
Under the leadership of interim director David Stern, MD, and scientific director Erik Knudsen, PhD, the UC Barrett Cancer Center at University Hospital is entering an era of unprecedented growth and development in both its research and its patient care capacities. The center includes scientists and physicians from various specialties—radiology, oncology, neurology, nursing, pharmacy, surgery—and entities associated with UC Academic Health Center, including Cincinnati Children’s Hospital Medical Center, the Cincinnati Department of Veterans Affairs, University Hospital and Hoxworth Blood Center.

“We want to transform cancer care in our region by providing the most advanced and compassionate care possible. And we’ll do that by building upon a foundation of innovative research and quality education that exists right now.”
Throwing the Spotlight on a Lady in the Dark

By M.B. Reilly
Photos by Andrew Higley
Righting an injustice done to the reputation of a famed composer compelled UC musicologist Bruce McClung to pen his just-released biography of a Broadway musical. And his peers—and general readers—are applauding his new book: *Lady in the Dark*. 
When a mere graduate student, bruce mcclung, PhD, found himself in opposition to the noted opinions of Europe’s most distinguished music critics.

It was 1987 at the Eastman School of Music, and the now University of Cincinnati associate professor of musicology was enrolled in a seminar studying the career and works of mid-20th century composer Kurt Weill—an artist whose American works were routinely disparaged by European critics.

As any student might, mcclung (who signs his name in lowercase) was at first willing to accede to this general view of Weill—that is until he actually listened to Weill’s score for a 1941 Broadway musical titled Lady in the Dark.

“What I heard,” recalled mcclung, “was a work that, while written for a popular, general audience, possessed an incredibly complex harmonic design. It was music that was both rich and demanding.”

For mcclung, it was a case of “hearing is believing,” and what he heard eventually led him to an intense, six-year effort to set the record straight on Weill in the just-released book, Lady in the Dark: Biography of a Musical.

However, what began as a Weill-centered research topic eventually grew to a fuller biography of this Broadway musical, a smash hit at the time due not only to Weill’s music but also to the contributions of a legendary cast:

- Leading lady Gertrude Lawrence, a famed actress and singer of the 1930s and 1940s who was a
power on Broadway, commissioning such works as Rodgers and Hammerstein’s *The King and I* • Lyricist Ira Gershwin • Actor and singer Danny Kaye, and • Famed playwright of the time Moss Hart, a pillar of 1930s theater.

So it is that in the book, mcclung not only defends Weill’s work, but he also chronicles the uncertain rise of a groundbreaking musical with the unusual theme of Freudian psychoanalysis at its core. The musical became so popular in its day that it ran 777 performances in New York and on tour, and the movie rights were sold in 1941 to Paramount Pictures for $285,000—a price that, at the time, was the highest ever bid for a literary work.

“The research began with a focus on Weill, and that’s certainly strongly incorporated into the book,” said mcclung. “But, in the same way that the musical *Lady in the Dark* took on a life and power of its own, so did the book. For example, Gertrude Lawrence is featured far more prominently than I first intended.

“But in the end,” added mcclung, “it seemed fitting to broaden the scope of the book. After all, Weill worked in the tradition of Mozart. He believed music was for all people, not something that only a group of connoisseurs should enjoy. I came to feel that this book should be the same, not something so narrow that only a musicologist could enjoy but something for a general audience.”

And mcclung succeeded. Mary Watkins, former director of UC graduate recruitment and retention, has already read the book and said she especially appreciates how the author reconstructed the historical context and how the personal histories of the creators shaped the work.

“I found that Broadway musicals are like people. All have a story to tell,” said Watkins. “The musical’s creation and performance were all before my time, so I knew nothing of the leading lady [Gertrude Lawrence] other than her name. In many ways, she was a co-creator of the work. I didn’t know about her stature at the time. Nor did I really know all of the influences—social, political and personal—that shaped this musical.

“And,” she went on, “as an amateur musician myself, I came away from the book very impressed by Kurt Weill’s music. Composition is such a demanding art form, and he was able to adapt that form to the business needs of the theater world, to the skills of the performers, the production time demands and the need to incorporate lyrics. He was truly a man of the theater, willing to make changes to his art in response to external factors. That’s not easy to do.”
Weill and Lady Liberty

The UC College-Conservatory of Music’s bruce mcclung began his research on Lady in the Dark motivated by a desire to “clear” the reputation of German-born composer Kurt Weill, who was thought to have “sold his soul to Broadway.” With his research, mcclung not only established the depth and complexity of Weill’s popular work, but he also found what he believes to be the motivation behind the tarnishing of Weill’s reputation in Europe.

“The musical materials in the book demonstrate without doubt the density and layered texture of Weill’s compositions. It was not for his music that he’s been disparaged in Europe. In fact, he’s been overlooked more because of the countercultural personal choices he made in his life,” claimed mcclung.

Those included Weill’s decision to move permanently to the United States when scores of other German intellectuals essentially repudiated America and returned to Germany after the defeat of the Nazis. In contrast, Weill bought a house in the United States and fully integrated into his new homeland, even so far as refusing to speak German with his fellow émigrés or even his own German-born wife.

“Weill became an ‘unrepentant’ American. He wrote in a letter to his wife that America was their home now. There was no turning back for him. He insisted on embracing this new homeland rather than clinging to and then returning to the old. He was one of the few German musical émigrés from the era who did so, and he was resented for that,” said mcclung.

ACKNOWLEDGMENTS

The research for the book Lady in the Dark was funded by a University Research Council Grant, by support from the College-Conservatory of Music’s dean, and by the Friends of CCM. The writing of the book was made possible with a sabbatical leave.
Geoffrey Block, professor of music at the University of Puget Sound, also applauded the book, stating, “thanks to mcclung, we are no longer in the dark about the artistic meaning and rich cultural context of this fascinating and timely show, which captivated America’s attention and left an enduring but previously unexplored legacy.”

In essence, the book is a look at what goes on backstage to create a runaway freight train of a success on Broadway—even when that train is loaded with baggage. That baggage included a demanding leading lady who initially waffled about taking on the title role. Not to mention that—at first—both the plot and initial motivation for the play seemed, well, not quite promising. The plot dramatizes the process of psychoanalysis (a process reserved only for the very well-to-do at the time) in which a woman seeks to uncover her difficulty in making certain life choices, specifically which type of man (father figure, glamour boy or mature individual) she really wants as a life partner. And Hart—who had a habit of starting and not finishing projects—actually wrote the play because he was ordered to do so by his own psychiatrist. The assignment was meant to force Hart—as a patient—to actually finish a job.

Fortunately, Hart passed his assignment and did finish the project. And so did mcclung—even though there seemed to be plenty of reasons to quit during the years of research and writing. As just one example: mcclung was not permitted to remove or even photocopy articles pasted into Gertrude Lawrence’s personal scrapbooks, now housed in the New York Public Library for the Performing Arts. So, he was then forced to use his laptop to painstakingly transcribe a significant portion of the 2,300 newspaper and magazine articles from the 1940s related to Lady in the Dark.

“I asked the staff if they’d put the scrapbooks on microfilm for me, but they said that there simply wasn’t enough demand for it in order to justify spending their time in that way,” recollected mcclung.

Worse yet, the library was only open about 24 hours a week, thus limiting mcclung’s research time. In the six weeks that he studied those materials, the author developed a feverish routine to capture as many specifics and as much general context as he could.

On days the library was open a full eight hours, he would eat a big breakfast but still be on time to be first in line as the library doors were unlocked. And even standing outside the doors, he’d open up his laptop, turn it on and then close it as he readied himself to, literally, sprint to the Lawrence materials.

“The elevators of the library were terribly slow. So, I’d run up the three flights of stairs to where the Gertrude Lawrence scrapbooks were kept. I’d pop open my laptop, which was already fired up and ready to go. I worked straight through in transcribing the most important articles. I’d merely summarize lesser articles. I
wouldn't take a break to eat. I had to make the most of my time. I was always there up to the very minute that the library was closing,” he stated.

That kind of dedication so impressed the few cast and crew members still alive that mcclung received both their thanks and additional historical treasures. For instance, Frank Spencer of San Francisco—who had worked as second assistant stage manager for *Lady in the Dark*—sent mcclung his original script containing all the changes and scene shifts made throughout the production.
Because of such help, mcclung uncovered a great deal of information, so much in fact that the first draft of his book was a whopping 120,000 words—even though his contract with Oxford University Press called for 80,000 words. “I tried to convince them to take the longer work, but they said, ‘No go.’ So, I had to cut a lot,” recalls mcclung.

All in all, that was the hardest part of the whole project, and the agonizing editing of his work took mcclung six months. “I was so close to the subject, and I found it all so fascinating, it was painful to cut so much.”

But in the end, mcclung did pare down the work, not only because he wanted to use the book to metaphorically put readers in the theater’s front row, but also to keep them there. He realized that the book—much like the musical that inspired it—was both a creative endeavor and a business proposition.

“As a musical, Lady in the Dark continually changed throughout its creation and production. This book is very much the same. And both have the same goal—to reach an audience. Moss Hart, Gertrude Lawrence, Ira Gershwin and Kurt Weill all had their own dramas in preparing their show for its opening, and so did I.”

**Other findings of note:**

- The crush for seats when *Lady in the Dark* first opened in January 1941 helped to establish the practice of advance sales on Broadway. Top ticket price for the show’s opening was $6.60, though some seats reportedly sold for $100 a pair on the street.

- The song, *Bats About You*, was only sung in the musical’s tryout opening in Boston and was subsequently cut.

- In the Moss Hart archives in Madison, Wis., mcclung discovered the true identity of the psychoanalyst who ordered Hart to begin and finish the work as part of therapy. It was long-believed that psychoanalyst Gregory Zilboorg was behind the genesis of the play, but letters in the archive proved that New York psychiatrist Lawrence Kubie actually instigated and promoted the production, even citing the work in his professional publications.

- *Lady in the Dark* was the first Broadway musical to do away with the overture and the opening production number. It opens with dialogue, and when the music finally does commence, it begins with two notes played by a single clarinet.

- *Lady in the Dark* was the first Broadway musical to integrate dream sequences to deliberately advance the plot.

- The musical represented lyricist Ira Gershwin’s return to writing full time after he virtually retired following the death of his brother, George, in 1937.

- None of the Gertrude Lawrence collection—boxes and boxes of materials—was catalogued. In one box, mcclung found her wallet still filled with items like her World War II blood-donation card.
Delicate Balance

By Dama Kimmon
Photos by Dan Davenport
Blood is a life force. Entire communities of people have learned to share it to save the lives of others.

Without it, hearts quit pumping and brains lose oxygen. But when there’s too much, blood can invade parts of the body it shouldn’t and carry toxins to organs—sometimes causing irreversible damage.

Stroke is a disease of either too much—or too little—of the good thing we call blood.

Its target: the brain.

Yet this disease that wages war against our knowledge center has proven itself elusive to some of the world’s greatest minds.

Each year, over 700,000 brains are “attacked” by stroke—formed when a blockage, or clot, disrupts the blood supply to the brain (ischemic stroke), or when a vessel bursts, sending blood to parts of the brain where it shouldn’t go (hemorrhagic stroke).

Preventing and treating stroke is all about balance,

TIPPING THE SCALES

Stroke is the third leading cause of death and the No. 1 cause of disability in the United States. Yet many of these “brain attacks” could be prevented. That’s why UC neurologists have set out to educate the public not only on signs and symptoms of the disease, but also on associated risk factors.

They are learning that it’s much easier to make people more aware of symptoms than it is to inform them on the lifestyle choices that put them at risk for stroke. And getting people to actually make changes that will lower their risk is even tougher.

UC’s Dawn Kleindorfer, MD, led a community-based research study targeting African-American women. To reach her audience, she sought out beauty shops and asked beauticians to ask their clients to take a baseline questionnaire to determine their knowledge about stroke. She then taught the beauticians warning signs, symptoms and risk factors and asked them to teach these stroke facts to clientele. At six-week and five-month follow-up appointments, clients were given another survey to determine what they learned.

“Community-based research is tough, but our surveys did show that the women retained a lot of the information they were given,” says Kleindorfer.

But, she says, they were best at remembering the signs of stroke and did worse at remembering the causes.
and helping stroke sufferers recover takes an equally measured response.

Sometimes called a “brain attack”—because its onset is sudden like a heart attack and because physicians want people to treat it with the same urgency—stroke is the third leading cause of death among Americans and leads the way in causing long-term disability.

And although stroke afflicts more people in the United States yearly than twice the population of Cincinnati, research shows that a majority still aren’t aware of the risk factors or symptoms of the disease.

UC scientists are working to learn not only about why stroke happens and to whom, but also about what happens to a person’s physiology after stroke, how different populations view their risk for the disease and what can be done to help victims recover months—even years—post-stroke.

To teach stroke signs and symptoms, Kleindorfer employs a common mnemonic that was developed at the University of Cincinnati in the mid-1980s to show emergency medical personnel what symptoms to look for.

The FAST method—keying in on facial and/or arm numbness, slurred speech, and the importance of time when seeking treatment—is now employed by health professionals and the general public across the country as a means for detecting stroke.

Knowing stroke symptoms is important, says Kleindorfer, but understanding risk factors and how to make lifestyle changes to prevent stroke is key to long-term changes in the incidence of the disease.

Kleindorfer thinks the FAST mnemonic really helps people as they learn what to look for and wonders if the struggle to understand risk factors would be made easier with a similar approach.

“Without a mnemonic, people don’t have anything to see or visualize as they try to remember what causes stroke,” says Kleindorfer. “And because risk factors serve as a reminder to make lifestyle changes, people just seem less interested in listening.”

Kleindorfer believes commu-
Community-based research is key to educating people about their health. “It’s a good way to get past the barriers of mistrust that sometimes exist between doctors or researchers and the community,” she says. “But there are going to be issues.”

For example, Kleindorfer had trouble getting follow-up information from some of the clientele who first filled out surveys in the beauty shop study. And determining public awareness depends very much on how you ask questions.

“When you ask people to pick from lists, like multiple choice, they do better,” she says. “But are they learning, or do they just remember something by that visual cue?”

“By asking open-ended questions, you make people generate an answer and you’re really able to see what they know.”

But because open-ended questions are more difficult for most people to answer, Kleindorfer says, many studies she’s conducted on public awareness show some very frustrating results.

Three public awareness studies (one each in 1995, 2000 and 2003) have shown slight improvements in stroke knowledge. But they have also found that despite more talk in the media about the stroke drug t-PA and its effectiveness if given within three hours of stroke onset, people aren’t getting to the hospital any quicker.

And people in the Tristate region aren’t making changes to daily behaviors that can lead to a stroke. During the 1990s, the smoking rate among Ohioans decreased very little, and the population got much fatter, both of which lead to climbing rates of diabetes, high cholesterol, and elevated blood pressure—all risk factors for stroke.


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**STRIKING A BALANCE**

Stroke prevention and treatment is about balance, and no one knows that better than UC neurology department chairman and professor Joseph Broderick, MD.

Broderick recently authored the American Heart Association’s guidelines for the treatment of hemorrhagic stroke and leads several large, worldwide studies of acute stroke therapy and genetics.

He was one of the key investigators in the late 1980s who led important research testing the effectiveness of t-PA—now the only FDA-approved treatment for breaking up the clots associated with ischemic stroke.

Brain damage occurs quickly in patients with stroke, so medications like t-PA must be used very quickly to have their greatest benefit. Because of this, UC physicians pioneered a new approach to stroke treatment. They handle each stroke case as they would a victim of a gunshot wound or major car accident. Thanks to this “trauma model,” patients who have a blockage in an artery supplying blood to the brain are treated with medications and/or devices to restore blood flow as quickly as possible. For those who have bleeding into the brain, the trauma model helps physicians to stop bleeding quickly and remove the collect-
ed blood clots in certain patients.

“We know that if we can give t-PA in the vein within two hours of stroke onset, patients are about three times more likely to get back to near their baseline than if they would have gotten no other treatment,” says Broderick. “However, when we treat patients within two to three hours, the benefit falls by half.

“We also know that people with ‘big’ strokes often still have blood clots after t-PA,” he adds. “Because of this, we have been leading government-funded studies that are examining whether t-PA plus devices and medication delivered by a small tube or catheter at the site of the blood clot in the brain can do a better job than t-PA alone.”

The group is also conducting studies to see if a combination of medicines that includes t-PA can be safer and more effective than t-PA alone.

“It’s true that t-PA has changed the lives of many stroke patients,” says Broderick, “but we can and must do better.”

**WALKING THE LINE**

UC neurologist Matthew Flaherty, MD, regularly walks the thin line of balancing medications as he works to prevent and treat stroke. In January, he published data concerning a medication sometimes used to prevent ischemic stroke—the kind caused by a blood clot.

Physicians use medications to prevent ischemic stroke in patients at risk for this condition, but managing these medications so that they don’t cause side-effects such as bleeding in the brain can be tricky.

Flaherty and a team of researchers found that the rate of brain hemorrhages associated with a blood-thinning drug sometimes used to prevent ischemic stroke quintupled during the 1990s, and in people over 80 the rate increased more than 10-fold. The results of his study were published in the journal *Neurology*.

The increase in hemorrhage, says Flaherty, is due to greater use of the drug warfarin, which is commonly prescribed to prevent blood clotting, but carries the side-effect of bleeding.

Use of the drug increased in the 1990s after studies showed it reduced the stroke risk caused by blood clots associated with atrial fibrillation, an aging-related condition that causes irregular heart rhythm.

“Warfarin is highly effective in preventing ischemic stroke among people with atrial fibrillation,” said Flaherty. “For many people, the benefits of preventing ischemic stroke continue to outweigh the risk of a hemorrhagic stroke.”

It’s that risk/benefit line that physicians treating stroke are forced to walk every day.

“Our findings should not discourage the use of warfarin when it’s appropriate,” says Flaherty. “Doctors can use these findings to make sure they are weighing the risks and benefits of warfarin use for their patients. For researchers, these results may stimulate efforts to develop safer alternatives to warfarin and better treatments for people with brain hemorrhage.”
Hemorrhagic (bleeding) stroke is the most deadly kind—primarily because no medical treatment has been approved to stop bleeding in these patients.

A major cause of hemorrhagic stroke is ruptured brain aneurysms, or blisters on blood vessels. Surviving this type of stroke is rare—30 to 40 percent of sufferers die within one month. This high mortality rate can be attributed to the accumulation of blood outside the blood vessel, which can cause the vessel to spasm and shut down blood flow to the brain. Called a cerebral vasospasm—this “secondary stroke” claims the lives of nearly half of the people it strikes.

Joseph Clark, PhD, a researcher in the neurology department, studies this type of secondary stroke and has identified some of the molecules that trigger vasospasm of the brain arteries.

“Normally the cerebral spinal fluid that envelopes the brain carries off wastes and exchanges them for nutrients at what's called the blood-brain barrier,” Clark says. “After a hemorrhagic stroke, however, toxins given off by the brain's bleeding contribute to the development of specific molecules that later cause the constricting vasospasm and second stroke.”

By understanding what causes these secondary strokes, Clark believes physicians can learn how to best predict who will have them and then adjust medications or other therapies to improve outcomes for those who do.

**RECOVERY: THE NEXT FRONTIER**

“All the good work we do with acute stroke takes care of 4 percent of people who need it,” says UC neurologist Brett Kissela, MD. “The major agencies that fund stroke research and reach out to patient communities would like to see that number closer to 20 percent.

“I think a realistic number is 10 percent. If we can treat 10 percent of patients, that would be great. I hope I can live long enough to see that. Twenty percent is a dream. But even so, that means 80 percent don't have anything.”

That's why, he says, the next frontier is trying to intervene to help people recover.

“Scientifically, we don't really get it,” says Kissela. “You have a stroke; the brain is dead. You can't revive it. What's dead is dead.

“Yet people can recover function. The rest of the brain can come in and take over.”

This concept—called neuroplasticity—is an intriguing one to neurologists and rehabilitation professionals alike.

And understanding how “plastic” the brain can be, and what triggers it to literally “rewire” itself, is something many at UC are trying to figure out.
The best tools scientists have to study this, Kissela says, are sophisticated imaging techniques. “Imaging can show us the process but doesn’t give us all the answers.”

But, he says, physicians might use imaging as a way to make predictions about who has the ability to recover after stroke—which is particularly important when studying novel devices. “If you don’t understand what’s going to predict recovery,” he says, “you could put a lot of people in a device trial who may simply never recover one bit. That doesn’t help them and will dilute your effect, which could lead to incorrect conclusions.

“We want to understand the biology of recovery enough to predict who should be enrolled in recovery clinical trials and not mistakenly reject any device or technique that could help.”

Questions about recovery, Kissela says, are what make stroke science interesting. “Science is a funny thing,” he says. “Sometimes different things drive it. And many times, people try to market products and use devices because they will pay off before the science is completely understood. Many trials are under way here that have to do with innovative devices designed by really innovative people trying to help patients recover. If we can help patients, we want to help them—even if we don’t understand biologically how and why these devices improve recovery.”

UC’s Stephen Page, PhD, leads the Neuromotor Recovery and Rehabilitation Laboratory (the Rehab Lab) at UC and the Drake Center—a Cincinnati-based, comprehensive rehabilitation hospital. He and his team develop and test stroke-recovery devices and techniques. They are learning more about the optimal recovery window—which Page says seems to be much bigger than many first thought.

Page’s team have a strong interest in the plastic properties of the brain and have visualized these properties in two studies of two completely different therapies—mental practice, and a modified version of constraint-induced movement therapy (CIMT).

During mental practice(also referred to as “motor imagery”)—patients repeatedly mentally picture themselves performing a task, like reaching for a cup.

Page and UC neurologist Jerzy Szafarski, MD, PhD, have used functional magnetic resonance imaging (fMRI) to take pictures of study participants’ brains before and after mental practice therapy and have noticed profound brain rewiring in people who have incorporated mental practice into their motor rehabilitation plans. They have found that this regimen results in dramatic movement gains even years after stroke.

A good thing, says Page, because mental practice is an
exercise that stroke patients can easily perform on their own at home, without therapists or expensive equipment.

During modified CIMT, patients are encouraged to use their affected arm for everyday tasks by restraining the unaffected arm. With this therapy, significant areas of rewiring appeared in patients’ fMRI scans—correlating with new movement abilities months and years post stroke.

“To our knowledge,” says Page, “we were the first to show that a reimbursable, outpatient therapy like modified CIMT can be potent enough to produce such rewiring. This is particularly important to stroke patients, since this therapy could be provided at most clinics.”

And he is quick to note that many clinics across the country are now using modified CIMT as a model of care.

For more information, visit www.rehablab.org.

**STROKE TEAM**

In 10 minutes, Dr. Joseph Broderick’s pager buzzes twice.

Two people in Cincinnati are being evaluated for stroke at an area emergency department—one of whom has already been assessed by a member of the Greater Cincinnati/Northern Kentucky Stroke Team. Then a third page comes in providing an update through a series of codes.

Described by some as the stroke “commando” model, the Stroke Team—a “special force” of neurologists, emergency medicine physicians, neuro-interventionalists and nurses—is on call around the clock, traveling to any one of the 17 hospitals in the team’s Tristate network to care for stroke as it happens and evaluate patients who may be candidates for available therapies or newer therapies being studied.

It’s this structure and teamwork that make Cincinnati’s Stroke Team such an impressive unit. And the team’s assignment—educate patients and the community, conduct research and care for stroke—is an example of how one program can fall so precisely in line with the overall mission of the UC Academic Health Center.

Neurology department chairman Broderick is most proud of the collaboration among hospitals, physicians and researchers in Cincinnati, which has changed stroke treatment, prevention, recovery and education around the world.

“In the past 20 years, more than 20,000 people have participated in ongoing stroke research in our community,” says Broderick. “As a result, not only have lives been saved here but also across the world. This balance between the community and health care at the Academic Health Center is a model not just for stroke, but also other diseases as we move into the next century. It makes me very proud to be a Cincinnatian.”
Laura Sauerbeck joined the Stroke Team 14 years ago after seeing the havoc wreaked by the disease. She was an emergency room nurse in a Cincinnati-area hospital and says she was fed up with telling patients and their families “only time will tell.”

“As health care practitioners, we don’t like things we can’t fix,” says Sauerbeck. “With stroke, there are so many unknowns. I thought researching it would provide me—and families of stroke victims—with important, more immediate answers.”

Since she joined, the team—which, at the time, was staffed by only two nurses and three physicians—has grown to include about 40 nurses at any given time.

Sauerbeck says the nurses are the bridge between the doctors and their research goals, and the patients and their families.

“Doctors have fantastic ideas,” she says. “The nurses network closely with hospitals and their institutional review boards to set those ideas into action.”

Cincinnati is known for many things—its rich German heritage, professional sports teams, major industry including General Electric and Procter & Gamble, and years of pork packaging. But local scientists and physicians see the city as a great place for research.

With stroke now affecting millions worldwide, preventing and treating this disease that’s come to be known as a “brain attack” is more important than ever.

Cincinnati, with a median income, minority population and percentage of high school and college graduates that statistically make it the all-American city, is a great place to study stroke.

But it’s not just the city’s demographics that make stroke care and research in Cincinnati appealing to so many scientists. Logistically, larger cities than ours are plagued with much more traffic, and many aren’t able to use their airspace for medical helicopters. As a result, strokes are often treated in suburban hospitals, creating a coordination nightmare for physicians and researchers hoping to study large populations.

And studying large populations is important, particularly for research projects like the genetic epidemiology study led by UC neurologist Daniel Woo, MD.

For a long time, there wasn’t much movement in the genetics
of stroke. Primarily, Woo says, because it has been considered a disease of the elderly. Finding living affected relatives was difficult because people who get strokes are often in their 60s or 70s and their brothers, sisters and parents are dead.

“Here in Cincinnati, we have population-based epidemiologic studies where we literally get to review about every stroke in town,” says Woo. He believes UC hosts the largest population-based case control study in the world.

Because of that, he says, UC scientists have the power to find specific differences among populations, adding to the validity to their findings.

And so far, they have learned a lot about the most severe kind of stroke—intracerebral hemorrhage. Most important: having a family history of this type of stroke is a risk factor.

“This has been well established for stroke in general in the literature,” says Woo. “But our study was the first to specifically show that a family history of intracerebral hemorrhage is a markedly increased risk factor.”

This study, Woo says, suggests that genetics could be the underpinnings of why some people have intracerebral hemorrhage.

The team has also linked variations in the gene apolipoprotein E to increased risk for this type of hemorrhage. Woo says the variations may account for as many as 40 percent of hemorrhages in the cerebral lobes of the brain—the cortex where most thinking occurs. He hopes that further research will provide a mechanism for regulating production of this gene.

The researchers have also found that the use of statins—cholesterol-lowering medications—also lowered the risk for bleeding strokes. Woo says this finding was surprising because high cholesterol is actually believed to protect against intracerebral hemorrhage.

“It’s a little-known fact that high cholesterol can actually be protective,” says Woo. “We would have guessed that the use of statins would lead to an increased risk for hemorrhage, but we found the opposite.”

Woo and his colleagues have also learned that African-Americans have almost double the risk of intracerebral hemorrhage compared with whites of the same age. He says the area of the brain most affected by hemorrhage in this population also happens to be the area most affected by hypertension (high blood pressure).

“African-Americans have higher rates of hypertension, but most importantly, higher rates of untreated hypertension,” says Woo. “We think that explains much of the increased risk.”

UC stroke physicians, nurses and researchers are all members of the Neuroscience Institute—a collaborative of nine academic departments at the College of Medicine, University Hospital and independent physician practice groups. The institute is dedicated to patient care, research, education and the development of new medical technologies.
THE IMPACT OF UC RESEARCH IS FELT FAR BEYOND THE TRISTATE. Fifty years ago, Albert Sabin, MD,—while on the faculty of UC College of Medicine and the staff of Cincinnati Children's Hospital Research Foundation—began testing an oral, live-virus polio vaccine. In 1963, Sabin's polio vaccine became available in the United States and has been used worldwide to save thousands of children from the crippling disease.

For his truly translational work, Sabin was awarded the Lasker Award for Clinical Medical Research in 1965.

Sabin, who died in 1993, began his career in biomedical research in 1926 at New York University. From 1939 to 1969, he was an associate professor of pediatrics, professor of research pediatrics and Distinguished Service Professor at UC.

A permanent display in the lobby of UC's Vontz Center for Molecular Studies showcases Sabin's work, and his papers, research materials, awards and honors are held in UC's Center for the History of the Health Professions—the region's largest collection of rare medical artifacts, manuscripts and photographs.
High school friends Chris, Pat and Marty were all very talented in math. While at college, Chris registers for 37% more algebra classes than Marty and attends twice as many advanced calculus classes as the average third-year student.

Pat completes three times as many accounting classes as either of the other two, and 1.65 times more than Chris.

The two taller friends have the same two instructors only 12% of the time, yet they all complete the math requirement six months sooner than any of their classmates.
All three plan to apply their math skills in their careers, but Marty wants the majority of work time spent solving complex situations faced in the real world.

How would Marty maximize the opportunity to reach this goal?
It happens every day: Injured and sick children sit in a hospital emergency room waiting to be X-rayed or for their films to be read.

And while children wait, parents worry.

Which is why Cincinnati Children’s Hospital Medical Center radiologists worked with UC’s College of Business to develop a process to improve the efficiency of radiology procedures.

Improve it they did. They reduced triage and exam processing times, decreased workflow disruptions and increased the quality of outcomes. And to date, the collaboration has also generated two patent applications, plus articles in two medical publications describing the development and success of Cincinnati Children’s new RadStream patient prioritization system.

It was all done with mathematical models, thanks to the business college’s quantitative analysis and operations management department (QAOM)—whose widely read output of research publications put it in the top 10 in its specialty in the world.

While QAOM faculty and students get their kicks using computer simulation, optimization and statistical models for solving planning problems, the issues they take on are far more than theoretical exercise in the classroom. Clients turn to UC’s team when a big problem needs an urgent fix.

“We’re Cincinnati’s ‘Numb3rs’ crew!” says QAOM department head Jeff Camm, PhD, referring to the television show in which an FBI agent and his math professor brother solve crimes using mathematical models.

“If you liked math in high school,” he says, “you were probably steered toward accounting or mathematics in college. But what if you really wanted to roll up your shirt-sleeves and get involved in business? Then you’re looking at quantitative analysis and operations management.

“When my relatives and friends ask me what it really is that I do, I tell them I solve word problems for a living. And it’s great fun!”
QUANTIFYING CARE

Working with the Cincinnati Children’s Radiology Informatics Research Core, QAOM developed a unique algorithm specifically for RadStream. It automatically prioritizes cases according to the patient’s medical severity and psychological state, and operational factors like patient waiting times and departmental turn-around goals. This automation frees up medical resources and helps guarantee patients are prioritized quickly and consistently.

“We knew we could benefit from collaboration with the College of Business,” says Mark Halsted, MD, chief of the Cincinnati Children’s Radiology Informatics Research Core. “These are people, for instance, who consult with shipping companies to make sure their trucks run the most efficient routes and remain full as often as possible. We realized they could help us improve our work flow and measure whether changes we implemented actually had a desired effect.”

“The algorithm’s performance showed high agreement with actual triage decisions made by experienced radiologists, which was a challenge given the inherent subjectivity of the task,” says Craig Froehle, PhD, the lead UC team member and an assistant professor in QAOM.

The effects of this inter-institutional project could be felt far beyond Cincinnati.

“Health care is a huge growth area for QAOM,” says Jeff Camm. “RadStream at Cincinnati Children’s is just one example. The ever-increasing cost has to be dealt with eventually, and mathematical modeling will certainly have a lot to offer in improving the current system.”
Teaching Decision Making

Operations research is a scientific approach to decision making.

“We teach a systems approach to decision making,” says QAOM department head Jeff Camm, PhD. “We ask the questions ‘what am I trying to decide?’ ‘what are the objectives?’ ‘how am I constrained?’ or ‘what are the rules of the game?’

“We then build mathematical models of the answers to these questions and analyze the problem.”

Planning problems, says Camm, can be mathematically difficult. “First,” he says, “there are too many options to list and evaluate. We use optimization for these. And second, uncertainty exists, so we use simulation to model uncertainty and statistical modeling to try to accurately predict what might happen.

“The future is in merging these technologies,” Camm says. “We need better research on how to optimize under uncertainty. In my opinion, we’re just now scratching the surface.”

Because of events like the 2001 terrorist attacks and Hurricane Katrina, companies and government agencies are increasingly concerned about managing risk. For example, companies are interested in a robust supply chain rather than just a cost- and service-efficient one.

“A robust supply chain handles shocks to the system, such as disruptions due to weather, terrorism or political disputes, better than a traditional cost-effective supply chain,” says Camm. “Likewise, our government is very interested in how to use our limited resources to best protect against further terrorist attacks.”

In fact, he says, thanks in part to UC’s contribution, P&G subsequently won the INFORMS Prize— from the Institute for Operations Research and the Management Sciences—for the most effective integration of operations research in company-wide decision making.

One of the QAOM department’s greatest successes has been a supply-chain optimization project for Procter & Gamble (P&G).

The QAOM team built a mathematical optimization model that would meet demand, customer service response-time goals and flow of goods through the supply chain—all while minimizing total supply-chain cost.

The outcome for P&G was $250 million per year in cost savings in its North American operations, “which led to the rebirth of their operations research,” Camm says. “P&G is now a leader in using analytics in supply-chain optimization in its operations around the world.”

In fact, he says, thanks in part to UC’s contribution, P&G subsequently won the INFORMS Prize— from the Institute for Operations Research and the Management Sciences—for the most effective integration of operations research in company-wide decision making.

“One of the QAOM department’s greatest successes has been a supply-chain optimization project for Procter & Gamble (P&G).”

“First,” he says, “there are too many options to list and evaluate. We use optimization for these. And second, uncertainty exists, so we use simulation to model uncertainty and statistical modeling to try to accurately predict what might happen.

“The future is in merging these technologies,” Camm says. “We need better research on how to optimize under uncertainty. In my opinion, we’re just now scratching the surface.”

Because of events like the 2001 terrorist attacks and Hurricane Katrina, companies and government agencies are increasingly concerned about managing risk. For example, companies are interested in a robust supply chain rather than just a cost- and service-efficient one.

“A robust supply chain handles shocks to the system, such as disruptions due to weather, terrorism or political disputes, better than a traditional cost-effective supply chain,” says Camm. “Likewise, our government is very interested in how to use our limited resources to best protect against further terrorist attacks.”

David Kelton, PhD, director of the business department’s master’s program in quantitative analysis (MSQA), points out the wide range of applications and industries in which UC’s mathematical-modeling tools can be applied.

“This program gives our graduates the flexibility to apply these tools in all kinds of companies and industries,” says Kelton, who with consultant Averill Law coauthored the book
Simulation Modeling and Analysis, considered the bible of their field. “It also keeps them flexible over their careers as the economic climate changes.

“In our program, we’re not training people just for the manufacturing sector or the transportation sector, or whatever,” says Kelton. “We’re providing a generic toolkit that can be used all over the place with tangible, spectacular results.”

UC alum Chris Lynd, now senior vice president of financial systems for U.S. Bank, says UC’s QAOM program has had a major impact on his success.

“I entered the business world with an attitude that I could solve any problem I came across,” he says. “In an environment where it was common to hear people say, ‘We can’t do that,’ the program helped me to confidently say, ‘I can do that, and I will have it for you by next week.’”

And, says Lynd, the program also helped him to understand the type of person he wants to hire.

“UC’s program does an excellent job of focusing on the application of theory,” says Lynd. “Too many other programs are pure theory. Some students are excellent at pure theory, but they simply don’t have what it takes to translate this knowledge to real-world problem solving. Theory-only individuals would not survive in our environment.

“Thanks to my own experiences, I can easily differentiate a real-world problem solver from a theory-based person. In fact, we have created an employee screening test to ascertain this information on potential candidates.”
Camm himself has applied optimization modeling to a variety of problems involved in the selection of nature reserve sites. Given the large number of potential sites, for example, it’s important to balance cost with the maximum number of unique species a site can sustain. Some of this work, described in an article that Camm coauthored in the journal Science, was included in a brief to then-President Bill Clinton.

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David Kelton, Director, Master’s Program in Quantitative Analysis

Fantasy Sports

Alumnus Paul Bessire earned an MSQA degree, which combines applied mathematics, statistics and computer applications in a business environment. Including what is often called operations research or management science, as well as applied statistics, this unique MS program helps students excel in all areas of the business world—not to mention sports.

“We believe that much of the variation found in a basketball team’s success can be explained mathematically by looking at the interactions of the five players on the court and not just individual player’s abilities,” says Bessire. For this project, he examined several methods for rating individual NBA players and used what is known as multivariate regression analysis to assist in building successful NBA teams.

Applications of the model include examining which players should play at each position, predicting the lineups that should have the greatest team success and specifying which skill areas the coaching staff should seek to improve through the annual NBA draft, free agency and trades.
AOM helped Hamilton County adapt to the new election procedures established by the 2002 Help America Vote Act. The legislation required many counties to switch from punch-card ballots to electronically scanned ballots. This meant that Hamilton County had to deliver electronic voting machines to nearly 1,000 precincts prior to Election Day. QAOM assistant professor Mike Fry developed the routes used to deliver the voting machines. His algorithm computed how many trucks were needed and where each truck should go so the voting machines could be delivered when poll workers were available to receive and secure them.

Several years ago, the group that sponsored Cincinnati’s bid to host the 2012 Olympics, Cincinnati 2012, asked the QAOM department to conduct a more formal risk analysis of the budget they submitted to the U.S. Olympic Committee, since it was necessary to ensure that the committee would not be at risk financially.

Using state-of-the-art risk analysis software, the team worked with Cincinnati 2012’s chief financial officer to identify revenue and expense uncertainties and predict the chances of overruns.

As a result of the analysis, says James Evans, PhD, director of UC’s Total Quality Management Center, the final budget submitted had at most a 2 percent chance of running in the red. Even though Cincinnati wasn’t in the Olympic Committee’s final four, a representative was quoted in the Oct. 27, 2001, Cincinnati Enquirer saying, “Cincinnati offered community strength … and they gave us one of the best budget analyses we’d seen.”
ON NURSING RESEARCH

Few know the rich and remarkable history of nursing and nursing research in Cincinnati. But where and how does the story begin? It’s probably best to start with Florence Nightingale, the founder of modern nursing and nursing research. She is the focus of many historical papers, books and even made-for-television movies. We know that she was the “lady with the lamp” who provided compassionate care for the British soldiers who were brought down the Bosporus Strait to Scutari during the Crimean War. She is known for bringing sanitary conditions to the hospital and reducing mortality. She was frequently sought by the leaders of her country to provide advice related to nursing education, care of the sick in the home and public health.

What’s less known was her insistence on documenting outcomes of care. She kept detailed notes and, in the early 1860s, developed the Coxcomb system (below, top) for graphing data. Nightingale’s contribution to developing data analysis techniques was recognized by the American Statistical Association when she was named one of the top 10 women contributing to the field.

In 1860, Nightingale established the School of Nursing at St. Thomas’
These programs of nursing research are diverse. However, Nightingale’s insistence on measuring outcomes of patient care is still evident.
Looking
a lot like a
phone keypad, these UC-
grown cubes actually reflect a differ-
ent technology altogether: carbon nanotubes.
Each one is about a half inch tall. In fact, a U.S. dime would
tower over them. A mighty different view of these cylindrical struc-
tures. But don’t be fooled by their size. These happen to be the largest growth of
vertically aligned carbon nanotubes in the world. Because they are unusually
strong (as structurally sound as an equal weight of steel), larger pieces
are critical to developing innovations in the transportation,
defense, safety, electronics, aerospace and medical
industries. Already, UC researchers are work-
ing on nanotube mass-production
methods—an industry
in itself.