HEALTH AND WELL-BEING
Medical Discovery
Innovative Design
Human Development

2007-08 ANNUAL REPORT
Health Research Boosts State’s Well-Being

Health disparities across North Carolina’s population. Limited access to health care in many parts of the state. Inefficiencies in using scarce health care resources. Responding to such issues, the UNC Tomorrow Commission, a 28-member blue-ribbon panel, has targeted health and well-being as one of seven challenges on which NC State and the rest of the University of North Carolina system should focus their education, research, and outreach efforts in the coming years.

NC State has a head start on the effort, having had health and wellness among its major research thrusts for years. “We look at health holistically, which produces groundbreaking research in genomics, proteomics, pharmaceuticals, nutritional foods, medical devices, accessibility for people with disabilities, and translational medicine that addresses both animal and human needs.” Vice Chancellor for Research and Graduate Studies Terri Lomax says. She notes that the University has research programs and a culture of partnerships in systems biology, comparative medicine, medical textiles, and biomedical engineering.

Leading NC State’s health-related research is the College of Veterinary Medicine (CVM), ranked fourth in the nation for its programs in clinical sciences, population health, and molecular biomedical science. The joint NCSU-UNC Biomedical Engineering Department, formed in 2004, is known for its research in biomedical imaging and devices, biosystems analysis, biomechanics, tissue engineering, and rehabilitation engineering. The Department of Molecular and Structural Biochemistry has one of the most comprehensive programs in macromolecular structure-function in North America. In addition, six large-scale, health-focused interdisciplinary graduate fellowship programs at NC State are currently funded by the National Institutes of Health, the U.S. Department of Education, and the Environmental Protection Agency, attracting and supporting top graduate students in biomedical fields.

Dr. Prema Arasu, director of Global Health Initiatives at NC State, is a parasitologist and infectious disease expert in the CVM. Arasu has spent several years working on international health policy and developing partnerships in China and India for public health research. She is now building teams of researchers across colleges to join partners in Africa, Asia, Europe, and Latin America to attack major international health problems like food safety and infectious diseases.

This issue of RESULTS features research projects in health and well-being. It also highlights achievements across the full range of NC State’s research in the 2007-2008 Research and Graduate Studies Annual Report. “We had a record year for research awards from a broad and balanced array of sources,” Lomax says. “We also continued to grow our population of talented graduate students who are the engine of our research enterprise.”
Dr. Paul Agris is a biochemist, but he sees himself as a quality control engineer for cellular activity. When mutant cells spur the growth of a tumor, or bacteria or viruses replicate and produce an infection, defective molecular products result. Issuing a massive “recall” to eliminate the defective products is often too difficult to succeed, Agris says. So, he suggests shutting down the cellular factories that are churning them out and fixing the machinery inside to stop the process altogether.

The equipment in need of repair in Agris’ scenario is the ribonucleic acid (RNA) in cancer cells, bacteria, and viruses. He has studied the molecule for four decades and says its ability to regulate protein synthesis makes it a prime target for disease intervention. “We don’t need to knock out huge quantities of proteins,” he says, noting many drugs are designed to bind to and disrupt specific proteins. “We can just go after a small bit of RNA in each cell to shut down the ability to express a protein.”

Targeting RNA is both simpler and more complex than going after a protein, Agris says. While proteins have 20 possible chemical building blocks, RNA has only four. That makes it harder to design a drug specific to RNA based solely on unique chemical properties, he says. Instead, researchers need to study the structure of the 3-D polymer, including the way it folds over on itself and how enzymes modify certain segments so potential targets can be identified. “You need to do a lot more upfront investigation to ensure the target is so distinct you don’t have any peripheral effects,” he says. On the other hand, once the target has been achieved, he says, RNA’s limited arsenal of chemistries makes it nearly impossible for the molecule to modify itself and become drug-resistant.

“We have a huge problem globally with antibiotic resistance but few new antibiotics.”

Drug resistance is a primary focus for Agris, who last year spun out his technology, including assays and reagents to test for candidate drugs, to a new company called Sirga Advanced Biopharma. The company recently won a National Institutes of Health grant to develop its process, and Agris wants to begin by studying HIV and a variety of bacteria, including methicillin-resistant Staphylococcus aureus (MRSA). Almost one-third of people with HIV develop resistance to one of more of the components in the drug cocktail designed to keep the virus in check, he says, and MRSA has become a major cause of infections in hospitals. “We have a huge problem globally with antibiotic resistance, but few new antibiotics are produced against innovative targets because there’s little profit in making them,” he says. “Finding a drug that is effective against these diseases is critical, and that is my goal.”
Inhaler Provides Pinpoint Drug Delivery

Anyone who has played the old labyrinth game knows just how hard it is to tilt the board and move the ball through the maze while avoiding holes to get all the way to the goal. Now, imagine trying to do it without any knobs to control the ball’s direction. That’s the challenge presented by inhalers, according to Drs. Clement Kleinstreuer and Stefan Seelecke, who say getting medicine to a specific site in the maze of airways in the lungs is almost impossible without a way to control its direction.

Along with colleague Dr. Bill Roberts, the two Department of Mechanical and Aerospace Engineering professors have devised such a control mechanism, and they say their smart inhaler is the ideal way to deliver drugs to treat lung cancer, diabetes, and other diseases. Kleinstreuer came up with the idea after U.S. Environmental Protection Agency officials asked him to predict how particles of pollution would deposit in the lungs. An expert in fluid dynamics, he flipped the scenario to examine therapeutic materials instead of toxic ones and found that, by running simulations that backtracked from a specific site in the lungs, he could determine the exact place in the mouth where the materials were released.

Seelecke and Kleinstreuer then designed an inhaler with a tiny nozzle to disperse medicine in aerosol form from a single point. A valve inside the smart inhaler also matches the air flow to a patient’s breathing patterns for maximum efficiency in delivering the dose. Regular inhalers mix a wider spray of aerosol drugs and air, he says, so about 80 percent of the therapeutic particles land in the throat or along the initial branches of bronchial airways and never penetrate deep into the lungs. “The drugs wind up attacking healthy tissue in the lungs instead of treating a tumor or other disease,” Seelecke says. Using a series of twisting glass tubes to mimic the larynx and lungs and a laser to track the path of the particles, Roberts confirmed the findings of Kleinstreuer’s simulations by demonstrating that the spray from the nozzle could travel through at least three levels of branching airways in the lungs to a specific point.

Getting medicine to a specific site in the maze of airways in the lungs is almost impossible without a way to control its direction.

The researchers are planning a clinical test with pulmonary specialists at the UNC School of Medicine to test the smart inhaler in patients and are mapping regions in the lungs so the nozzle can be set to deliver targeted doses of medicine for individual patients. “Inhalation is becoming a more desirable way of bringing medication into the system,” Kleinstreuer says. “It’s a much more efficient and direct way than swallowing pills or injecting drugs.”
The Code Red and Code Orange air-quality advisories that plague urban areas nationwide each summer mean hazy skies, scratchy throats, and wheezing coughs to most people. But to Dr. Montserrat Fuentes, a professor of statistics in the College of Physical and Mathematical Sciences, they also mean an increased risk of death for some people.

Fuentes was a member of a National Research Council panel that last spring established a cause-and-effect link between ground-level ozone and mortality rates. She also serves on a science advisory board which has recommended that the U.S. Environmental Protection Agency (EPA) slash the ozone standard in the Clean Air Act from 85 to 65 parts per billion. The recommendation is based on a cost-benefit analysis pitting human lives against the economics of meeting tougher restrictions. “The government has never taken mortality into account when setting air-quality standards,” she says. “Officials say there’s not enough evidence to connect pollution and mortality.”

Fuentes has worked for years to prove such a connection. She has used statistics to solve environmental problems since working at the National Center for Atmospheric Research in Boulder, Colorado, almost a decade ago, and she now splits her time between NC State and EPA labs in Research Triangle Park. In recent years, she has developed complex statistical models to examine the relationship between short-term exposure to ozone and fine particles in air—soot, dust, and pollen—and health problems like asthma and heart disease. “It’s much more complicated than just seeing that the ozone level is high and this person died,” she says, noting weather, exposure levels, and factors like smoking need to be considered.

“The government has never taken mortality into account when setting air-quality standards.”

Epidemiologists at UNC-Chapel Hill and Duke, along with Drs. Chris Frey and Yang Zhang of NC State, provide the inputs for her models. Frey, an environmental engineering professor, helps determine pollution exposure using data from hundreds of air-quality monitoring stations nationwide. Zhang, an assistant professor in the Department of Marine, Earth and Atmospheric Sciences, uses his own models to characterize the pollution, including the types of particulate matter in the air, which can vary from one region to the next.

Plugging that data into her equations, Fuentes has determined that reducing daily ozone levels by 10 parts per billion would cut mortality rates by about 1 percent. Likewise, her models have shown a 6.6 percent jump in mortality when the monthly average exposure to fine particulate pollution increases by 10 parts per billion. With grants from the EPA and the National Institutes of Health, she now is examining particulate pollution more closely. “Instead of setting an air-quality standard based on the total level of particulate matter,” she says, “we should be regulating the sources like vehicle emissions and industrial plants.”
Research Campus to Super-Charge Fruits, Vegetables

ways to protect their own health,” says Dr. Mary Ann Lila, professor of food science and founding director of PHHI. “Through our public-private partnership with Dole Food Company, Inc., we have a pipeline to getting benefits directly to consumers.”

Top researchers from eight North Carolina universities will collaborate with government scientists and private businesses to determine how to boost the nutritive value of fruits and vegetables.

David Murdock, the owner of Dole, is investing more than $1 billion to create NCRC on the site of a former textile mill. Seven North Carolina universities will join NC State on the campus. Several biotechnology and crop science companies and U.S. and foreign government agencies are considering locating nearby, says Dr. Steve Lommel, interim associate dean for research in the College of Agriculture and Life Sciences, who is coordinating NC State’s efforts at NCRC. “We’ll be working on next-generation problems of human nutrition and health that cannot be addressed by a single university,” Lommel says. “No place is better positioned to do this.”

In addition to setting up NCRC as a giant petri dish where researchers can combine their talents to produce results, Murdock has outfitted the 350-acre campus...
with state-of-the-art equipment. The instrumentation includes a 950-megahertz nuclear magnetic resonance spectrometer—the most powerful machine of its type in the world—to study complex proteins and molecular activity in great detail, as well as advanced imaging and genomics equipment. “Although there will be plenty of graduate students to mentor, this is clearly more a research institute than a university campus,” Lommel says. Murdock also provided NC State with $2 million to supplement faculty salaries and attract top researchers like Lila to PHHI. The North Carolina General Assembly has appropriated $1.8 million in recurring funds to supplement Murdock’s gift.

Lila, who spent 24 years at the University of Illinois as a plant biologist, says she was drawn to NC State by the “unprecedented opportunity” offered by NCRC. “We have the ability to do things here that you can’t do anywhere else,” she says, noting that PHHI’s capabilities helped land a $1.4 million grant even before the institute officially opened. Under the Medicines for Malaria Venture grant, NC State will work with Rutgers University and the University of Cape Town in South Africa in an effort to find anti-malarial compounds in plants.

“We have the ability to do things here that you can’t do anywhere else.”

A Chicago native who dreamed as a girl of being a florist, Lila has focused her research for more than a decade on biologically active compounds in produce. Fruits and vegetables have no natural defenses other than an array of chemicals that they produce when under stress. “The same compounds that protect plants have therapeutic benefits for humans,” she says. Since many of the compounds’ functions overlap, researchers must determine which are the key compounds and how they work together to become more potent. “There’s no magic bullet,” she says. “There’s always an interaction of compounds, which is why there’s no tendency to build resistance to them.”

Lila has traveled the globe, studying plants in locales as diverse as Kyrgyzstan, New Zealand, and sub-Saharan Africa to learn the medicinal uses of fruits and vegetables among different cultures. Some produce has antioxidant properties, while the active compounds in others turn on enzymes or open or close metabolic pathways. Although epidemiological studies have shown certain foods lower cancer risks or help diabetics, scientists have never been able to figure out why. “We now have the instruments and the expertise here to do that,” Lila says. “We can then use animal models to see how the compounds work in the system.”

The NCRC campus will include extensive greenhouses and test plots, allowing PHHI scientists to apply the latest plant breeding technologies to produce specific fruits and vegetables with higher concentrations of the key compounds. NC State researchers will then work with farmers across North Carolina to begin growing the improved crops commercially. “Mr. Murdock has shown tremendous vision,” Lila says. “It’s up to us to realize it.”
The concept sounds like it’s straight out of the science fiction that Dr. Elizabeth Loboa loves to read and watch so much. Take stem cells from discarded fat and create bones from them. Yet, the assistant professor in the Department of Biomedical Engineering is producing real bone cells in her lab, hoping to one day provide body parts to wounded soldiers, help children with skeletal birth defects, or treat an aging population dealing with osteoporosis.

Loboa places the adult stem cells in devices that tug or twist them repeatedly until they start differentiating into bone cells and producing the proteins found in natural bone. The tension, compression, and shear forces mimic the stresses the stem cells undergo in the human body, says Loboa, a mechanical engineer whose interest in stem cells grew out of computer simulations she developed to measure tissue regeneration and growth under various mechanical loads. “Our bodies provide mechanical, chemical, and electrical cues,” she says, “to give stem cells an idea of how they should differentiate into various types of cells.”

Dr. Laura Clarke and Russell Gorga have teamed up with Loboa to see if they can replicate the electrical cues and accelerate the process of creating bone cells. Gorga, an assistant professor in the College of Textiles (COT) who specializes in polymer physics, builds tiny “scaffolds” of nonwoven fibers that allow the stem cells to grow in more of a 3-D setting than a culture dish provides.

Fat-derived stem cells that have been stained purple can be seen growing rapidly on scaffolds of nonwoven polylactic acid fibers over a 24-hour period. The scaffold on the right, which has been oxygen plasma treated, causes more stem cell growth and proliferation than the untreated scaffold at left.

Dr. Elizabeth Loboa and Ph.D. student Seth McCullen try to replicate the mechanical, chemical, and electrical cues the body uses to tell stem cells to become bone cells.

He and COT graduate Seth McCullen, now a Ph.D. student in Loboa’s lab, came up with the idea of adding carbon nanotubes to a biodegradable polymer as it’s sprayed into a web, making the resulting scaffold stronger and electrically conductive.

Adult stem cells from fat are placed in devices that tug or twist them repeatedly until they start differentiating into bone cells.

Clarke, a physicist in the College of Physical and Mathematical Sciences, then applies an alternating current of about 10 volts per centimeter to the scaffolds and stem cells. Clinical tests have shown such electrical pulses help bone fractures heal more quickly, she says. The team’s experiments have shown bursts of calcium release resulting from the oscillating current. “The electric fields put the stem cells under stress,” Clarke says. “All we’re trying to do is trigger a natural response to the cell’s surroundings.”

Loboa harvests the stem cells from fat extracted from patients undergoing liposuction at UNC Hospitals in Chapel Hill. Such a universal source could make it easier to build bones for individual patients that their bodies wouldn’t reject, she says. “We’re basically recycling waste tissue,” she says. “The adult stem cells also might be able to regenerate cartilage, ligaments, and muscle tissue.” Science fiction is quickly becoming reality.
Biomedical engineering graduate Kat Sauer and her team devised a way for ambulances to chill saline IVs given to cardiac patients to lessen the neurological damage from a heart attack.

Even before she heads off to med school, Kat Sauer has a medical device invention to her credit. Then again, so does every other student who has taken the senior design course in the Department of Biomedical Engineering (BME) in the last two years. Course director Andrew DiMeo’s efforts to make the course more entrepreneurial in that time have produced 17 invention disclosures and a new partnership with Wake Medical Center.

“Working together, we can develop practical solutions to health care challenges.”

Instead of gathering a list of possible design projects from various end-users and assigning them to students, DiMeo wanted to emulate the U.S. Food and Drug Administration’s design control process for medical devices. That involves defining a problem, cataloging inputs, and describing how each one led to the final output. DiMeo used the process himself—he worked as a project manager for a medical device company and co-founded a company that provided mechanical engineering services to device companies—before coming to NC State. “There are lots of different design processes,” he says. “The best practice is hands-on, need-based design.” He now sends teams of BME students to find problems in various clinical settings and then develop solutions.

Sauer’s team, for example, determined that WakeMed Emergency Services needed an efficient, portable way to chill saline for cardiac patients. Research has shown that inducing mild hypothermia shortly after a heart attack reduces the resulting neurological damage. Wake County paramedics have to use separate vehicles with refrigeration units to deliver iced bags of saline when an ambulance responds to a cardiac emergency, Sauer says, and there’s no way to regulate the temperature of the saline as it goes through an IV. The students devised a system in which a chemical reaction in an enclosed cylinder—similar to a first aid cold pack—chills saline as it moves through three metal coils inside. “It was the school of hard knocks. We had to get in there and figure out something that works,” Sauer says. “The problem-solving skills will no doubt help me in my career and in life.”

WakeMed was so impressed with the results of DiMeo’s students that it signed up every NC State team this year and made a donation to BME to defray the cost of supplies for the senior design class. Susan Jackson, WakeMed’s vice president and chief learning officer, says the partnership solves problems WakeMed officials didn’t even recognize, while also giving the hospital system a leg up on hiring talented biomedical engineers. “They’re coming in with new eyes and innovative minds,” she says. “Working together, we can develop practical solutions to health care challenges.”
It may not look like it, but first-year graduate student Ashley Tucker is advancing cancer research as she drops worms into containers with varying concentrations of five experimental compounds. If Dr. John Cavanagh and Nick Valvano are correct, her work also could be crucial to creating a new generation of cancer researchers.

Nick Valvano wanted to honor his brother’s relationship with NC State by doing something different for the future of cancer research.

The V Foundation for Cancer Research, headed by Valvano, has given $1 million to the University to launch the Jimmy V-NC State Cancer Therapeutics Training Program. The program is named in honor of Valvano’s late brother and V Foundation founder, former NC State basketball coach and athletic director Jim Valvano, who died of bone cancer in 1993. The initiative is designed to encourage students to pursue careers in cancer research by involving them early on in interdisciplinary, hands-on studies and allowing them to follow their interests. “Nobody thinks of NC State as a cancer research center because we don’t have a medical school, but we’ve got research faculty in several disciplines looking at every aspect of the disease,” says Cavanagh, a professor of biochemistry and the coordinator of the program.

Cavanagh used that breadth of research expertise and the idea of teaching students to become cancer researchers to pique Nick Valvano’s interest. The V Foundation regularly hands out grants to individual scientists to help advance their work, but Valvano wanted to honor his brother’s relationship with NC State by doing something different for the future of cancer research. He and Cavanagh spent two years devising a program where students as future researchers—not the research itself—were the focus. “My brother would be so excited,” Valvano says, “that someday a breakthrough in how cancer is diagnosed or treated will be developed by a scientist who was involved in this program at NC State.”

Finding a cure for cancer is becoming more difficult even as research advances appear to bring the goal closer, Cavanagh says, because fewer U.S. students are entering the field. The dual obstacles of decreased federal spending—only one in 10 promising cancer research proposals is funded now, compared with one in five in 2002—and tedium in labs have students looking elsewhere for their careers. “If we let them follow their curiosity and find what they’re interested in doing,” he says, “we can actually accelerate research by exposing them more quickly to more things.”

“We have the chance to develop the next generation of researchers.”

The Jimmy V Program achieves that by training high school, undergraduate, and graduate students in the labs of Cavanagh and three other NC State faculty involved in cancer research: Dr. Jon Horowitz, an associate professor of oncology in the College of Veterinary Medicine; Dr. Jon Lindsey, Glaxo Distinguished University Professor of Chemistry; and Dr. Christian Melander, an assistant
professor of chemistry. The students work on research teams with their peers and mentor their younger counterparts as they move from one lab to another. They can conduct their own research projects in the newly constructed Structural and Integrative Biosciences Laboratory in Polk Hall and routinely meet to discuss overall progress and how to proceed. “We’re building a community of researchers,” Horowitz says. “It’s not individual students floundering about as they learn about research.”

Students work on research teams with their peers and mentor their younger counterparts as they move from one lab to another.

Drawing on the expertise of various faculty gives students a broader view of cancer research and a systems approach to solving biological problems. “Battling cancer involves more than just beating back a tumor, and different professors attack the problem differently,” Cavanagh says. Horowitz, for example, is studying skin and prostate cancers in mice and zebrafish to understand the genetic mechanisms of the disease. Meanwhile, Lindsey is working with compounds activated by infrared light that can destroy tumors. Melander is pursuing two paths: studying a class of molecules that could become potent chemotherapy treatments and making molecules to battle the secondary infections cancer patients often contract.

A member of the inaugural class of Jimmy V Cancer Research Scholars, Ashley Tucker is working in Cavanagh’s lab to assist Melander’s chemotherapy project. Her worms are determining whether the compounds he’s developed are toxic and are finding the optimal dose of each compound. Tucker is in the functional genomics Ph.D. program and had planned to study neurodegenerative diseases like Alzheimer’s, but the Jimmy V Program has captured her interest. “You don’t often get to collaborate between labs like this,” she says, “which makes it a really cool project for a student.”

The Jimmy V Program is one of several medical research training programs underway at NC State. Faculty involved in the programs call them a chance to impact science far beyond the findings of their individual research projects. “We have the chance to develop the next generation of researchers,” Melander says. It’s an opportunity Jim Valvano, who urged people to never give up in the fight against cancer, would welcome.
Where some see a park bench in the shade of an oak, Drs. Myron Floyd and Karla Henderson of the College of Natural Resources see an invitation to sedentary activity. Where others see an open, grassy field for a weekend picnic or lying in the sun, the researchers see opportunities for physical activity that are underutilized.

“There’s been a lot of research on physical activity, but little that looks at how parks contribute to that.”

Together with colleagues in the Department of Parks, Recreation and Tourism Management, Floyd and Henderson have created Investigating Places for Active Recreation in Communities (IPARC), a program that studies ways communities can design and manage parks and recreational programs better to promote active lifestyles by youths and adults. “There’s been a lot of research on physical activity,” Floyd says, “but there’s been little that looks at how parks and natural environments contribute to that.”

In a study funded by the Robert Wood Johnson Foundation, which has made ending childhood obesity a top priority, Floyd found that about half of the people visiting Chicago parks and nearly three-fourths of those in Tampa were engaged in sedentary activities. Those numbers relate to how the parks are designed and operated, he says. Tampa’s parks feature more picnic areas and shelters, while Chicago’s have more athletic fields and walking paths. “We don’t characterize them as good parks or bad parks but look only at how conducive they are to activity,” he says. Soccer fields, basketball courts, and walking paths score high, he says, while baseball fields and shelters promote less activity.

IPARC researchers have also found that teens are more sedentary in parks than 6- to 12-year-olds and children are less active when adults are around, reining them in and trying to organize their play. Henderson says parks must meet the needs of these age groups, as well as those of young and older adults, so IPARC hosted a conference last April for parks officials to provide information on how to do it.

The IPARC program studies ways communities can design and manage parks and recreational programs better to promote active lifestyles by youth and adults.

Sharing the research findings should influence public policy discussions on how parks can be built or redesigned with improved public health in mind, Henderson says. She and Floyd point to a 2007 survey by IPARC that found that less than half of North Carolina’s local parks directors felt residents would pay more for parks featuring amenities to encourage activity. “Different groups of people want different things out of parks,” Henderson says. “We hope our research can put the pieces together to help officials configure parks to serve everyone better.”
Putting Active Designs into Play

Good health can be as easy as child’s play, according to College of Design professors Robin Moore and Nilda Cosco. Leading the Natural Learning Initiative (NLI), they work with Swedish scientists to create play areas that encourage plenty of activity for children while limiting their exposure to harmful ultraviolet (UV) rays.

“We could have a generation of children that won’t survive their parents. We believe design can be used as a health intervention.”

More than 15 percent of American children are considered obese, putting them at risk for health problems like diabetes and heart disease. The figure is more than double the percentage of 30 years ago and continues to grow. “We could have a generation of children that won’t survive their parents,” Cosco says. “We believe design can be used as a health intervention.” Getting children outdoors is a key to battling obesity, and outdoors play also helps children develop socially and cognitively, says Moore, a landscape design researcher who founded NLI eight years ago.

As part of a study funded by the National Institute of Environmental Health Sciences, NLI researchers followed preschool children on playgrounds at 30 day-care centers. By combining geographic information system (GIS) technology and handheld devices, the researchers gathered data on exactly where children played and the environmental characteristics of each location. Using evidence from statistical analysis, they can design the most activity-enticing play areas possible. The designs include curvy, exploratory pathways connecting play houses, climbing equipment, and soft-surfaced open lawn areas, all within shady, natural surroundings.

But being outdoors can have health risks as well. Overexposure to the sun at an early age can increase the chances of developing skin cancer later in life, Moore says. Through a colleague of Cosco’s, the NC State researchers linked up with Swedish scientists who were looking at different environments for playgrounds and ways to minimize the risks of UV radiation. Using seed money from the Swedish public health agency, the combined research team is building on Moore and Cosco’s previous GIS-based work.

“The design of the physical world can be managed and manipulated for people’s benefit.”

To design for appropriate sun and shade in playgrounds, researchers monitor the movements of preschoolers and outfit the children with shoulder badges that degrade in sunlight to measure their UV exposure. Moore says the study could help guide public policy to require a certain amount of shaded play area at day-care centers. “Our whole focus is preventive health,” he says. “The design of the physical world can be managed and manipulated for people’s benefit.”
Surgical Robots Take Devices to Heart

As a boy, Dr. Greg Buckner dreamed of becoming a doctor and trying to save people’s lives. “My father was an engineering professor, and he talked me out of a medicine career by convincing me I could do a lot in medicine as an engineer,” he says.

“I’ve always used that argument to guide my research.” By leading a team of NC State researchers that has patented two devices to assist with robotic heart surgeries, the associate professor of mechanical engineering is achieving his dream.

While most patients undergo open-heart surgery to repair a defective mitral valve, a growing number have a procedure that uses remote-controlled robotic instruments—slender mechanical arms inserted through small openings in the ribs—to cause less pain and tissue trauma. Buckner’s interest in the technology led him to observe robotic heart surgeries at East Carolina University—a pioneer in the field—to see how he could help improve the technology.

Although it reduces trauma, using robotic instruments adds about an hour to the valve-repair surgery, which increases the risk of health complications for the patient, disqualifying many from the procedure. Buckner assembled a team that included Dr. Bryan Laffitte, associate professor of industrial design, and Dr. Denis Cormier, associate professor of industrial engineering, to develop devices to shorten the robotic surgery.

One time-consuming aspect is securing a band around the valve to help it maintain its shape, a process that involves tying dozens of knots in sutures. “It’s like tying your shoelaces with tweezers,” Buckner says. Laffitte and his design students dreamed up a device with a rotating disc that allows knots to be tied without having to let go of the suture and grasp it again. Cormier then used his rapid prototyping system to manufacture the device—a dime-sized plastic
cartridge that snaps onto the end of the robotic instrument to tie knots. The NC State team also developed a retractor to expand the interior of the heart enough for surgeons to see what they’re doing and provide more space for the robotic instruments. Surgeons currently have to work a metal plate through the body and prop it up inside the heart. The NC State researchers created a metal rod that the robotic scope can slide into the heart, where four motorized wire wings can quickly unfold to open up the surgical field.

Design students dreamed up a device that allows knots to be tied without having to let go of the suture and grasp it again.

Buckner is lining up clinical trials for the inventions. “These devices have the potential to significantly reduce surgical times,” says Dr. Richard Cook, a cardiothoracic surgeon at the University of British Columbia who helped test them during his fellowship at ECU. “They could make robotically-assisted heart surgery and faster recovery available to many more patients.”
Diabetes Treatment Fits to a T Cell

**Diabetes is the seventh-leading cause of death in the U.S. and is a major contributor to heart disease, blindness, and even leg and foot amputations.** Long before the chronic disease attacks various parts of the body, however, the body attacks itself to cause diabetes. Dr. Paul Hess, an assistant professor in the College of Veterinary Medicine, wants to stage his own attack and destroy the cells believed to be responsible for Type 1 diabetes, which afflicts as many as 3 million children in the U.S.

Type 1 diabetes develops when T cells, white blood cells that normally protect the body from various illnesses, get a signal to destroy cells in the insulin-producing areas of the pancreas called islets. Researchers aren’t sure why the signal is issued, but Hess says there are a couple dozen genetic factors that place some children at higher risk. “About 90 percent of the T cells your body makes are either killed or turned off because they are capable of attacking healthy tissue,” he says. “In some people, these T cells aren’t eliminated or restrained, and they then ignore all of the body’s signals that say, ‘Don’t do this.’”

**Type 1 diabetes develops when T cells get a signal to destroy cells in the insulin-producing areas of the pancreas.**

Most of Hess’ research has been in oncology, but he says diabetes treatments offer him a look at “the opposite side of the coin” from cancer. Tumors are usually ignored by the body’s immune system, he says, while an autoimmune disorder involving T cells causes Type 1 diabetes. “To develop a cancer vaccine, you need to overcome the body’s tolerance of tumor cells,” he says. “Conversely, you need to promote tolerance of healthy tissue to defeat diabetes.”

A synthetic molecule known as a tetramer can deliver a toxin that knocks out the rogue T cells.

Type 1 diabetes. The best way to do that is to target the rogue T cells. With funding from the Juvenile Diabetes Research Foundation, Hess used a synthetic molecule known as a tetramer to deliver a toxin that knocks them out. The four proteins that form the outer surface of the tetramer can be directed to bind to specific T cells. Saporin, a protein that shuts down cellular activity, is then inserted into the cell’s middle. Tests in mice have shown that diabetes-causing T cells that are targeted by the tetramer take in the saporin and are killed, delaying the onset of the disease.

Hess is working with an immunologist from UNC-Chapel Hill on a National Institutes of Health grant to identify the specific type of T cell that attacks the pancreas. “There is a mixture of T cells in the islets, and there’s good evidence that one type gets the process started and then enlists the others to join in the attack,” he says. “We need to find the real culprit to protect children from this debilitating disease.”
With over 70% of faculty members engaged in externally funded research, NC State saw its research proposals and awards grow 11% in 2007-08—to over $213 million. The University’s sponsored research is the key to its excellence in education, discovery, and economic development.


For more detailed information about graduate programs, please visit [http://www.ncsu.edu/grad/faculty-and-staff/facts.html](http://www.ncsu.edu/grad/faculty-and-staff/facts.html).

### 2007-08

**Sponsored Research**

- Proposals Submitted: 2,851
- Awards Received: 1,909
- Grant and Contract Dollars Requested: $713.0M
- Grant and Contract Dollars Awarded: $213.7M
- Grant and Contract Research Expenditures: $366.1M
- Recovered Indirect Cost Expenditures: $29.5M

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### Inventions, Patents and License Agreements

- **License Agreements**: 153
- **Invention Disclosures**: 73
- **US and Foreign Patents**: 47
Where NC State Ranks

- 9th in total research expenditures among public universities without medical schools, NSF, 2007
- 4th in industry research funding among universities without medical schools, NSF, 2008
- 6th in best overall public university value, Princeton Review, 2009
- 11th among American public research universities without medical schools, The Center for Measuring University Performance, 2007
- 111th in the Top 500 World Ranking, Center for World-Class Universities, 2008

* All graduate students, including Doctors of Veterinary Medicine and distance education enrollment, as a percentage of total student enrollment

Fall 2008 Graduate Enrollment by College*
Degrees Awarded 1999-2008

Fall 2008
Graduate Enrollment

2007-08 U.S. Minority
Graduate Enrollment*

*All graduate students, including Doctors of Veterinary Medicine and distance education enrollment.
On the cover: Health and wellness is one of seven challenges on which NC State and the UNC System are focusing their education, research, and outreach efforts in the coming years. NC State looks at health holistically, producing groundbreaking research in systems biology, pharmaceuticals, nutrition, biomedical engineering, comparative (animal-to-human) medicine, medical textiles, and accessibility for people with disabilities.