Dear Friends of SUNY Downstate,

I am pleased to share with you our inaugural issue of Downstate Research. Research is one of the central missions of an academic medical center. It is an area in which Downstate has excelled in the past, in which it is continuing to make important and exciting advances, and to which it is committed in the future.

In these pages, you will read about some of the current research being conducted at SUNY Downstate Medical Center. From women’s health to understanding the working of the human brain, to the molecular basis for heart disease and cancer, Downstate scientists are exploring the basic ways in which the human body works and applying what they have learned to meet the most daunting clinical challenges. The array, distinctiveness, and breadth of research at Downstate is impressive – but equally impressive is the talent and dedication of the faculty, staff, and students who engage in it.

The individuals and the research profiled in these pages are exceptional. They are also representational. At SUNY Downstate, every college, school, and academic program offers faculty and students the opportunity to engage in research. It is part of who we are and, most importantly, why we are. I applaud all who contribute to Downstate’s research efforts. I want to thank especially all those donors whose philanthropy helps support us.

As befits a great academic medical center—and sometimes against large obstacles—Downstate provides its researchers with support, encouragement, and the tools needed for success. The future holds the promise of enormous strides. I am confident that Downstate will play a major role.

Very truly yours,

John C. LaRosa, MD, FACP
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Every year, almost 30 percent of deaths worldwide are caused by cardiovascular disease—heart attack, stroke, high blood pressure, heart failure, and rheumatic heart disease. The causes and treatments of these illnesses are sometimes relatively straightforward. Proper diet and exercise can prevent a great deal of heart disease, as can abstaining from smoking and keeping one’s weight at the appropriate level. Sadly, these practices alone cannot stop the world’s and the nation’s number-one killer.

That is where Downstate’s internationally renowned cardiovascular research faculty comes in. Scientists are studying the basic molecular processes of cardiac muscle cells and atherosclerosis, with the ultimate goal of uncovering new therapies for heart disease. Among their concerns: how does the body process lipids and triglycerides, both major contributors to obesity and hardening of the arteries; what causes, and what can cure, atherosclerosis; and how can cardiac hypertrophy—the pathological enlargement of the heart—be understood, stopped, and reversed. The answers these researchers find are certain to make inroads into understanding and curing the world’s largest health problem.
THE HEART OF THE MATTER: expanding medical science’s knowledge of the cardiovascular system
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After three days in the hospital, Dr. Siddiqui was diagnosed with “a simple gastrointestinal problem,” he says, not the cardiac disease he feared.

Up until that point, most of Dr. Siddiqui’s research had been in the area of protein synthesis—how cells use DNA and RNA to create proteins that serve different biological functions. But after his experience of severe chest pain, he says, “I became interested in the more clinical aspects” of heart disease.

Since then, Dr. Siddiqui and his collaborators have made significant contributions to medical science’s understanding of how cardiac genes function and are regulated. He has discovered key molecular pathways that govern the development of cardiac hypertrophy—enlargement of the heart—as well as the development of cardiac ischemia, a diminution in the heart’s blood supply. It is Dr. Siddiqui’s belief that this basic research will aid in the development of better medications for those two prevalent conditions.

“Right now, if you look at how these pathways work,” he says, “you can develop antagonists, you can develop inhibitors, you can develop activators—all chemical compounds that could potentially be quite useful.”

The heart is a muscle. Under increased strain, it grows. But not by creating new cells. Rather, heart cells increase in size. That process, called hypertrophy, can either be adaptive—appropriate and beneficial—or maladaptive and pathological, causing disease.

“One type of hypertrophy—adaptive hypertrophy—is in response to work overload on the heart,” he explains. “It is the heart’s adaptation to sustain the work demand.” Weight gain, artery blockage, and high blood pressure can all
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increase the demands placed on the heart. “But when the work demand becomes chronic,” Dr. Siddiqui continues, “the heart cannot adapt anymore and the type of hypertrophy that develops is called pathological hypertrophy.” Chronic over-taxing of the heart “leads to heart failure,” Dr. Siddiqui explains.

The problem is a significant one. In the United States alone, an estimated 5 million people suffer from heart failure as a result of pathological hypertrophy. In trying to understand the mechanisms that create this problem, Dr. Siddiqui and his collaborators have gone back to the genes involved in the development of the heart. “In the patient, there is enlargement of the heart muscle cell” he explains, “which is accompanied by a change in the pattern of gene expression.”

One of the things that occurs, Dr. Siddiqui says, is that “specific genes are activated to make new proteins to meet the increased work demands on the heart.” By discovering the molecular pathways that activate these changes, Dr. Siddiqui and his collaborators have laid the groundwork for life-saving new drugs. “Finding a medication that will inhibit the activation of a particular signaling pathway could allow us to reverse the effect of other stimuli and potentially inhibit cardiac hypertrophy,” he says.

Dr. Siddiqui believes this work could be significant for those who suffer from cardiac enlargement. “It is far away, but it could lead to developing an anti-ischemic, cardioprotective agent,” Dr. Siddiqui says. “This has great promise.”
In the United States alone, almost 700,000 individuals each year die from atherosclerosis and related cardiac problems.

In China, too, atherosclerosis is a major killer, one that felled researcher Xian-Cheng Jiang’s father at a young age. “It was very quick,” Dr. Jiang, associate professor of anatomy and cell biology, recalls. “This is my motivation to study this problem.”

Atherosclerosis results, in large part, from the build-up of lipids—fats and fat-like materials—in the bloodstream and along the artery walls, causing blockages and life-threatening deposits known as plaques.

Dr. Jiang’s research into the subject of lipid metabolism, from lipids’ beginnings in the digestive system through their elimination, may lead to new drugs that can treat atherosclerosis and may help individuals currently unaided by the popular cholesterol-lowering statin compounds. With great enthusiasm, Dr. Jiang says, “We are trying to find a new drug target.”
Many lipids are familiar from discussions in the popular press—HDL and LDL cholesterol (the good kind and the bad kind, respectively), as well as triglycerides, which are simply fats.

But as a biochemist, Dr. Jiang understands that these well-known lipids are not the sole source of the problem. “Some people have normal cholesterol levels, but they still suffer from atherosclerosis,” he explains. “In other words, there is another mechanism; other lipids are involved in the process.”

These other lipids, including sphingomyelin and a phospholipid called phosphatidylcholine, are what Dr. Jiang studies. To get a sense of just how important these lipids are in the development of atherosclerosis, Dr. Jiang and his colleagues compared sphingomyelin levels in 600 chest-pain patients. Those whom doctors determined had stenosis, a plaque-induced narrowing of the arteries, had significantly increased sphingomyelin levels compared to those without stenosis.

“So the real question is, ‘why?’” Dr. Jiang asks. What elements of sphingomyelin metabolism lead to hardening of the arteries?

Using bioengineered mice, Dr. Jiang has studied the five-step process of sphingomyelin formation. Already, he and his colleagues have identified a drug that, at least in the mouse population, acts on the first part of the process, lowering levels of circulating sphingomyelin. “We found a dramatic decrease due to the inhibition of biosynthesis,” Dr. Jiang says. “Also, we found that atherosclerosis in these mice is dramatically decreased.”

Dr. Jiang says he and his colleagues still have much work to do in understanding sphingomyelin metabolism. Could an intervention closer to the end of the five-step process offer better results? This is, after all, a complex research area.

As are the other areas Dr. Jiang is exploring: molecular communication between lipids, which researchers call “cross-talk,” and phospholipid metabolism. “We find that in cardiac cases, a protein called plasma phospholipid-transfer protein is increased,” Dr. Jiang notes. He hopes he and his colleagues can develop communication inhibitors that stop the development of life-threatening plaques.

“The immediate goal,” he says, “is drug discovery.”
Lipid researcher Mahmood Hussain, PhD, professor of anatomy and cell biology, is concerned about how fat we are. And with good reason.

According to the World Health Organization, since 1980 obesity has risen threefold or more in major parts of the globe. Three hundred million of the world’s people are currently obese; an additional 700 million are overweight. That’s 15 percent of the world’s population.

Here in the United States, the numbers are even more staggering. Thirty percent of the adult population aged 20 and over is obese—some 60 million Americans. Another 35 percent of the population—70 million—is overweight.

The costs, both in terms of human health and hard, cold cash, are similarly astounding. Obesity is linked to increased risks of type II diabetes, heart disease, stroke, respiratory problems, and cancers of the breast, colon, and endometrium. According to a 2004 study, obesity accounts for more than 9 percent of all medical expenditures in the United States—$92.6 billion a year, in 2002 dollars.
Toward the end of preventing and treating obesity, Dr. Hussain studies the way the body processes fats. “We are looking at the very early steps—when we eat, what happens,” Dr. Hussain explains. In particular, he says, “most of my work is in lipids [the fatty compounds known as triglycerides and cholesterols] and lipoproteins [fat-transporting protein particles].”

From a scientific point of view, Dr. Hussain says, when attempting to combat the problems of obesity, it makes sense to explore how fat enters the body. “Our major interest is how lipids get into the intestinal cells”—the place from which they begin to become digested—“and how they are packaged into the lipoproteins called chylomicrons, which are made in the intestines.” He and his colleagues are conducting research into the basic science of this. “Because if you can control this, you can control the amount of fat getting into the body.”

Dr. Hussain and his colleagues have broken the process of lipid absorption and processing into a few basic steps. “We’re trying to understand the different molecules involved so that we can target them,” Dr. Hussain says. What he has found is that two molecules—one called apolipoprotein B and another called microsomal triglyceride transfer protein, or MTP—are essential in moving lipids out of the intestinal cells and into the bloodstream.

Ideally, Dr. Hussain would use his research to help develop a lipid blocker that would stop fat from being packaged in intestinal cells. The benefits could be twofold. It would assist in solving the problem of lipid build-up in the arteries, a major cause of heart disease. “If you can block cholesterol uptake in the intestines, you may not even need the statins,” he says, referring to the widely prescribed cholesterol-lowering drugs.

While some drug companies are currently at work on compounds that block fat absorption, those drugs have unpleasant side effects. “If we can come up with some ways of controlling this without causing gastric side effects, it will be great,” he says.
Cogito ergo sum—I think, therefore I am. In the 17th century, when philosopher René Descartes wrote his famous phrase, the workings of the mind—of learning, of memory, of thought—were the subject of much speculation but little empirical investigation.

In the three and a half centuries since, science has made tremendous strides in understanding the workings of the human brain. Nevertheless, the processing of information, the imprinting of memory, the ebb and flow of emotion remain, as one researcher has said, the “last, great frontier.” At SUNY Downstate Medical Center, more and more of that unexcavated territory is charted every day. How is memory encoded? Can human thought processes guide machines? What causes Alzheimer’s disease? Is mental illness the result of neuronal misfiring?

Internationally renowned for their research in learning and memory, Downstate faculty are pioneers in exploring these questions and more, and in bringing new understanding to the brain, its functions and disorders.
memory and learning
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Four and a half million Americans suffer from Alzheimer’s disease—memory impairment, disorientation, and loss of ability to learn—that can lead to profound personality changes, agitation, and inability to care for one’s self.

Though first described a century ago in Germany by Dr. Alois Alzheimer, much about the disease still remains a mystery. Helping to unravel this mystery is Suzanne Mirra, MD, PhD, professor and chair of pathology.

Dr. Mirra, an internationally recognized neuropathologist, has been a pioneer in the field of Alzheimer’s research. She led neuropathologists in an NIH-sponsored, multi-center study standardizing the way in which Alzheimer’s disease is diagnosed. Her lab was one of the first to identify the microtubule-associated protein tau as the major component of the neurofibrillary tangles, a hallmark of the disease seen under the microscope in the brains of Alzheimer patients.
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Dr. Mirra’s initial interest in Alzheimer’s disease was piqued by one of her medical students at Emory University in Atlanta. Later, several family members developed the disease, further strengthening her commitment to study this devastating disorder.

Upon her arrival at Downstate eight years ago, Dr. Mirra was excited to learn of the work of neurologist Todd Sacktor, MD, involving a critical memory molecule known as protein kinase M zeta. “It seemed logical to explore the role of this protein in the commonest disorder of memory—Alzheimer’s,” says Dr. Mirra.

Their collaboration, which included MD/PhD student John Crary and neuropathologist Charles Shao, MD, PhD, has led to some exciting findings. The investigators found PKM zeta in neurofibrillary tangles in Alzheimer brains. Especially intriguing was the discovery that the protein was restricted to tangles in the limbic system, a region of the brain associated with memory.

Moreover, while it is common to find a few tangles in the brains of elderly individuals who don’t have Alzheimer’s disease, PKM zeta was not found in tangles from normal elderly. These data argue for a critical role of PKM zeta in the memory impairment associated with Alzheimer’s disease.

“The collaboration with the Sacktor lab has been especially satisfying—perhaps because it represents the merging of different disciplines, with each scientist making a unique contribution,” says Dr. Mirra. She and her colleagues are encouraged that their work may lead to new therapeutic strategies for the treatment of Alzheimer’s disease.
Why do we remember? What causes things to stick in the brain, or, conversely, to fall away from consciousness?

These are questions that have always fascinated neurologist Todd Sacktor, MD, professor of physiology and pharmacology. As a boy, he read everything he could about neuroscience and even tried, with limited success, to perform a memory experiment on his 3-year-old brother.

Dr. Sacktor has used this life-long fascination to become an international leader in the field of memory research. His most important discovery—that a single enzyme called protein kinase M zeta (PKM zeta) is the molecule that fixes memory in the brain—may have wide-ranging implications. Dr. Sacktor’s efforts to understand memory may change the way we think about the complex subject and revolutionize many of the ways medical science treats its disorders.

“What is it in the brain that is storing information?” That is a question that Dr. Sacktor has pursued for more than two decades. Most of Dr. Sacktor’s initial work has been on a process called long-term potentiation—the mechanism by which connections between brain cells are strengthened, and which is widely considered the physiological basis of memory.
“Each brain cell is hardwired, probably through evolution, to be connected to certain other brain cells,” Dr. Sacktor explains. This is why the brain has a propensity to store visual information, for instance, in the back of the brain. Or to store decision-making information in the front.

The more individual connections are reinforced, the stronger they become, and the more intensely they are remembered. The question of memory, Dr. Sacktor explains, really boils down to: “What is the basis for the permanent enhancement of these connections? What is the molecule that causes it?”

In 1993, Dr. Sacktor found what many neuroscientists now believe to be the answer to that question: an enzyme called PKM zeta. “Its unique structure allows the enzyme to be persistently active, thus sustaining increases in the strength of the synaptic connections between neurons, and causing long-term increases in the response to the same stimuli.”

Dr. Sacktor’s discovery will likely have wide-ranging implications, particularly in the area of Alzheimer’s disease. The degenerative brain disorder afflicts 4.5 million Americans, at great personal and financial cost—$100 billion annually in the United States alone. Working with SUNY Downstate’s chairman of pathology, neuropathologist Suzanne Mirra, they found PKM zeta in the neurofibrillary tangles that are the hallmark of Alzheimer’s disease.

Says Dr. Sacktor, “We asked a very simple question: ‘Is this molecule screwed up in the brains of Alzheimer’s disease patients?’ And the answer is, it is.”

The mechanism for memory loss in Alzheimer’s disease may be the binding of PKM zeta to the neurofibrillary tangle, he explains. Blocking that binding process through new drug treatments or other interventions may help stop memory loss in those with early symptoms of Alzheimer’s. “This would be an entirely new way to approach the problem,” Dr. Sacktor says.

The neuroscientist’s work with PKM zeta may also be instrumental in developing new treatments for the shattering chronic pain syndrome known as reflex sympathetic dystrophy (RSD). In RSD, researchers believe, the nervous system constantly re-experiences—replays—the pain first felt during a simple trauma, such as a fall, a bone break, or minor surgery.

Using information about how PKM zeta works, one could potentially “flip all those pain pathways from being supersensitized to being normal,” Dr. Sacktor says.

Dr. Sacktor likens his work to the field of computer science. “What we are studying is the hard disk,” he says.

“We are trying to figure out how the zeros and ones are stored—the physical substrate of memory. Once you understand that,” he says about his field of neuroscience, “a great many other emergent properties of the brain will follow.”
André Fenton, PhD, assistant professor of physiology and pharmacology, has always been interested in the big questions. At McGill University in Montreal, he started off as a philosophy student, wondering about the mind-body problem and the nature of experience. “What fascinated me and still fascinates me is whether experience is in any way objective,” Dr. Fenton says.

But neurobiology, the study of the brain’s inner workings, captured his attention after he sat in on a couple of lectures about the subject. “I became fascinated by what neurobiologists could do: namely, answer some of those philosophical questions I’d been interested in, but using methods that actually gave some notion of what the true answer might be.”
Such intellectual pursuits might strike some as navel-gazing. But Dr. Fenton and his collaborators are turning their curiosities toward some of the most pressing and compelling problems of our time: mental illnesses, such as psychosis, schizophrenia, and autism; and nervous-system dysfunctions, such as chronic, debilitating pain syndromes. The answers they have begun to find may offer hope to those whose lives have been mired in physical and emotional pain.

Dr. Fenton starts his research with a novel premise: that understanding how the brain makes sense of, categorizes, and retrieves information can lead us to better comprehend mental function and improve treatment of mental dysfunction. Toward that end, Dr. Fenton and his labmates study how rats store and make sense of external information.

“We all have lots of experience stored in our brain cells,” Dr. Fenton explains. “And we have a very good ability to selectively activate certain types of experiences or certain types of memories or knowledge and keep suppressed all the other stuff that’s inappropriate. How do we do that? That’s what I’m interested in understanding.”

Dr. Fenton and his graduate students have been finding out by studying the firing of neurons in rats’ brains. What they have discovered is that in rats, the brain functions much like a multi-tasking computer, first devoting a small slice of attention to one subject, and next to another. Dr. Fenton speculates that this is how human brains function as well.

This theory may offer insight into the problem of brains that function, as Dr. Fenton says, “improperly.” What if, rather than firing in sequence, certain neurons fired simultaneously? “If they’re not working right, we’ll get a mixing of patterns that are inappropriate—like my grand-mother with Cleopatra, or, in the case of a schizophrenic, the CIA with a radio.”

Dr. Fenton contends that psychosis or schizophrenia, even autism, might be caused by “not being able to keep neural patterns separate,” by neurons firing together that are not supposed to fire together. In a recently published paper in the *Journal of Neuroscience*, Dr. Fenton and his colleagues reported that injecting a toxin that caused the coupling of unrelated brain cells resulted in “cognitive disorganization” in affected rats.

Such knowledge may allow researchers to develop more accurately targeted drugs to treat the mental problems that devastate millions worldwide. “We can try and invent drugs that will prevent precisely that problem of neurons firing together when they shouldn’t,” Dr. Fenton says. “Which is quite a different way of trying to invent an anti-psychotic.”

In collaboration with pioneering Downstate neurology researcher Todd Sacktor, MD, Dr. Fenton has also turned his attention to the issue of how memory is stored. Surprisingly, this question impacts on the problem of certain chronic, debilitating pain syndromes.

Researchers believe that in some pain syndromes, the nervous system is not experiencing new pain but rather re-experiencing the memory of earlier pain. With Dr. Sacktor, Dr. Fenton has begun testing a theory about how memory is encoded in the brain and might possibly be removed from the brain. Their initial findings bear out their hypothesis. “This is very, very exciting, with huge implications,” Dr. Fenton says. “One can now work toward interfering with memory in a targeted way.”

Indeed, for the hundreds of thousands of chronic pain sufferers, the results found in Dr. Fenton’s and Dr. Sacktor’s labs might eventually heal not just their nervous systems, but their lives as well.
Training a new generation of neuroscientists is an important part of Dr. Fenton’s work. Though he teaches his students a host of technical skills—how to use tetrodes for recording electrodes, how to design computer programs to best record their experiments—perhaps the most important skill Dr. Fenton teaches is how to approach a scientific problem.

“With André, it’s not just ‘I’m giving you a project—do it,’” says PhD student Hsin-Yi Kao. “He always asks me, ‘Why are we running this experiment? What kind of questions are we asking?’”

That know-how will not only make Dr. Fenton’s graduate students better scientists, it will spread Downstate’s influence in the scientific world.
To John Chapin, PhD, professor of physiology and pharmacology, the brain is the most important thing. It is what makes us what we are, but how does it work? Though the brain has been considered as a kind of computer, it is much more powerful because it is intelligent. It can instantly recognize subtle expressions in a human face, coordinate the fine movements of a gymnast, and even appreciate art. Why are brains so much smarter? If we could answer that question, we could make better robots, cure neurological diseases, and understand our own behavior.
In the 1980s, many scientists thought that information in the brain was stored in single neurons, just as bits of information in a computer are stored in tiny transistors. Dr. Chapin, however, proposed that information in the brain is not stored in single nerve cells, but instead is distributed across millions of them.

To prove this idea, he developed a method for implanting arrays of electrodes in the brains of rats, allowing him to record the signals from each of a large number of nerve cells simultaneously. This completely changed the way neurophysiologists did their experiments. Previously they would record information from one neuron at a time and then average across many trials. Now they could record from so many neurons simultaneously that they could extract clear and accurate information from the brain in real time.

This approach has proved to be useful not just for understanding how information is processed in distributed brain networks, but also for helping people with paralyzing brain diseases such as spinal cord injury and Lou Gherig’s disease (ALS).

In 1999, Dr. Chapin and his colleagues were the first to use this multi-neuron recording method to extract “motor commands” from the brains of experimental animals, allowing them to directly control the movement of a robot arm, “by thought alone!” as reported by the BBC. This demonstration has since spawned the new science of “brain-machine interfaces (BMIs)” and with it, a whole new area of biomedical technology. Scientists and corporations around the world are now working on various methods to use brain interfaces to restore motor function in paralysis victims.

Meanwhile, Dr. Chapin’s lab is going to the next level by developing another brain interface that will restore the sense of touch to patients with spinal cord injuries who have lost both motor and touch-sensory function. This involves using electrodes to stimulate regions in the brain involved in perceiving touch and arm position. Recent experiments suggest that such stimuli do indeed produce perceptions of touch or arm movement. When this “somatosensory prosthesis” is fully developed it will be combined with a motor prosthesis (BMI), and patients with spinal cord injuries may be able to use their brains not only to directly control a robot arm (or their real arm) to reach and grasp a cup of water, but also to “feel” that cup.

In the process of developing this sensory prosthesis, Dr. Chapin stumbled on another innovation that could have profound implications in law enforcement and national security.

While studying whether rats can “feel” as if their whiskers are being touched when an electrode stimulates their cortical whisker area, Dr. Chapin found that such stimuli can not only be felt, but can be used to train the rat to go left, right, or straight—just as a rat would turn to the right if his right whisker were touched. When Dr. Chapin and colleagues put a wireless brain stimulator and video camera on a rat’s back, they found that the rat could be remotely guided through virtually any indoor or outdoor space that a rat can enter. Finally, they trained the rats to use their highly acute sense of smell to detect explosives.

As a result, a project originally intended to benefit paralysis victims has now yielded a novel technology that can be used to help find victims buried in rubble caused by a natural disaster or terrorist attack.
Second only to cardiovascular disease, cancer is among the leading causes of death in the United States. Around the globe, it is responsible for 13 percent of all mortality, having caused 7.6 million deaths in 2005, with numbers projected to rise to 9 million deaths in 2015 and 11.4 million deaths in 2030, according to the World Health Organization.

Despite these figures, there is great optimism in the field of cancer research today. Recent breakthroughs in the understanding of how cancers develop and spread have led to the beginnings of a new age for cancer treatment, with innovative screening and diagnostic techniques and unique, tailored treatments that combat specific molecular problems, rather than attempting to kill all fast-growing cells indiscriminately.

At SUNY Downstate Medical Center, researchers are making similar strides, not just in understanding the basic science of cancer, but also in translating that knowledge into clinical practice. Researchers are exploring the inner workings of the human immune system implicated in lymphomas and leukemias. They are investigating tumor suppressors and activators, attempting to understand liver cancers among those chronically infected with hepatitis C, and, using tailored treatments, they’re offering startling results in laboratory animals.

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UNRAVELING THE CRAB: bringing cancer research into a new era
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Indeed, at Downstate, researchers are ushering the much hoped-for future of cancer prevention and treatment directly into the present.
So says molecular biologist Miriam Feuerman, PhD, associate professor of biochemistry, an internationally recognized researcher in the field of liver regeneration.

For years, Dr. Feuerman has been involved in painstaking research into the basic science of liver growth and the cancer-causing disruptions that occasionally mark the liver’s growth pattern. Now, in collaboration with clinicians at Downstate’s University Hospital of Brooklyn, she’s taking her knowledge “from the bench to the bedside,” in an effort to understand why individuals on methadone maintenance who are infected with the hepatitis C virus (HCV) appear to have lower liver-cancer rates than those who don’t take methadone.

The potentially protective effect of methadone is a curious finding that, on its face, might not seem particularly earth-shattering. But only to people without a clear understanding of liver cancer and of one of its primary causes, HCV. In the United States alone, liver cancer causes 3 percent of the total number of cancer deaths among men. Anywhere from 2.7 million to 5 million Americans suffer from chronic HCV infection. Of those, between 1 and 5 percent will die of HCV-induced hepatocellular carcinoma. Worldwide, as many as 200 million people—a staggering 3.3 percent of the world’s population—have contracted the disease.
MIRIAM feuerman
Dr. Miriam Feuerman with two of her MD/PhD students: James Park and Eric Anderson. Both have already received their PhD degree and will graduate from medical school in May 2006.

“I’VE ALWAYS BEEN INTERESTED IN CANCER.”

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Understanding and locating the cause of methadone’s potentially preventative effects could lead to life-saving treatments. “The potential for this research is big,” Dr. Feuerman says, with some understatement. “We just have to get on it.”

The liver is the ideal organ to study for someone who has always been interested in cancer, Dr. Feuerman says. That is because the liver is unique in its ability to replicate itself—to regrow—after trauma, surgery, or exposure to toxins. Imagine a section of kidney or intestine removed during surgery. The wound heals, but the part removed will forever be missing. The liver, on the other hand, can reproduce itself almost entirely.

“What attracted me to using the liver as a model for cancer was that you could think of regeneration as a normal growth process and cancer as a growth process gone a little bit berserk,” Dr. Feuerman explains. Finding what is different in the two processes might help explain liver cancer and perhaps other cancers as well.

In her lab, Dr. Feuerman has endeavored to do just that. With collaborators, she identified a heretofore unknown gene called MCM8, which is implicated in the complicated mechanism of tumor growth. Now, instead of looking at the liver and the way its genetic material creates building blocks for both normal and deranged cells, Dr. Feuerman and her Downstate colleagues, Drs. Nora Bergasa and Cherif El Younis, will take a new tack. Rather than looking at the liver itself, they will explore the protective effects of an external substance, methadone.

In this exploration, there are once again complicated questions of molecular biology in play, some of which Dr. Feuerman translates into more understandable English: “How is it that exposure to methadone influences the development of liver cells and the cell division property of those liver cells?” she asks.

The answers could save millions of lives.
The protein molecules cancer researcher Stacy Blain, PhD, assistant professor of pediatrics and anatomy and cell biology, is interested in share an unusual quality: both function sometimes as tumor suppressors and other times as tumor activators.

“That wasn’t my original reason for studying them,” Dr. Blain says. “I’m interested in these proteins because they are multifaceted, as cancer is.” Indeed, with the goal of helping better diagnose and treat breast cancer and other malignancies, the molecular biologist has focused on two “Janus-like” compounds (Janus was a Greek god who had two faces)—one a gene called p27 and another a protein called TGF-beta—both of which may be implicated in the vast majority of human cancers. For instance, p27, found always in normal cells, appears to be missing in 60 percent of all carcinomas. TGF-beta, which is involved in several biological processes, such as involution (tissue repair and immune modulation), can arrest tumor growth or promote it.

“These molecules are master regulators,” Dr. Blain notes. “That makes them more interesting from a scientific point of view and potentially more rewarding from a clinical perspective.”

In order for cancer cells to develop and replicate, they need to pass through a series of regulatory checkpoints and roadblocks, one of which is p27. When working properly, it halts a cancer cell’s progress. But when something is awry, p27 waves the potentially malignant cell through to the next checkpoint.
Often “checkpoint” problems come in the form of genetic mutations, Dr. Blain observes. Indeed, genetic mutations cause most tumor-suppressor problems. But something odd happens when p27 malfunctions. “Very rarely do you find mutations in p27 at the genetic level,” she explains. “Usually, it’s made properly but it’s degraded. Or it’s put into the wrong compartment of the cell—it’s present in the cytoplasm when it should be in the nucleus.”

That malfunction serves not only to promote cancer, but also, interestingly, to identify its most aggressive forms. “In breast cancer,” Dr. Blain continues, “the loss of p27 appears to correlate very closely with poor prognosis.”

Dr. Blain believes p27’s most immediate use is as a prognostic marker for women with breast cancer, especially for the majority, whose cancer has not yet spread to the lymph nodes. “In 30 percent of these women, the cancer recurs within five years,” Dr. Blain notes. But because medical science doesn’t yet know which 30 percent are at greatest risk, many women who don’t need it receive unnecessary and potentially harmful chemotherapy and radiation treatment.

Dr. Blain says, “If we could screen for p27, and you didn’t have any, the clinicians could probably tell you ‘You have a very bad cancer and we need to treat it aggressively.’” Women whose tumor tissue showed high p27 levels might be spared additional therapies. Likewise, the gene might serve as a treatment target itself. “Because it’s not mutated,” Dr. Blain says, “it may be more conducive to therapeutics.”

TGF-beta is another compound with a complex action. “Our body makes and uses it all the time to control almost all cellular processes,” Dr. Blain observes. Functioning normally, TGF-beta not only stops cell division, it also promotes the destruction of cells the body no longer needs. But when malfunctioning, Dr. Blain says, “it causes cancer cells to become mobile and leave the primary tumor,” resulting in metastasis. Dr. Blain recently received a grant from the Susan G. Komen Breast Cancer Foundation to study whether the TGF-beta signaling pathway might be harnessed to treat or even prevent breast cancer metastasis, the cause of more than 333,000 annual breast-cancer deaths worldwide.

“This is a long way away,” Dr. Blain says about the possible fruits of her research. “But you’ve got to think big.”
Christopher Roman, PhD, assistant professor of microbiology and immunology, wants to understand how your immune system works. Not just how it works, but what can go wrong with it.

“T-cells are the mastermind cells of the immune system. And what we have developed is a line of research that tries to understand how T-cells’ biology is regulated,” says Dr. Roman. “That is, how their involvement in immune response is controlled.”

The immune system is elaborate, almost military in structure, with chains of command and separate battalions organized around specific tasks. “Normally, in the immune system, there are these alarms that are caused by foreign invaders,” Dr. Roman explains. “That gets the T-cells going and the T-cells garner the troops.” Other types of white blood cells, Dr. Roman says, “do the ‘dirty’ work of recognizing the mess, cleaning it up, and eventually clearing it from the body.”

In particular, Dr. Roman is interested in a molecule that T-cells make called CD40 ligand. “What this molecule does is endow other cells with the power to kill or to do something to get rid of infection,” he says.

“YOU’RE NOT JUST ASKING ‘HOW CAN I MAKE THIS PATIENT BETTER?’ BUT, ‘WHAT’S CAUSING THIS DISEASE?’”
Because of the immune system’s integral involvement in so much of human health, its dysfunctions can cause severe, often life-threatening diseases—rheumatoid arthritis, lupus, and multiple sclerosis, to name just a few. In the United States alone, an estimated 14 to 22 million people suffer from autoimmune disorders.

“If we learn more about what tells T-cells do to make CD40 ligand, then we can come up with strategies to intervene,” he says. “There are lots of illnesses where this might play a role, like Crohn’s disease, inflammatory bowel disease, and atherosclerosis. CD40 ligand has even been implicated in Alzheimer’s disease.”

According to Dr. Roman, immune disorders are often caused by T-cell malfunctions. “Either the T-cells don’t send out any instructions, they don’t send out the right instructions, or they send out instructions all the time.” They identify something that is internal to the body as foreign and fight it constantly.

That is what happens in the case of rheumatoid arthritis and lupus. “CD40 ligand gets made when it is not supposed to be—in the absence of infection—and drives the development of B-cells [another type of infection-fighting white blood cell] that make self-reactive antibodies. These auto-reactive complexes are actually what is dangerous.”

Dr. Roman and his collaborators have not limited their investigations to CD40 ligand, however. They are also exploring other aspects of immune functioning: “We are trying to understand where B-cells come from,” he says, matter-of-factly. These major players in the immune system share a common ancestor with T-cells, but serve a vastly different function, Dr. Roman explains. “B-cells make special molecules, antibodies, that coat foreign material and allows other killer cells to glom on to microbes and destroy them.”

Dr. Roman’s research may also lead to new understandings of white-blood-cell cancers—lymphomas and leukemias. “Many of the processes that we study that control lymphocytes-developmental decisions are actually deranged in cancer,” he says. “We are studying the normal process to learn how it can get messed up.”

For Dr. Roman, whose interest in the functioning of the human body began in childhood, investigating the immune system’s minute workings is a source of constant fascination. “I have a natural curiosity about how things work,” he says. And there is an even greater reward for his work: “With the information we generate, we can hopefully get new ways to treat immune system diseases.”
“OUR PRIMARY INTEREST WAS IN ADDRESSING PROBLEMS WITH RAS-P21. THIS PROTEIN HAS BEEN IMPLICATED IN ONE OUT OF THREE HUMAN CANCERS.”
Pathology professor Matthew R. Pincus is curing mice of cancer, using bioengineered peptides, parts of a protein called p53 that control cell division. And not just mice that are a little sick, but mice whose bodies are riddled with human pancreatic tumors.

What is so impressive about the results of Dr. Pincus’s research is that of all human cancers, pancreatic cancer has the worst prognosis. Almost 34,000 Americans will be diagnosed with the disease in 2006; only 24 percent will live out the year, and fewer than 5 percent will survive for five years after their cancers were first detected. In mice implanted with human pancreatic tumors, the outlook is similarly bleak.

Yet Dr. Pincus’s mice are fine, he says. Not only are they tumor-free, but “their weight gain is exactly what you’d expect in a normal mouse, and they behave completely normally.” What is even more startling about the work Dr. Pincus and his colleague Josef Michl, MD, associate professor of pathology, have done is that their treatments involve none of the punishing chemotherapy and radiation that today are the hallmark of most cancer treatments. Instead, their new peptides kill only cancer cells and leave normal cells undisturbed.

Dr. Pincus’s and Dr. Michl’s work in the lab shows that the peptide approach may apply not only to the devastating problem of pancreatic cancer, but to a large number of human cancers including those of the lung, breast, colon, and prostate—in other words, many of cancer’s leading killers. Dr. Pincus is also applying his peptide approach to malfunctions of another important protein involved in many cancers, called ras-p21. “Our primary interest was in addressing problems with ras-p21,” he explains. “This protein has been implicated in one out of three human cancers. It causes more than 90 percent of pancreatic cancers, about 75 percent of colon cancers, and about a third of lung cancers.”

His approach, should it prove successful in human clinical trials, could revolutionize the way cancer is treated and transform our expectations of what a cancer diagnosis may mean. “While our results are very promising, I don’t want to make any false
claims,” he cautions. “We’re eager to begin clinical trials as soon as possible.”

Back in the early 1980s, when Dr. Pincus was a scientist at the National Institutes of Health, he and the rest of the scientific world learned an important new fact. In a cell’s DNA, “a single amino substitution”—the presence of one type of amino acid when another is appropriate—“makes that protein oncogenic,” that is, it allows the protein to cause cancer. “It meant there was a link between protein structure in cells and cancer,” he says. “That’s when I became interested in the problem.”

So far, that interest has had impressive results. Using a vector—a biochemical vehicle that helps replace damaged proteins with the new ones he and Dr. Michl have created—the two scientists have succeeded in treating cancers in human cancer cells in Petri dishes. Their approach has killed cancers in cell lines not just for pancreatic cancer, but for colon cancer, one type of brain tumor, cervical cancer, breast cancer, and a cancer of the blood vessels.

The peptides kill the cancer cells without damaging healthy cells. “The peptides are causing very selective cancer cell death,” Dr. Pincus explains. “There is no adverse effect from the peptides at all.” The same has happened in their experiments using laboratory mice.

Dr. Pincus’s greatest hope now is that he can raise the money to get these peptides into human clinical trials within the next year. “We want to emphasize them in terms of real treatment,” says Dr. Pincus, who initially came to Downstate in its first class of MD/PhD students. “We want to push right now.”
WOMEN’S LIVES, WOMEN’S BODIES: addressing women’s unique health challenges

The field of women’s health has come a long way since the late 1960s, when activists, practitioners and researchers first began focusing public attention on women’s unique and often-neglected health and medical needs. Nowhere is that more true than at SUNY Downstate Medical Center, the only New York State educational and research institution to receive a prestigious BIRCWH (Building Interdisciplinary Research Careers in Women’s Health) grant from the National Institutes of Health. The five-year, $2.5 million grant brings together seasoned scientists and physicians to help train younger scientists and clinicians in women’s health research.

At SUNY Downstate, these young researchers have much expertise upon which to draw. Downstate’s clinical and biomedical scientists are actively investigating such diverse women’s health issues as the influence of the female hormonal cycle on mood, learning, and memory; women’s unique experiences of pain and addiction; prognostic markers for early stage breast cancer; and improved breast cancer screening and detection through new medical imaging technology.
WOMEN
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Dr. Alan Gintzler and Nai-Jiang Liu, PhD, a BIRCWH scholar.
HERE’S A CONUNDRUM IN THE FIELD OF PAIN RELIEF: WOMEN ARE SIGNIFICANTLY LESS SENSITIVE TO PAIN THEN MEN ARE. YET, WHEN IT COMES TO CHRONIC PAIN SYNDROMES, WOMEN SUFFER AT A FAR HIGHER RATE.

Pain researcher Alan Gintzler, PhD, professor and interim chair of biochemistry, has been trying to understand why. “The statistics are staggering,” he says. “In chronic pain syndromes such as temporomandibular joint syndrome, or TMJ, something like 80 to 90 percent of the cases are in women.”

Dr. Gintzler, who is also a program director of a Women’s Health Research Training Grant (BIRCWH), hopes his research into women’s paradoxical experiences of pain will help improve the treatment of pain in both women and men. “Pain treatment continues to be very primitive,” he explains. Unfortunately, “there are lots of pain syndromes that are very poorly managed.”

Dr. Gintzler didn’t set out to be a pain researcher. But as a young scientist he made a startling finding: Pregnant laboratory animals were far less sensitive to pain than animals that weren’t pregnant. Eventually, he tested the pain thresholds of pregnant rats and found it increased as their pregnancies progressed, peaking just before childbirth. Such is the case in pregnant women, as well. Why does this happen? High levels of estrogen and progesterone released during pregnancy, Dr. Gintzler explains, “act on spinal neurons to activate analgesia.”

But Dr. Gintzler didn’t think hormonal differences alone accounted for the dissimilarity between women’s and men’s experiences of pain. To test that hypothesis, he made male rats hormonally “pregnant”—giving them hormones that mimicked the hormones female rats produce internally during gestation. “Low and behold,” he says, “they had very, very robust analgesia. As great, if not greater, than the females.”

That result might seem to contradict Dr. Gintzler’s original hypothesis. But in the process of conducting his experiments, he and his collaborators have discovered that the central nervous system’s pain pathways aren’t entirely the same in females and males. Females have an additional system that processes pain. And not only that. The receptors that females and males have in common work differently. Observes Dr. Gintzler, “the components in the female are multiplicative.” In other words, they work together synergistically. Give a female a small amount of pain relief, and she’s likely to get a disproportionate benefit. In males, pain relief “is purely additive,” Dr. Gintzler says. The same analgesic input gives far less relief.
Dr. Gintzler is one of several researchers pursuing the question of why, then, women suffer from chronic pain at disproportionate rates.

“Nobody has a complete handle on why women experience much more chronic pain,” he says. Indeed, the medical literature offers no firm conclusions. But Dr. Gintzler theorizes that the synergistic pathways that aid women in late pregnancy and childbirth may be the same ones that plague them when they develop chronic pain. Just as a small increase in the activity of the analgesic system gives females greater relief, so a small deficiency “has a much bigger effect in the opposite direction,” Dr. Gintzler says.

Dr. Gintzler’s interest in women’s and men’s differing experiences with pain dovetails with his other major research interest: how the body becomes tolerant of opioid-based narcotics. “One of the more intriguing aspects” of the analgesic effects of increased estrogen and progesterone exposure “is the noticeable decrease of tolerance development,” Dr. Gintzler explains. “This could suggest sex-based differences in tolerance and perhaps even addiction mechanisms.”

Dr. Gintzler’s twin interests may well increase medical science’s knowledge of sex-based differences in pain and analgesia. Perhaps one day, he says, “that difference can be exploited to optimize pain treatment.”
BIOCHEMIST HENRI TIEDGE DID NOT SET OUT TO BECOME A BREAST CANCER RESEARCHER. THE BULK OF HIS WORK HAS ALWAYS BEEN IN THE AREA OF LEARNING AND MEMORY—IN HOW CERTAIN TYPES OF RNA MAY REGULATE THE PRODUCTION OF PROTEINS AT THE BRAIN’S SYNAPSES. BUT AN UNEXPECTED RESULT HAS GIVEN HIM A NEW RESEARCH INTEREST.

BC200 RNA, a type of RNA that Henri Tiedge, PhD, professor of physiology and pharmacology, and neurology, has long studied, is usually present only in nerve cells and germ cells. Yet after a series of investigations, he and his colleagues “had reasons to believe these RNAs should also be expressed,” that is, they should also be present, in certain cancer cells.

In fact, the types of cancer cells that expressed the most BC200 RNA were breast-cancer cells.

Now, Dr. Tiedge’s newly undertaken research may alter the way doctors diagnose the hundreds of thousands of women around the world who each year discover they have pre-invasive, in situ breast cancers.
In situ breast cancers begin inside the breast’s milk-producing and -carrying lobules and ducts. These cancers are usually detected through screening mammography, and at the time of diagnosis, have yet to break through the structures in which they have formed. Untreated, only some—estimates range from about 30 to 60 percent—will go on to become potentially life-threatening tumors, the kind that can invade other tissues.

“The question is,” Dr. Tiedge asks, “concisely, which ones?”

Indeed, researchers and physicians don’t yet know what characterizes these more aggressive cancers. What types of molecular compounds and cell structures are linked to more virulent disease?

This is where Dr. Tiedge’s research may offer valuable clues: BC200 RNA seems to be present in the most potentially invasive forms of the disease. “When we look at a cell that’s become invasive or is going to become invasive, those cells are not just making a little BC200 RNA, they’re making a lot of it,” Dr. Tiedge explains.

If his research bears out, BC200 RNA may well become an important marker, something pathologists and clinicians can use to prognosticate the likely course of the disease. They may be able to deduce the all important question of whether the cancer will spread. To do this, they’re putting together a prospective study, “where you get biopsy material, look at the tissue, and ask these women if we can follow them for 10 years,” Dr. Tiedge explains.

Dr. Tiedge also includes Ms. Lin in his meetings with collaborators. “He thinks that’s beneficial to me and I do, too,” Ms. Lin says. That independence allows her a more nuanced understanding of her work. In addition, she says, “it broadens my professional contacts and strengthens my ability to ask questions.”

At Downstate, Ms. Lin believes, “I’m learning the skills I’ll need for the future.”
HORMONALLY-RELATED MOOD CHANGES, SUCH AS PREMENSTRUAL SYNDROME (PMS), HAVE RARELY BEEN THE FOCUS OF SERIOUS SCIENTIFIC INQUIRY.

This despite the fact that a full 30 percent of American women experience PMS on a regular basis, with 10 percent being severely affected and an additional 5 to 7 percent undergoing such intense symptoms as to warrant the psychiatric diagnosis of premenstrual dysphoric disorder.

Neuroscientist Sheryl Smith, PhD, professor of physiology and pharmacology, is out to change all that. In her lab, PMS is the major priority. And what she’s found may come as a surprise, and as a kind of recognition, to millions of PMS sufferers and non-sufferers alike: The set of brain cell receptors involved in PMS, called GABA receptors, are the same ones affected by tranquilizers such as Valium, Xanax and Ativan, as well as by alcohol and the hormonal changes that can accompany menopause and childbirth.

“All this happens in the part of the brain called the limbic system,” Dr. Smith explains, “which is important for things like spatial memory as well as for mood. So there are repercussions on mood, on memory, and learning.”
What causes PMS? Dr. Smith and her team have learned that during the second half of the menstrual cycle, after ovulation, a metabolite of the naturally occurring hormone progesterone, called allopregnanolone, binds to GABA receptors. “When allopregnanolone is at high levels,” Dr. Smith says, “there’s less brain excitability in a normal person.” Researchers have reported, for example, fewer instances of epileptic seizures during this so-called luteal phase of the menstrual cycle.

At the very end of the cycle though, progesterone’s soothing effects come to an abrupt stop. Dr. Smith explains, “The progesterone levels become very low, and this progesterone metabolite is also declining. That’s when many women have a change in mood.” Similar declines in allopregnanolone levels also occur during the period immediately following childbirth, which in some mothers results in postpartum depression; after repeated stress; and during menopause, when changes in mood and cognition are also common.

Dr. Smith and her fellow researchers think what happens at the end of the menstrual cycle is a type of withdrawal. “Amazingly, what you see in the brain looks a lot like alcohol withdrawal,” Dr. Smith says. In fact, as in withdrawal, one type of building block in the affected GABA receptor, called the alpha 4 subunit, increases markedly during PMS, and levels of the more soothing alpha 1 subunit decrease. “In rats, when you see alpha 4 increasing, the rats have increased anxiety and it’s easier to produce a seizure. There are also changes in learning.”

Dr. Smith is currently investigating how to prevent increases in the alpha 4 subunit in the face of changing hormone levels. A compound called antisense appears to prevent such withdrawal symptoms. “In laboratory animals,” Dr. Smith says of her research, “you can put antisense into their brains and it prevents alpha 4 from being increased. Normally, these animals would be very anxious. But the antisense prevents the formation of alpha 4 subunits. And when that happens, you don’t see the anxiety or seizure activity.”

Dr. Smith’s research has led her to a few important conclusions about PMS and other related problems. Because GABA receptors that contain higher levels of alpha 4 are sensitive to low levels of alcohol, women experiencing the mood changes associated with PMS or menopause might well benefit from an occasional drink, when symptoms are most severe. But only one drink.

“There is some increased response to very low doses” of alcohol, she says. In fact, women who experience severe PMS are at higher risk for alcoholism, perhaps as a result of self-medication in the face of increased sensitivity to alcohol.

Dr. Smith hopes to further explore the basic science of PMS. For women who suffer from PMS, and for the millions of others with the related mood changes and cognitive impairments that occur during menopause and after childbirth, that research will be a welcome prospect.
WHAT IF THERE WERE A WAY TO SCREEN FOR AND DETECT BREAST CANCER THAT COULD FIND THE DISEASE IN ITS EARLIEST STAGES, COULD AVOID EXPOSING PATIENTS TO THE POTENTIALLY CARCINOGENIC EFFECTS OF THE X-RAYS NOW USED IN MAMMOGRAPHY, AND WAS SIGNIFICANTLY MORE ACCURATE THAN CURRENT MEDICAL IMAGING TECHNOLOGIES?

Pathology professor Randall Barbour, PhD, may have found a way to do all that and more. Dr. Barbour, who is also research professor of electrical engineering at Polytechnic University, is the inventor of a relatively new field of medical imaging technology called diffuse optical tomography (DOT). DOT is a noninvasive approach that uses near-infrared light and computer algorithms to visualize tissue.

DOT has vast potential, including the diagnosis of the multiple health problems faced by extremely premature infants and improved visualization of degenerative neurological disorders. Georgetown University researchers are even using it to study what happens in the brain when individuals commit acts of deception.
Nowhere is DOT’s potential greater than in the diagnosis of breast cancer and the assessment of treatments. “The likelihood is,” says Dr. Barbour, “optical tomography is going to almost certainly be the preferred way to monitor the response to chemotherapy and the preferred technique, period, for breast cancer screening.”

Randall Barbour had an epiphany. One day, while adjusting his car’s headlights in the dense fog, he realized that light from a distant source was better at penetrating the low-lying cloud than light from a nearby source. Familiar with pulse oximetry, a non-invasive medical technology that uses near-infrared light to monitor the oxygen content of a patient’s blood, Dr. Barbour thought he might be able to use near-infrared light to penetrate the dense cloud that is human body tissue. “In effect, we took the basic idea of pulse oximetry and extended it to a functional imaging tool,” he says.

But that wasn’t easy. The problem was how to read the light that penetrated the tissue. Light, after all, diffuses in complicated ways. Dr. Barbour’s scientific quandary was “How could you possibly unscramble those randomly scattered patterns of light to allow you to reform the information, if you will, to get an image?”

Dr. Barbour, a biochemist by training, presented his ideas at a scientific forum in the mid-1980s; a few months later, a physicist friend explained how that might happen. Shortly thereafter, Dr. Barbour and his collaborators wrote the first computer code that enabled the process. “Sure enough,” Dr. Barbour recalls, “within a short period of time, we knew it would work.”

Indeed, since the late 1980s, the innovations have raced forth. “Typically, it takes about 20 years to work out all the bugs and come up with a new imaging scan,” Dr. Barbour explains.

Now, working onsite at SUNY Downstate and at its nearby Advanced Biotechnology Incubator, using funding from such innovative sources as the Susan G. Komen Breast Cancer Foundation and the United States Department of Defense’s breast cancer research program, Dr. Barbour and his team are ready to move their technology into the future. This year, Dr. Barbour’s imaging venture, NIRx Medical Technologies, has begun to enroll healthy women and women with breast cancer in clinical trials that will compare DOT’s accuracy to that of currently available detection technologies, including mammography and magnetic resonance imaging. “Already, we have sensitivity and specificity values”—measures of accuracy—“over 90 percent, which is considerably better than x-ray,” he says.

The trial results won’t be available for another year or so. “But right now,” Dr. Barbour says, “I’m quite optimistic.”
To support Downstate’s scientists and their ground-breaking discoveries, please call 718-270-4418, or go to: www.downstate.edu/giving/default.html