

translational and molecular imaging institute

accelerating  
science

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advancing  
medicine



MOUNT SINAI  
SCHOOL OF  
MEDICINE

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passion

# Fierce Competition

# Fierce Cooperation

We intend to create a research environment  
that encourages collaboration and rewards  
work that challenges conventional wisdom.  
—dennis s. charney, md

message from the dean



dennis s. charney, md

The Anne and Joel Ehrenkranz Dean of Mount Sinai School of Medicine  
and Executive Vice President for Academic Affairs of The Mount Sinai  
Medical Center

## Where Does the Future Happen?

I am very proud to introduce Mount Sinai School of Medicine's vision for its twelve translational research institutes. These institutes embody our mission as a leader in basic and clinical research and lie at the heart of the larger strategic plan for The Mount Sinai Medical Center.

Translational medicine has been synonymous with Mount Sinai since the founding of the Hospital in the mid-nineteenth century, when our doctors turned to their microscopes to better understand the conditions they had just encountered in their patients.

The halls of our medical school are lined with portraits of Mount Sinai pioneers who first described clinically complex disorders, including Crohn's disease, Churg-Strauss disease, Tay-Sachs disease, and Brill's disease.

This passion for patient-focused research inspired another generation of physicians, who created Mount Sinai School of Medicine. Today, we are building upon this legacy with a research model that moves beyond the conventional departmental structure that typically governs medical schools.

Our plan originated in 2005, when I invited over 100 of Mount Sinai's leading researchers to form twenty-two working groups that would address our future. Together, we agreed that Mount Sinai had an unparalleled opportunity to transform itself into an even more powerful translational medical institution.

The basic infrastructure of The Mount Sinai Medical Center, a medical school embedded in a hospital, is tailor made for collaborative projects that can progress rapidly, unencumbered by a complex bureaucracy. In fact, Mount Sinai is unique among academic medical centers in not being accountable to either a university administration or a governmental organization.

During two years of intense study and discussion, we identified areas of research where Mount Sinai can truly be a world leader. This analysis formed the basis of the twelve research institutes that you will learn more about in subsequent chapters.

Each institute is designed to facilitate breakthrough science. We intend to create a research environment that encourages collaboration and rewards work that challenges conventional wisdom. Scientists from different departments and disciplines will be provided the intellectual freedom, the physical space, and the financial support they need to pursue their best ideas. Further, these research institutes will be characterized by organizational flexibility in order to maximize our capacity to respond quickly to scientific advances.

As the medical sociologist Rogers Hollingsworth observes, the most successful scientists possess “high cognitive complexity,” which gives them the capacity to see important relationships among disparate fields of knowledge. Both the physical design and intellectual atmosphere of our institutes reflect this insight, by encouraging the constant and open exchange of ideas. I believe we have greatly increased the potential for major discoveries at Mount Sinai by designing our research model to reflect Hollingsworth’s findings.

Seven of our institutes are disease oriented, focusing on the brain, cancer, child health and development, the heart, immunology, metabolism, and emerging pathogens.

Five institutes will complement and advance the work of the disease-oriented institutes: experimental therapeutics, molecular imaging, personalized medicine, stem cell research, and disease prevention and public health.

Our decision to target areas where Mount Sinai can excel also governs research priorities within the institutes, which build upon established clinical and research strengths, the expertise of our new recruits, our unique location at the intersection of New York’s most and least affluent zip codes, and our long-standing commitment to all of the communities that Mount Sinai serves.

Above all, Mount Sinai will continue to encourage and support the bold thinking and disciplined science that can fundamentally

change the face of medicine. Heart and brain researchers, for example, are working toward restoring tissue and repairing functions thought to have been lost forever. Experts in children's health are uncovering the genetic and environmental underpinnings of asthma, the primary cause of school absenteeism in New York City. Diabetes researchers are unraveling the complex web of factors that contributes to a national health crisis. Cancer investigators are using new knowledge of stem cells to fundamentally transform the fight against one of the leading causes of death worldwide.

These and myriad other investigations will take place on a campus invigorated by the new Center for Science and Medicine, which is designed to promote translational research. This 450,000-foot facility will house six full floors of laboratory space built to encourage scientists to share ideas and findings on an informal basis.

The Center will also be home to our cancer clinics and labs, and our new imaging center. This will facilitate communication between researchers and their clinical partners and will enable patients and doctors to take full advantage of the latest technologies. Overall, the Center for Science and Medicine, scheduled to open in 2012, will increase our research capacity by 30 percent.

Mount Sinai School of Medicine is a magnet for visionary scientists and clinicians, and I am honored to be working with such a passionate and productive group of colleagues.

vision

# Rigorous Thinking

# Revolutionary Medicine

Many discoveries are now within our grasp, including those that will increase the plasticity of the human brain, rejuvenate damaged heart tissue, and protect society from devastating pandemics.

—kenneth l. davis, md

message from the president and ceo



kenneth i. davis, md  
President and Chief Executive Officer of The Mount Sinai Medical  
Center and the Gustave L. Levy Distinguished Professorship

## A Portrait of the Future

We are living at a watershed moment in medical science. The elaboration of the human genome has created a revolution in biology that is equivalent to the revolution in physics that occurred in the early years of the twentieth century. Between 1890 and 1920 a sequence of basic discoveries set the stage for nuclear energy, transistors, and rapid communication, transforming life to such an extent that someone living a century ago could not have imagined the world of today.

The current revolution in the biomedical sciences reflects an increased understanding of how genes are controlled and how proteins are made and can be changed, and it presents unprecedented opportunities for the development of new classes of drugs and diagnostic tools. Armed with such new innovations, the medical profession can treat and cure some of the most serious diseases and conditions known to humanity, improving outcomes and extending millions of lives.

Those of us at the leading edge of research in the life sciences, especially at academic medical institutions, see extraordinary opportunities before us every day. I am particularly proud that The Mount Sinai Medical Center has both the intellectual and financial resources to deliver on these opportunities.

Our new institute structure, as envisioned by my colleague Dennis Charney, will accelerate the pace of breakthrough ideas. We have carefully chosen the areas of research in which we can excel, and we have recruited world-renowned scientists and clinicians to join our distinguished faculty. Many discoveries are now within our grasp, including those that will increase the plasticity of the human brain, rejuvenate damaged heart tissue, and protect society from devastating pandemics.

Financially, The Mount Sinai Medical Center is in sound condition, giving us the capacity to recruit world-renowned talent, support young scientists, build new facilities, and fund novel ideas.

Furthermore, successful translational medicine, by its very nature, promises to increase intellectual property and royalties, hospital revenues from new treatments and therapeutics, National Institutes of Health funding, and future philanthropy.

Our success and our stability as an academic medical institution reflect both the wisdom of the institute plan and the strength of the entire Mount Sinai team. Thanks to their efforts and foresight, we have every reason to be optimistic about the future of Mount Sinai and the future of medical science.

legacy

# Breaking Ground

# Building Greatness

The creation of twelve translational  
research institutes is a bold move forward and a  
natural evolution of Mount Sinai's legacy.  
—pet er w. may

message from the chair



pet er w. may  
Chair of the Boards of Trustees

## Building the Right Place at the Right Time

For over 150 years, Mount Sinai physicians have advanced science, and accelerated the pace at which research breakthroughs have been developed into novel therapies that benefit our patients. The creation of twelve translational research institutes is a bold move forward and a natural evolution of Mount Sinai's legacy.

Today, the revolution in the biological sciences is opening new avenues for investigation and even greater opportunities to improve patient care. At this critical moment, Mount Sinai is ideally positioned to shape the future of medicine.

Our endowment has grown to \$1.1 billion. This important measure of stability reflects both sound financial management and the long-term generosity of so many of our supporters.

Last year alone, Mount Sinai raised a record \$147 million in philanthropy, and soon we will launch a \$1 billion capital campaign to fuel Mount Sinai's comprehensive strategic plan. Many of the families responsible for our extraordinary growth are continuing a tradition that dates to the founding of the Hospital in the nineteenth century.

We are about to break ground for the new Center for Science and Medicine, a state-of-the-art facility that will serve as a focal point for our translational research efforts. The Center will include six full floors of laboratory space and will house all of Mount Sinai's cancer-related research, clinics, and advanced imaging technologies. With almost a half million square feet of space, the Center will increase our overall research capacity by a full 30 percent.

Recently, The Mount Sinai Hospital and Mount Sinai School of Medicine received an "A"-category rating from Moody's Investors Service. This is a tremendous achievement and represents the fruition of all of our financial improvement efforts. Among our particular strengths, Moody's praises our "focused and driven management team committed to financial success."

Of course, the most important component of Mount Sinai's growth is the superb quality of our scientists and physicians. Over the past two years, Mount Sinai has recruited scores of world-renowned researchers and clinicians who have chosen an environment that offers the freedom to explore new avenues of inquiry and the opportunity for cross-disciplinary collaboration.

As Board Chair, I am proud that Mount Sinai is in a position to fully support the unified vision of Dr. Davis and Dr. Charney, and encourage the work of so many remarkable medical pioneers.

# the center for science and medicine

The new Center for Science and Medicine will be a state-of-the-art, modern facility that will house both clinical care and basic research programs. Designed to increase interaction and collaboration among faculty and staff practicing a variety of disciplines, the building will feature wide open spaces, significant laboratory and clinical care space, as well as a roof lounge.



Construction for the Center for Science and Medicine is scheduled to begin in 2008 and is expected to take approximately three to four years. The 450,000-square-foot facility will increase Mount Sinai School of Medicine's research capacity by about a third.



# translational and molecular imaging institute

**Zahi A. Fayad, PhD**

Interim Director

Picture  
the  
future.



The Translational and Molecular Imaging Institute is advancing the science of imaging, from the development of new visualization technology to improved contrast agents. Once confined to clinical radiology and basic cell biology, biomedical imaging now enables in vivo detection of structures and events in biologic systems, ranging from individual macromolecules to whole organisms. Imaging tools can even facilitate studies of gene expression at the subcellular level, helping scientists unveil the secrets of all living systems. Institute researchers collaborate with investigators throughout The Mount Sinai Medical Center to increase the potential for making a major discovery.

## Vision and Resources

Biomedical imaging in the twenty-first century offers unparalleled opportunities to transform clinical medicine. Today, the latest technologies are able to reveal biochemical alterations in metabolic pathways in response to therapy; localize brain activation during cognitive, motor, or sensory tasks; and track multiple cell types in real time as the cells migrate throughout the body.

The Translational and Molecular Imaging Institute will serve as a research catalyst for a new generation of translational and molecular imaging methodologies. Imaging modalities, including magnetic resonance imaging (MRI), nuclear, X-ray-based, and optical techniques, will be applied in both preclinical basic science and clinical research settings to improve diagnostic accuracy, to increase the understanding of pathophysiology and metabolism, and to measure therapeutic efficacy, such as measuring a cancerous growth to test whether a new drug has effectively shrunk a tumor. The Institute will also support and integrate advances in imaging physics, engineering, nanomedicine and nanochemistry, and image analysis.

Researchers and clinicians from all the Institutes will have greater and more comprehensive access to complex imaging equipment, including MRI and magnetic resonance spectroscopy (MRS), X-ray computed tomography (CT), positron emission tomography (PET), single photon emission computed tomography (SPECT), and emerging modalities like bioluminescent and fluorescent imaging of intact organisms.

“We will be among the first in the world to combine an MRI and a PET in a single machine. This will provide high-spatial and high-contrast imaging with MRI and metabolic information from PET, which will lead to earlier detection of disease and also more targeted treatments,” says Zahi A. Fayad, PhD, Interim Director of the Translational and Molecular Imaging Institute and Professor of Radiology and Medicine (Cardiology). “By combining MRI and PET, we can further probe disease mechanisms. For example, with Alzheimer’s disease, an MRI gives us anatomical information about the brain, and the PET measures blood flow activity. This helps us track plaque development and pinpoint plaque formation, and it will ultimately lead to earlier detection, earlier diagnosis, and better treatments.”

# Collaborative Opportunities

## **Radiology**

The Institute facilitates the direct involvement of attending radiology physicians, residents, and clinical and basic researchers, which results in more coordinated and improved patient care. Imaging specialists have long worked with Mount Sinai's psychiatrists and cardiologists to diagnose and treat patients. The Institute will expand on this by allowing for interdisciplinary teams to use neuroimaging and structural and functional MRI and MRS techniques in order to develop diagnostic methods and treatments for patients with cardiovascular disease and brain disorders. Alzheimer's disease, mood disorders, and atherosclerosis are particularly promising targets for radiology.

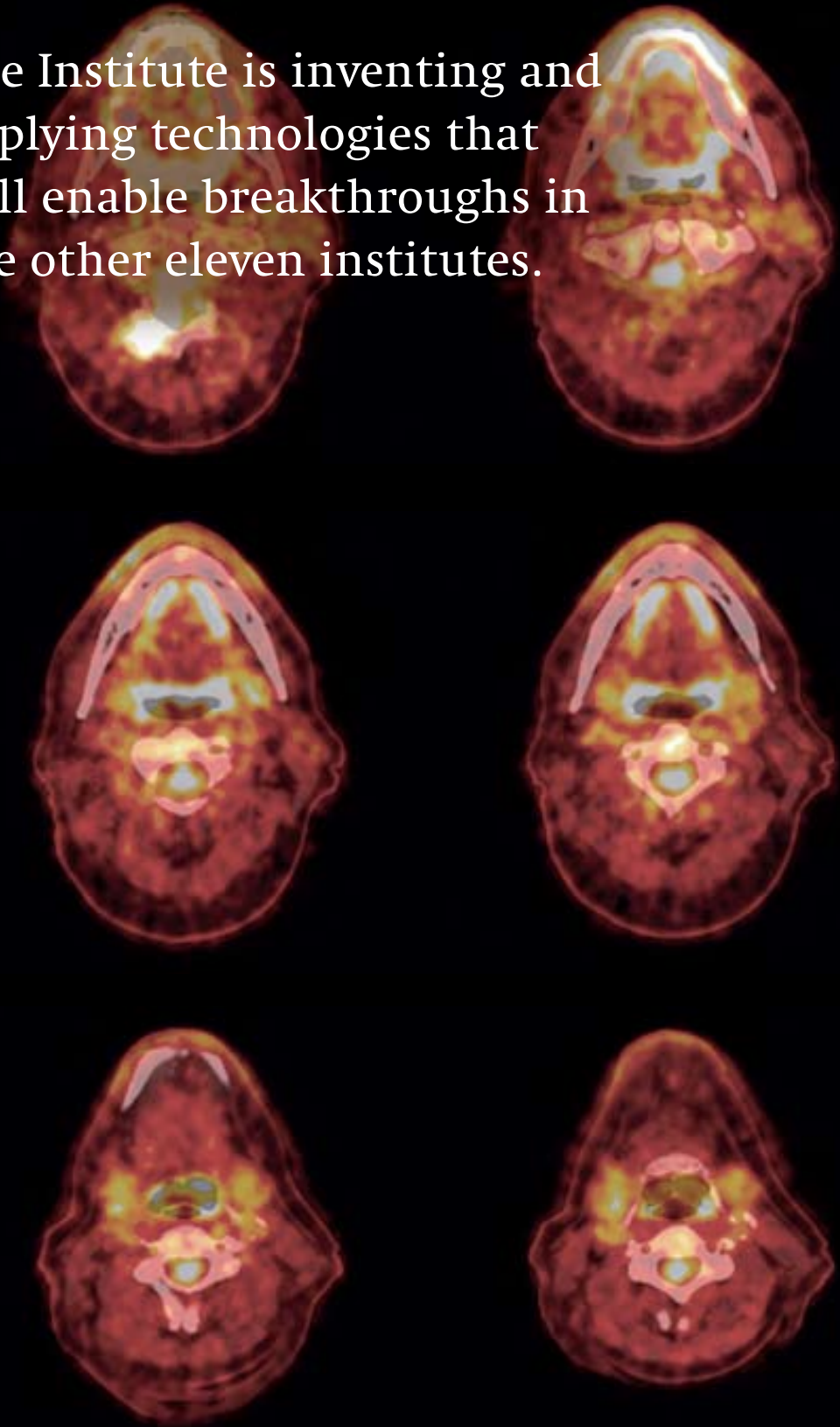
The Institute is also emphasizing chemical probes and nanomedicine, new technologies that can improve the sensitivity of detecting imaging-specific molecular events in vivo by one or two orders of magnitude as well as introducing new nanoparticles for improved drug delivery.

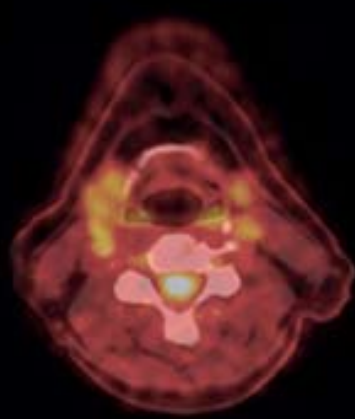
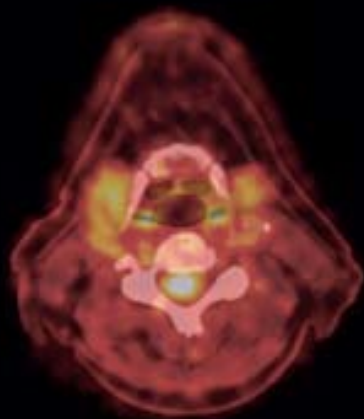
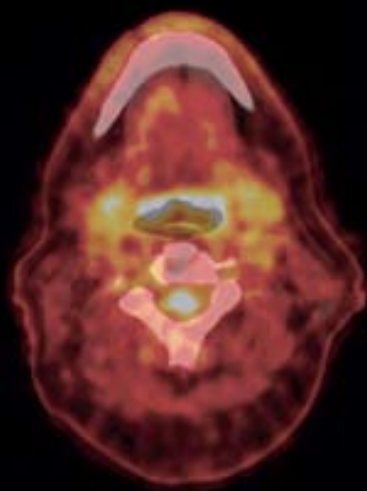
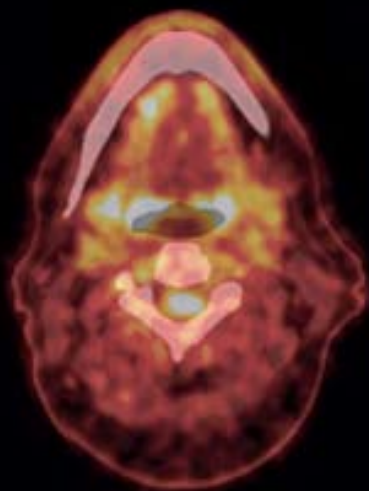
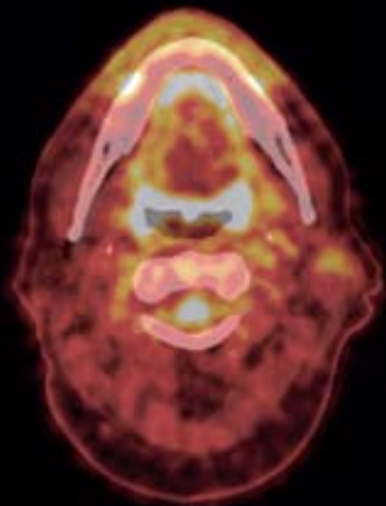
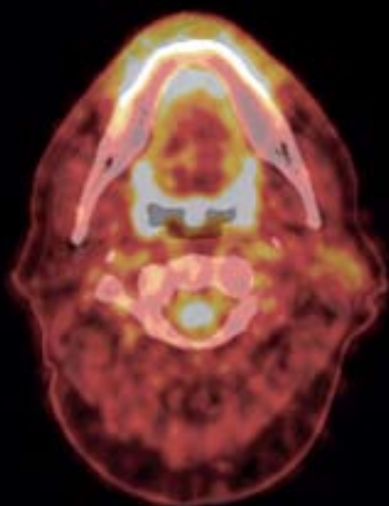
## **Neuroscience**

Imaging advances are playing an increasingly important role in neuroscience research. Functional MRI offers a noninvasive look into the workings of the brain, the areas that are connected, and how those regions communicate. New methods in nerve fiber assessment allow white matter tracking to show disruptions or changes during disease progression. Together, imaging experts and neuroscientists can identify brain activity differences between Alzheimer's patients and healthy individuals, which will help identify patients at risk.

Another example of collaboration is the new interdisciplinary project on autism, which is using imaging techniques to find better ways to individualize and improve treatment strategies. The project, which combines basic science with clinical research, builds on the idea that in the autistic brain, neural circuitry involving the hormone oxytocin and its cell surface receptor differs from that in non-autistic brains. To measure neural circuitry changes, psychiatry faculty members are using MRI to test the effects of oxytocin in patients with autism. At the same time, in the laboratory, imaging specialists from the Institute are developing an MRI-based ligand to visualize the density and distribution of

The Institute is inventing and applying technologies that will enable breakthroughs in the other eleven institutes.





oxytocin receptors in a rodent model. The efficacy of this ligand may allow clinicians to screen their patients for more personalized treatment strategies.

### **Cardiovascular Studies**

Mount Sinai pioneered the use of MRI to detect hidden plaque buildup within the arterial wall in a noninvasive way. Building on that work, collaborative research is now combining cardiovascular MRI with other technologies to noninvasively investigate both the lumen and the vessel wall.

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# MRI

Other projects also illustrate how the Institute is helping to change the way cardiovascular research is conducted. Researchers are applying lipid-based nanoparticles to develop new ways to predict, prevent, and treat cardiovascular disease. For example, lipid-based molecular complexes, made with the primary protein component of HDL, can be rendered visible by MRI, CT, PET, and optical imaging when tagged with material such as gadolinium ions, iron-oxides particles, copper 64 nuclide, and near-infrared probes. These molecules can then be further modified with small peptides or antibodies for targeting specific tissues, cells, and proteins. In pilot studies, Institute researchers localized HDL nanoparticles, specifically in the atherosclerotic vessel walls of living animals and in inflamed high-risk plaques. They found that HDL-like nanoparticles may be effective for imaging atherosclerotic plaques and are also more practical, safer, and less costly than other, more complex contrast agents.

In another project, researchers associated with the Institute are using noninvasive imaging tests based on MRI, CT, and fluorodeoxyglucose (a glucose analog) PET to compare atherosclerosis regression in patients receiving statins and other novel cardiovascular drugs. These technologies create windows through which clinical researchers can monitor the effects of various drugs and dosages on plaque behavior in different vessels throughout the body.

### **Cancer Detection and Therapy**

The long-term goal for the Institute and cancer therapy is the development of image-agent tagged chemotherapies whose dosage or composition can be altered based on real-time measurements of tumor response. Treatments will target both the cellular and molecular levels.

Because the Institute has extensive imaging technologies for use in both preclinical and clinical studies with cancer patients, it expects to streamline the process of moving from target and compound identification to individualized treatment of patients. In the near future, bioluminescent and fluorescent imaging may help find reporter genes that can reveal gene activity at the earliest phases of transition from hyperplasia to neoplasia.

### **Genetics**

Based on Mount Sinai's success in using microMR for cardiovascular and neurological studies, the Institute will develop MR technology opportunities for in vivo studies that visualize reporter gene expression in space and time.

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Opening new avenues in small-animal research, some projects will employ nuclear imaging techniques like PET and SPECT or bioluminescence and fluorescence to create genetic reporter probes. Projects over the next few years may modify and find novel uses for microPET, microSPECT, microCT, and micro-ultrasound (US) for expanding the application of reporter gene technology. The next generation of reporter probes will help researchers understand when and where genes are expressed and how patterns of expression interact at the cellular level. This technology might also be applied to assess many aspects of phenotypic differentiation in animal models of disease, including morphologic and metabolic differences.

### **Metabolic Diseases**

The Institute envisions projects that apply new ways to detect cardiovascular, renal, and cerebrovascular disease that will refine detection of metabolic diseases at all stages. There are opportunities to use imaging to noninvasively assess insulin-resistant patients and find out how they differ from healthy individuals. Imaging can also be used to examine how various diet and exercise programs return patients to their normal metabolisms, while radio- and MR-labeled compounds can noninvasively map out metabolic pathways.

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