ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY

Jack and Pearl Resnick Campus
1300 Morris Park Avenue
Bronx, New York 10461

Albert Einstein College of Medicine
Strategic Research Plan

Published by:
Office of the Dean

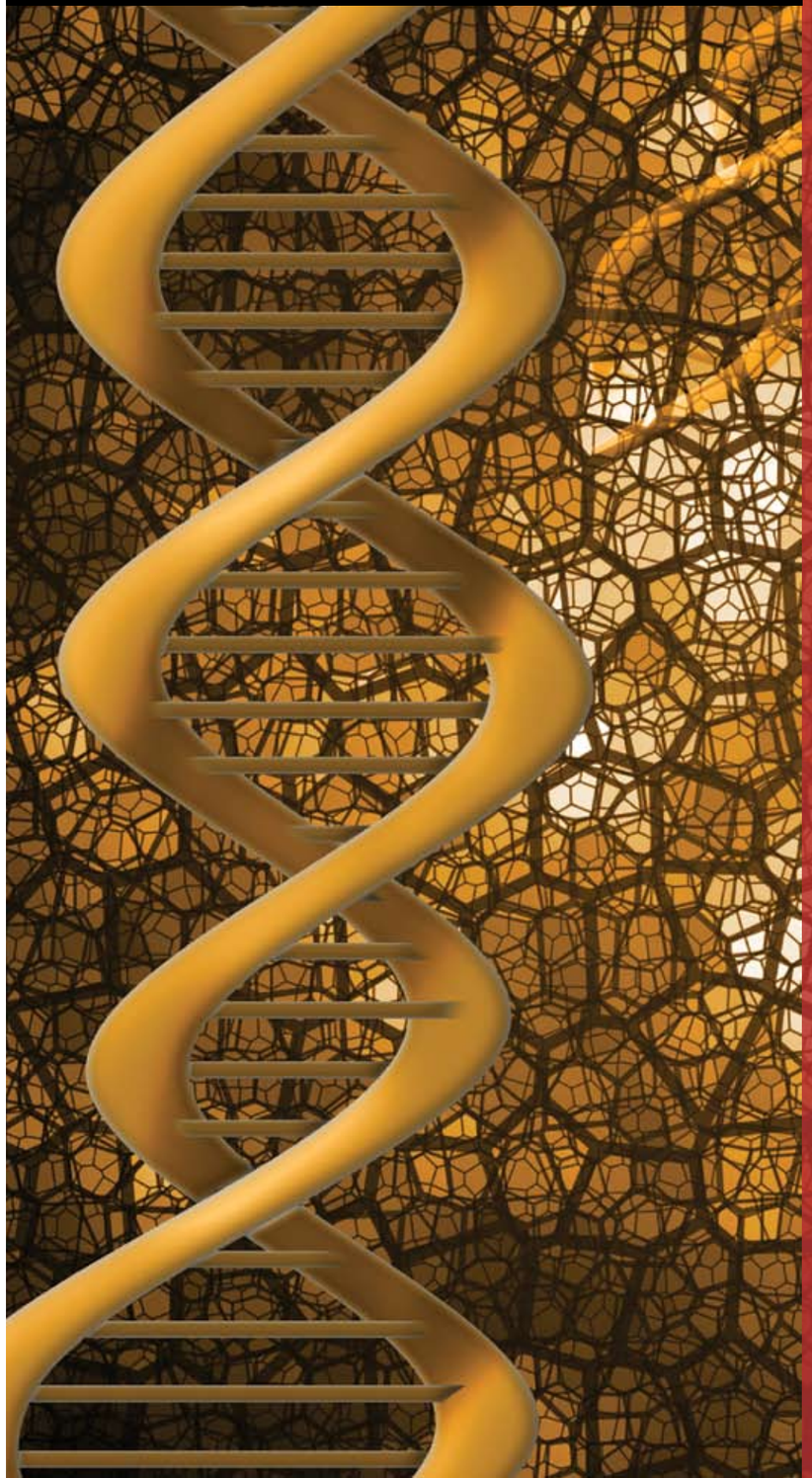
Science Writer:
Michelle A. Cissell, Ph.D.
M.A. Cissell Consulting

Design:
GRAPHIC ARTS CENTER
Creative Director: Peter Dama
Albert Einstein College of Medicine

Art Director:
James Wawrzewski
Cobalt Design Group

Printing:
OFFSET IMPRESSIONS, Inc.

Albert Einstein College of Medicine
of Yeshiva University



Strategic Research Plan

Albert Einstein College of Medicine
of Yeshiva University

Strategic Research Plan

"Concern for man and his fate must always form the chief interest of all technical endeavors. Never forget this in the midst of your diagrams and equations."

—Albert Einstein

Contents

Letter from the Dean 2

Executive Summary 4

Introduction 10
- History of Biomedical Research and Education at Einstein 11
- The Challenge of Biomedical Research in the 21st Century 12
- Development of a Strategic Plan for Einstein Research: A Transformative Era 14
  - A New Environment for Biomedical Research Funding 14
  - Changing Landscape at Einstein 15
  - Strategic Planning Process 15
  - The Matrix: A Framework for Strategic Research Planning 16

Translating Research from the Bench to the Bedside 18
- Barriers to Clinical Research at Einstein and its Affiliate Network 19
- Einstein-Directed Clinical Care Programs 20
  - Children's Evaluation and Rehabilitation Center (CERC) 20
  - Division of Substance Abuse (DoSA) 21
- Institute for Clinical and Translational Research (ICTR) 21
- Clinical Research Education, Training, and Career Development 22

Advancing the Science and Technology of Research 23
- Structural Biology and Proteomics 25
- Imaging 29
- Chemical Biology and Chemical Genomics 31
- Stem Cells and Regenerative Medicine 35
- Human Genetics 39
- Behavioral and Social Determinants of Health and Health Disparities 43
- Computational Biology and Systems Biology 47

Improving Human Health Through Research 49
- Aging 51
- Cancer 53
- Cardiovascular Disease 59
- Diabetes, Obesity, and Other Metabolic Diseases 61
- Infection and Immunity 65
- Liver Diseases 69
- Neuropsychiatric Diseases 73
- Reproductive Medicine and Health 77

Realizing the Vision for the Future of Einstein Research 81
- Implementation in the Michael F. Price Center for Genetic and Translational Medicine (CGTM)/Harold and Muriel Block Research Pavilion 83
- Implementation in Facilities Other than the CGTM 83
- New and Enhanced Research Programs 84
- Enhancing the Infrastructure for Science 84
- Implementation Phasing and Timeline 85

APPENDIX: Strategic Research Plan Contributors 86

Letter from the Dean

From the time of its creation in 1955, the quality and impact of the research performed by the faculty of the Albert Einstein College of Medicine has been extraordinary. Within fifteen years of its founding, Einstein was ranked as high as 5th in the Nation in research funding from the National Institutes of Health (NIH), a rigorous and objective measure of quality. The impact of research at Einstein has always been disproportionately high relative to the size of the School's faculty and resources. While Einstein has managed to maintain a position in the top quarter of the NIH funding rankings without the significant growth in size of faculty and research space that has characterized many other top tier schools, two major changes in the research landscape provided a compelling rationale for a different approach:

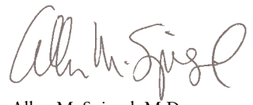
- In the genome era, the massive amounts of data that can be obtained with powerful new techniques offer unprecedented opportunities for understanding human disease, but seizing these opportunities requires research groups different in scale from the traditional individual investigator labs.
- Basic science research remains the main engine for discovery and innovation, but translation of basic science discoveries to benefit human health is critical, if the public's investment in research is to be sustained. Translational research is more than a "buzzword"; it poses a great challenge to institutions everywhere seeking closer integration between basic and clinical research. The public expects that just as research over the past decades has improved human health and led to such "medical miracles" as successful organ transplantation, translational research in the genome era will fundamentally change the way medicine is practiced, so that prevention of organ failure rather than treatment or replacement of a diseased organ becomes the rule.

Recognizing the need for growth and for meeting the challenge of providing the infrastructure for successful translational research, Einstein's Board of Overseers had the vision to secure ten acres of property across from the main campus where the new, 212,000 square foot Michael F. Price Center for Genetic and Translational Medicine (CGTM)/Harold and Muriel Block Research Pavilion will be completed later this year.

Funds were also approved for renovation of the Mazer Building which will house the infrastructure for our new Institute for Clinical and Translational Research (ICTR). This major investment in Einstein's future by the Board of Overseers demanded development of a Strategic Research Plan that would provide a guide for the School's physical growth and the expansion of its faculty over the next five years. The document you are holding (or viewing online) is the culmination of a nearly year-long process in which a large number of Einstein faculty from across the entire research spectrum were deeply engaged. It also benefited from the engagement of our Board leadership, including a highly interactive, full day Board retreat.

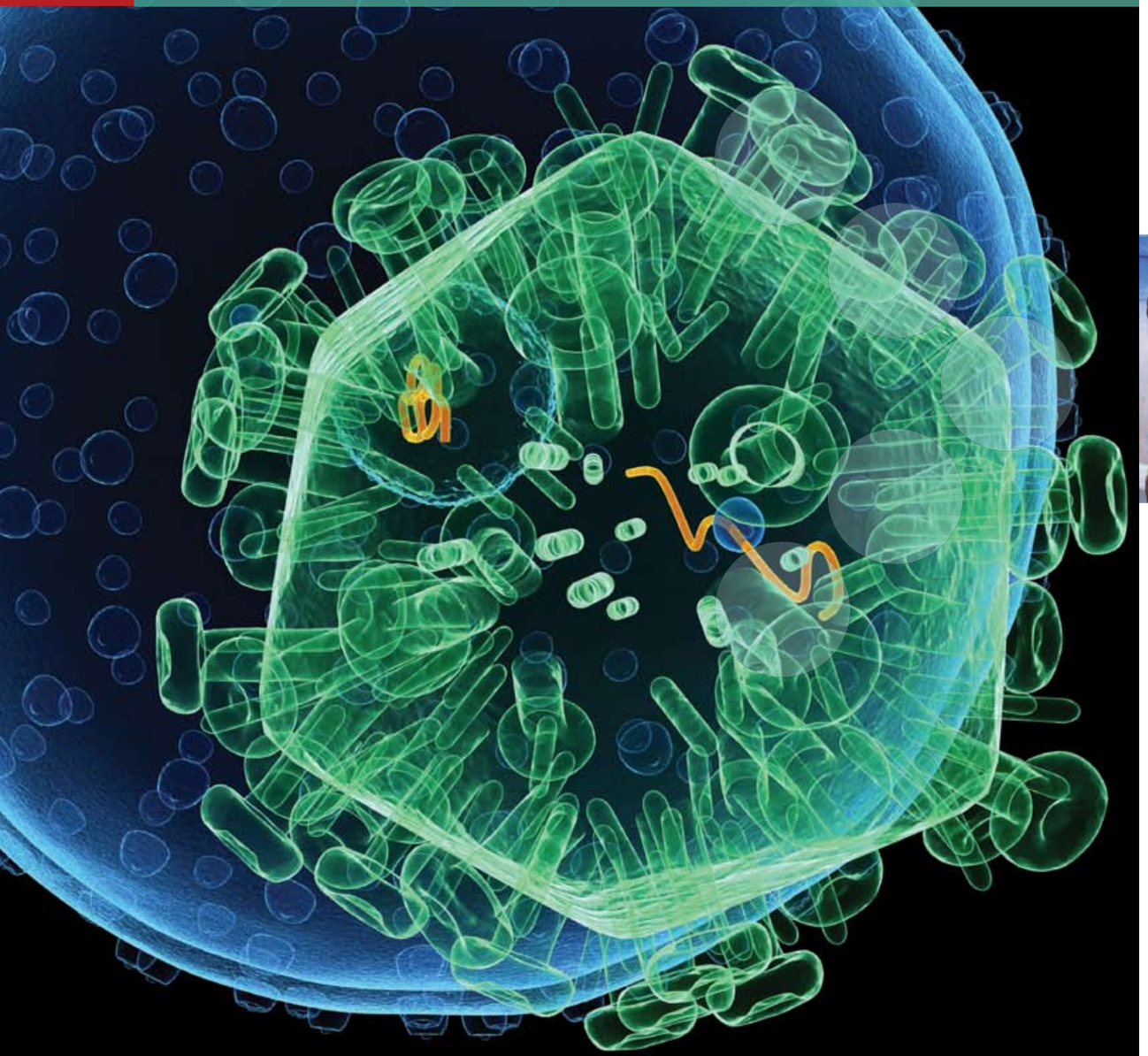
The Strategic Research Plan defines a set of priorities that will shape our recruitment of new investigators for the CGTM and ICTR, but it does more. It provides a vision for Einstein's future; a future in which:

- Einstein research is characterized by true collaboration and synergy between basic and clinical investigators
- Einstein research informs both our educational mission in training the next generation of physicians and scientists, and our clinical agenda in partnership with our medical center affiliates
- Einstein research leads to measurable improvement in the health of our local Bronx Community, of our Nation, and of people throughout the World.



Allen M. Spiegel, M.D.
The Marilyn and Stanley M. Katz Dean
April 2007

Executive Summary



The Albert Einstein College of Medicine biomedical research community has engaged in an intensive, collaborative, and rigorous strategic planning process to create a vision that will guide Einstein research over the next 5 years. The resulting Strategic Research Plan builds on more than 50 years of scientific excellence at Einstein to position the College at the leading edge of biomedical research with the ultimate purpose of improving human health and reducing the burden of disease.

Einstein is one of the nation's leading research institutions, ranking 27th out of 123 medical schools in NIH funding received in 2005. In the same year, the College ranked 6th in NIH funding obtained per principal investigator (see Figure 2, page 13). The gap between these rankings suggests that individual investigators have built productive, scientifically meritorious research programs and that Einstein's overall standing could be further improved by the targeted recruitment of additional researchers who would complement the strengths of these existing faculty and programs. To achieve this goal, Einstein must also identify and exploit new technologies and research disciplines that have emerged from the explosion in biomedical knowledge that has occurred since its founding 52 years ago.

Through the development and implementation of this Strategic Research Plan, Einstein has an opportunity to foster a bidirectional, cross-disciplinary research environment (see Figure 4, page 14) that meets the challenges of the increasingly collaborative and technology-oriented nature of the biomedical research enterprise. By strategically expanding the research faculty and ensuring access to state-of-the-art technologies, Einstein will strengthen the research base, enhance its leadership position in the research community, and continue a long tradition of translating fundamental scientific discoveries into meaningful clinical breakthroughs that improve the human condition.

Development of a Strategic Research Plan for Einstein: A Transformative Era

Several factors have created a timely opportunity for the College to evaluate the status and direction of its research programs. In 2006, Einstein recruited its seventh Dean, Allen M. Spiegel, M.D., to succeed Dominick P. Purpura, M.D. who had led the College for 22 years. Dr. Spiegel is an internationally-recognized physician-researcher and the former Director of the National Institute of Diabetes and Digestive and Kidney Diseases. His leadership coincides with the construction and renovation of new facilities that will facilitate significant faculty recruitment and resource development. The Michael F. Price Center for Genetic and Translational Medicine (CGTM)/Harold and Muriel Block Research Pavilion will open in late 2007 with 212,000 square feet of new space. Approximately forty new faculty are expected to be recruited to direct disease-oriented research programs in such areas as cell transplantation, liver diseases, human genetics, infectious diseases, mouse genetics and models of human disease, diabetes and metabolism, cardiovascular disease, and cancer. Renovation of the Mazer Building to house the new Institute for Clinical and Translational Research will provide centralized infrastructure for bidirectional bench-to-bedside research. Both facilities will improve Einstein's ability to engage the local Bronx community in cutting-edge research that will advance our understanding of human biology and address the unmet medical needs of this diverse population.

This Strategic Research Plan responds to these current challenges and opportunities in a way that supports existing investigators and research programs while also providing for an expansion of research resources and personnel that will benefit the entire Einstein community. The planning process, which began in June 2006 at meetings of the Faculty Senate, the Science Council, and departmental chairs, was intended to emphasize the need to increase linkages between basic and clinical research programs in ways that would address the overarching purpose of enhancing Einstein contributions to improving human health. The plan was also intended to: increase the College's competitiveness for funding; increase competitiveness for top-quality faculty, graduate student, and postdoctoral fellow recruitment; define a recruitment plan for the CGTM and other space; define space and infrastructure needs; and enhance fundraising efforts.

A Strategic Research Planning Matrix (see Figure 6, page 17) was developed to illustrate the linkage between health-related research programs and science/technology research areas that are important disciplines in their own right, but that also provide universally-applicable research resources and tools. Focus areas in the Matrix represent: existing strengths that could be expanded; major gaps deemed critical to achieving the goal of improving human health through research; fields in which Einstein investment would result in a unique or innovative approach; topics that would enhance multi- or interdisciplinary research; and areas that would promote bidirectional translation between basic and clinical research.

Eight health-related focus areas were chosen: *Aging*; *Cancer*; *Cardiovascular Disease*; *Diabetes, Obesity, and Other Metabolic Diseases; Infection and Immunity*; *Liver Diseases*; *Neuropsychiatric Diseases*; and *Reproductive Medicine and Health*. In addition, seven major science/technology theme areas were developed: *Behavioral and Social Determinants of Health and Health Disparities; Chemical Biology and Chemical Genomics*; *Computational Biology and Systems Biology*; *Human Genetics*; *Imaging*; *Stem Cells and Regenerative Medicine*; and *Structural Biology*. Working groups of faculty with experience in each area were charged with developing forward-looking visions that would advance Einstein research on human health and disease. In addition, the science and technology groups created detailed implementation plans that included proposals for new organizational structures or resource development to achieve their visions and to support the programmatic goals of the health-related focus areas.

Linkages between the two axes that create a true matrix are noted throughout the Plan. Importantly, synergies between the health-related focus areas and the science/technology themes guided the choices and priorities highlighted in the final, integrated implementation plan. Only by investing in both fundamental research that may have unexpected payoffs as well as disease-oriented studies with direct application to human biology can Einstein maintain its leadership position in the biomedical research enterprise.

Translating Research from Bench to Bedside

Translation of basic science discoveries into clinically-relevant applications requires a multidisciplinary team of scientists with diverse expertise, centralized resources, and state-of-the-art clinical research tools. For Einstein to retain its competitiveness as a major research institution, the College must foster a vigorous translational and clinical research program that builds on its basic science strengths and capitalizes on the availability of unique patient populations in the Bronx and other New York City communities.

Einstein's partnerships with multiple, independent academic health centers offer both opportunities to develop new research programs and challenges in the need to provide research faculty with coherent, integrated resources. In addition, the College has direct responsibility for two clinical care sites: the Children's Evaluation and Rehabilitation Center (CERC) and the Division of Substance Abuse (DoSA), both of which offer important resources for translational and clinical research. Key objectives of this strategic plan are to identify ways to collapse barriers to clinical research at the affiliated medical centers, and to fully integrate all of these programs into Einstein's research agenda.

While responding to these local challenges for translational and clinical research, Einstein must also consider the NIH recommendations to the academic community that include: developing a biomedical academic culture that emphasizes scholarship, coupled to a reward system that values membership in teams; resource allocation in a centralized fashion, but that is responsive to divergent needs; and facilitation of research that bridges translational and clinical investigators.

In response, Einstein has established a new Institute for Clinical and Translational Research (ICTR) to integrate existing non-disease-oriented clinical research units into a seamless infrastructure; oversee training and career development in relevant research fields; formalize a partnership with the Montefiore Medical Center for the support of clinical research and training; and promote collaboration. The resources of the ICTR will be available to all Einstein faculty.

Advancing the Science and Technology of Research

The science and technology themes have the potential to create innovative, enabling technologies that can accelerate research across a wide spectrum of human diseases.

Each working group articulated a vision that would enrich Einstein's research efforts and an implementation plan to achieve that vision.

The ***Structural Biology*** group proposes to develop state-of-the-art infrastructure that will strengthen Structural Biology resources and expertise at Einstein, maximize access to and use of this infrastructure by the Einstein research community, and leverage these resources to enhance the development of new therapeutics to treat human disease. Development of an **Einstein Protein Production Facility** will facilitate utilization of existing resources for structural biology and proteomics and accelerate robust, in-house design and development of novel therapeutics. In addition, acquisition of **technology for the rapid generation of new mouse models** will greatly enhance mechanistic research to understand complex phenotypes in animal models of human disease and behavior.

The vision for ***Imaging*** research is to develop an integrated resource that will extend the resolution and interpretation of clinical imaging beyond that currently possible by enabling continuous imaging from nanometers to centimeters in living tissues. A multi-modal **Integrated Imaging Resource** will be created by combining biophotonics technologies for subcellular imaging with whole body imaging approaches. This resource will enable researchers to correlate molecular events with changes at the cellular and tissue level, thus establishing cause-and-effect relationships in disease.

The ***Chemical Biology and Chemical Genomics*** group aims to promote robust and efficient translation of Einstein's basic research discoveries into clinical applications, including drug development, by establishing in-house resources for chemical library screening. A new **Einstein Chemical Screening Facility** will be available to all investigators at the College to identify chemicals that can serve as molecular probes, activators and inhibitors, or lead compounds for novel drugs.

The ***Stem Cells and Regenerative Medicine*** group intends to advance the use of stem cells for improving human health, obtaining new research tools for diagnosing disease, developing cell therapies, and thus positioning the College at the forefront of 21st century regenerative medicine. An **Einstein Institute for Stem Cells and Regenerative Medicine** will be created to provide a central "home" for stem cell research in order to support individual investigators, facilitate the assembly of multidisciplinary teams through increased communication and collaboration, provide shared resources and technologies, and develop educational, enrichment, and training opportunities.

The objective for ***Human Genetics*** research is to advance translational research at Einstein by facilitating the study of common diseases that result from genetic and environmental interactions, genomic variation, and epigenetic alterations. Establishing an **Einstein Translational Genetics Center** will provide necessary infrastructure to link clinical investigators and basic research by enabling cohort studies. The Center will make intellectual resources available for genetic study design from inception to publication and provide access to other essential core services and technologies for human genetics research.

The vision for research in the field of ***Behavioral and Social Determinants of Health and Health Disparities*** is to create a seamless, interdisciplinary research environment that enhances investigator-initiated and collaborative social-ecological approaches to behavioral and social determinants of health and disease, with a focus on reducing health disparities. Development of an academic infrastructure, such as an **Institute of Behavioral and Social Science Research**, will bridge barriers and gaps between departments and disciplines to create a supportive environment for multidisciplinary behavioral and social science research. The Institute will encourage collaboration between biomedical scientists and social/behavioral investigators and facilitate unique, coordinated approaches to research on human health and disease.

The ***Computational and Systems Biology*** group proposes to advance our understanding of living systems by developing new approaches that combine theoretical and experimental methodologies to reveal the properties and functions of the component parts of biological systems and the higher level behavior of complex biological systems that emerges from the interactions of their parts. Implementing this vision at Einstein may require a formal structure to coordinate research, administration, and educational programs in these disciplines. An advisory committee will assess the feasibility of creating a new **Department, Institute, or Center of Computational and Systems Biology** to address these needs.

Improving Human Health through Research

The health-related focus areas represent fields of historic research strength at Einstein, high national priority, and important funding opportunity. Working groups in these areas defined forward-looking visions and major research goals that could be addressed with enhanced resources of the science and technology themes.

The ***Aging*** research group aims to identify and prevent or delay the onset of chronic, debilitating, age-related diseases and promote healthy aging. Research goals include: discovery of genetic factors associated with increased longevity and lower rates of age-related diseases; development of new treatments to counteract the metabolic decline of aging; identification of new methods for early diagnosis and treatment

of Alzheimer's disease and age-related frailty; understanding the molecular mechanisms of cellular aging; and development of novel animal models to understand immune system failure in aging and to design and test new interventions to reverse this process.

The vision of the ***Cancer*** research group is to strengthen research and technical capabilities at the Albert Einstein Cancer Center and link basic, clinical, translational, and population based research in order to bring to fruition new, effective approaches to the prevention and treatment of cancer. Major research goals include: the development of new therapies; establishment of a Cancer Clinical Trial Unit to test experimental therapeutics; targeting the immune system to fight cancer; blocking metastasis of primary tumor cells to distant sites in the body; understanding the tumor microenvironment and cell-cell interactions; identification of epigenetic changes in the genome that contribute to cancer; population-based and epidemiologic research to identify risk factors; and development of behavioral interventions for cancer prevention.

The ***Cardiovascular Disease*** group proposes to discover underlying mechanisms, treatments, and preventive approaches for the most common and devastating cardiovascular diseases using an integrated, multidisciplinary approach employing cutting-edge technologies and capitalizing on the Bronx location. Two overarching research themes were identified: to investigate the complex mechanisms involved in heart failure, using a combination of basic, translational, and clinical approaches; and to understand the causes and prevention of atherosclerotic vascular disease and its sequelae, including heart attack and stroke.

The goal of research on ***Diabetes, Obesity, and Other Metabolic Diseases*** is to prevent or reverse the current epidemic of diabetes mellitus, obesity, and related metabolic disorders. Important research goals include: development of new treatments for type 1 diabetes such as stem cell therapy to replace pancreatic beta cells; elucidation of the cellular mechanisms of obesity and developing strategies to prevent or reverse obesity; investigation of the causes of insulin resistance and its clinical sequelae, such as type 2 diabetes, obesity, and other serious conditions; prevention or reversal of tissue damage caused by diabetes and obesity; and development and testing of culturally sensitive models for diabetes management to improve patient outcomes.

The ***Infection and Immunity*** group envisions a strategy to shift human biological research from organ concepts to a new focus on the human symbiont and associated systems. High-priority research goals include: engaging in multidisciplinary research to understand diseases caused by dysregulation of the immune system; establishment of a Vaccine Institute to design and test new vaccines for the prevention of infectious diseases; understanding the genetic basis of individual susceptibility to infectious diseases; examination of the interactions between microbes and the immune system at the mucosa that impact human disease; discovery and treatment of emerging infectious agents; and development of new therapies to treat HIV/AIDS.

The vision for research on ***Liver Diseases*** is to harness Einstein's significant and unique research strengths in basic liver biology and pathobiology to advance the diagnosis and treatment of liver diseases. Research goals to be pursued include: development of novel approaches to cell and gene therapy for liver diseases; defining the mechanisms of fat accumulation in liver cells and the development of nonalcoholic fatty liver disease (NAFLD); understanding the mechanisms of liver cell injury and death; finding ways to stimulate liver regeneration and development of new treatments for hepatitis viruses and liver cancer; and identification of differences in drug transporters that predict which patients are at increased risk of liver toxicity from pharmaceutical drugs.

The goal of research on ***Neuropsychiatric Diseases*** is to define pathogenesis, prevent disease, and promote cures by exploiting endogenous neural stem cell repair mechanisms, emerging genetic and epigenetic reprogramming and recoding strategies and innovative pharmacogenomic tools. Goals to achieve this vision include: identification of the alterations in neural cell patterning that lead to developmental disorders like autism or mental retardation; understanding the basis for susceptibility to late-onset neuropsychiatric diseases, such as Parkinson's disease or schizophrenia; defining mechanisms of immune surveillance and self-repair in the nervous system; understanding how the neural network maintains normal flexibility and how this process breaks down in disease; and identification of genetic and environmental factors that contribute to psychiatric and behavioral disorders.

The ***Reproductive Medicine and Health*** group aims to create a national program of excellence for research on the influence of reproductive hormones on susceptibility to disease, course of disease, and treatment outcomes. Major research goals include: understanding the basic biology of human reproduction to design new strategies for contraception and treatment of fertility/infertility and menopausal symptoms; defining conditions within the intrauterine environment that impact adult-onset diseases; studying the role of reproductive hormones in the prevalence, severity, progression, and outcome of diseases in women compared to men; understanding the role of the immune system in cancers that solely or primarily affect women, such as ovarian or breast cancer; and investigation of the effect of reproductive hormones on nervous system function.

Realizing the Vision for the Future of Einstein Research

The strategic planning process evolved over 9 months from an initial assessment of current resources to the development of an implementation plan that defines faculty recruitment in departments and centers, space allocation, shared resource needs, and budget projections to accomplish the programmatic visions set forth in the Plan (see Figure 8, page 82). Ultimately, the result of this process will be a state-of-the-art research environment that will foster scientific investigation at all levels from the bench to the bedside and from the clinic to the community.

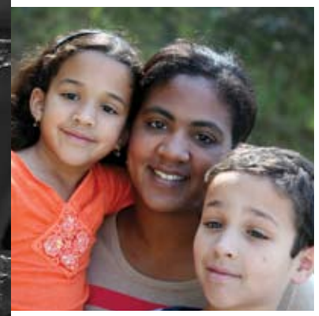
A major outcome of the planning process is the creation of a coherent plan to populate the CGTM with faculty investigators, trainees, core resources, and shared facilities. Specialized facilities, many developed in direct response to the essential needs of the science and technology themes, will be housed in CGTM space (see Figure 10, page 84). In addition, targeted recruitment of new faculty will fill programmatic needs as identified by the health-related focus groups (see Figure 11, page 84).

The Plan cannot be fully implemented within the CGTM, so existing space in other Einstein facilities will be strategically allocated to foster high-priority research programs. For example, the Institute for Clinical and Translational Research and related programs will be centrally located in the renovated Mazer Building. Most importantly, the College will work with a major architectural planning firm that specializes in university planning to develop a 10-year master facilities plan. This plan will address needs for expanding clinical research, providing additional housing for trainees and faculty, and building new amenities for the College community, and will also consider long-range options for future research laboratory construction.

In addition to physical plant considerations, the objectives of this Strategic Research Plan will be met by enhancing opportunities for intellectual collaboration and the development of multidisciplinary teams that can tackle complex research questions. Such teams will provide training for young investigators, leverage common resources and complementary skills, speed bidirectional translation of research results, and enable Einstein to rapidly respond to new research and funding opportunities. Several new Centers, Institutes, or other entities will be built to capitalize on existing faculty expertise; new research teams will evolve as recruited faculty build novel programs in the context of current resources (see page 84). Administrative matters—review of criteria for promotion, faculty development, funding for bridging postdoctoral fellows, upgraded information technology support, and other key issues—will also be addressed to ensure that the goals of this Plan can be accomplished in an effective and timely manner.

Prioritization of the many top-tier initiatives outlined in this Plan will require consideration of available funds, space, and the timing of the recruitment of new faculty (see Figure 12, page 85). This plan is therefore not fixed and immutable. Going forward, the Plan will be adjusted in order to continue Einstein's leadership in biomedical research. Achieving these goals will require strategic partnerships with our affiliated medical centers, with regional, national, and international academic collaborations, with the philanthropic community, and with industry. Finally, we must continue to engage the public—and particularly the people of The Bronx—in our pursuit of improving human health and reducing the burden of disease.

Introduction



The Albert Einstein College of Medicine biomedical research community has engaged in an intensive, collaborative, and rigorous strategic planning process to create a vision that will guide Einstein research over the next 5 years. The resulting Strategic Research Plan builds on more than 50 years of scientific excellence at Einstein to position the College at the leading edge of biomedical research with the ultimate purpose of improving human health and reducing the burden of disease.

History of Biomedical Research and Education at Einstein

The Albert Einstein College of Medicine was conceived as an academic medical institution that would provide world-class medical education and conduct research of the highest scientific caliber without regard to religion, race, or other personal characteristics of its students and faculty. Throughout its history, this socially-conscious and humanitarian commitment has guided the College, which quickly became and has remained one of the nation's leading institutions for biomedical research, education, and training.

Since opening its doors in 1955, the College of Medicine has grown from a class of 56 to more than 1,000 students pursuing the M.D., Ph.D., or M.D./Ph.D. degrees, in addition to 360 postdoctoral fellows receiving advanced training. The Sue Golding Graduate Division administers the Ph.D. degree through an interdisciplinary/interdepartmental program that trains students in the knowledge and skills needed to become independent biomedical scientists. Similarly, the Einstein Medical Scientist Training Program (MSTP) has been continuously funded since 1963 to prepare physician-scientists for careers in biomedical and clinical research. It was one of the first NIH-funded programs for M.D./Ph.D. training and remains one of the largest. The Belfer Institute for Advanced Biomedical Studies oversees the academic and quality-of-life aspects of Einstein postdoctoral fellows to ensure that they are adequately prepared and highly competitive for scientific careers in academia, industry, and education.

Just as the educational program at Einstein has grown, the research base has also expanded over the past half-century to now comprise 370 funded basic science and clinical research principal investigators based at Einstein in 2006. These researchers—working in 10 basic science and 21 clinically-oriented departments—garnered more than $156 million in peer-reviewed NIH grant funding and $20 million of extramural, non-NIH research funding in 2005. In addition, NIH supports six federally-designated Centers at Einstein as well as a number of institutionally- and philanthropically-supported centers and institutes (Figure 1). The diversity of research areas represented in these programs attests to the breadth of scientific expertise at Einstein. These centers represent focal points for interdisciplinary faculty collaboration and provide critical infrastructure and shared resources for the entire Einstein research community.

Einstein partners with five regional medical centers: Montefiore Medical Center (MMC), North Bronx Health Network comprising Jacobi Medical Center (JMC) and North Central Bronx Hospital (NCB), Bronx-Lebanon Hospital Center, North Shore-Long Island Jewish Health System (NS/LIJ), and Beth Israel Medical Center (BIMC). These medical centers, along with

FIGURE 1
Einstein Centers and Institutes

Albert Einstein Biodefense Proteomics Research Center
Albert Einstein Cancer Center*
Bronx Comprehensive Sickle Cell Center*
Cardiovascular Research Center
Center for AIDS Research*
Center for Reproductive Biology
Children's Evaluation and Rehabilitation Center
Diabetes Research and Training Center*
General Clinical Research Center*
Gruss Lipper Center for Biophotonics
Gruss Magnetic Resonance Research Center
Human Genetics Program
Institute for Aging Research
Institute for Brain Disorders and Neural Regeneration
Institute for Clinical and Translational Research
Institute for Community and Collaborative Health
Institute for Smooth Muscle Biology
Institute for Stem Cell Biology
Jack and Pearl Resnick Gerontology Center
Marion Bessin Liver Research Center*
Michael F. Price Center for Genetic and Translational Medicine (CGTM)/ Harold and Muriel Block Research Pavilion
Rose F. Kennedy Center for Research in Mental Retardation and Developmental Disabilities
Seaver Center for Bioinformatics

*NIH-designated centers

three mental health facilities and four long-term care facilities, provide state-of-the-art clinical training for Einstein medical students. In addition, the affiliated medical centers represent exceptional opportunities for Einstein researchers to engage in collaborative translational and clinical research that directly addresses the health and medical needs of the community.

On the strength of its research programs, Einstein ranked 27th out of 123 medical schools in terms of total NIH funding in 2005. Yet, the College ranked 6th in funding per principal investigator (Figure 2). This suggests that Einstein researchers are highly productive and that the overall standing could be improved by the recruitment of similarly productive faculty members who could complement and expand the existing research programs.

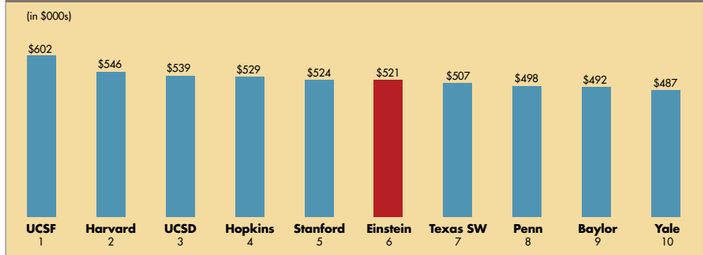
The measure of an institution's success does not lie solely in the amount of grant funding that it is able to procure. Einstein's long history of leadership in biomedical research has generated many important scientific discoveries and clinically-relevant breakthroughs. Significant advances resulting from Einstein research include:

- *Basic Research*: development of landmark techniques to grow human tissues under laboratory conditions, an advance that helped make possible all subsequent research in cell biology; and participation in the historic international project to map the human genome.
- *Aging:* identification of the key missing protein in the brain of Alzheimer's patients, a finding that influenced all subsequent Alzheimer's disease research.
- *Cancer:* identification of the anti-tumor mechanism of Taxol, one of the most significant anti-tumor drugs of the past decade; and development of a new class of inhibitors for treating cancer without the side effects of most chemotherapy agents.
- *Cardiovascular Disease:* demonstration of the association between reduced levels of high-density lipoprotein ("good" cholesterol) and heart disease; and first use of gene therapy to treat abnormally high cholesterol in the laboratory, leading to an effective treatment for human patients.
- *Diabetes*: development of ground-breaking new protocols for diabetes treatment based on more sophisticated methods of monitoring blood glucose levels; and identification of new modifiers of insulin function that can lead to better treatments of type 2 diabetes and obesity.
- *Infectious Disease:* development of innovative new therapies to combat drug-resistant tuberculosis; and identification of pediatric AIDS as a distinct disease and establishment of the first day care in the world for children with AIDS.
- *Neurological Disease:* development of a new class of pain relievers that will reduce the addictive potential of narcotic analgesics; and discovery of structural abnormalities of brain cells that explain deficiencies in cognitive development.
- *Pediatrics:* prevention of untold cases of blindness in premature infants through a revolutionary understanding of the oxygen requirements for very low-birth weight infants; and fundamental research on the harmful effects of lead in the environment that spearheaded public health efforts to combat lead poisoning, especially in children.

The Challenge of Biomedical Research in the 21st Century

In the 52 years since Einstein was founded, major advances in science and technology have revolutionized the understanding of the mechanisms of human health and disease and led to the discovery of new methods to detect, prevent, and treat disease more effectively. As importantly, this explosion of knowledge and innovative technologies has created entirely new research disciplines and has fundamentally altered the way biomedical research is conducted. The stereotype of an individual scientist working in an atmosphere of isolation and driven solely by personal curiosity is no longer valid or even practical. Biomedical research has become increasingly collaborative, technology-oriented, and focused on improving the human condition.

FIGURE 2
Ranking of NIH Grant Funding per Principal Investigator



Note: PI number includes individuals holding 1 or more Federal grant of any type
Source: Carl Mankowitz, M.D., CSC consulting report to Einstein, December 2005

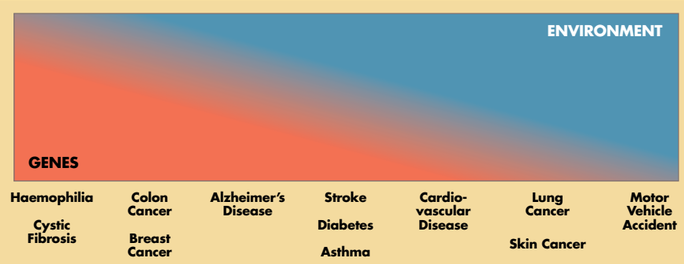
The landmark mapping of the human genome, which was completed in 2003, revealed the presence of an estimated 20,000 to 25,000 genes in human DNA, far fewer than was originally predicted. Genetic contributions to the full range of human diseases were found to include not only variations or mutations in the DNA sequence, but also "epigenetic" changes or modifications to the DNA structure. Many diseases arise from complex interactions between multiple genes that have both genetic mutations and epigenetic modifications, any one of which may contribute only a small fraction of the risk for disease. In addition, scientists have increasingly appreciated the role of the environment in health and disease. Voluntary behaviors such as smoking, excessive sun exposure or unhealthy dietary habits are only part of the environment that affects disease risk. The role of other factors, such as family and social networks or poverty, are being recognized and studied. Genetic and environmental factors interact in intricate and largely unknown ways to trigger a continuum of human diseases and conditions (Figure 3). Some diseases, such as haemophilia or cystic fibrosis, are nearly entirely determined by genetic mutation, while others, including accidents and trauma, are mainly attributable to the environment.

Unraveling the web of genetic and environmental factors for a given disease and using that information to develop new therapies cannot be accomplished by any one investigator, or even a single scientific discipline. Progress in biomedical research in the 21st century requires cross-disciplinary, bidirectional research that translates basic science discoveries from the laboratory to the clinic and back again (Figure 4). Successful investigators must both build on and feed into the work of their colleagues.

For example, when a human geneticist identifies a gene associated with a particular disease, that information can spark cellular/molecular and biochemical research to understand the basic structure and function of the gene and its protein product. Animal models of the disease can be developed to study the gene in a physiological context and to test potential therapies. At the same time, population biologists can study large groups of people to identify environmental risk factors that interact with the gene and modulate its effects. Data from all sources must be integrated and translated into clinical settings where they can be validated in human patients. Conversely, a clinician who observes a new syndrome in patients can set the cycle in motion in the opposite direction. Regardless of where the cycle begins, real progress depends on robust communication and interaction among scientists with a wide variety of expertise and skills

Throughout this process, the research community must keep its eye on the main goal: improving the ability to diagnose, prevent, treat, or cure disease. This objective is complicated by the increasing costs of healthcare in this country that threaten to put new therapies out of the reach of many Americans. In 2004, the total national

FIGURE 3
Continuum of Genetic and Environmental Contributions in Common Diseases



Source: Bernice Morrow, Ph.D., Albert Einstein College of Medicine

expenditure on healthcare was $1.9 trillion or 16 percent of the gross domestic product (GDP). By 2015—less than a decade away—these numbers are expected to climb to $4 trillion, representing 20 percent of GDP.*

Currently, most medical intervention occurs very late in the time course of disease at a high economic cost as well as a heavy burden of disability and death (Figure 5, grey line). While biomedical research has led to the development of novel diagnostic tools and more effective treatments that allow earlier intervention, many of these advances have not been efficiently translated into routine clinical practice. Nonetheless, researchers are working toward a future when most diseases can be detected at or before onset, allowing prevention or treatment to occur at the earliest possible stage and substantially reducing the costs and burden of disease and improving patient outcomes (Figure 5, blue line).

Achieving this vision of the future and making it a reality for all patients is the fundamental challenge faced by the entire international biomedical research community. Einstein, as a longstanding leader in the field, is poised to meet this challenge by assessing the strengths and gaps in its research programs and strategically charting a course forward.

Development of a Strategic Plan for Einstein Research: A Transformative Era

The Albert Einstein College of Medicine, a research-intensive medical school with a long track record of accomplishment, is entering a new, transformative era. A convergence of external and internal factors requires the College to evaluate the status and direction of its research programs. In order to enhance its position as a major force in biomedical research in the 21st century, Einstein must respond to these challenges and opportunities with a thoughtful and visionary strategic plan that strengthens existing research and paves the way for a productive expansion of resources and talent.

A New Environment for Biomedical Research Funding

Academic biomedical research in the United States is funded in large part by the National Institutes of Health (NIH), a federal agency within the Department of Health and Human Services. From fiscal years 1999 through 2003, the U.S. Congress enacted historic appropriations that effectively doubled the NIH budget in 5 years—twice the usual rate of budgetary increases. This surge of funding led many institutions around the country to rapidly build new infrastructure and increase the size of their research faculty. However, the budget doubling period ended abruptly with essentially flat budgets in 2004 and 2005. In 2006, the NIH budget appropriation was reduced by 0.1 percent—the first enacted reduction since 1970**. This new budget reality severely curtails the agency's ability to fund new research projects and to competitively renew existing grants, even those that have been productive, for the foreseeable future.

Under the leadership of Elias A. Zerhouni, M.D., NIH Director since 2002, the NIH has set out to catalyze fundamental change in biomedical research through its "Roadmap for Medical Research." The Roadmap seeks to accelerate the progress of medical research by tackling cross-cutting challenges aimed at translating scientific discovery into real benefits for people. Three overarching themes guide Roadmap programmatic decisions and funding:

- *New Pathways to Discovery:* Understanding the complexity of human health and disease requires a new "toolbox" for medical research, drawing from the disciplines of chemistry, imaging, structural biology, bioinformatics, computational biology, and systems biology.
- *Research Teams of the Future:* Increasingly, problems in biomedical research must be addressed from a multidisciplinary perspective that can only be provided by teams of scientists working in collaboration to test innovative, high-risk ideas that have the potential to lead to ground-breaking advances.
- *Re-engineering the Clinical Research Enterprise:* To successfully translate research into improved health, the clinical research system must be upgraded with new information technologies, partnerships that link researchers to patients and the community, more efficient clinical research networks, and enhanced training for clinical and translational researchers.

Einstein, which derives a significant portion of its operating budget from federal grants, must respond to the changing funding environment and shifting priorities of the NIH; however, it is important to note that the federal government is only one of many potential sources of research funding. The pharmaceutical industry reported spending $51.3 billion on research and development in 2005, largely associated with drug development and clinical trials. Pharmaceutical and biotechnology companies frequently partner with academic institutions to carry out trials in appropriate patient populations. Numerous voluntary health agencies as well as public and private foundations support biomedical research on a wide range of health and disease topics. Finally, state governments are becoming increasingly involved in research funding. In his State-of-the-State address on January 3, 2007, New York governor Eliot Spitzer proposed the creation of a Stem Cell and Innovation Fund, which would add New York to the growing number of states that directly support stem cell research. The NY Stem Cell and Innovation Fund Corporation will propose a $1.5 billion bond in the November 2008 election. The fund would support $500 million over 10 years to support stem cell research beginning in 2008-09. To successfully compete in this new era of biomedical research, Einstein must identify and respond to all potential funding sources.

Changing Landscape at Einstein

In 2006, Einstein recruited its seventh Dean, Allen M. Spiegel, M.D., to succeed Dominick P. Purpura, M.D. who had led the College with vision and commitment since 1984. Dr. Spiegel is an internationally recognized researcher and endocrinologist who conducted a highly productive translational research program on signaling dysfunction in human disease. His 33 year tenure at NIH culminated as Director of the National Institute of Diabetes and Digestive and Kidney Diseases, the fifth largest NIH institute with an annual budget approaching $2 billion. Given his record of achievement both as an active physician-scientist and as a research funding administrator, Dr. Spiegel's new leadership makes this an opportune moment to re-assess the College's goals and strategic objectives and to chart a way forward for Einstein's research programs in the context of the shifting funding environment.

New facilities already under construction are setting the stage for significant faculty recruitment and expansion of research resources. The most prominent addition to the Einstein campus is the Michael F. Price Center for Genetic and Translational Medicine (CGTM)/Harold and Muriel Block Research Pavilion, which is scheduled to open in late 2007. This new 212,000 square foot research building will contain both wet and dry laboratories, 10 specialized scientific facilities, and a 100-seat auditorium. Approximately forty faculty scientists will be recruited to direct research programs in major disease focused areas, including cell transplantation, liver diseases, human genetics, infectious diseases, mouse genetics and models of human disease, diabetes and obesity, cardiovascular disease, and the genetics and biology of cancer. Key features of the CGTM are the availability of "open laboratories" on each floor and adjoining space for computational and systems biologists that is designed to increase communication and collaboration among the researchers.

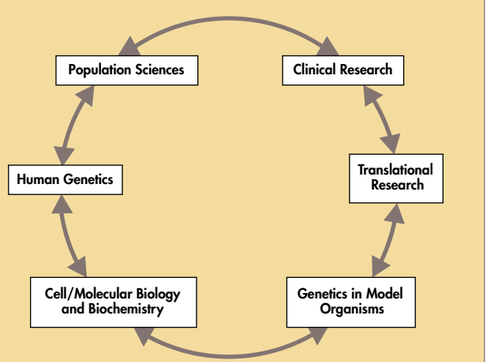
In addition, renovation of the Mazer Building to house the new Institute for Clinical and Translational Medicine (ICTR) will enhance the College's ability to support bidirectional bench-to-bedside research.

One aspect of the Einstein landscape that has not changed—unless perhaps to grow more critical—is its location in the Bronx, one of the most impoverished communities in the U.S. The Bronx has a racially- and ethnically-diverse population that bears a disproportionately heavy burden of disease. Diabetes, heart disease, HIV/AIDS, asthma, and preterm birth are just a few examples of the many conditions that are prevalent in this population and compounded for many individuals by lack of access to adequate health care. Einstein has both an opportunity and a responsibility to engage the community in cutting-edge research that will advance knowledge of human health and disease and, as importantly, address the unmet medical needs of the surrounding population.

Strategic Planning Process

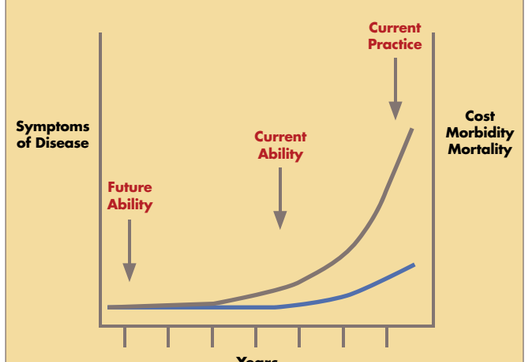
The Einstein strategic research planning process was initiated in June 2006 at meetings of the Faculty Senate, the Science Council, and departmental chairs. The immediate goal was to develop a list of high priority research areas for Einstein focus and an implementation plan defining how the College could be successful in those areas. The planning process specifically emphasized the need to increase linkages between basic and clinical research programs to address the overarching purpose of enhancing Einstein contributions to improving human health. The plan was also intended to: increase

FIGURE 4
Bidirectional Cycle of Biomedical Research Involving Genetics



Source: Richard Kitsis, M.D., Albert Einstein College of Medicine

FIGURE 5
Model of Medical Practice and Ability for Disease Prevention



Source: Raymond DuBois, M.D., Vanderbilt University Medical Center

*Source: National Coalition on Health Care
**Loscalzo, J. NEJM 2006; 354: 1665-1667

the College's competitiveness for funding; increase competitiveness for top-quality faculty, graduate student, and postdoctoral fellow recruitment; define a recruitment plan for the CGTM and other space; define space and infrastructure needs; and enhance fundraising efforts. Importantly, increasing the performance of Einstein as a whole would transcend issues related to the needs of individual investigators and departments.

With these guiding principles at the forefront, the College has engaged in an inclusive, transparent process to develop a coherent and meaningful Strategic Research Plan. More than 150 faculty members representing all academic departments (see Appendix) have directly participated in the formulation of the Plan. Moreover, interim documents tracking the progress of the planning effort have been posted on a website that is accessible to all.* Investigators have been encouraged to communicate with working group members and the Dean's Office staff to provide feedback and ideas.

At its June meeting, the Science Council proposed and discussed an extensive list of potential topics for the plan. After an iterative process to determine the highest priorities, working groups were assembled around each of 10 theme areas. These initial working groups were given the task of preparing a presentation on the current status and potential future direction of their assigned area at Einstein. At a one-day retreat in mid-July, the working groups presented their findings to a group of researchers from Einstein and the clinical affiliates for the purpose of understanding each of the 10 themes and the synergies and interactions among them. Out of the discussion at the July retreat, a matrix of health-related and science/technology focus areas emerged that would form the basis of the final Strategic Research Plan (Figure 6). Working groups—reconfigured for each of the health-related and science/technology focus areas on the new matrix—met repeatedly over the course of 3 months to craft a proposal for development of their area. A second, longer retreat was convened in early October to present and critique each of the working group plans and to begin a discussion of implementation priorities. At a Board of Overseers retreat in late October, Dr. Spiegel presented a preliminary look at the diverse goals identified by the working groups. Since that time, the Dean's Office staff has integrated the visions and research objectives from the individual working group plans into a single, cohesive implementation plan that will guide Einstein's progress into the new era of translational, and transformative, research.

The Matrix: A Framework for Strategic Research Planning

A central goal of this plan is to forge stronger links between basic science and clinical medicine at Einstein. The Strategic Research Planning Matrix emphasizes the need for both health-related research programs that maintain focus on the human condition as well as science/technology research areas that are important disciplines on their own, but that also provide essential research tools and resources. Selection of focus areas for inclusion in the Strategic Research Plan was based on several criteria:

- existing strengths that could be expanded;
- major gaps deemed critical to achieving the goal of improving human health through research;
- fields in which Einstein investment would result in a unique or particularly innovative approach;
- topics that would enhance multi- or interdisciplinary research; and
- areas that would promote bidirectional translation between basic and clinical research.

Eight health-related focus areas were chosen: *Aging; Cancer; Cardiovascular Disease; Diabetes, Obesity, and Other Metabolic Diseases; Infection and Immunity; Liver Diseases; Neuropsychiatric Diseases; and Reproductive Medicine and Health*. It is important to note that these areas do not encompass every disease that is or could possibly be studied at Einstein. Rather, these focus areas represent general fields of historic strength that are also topics of high national priority and funding opportunity. These focus areas are not mutually exclusive, but have considerable overlap. For example, the problems of aging include increased rates of cancer, diabetes and other metabolic diseases, neurological conditions such as Alzheimer's and Parkinson's disease, and cardiovascular disease. Each health-related working group was charged with developing a vision for their area and describing how that vision could be realized through the resources of the science/technology areas. The groups were also asked to formulate an implementation plan to identify available and required resources.

Seven major science/technology theme areas were developed: *Behavioral and Social Determinants of Health and Health Disparities; Chemical Biology and Chemical Genomics; Computational Biology and Systems Biology; Human Genetics; Imaging; Stem Cells and Regenerative Medicine; and Structural Biology.* Like the health-related focus areas, these themes are highly interconnected both among themselves and with all of the health topics. Each of these research disciplines has the potential to create innovative, enabling technologies that accelerate research on health and disease. Although the charge to each of the science/technology working groups varied slightly, the overall goal for each group was to articulate a forward-looking vision that could be programmatically tied to one or more of the health-related focus areas. Each working group also devised a specific and detailed implementation plan that included, where appropriate, proposals for new organizational structures or resources to achieve their vision.

*http://www.aecom.yu.edu/home/researchsp

FIGURE 6
Strategic Research Planning Matrix

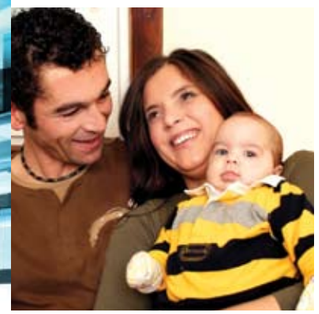
Science/Technology Theme Areas	Health-Related Focus Areas: Aging	Cancer	Cardiovascular Disease	Diabetes, Obesity & Other Metabolic Diseases	Infection and Immunity	Liver Diseases	Neuro-psychiatric Diseases	Reproductive Medicine & Health
Structural Biology								
Imaging								
Chemical Biology & Chemical Genomics								
Stem Cells and Regenerative Medicine								
Human Genetics								
Behavioral and Social Determinants of Health and Health Disparities								
Computational Biology & Systems Biology								
Cell-Cell Interactions								
Signaling								

Two additional areas were identified as important science/technology themes: *Cell-Cell Interactions*; and *Signaling*. Through the efforts of the working groups, it became clear that many Einstein investigators are engaged in valuable basic and clinical research related to these areas, which also fundamentally intersect with all health-related areas and several science/technology themes. However, as the planning process unfolded, the decision was made that stand-alone implementation plans would not be developed for these broad, wide-ranging research fields. As plans for the other areas are defined, synergies with Cell-Cell Interactions and Signaling research will be sought out in order to capitalize on the strengths of the current Einstein faculty.

Although the bulk of this plan describes the individual focus areas, inter-relationships between the two axes that create a true matrix are noted throughout the document. Synergies between the health-related focus areas and the science/technology themes guided the choices and priorities highlighted in the final, integrated implementation plan. Only by investing in both fundamental research that may have unexpected payoffs in addition to disease-oriented studies with direct application to human biology can Einstein maintain its leadership position in the biomedical research enterprise.

Translating Research from the Bench to the Bedside

The translation of fundamental biological discoveries made in the laboratory into new applications that impact human health cannot be accomplished by a single investigator. Conducting research in human subjects requires diverse tools and expertise that can only be supplied by a multidisciplinary team of scientists and centralized resources. For Einstein to retain its competitiveness as a major research institution in the 21st century, the College must foster a vigorous translational and clinical research program that builds on its basic science strengths and capitalizes on the availability of unique patient populations in the surrounding community.



Barriers to Clinical Research at Einstein and its Affiliate Network

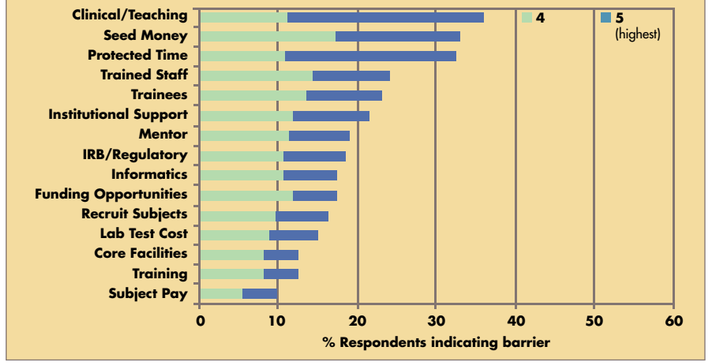
The challenges for clinical and translational research over the past two decades have been well documented, and include the dearth of appropriately trained health professionals, the fragmented nature of the resources available, and the lack of continuity between the various components of the academic medical community.

Einstein's academic health center partners offer opportunities and challenges in developing new research partnerships. Since each is an independent health care system, providing faculty with coherent and integrated resources is essential. In order to assess the needs of this large faculty, an on-line survey conducted as a part of the strategic planning process assessed the perceived barriers to clinical and translational research among 4,430 faculty members (including all full-time, part-time, and voluntary faculty). To examine the corresponding affiliate-based resources, detailed Institutional research profiles were sought from the respective medical center CEOs. The survey data presented below are only for full-time faculty (N=2,532: College payroll (Einstein), 550; MMC, 849; NS/LIJ, 369; BIMC, 345; and JMC, 229).

Based on the CEO-generated Medical Center data, and the self-report from the affiliate-based faculty survey, some 25% of faculty members are engaged in research for a portion of their academic activity, and 30-40% conduct research for a substantial portion of their effort. In general, the vast majority of faculty at the affiliated medical centers reported translational and clinical research as their focus, while 90% of the Einstein-based faculty reported that their primary research was basic. However, 65% of Einstein-based faculty reported some clinical and translational research in their portfolios, and varying portions of affiliate-based faculty (10% to 30%) indicated that their research is basic.

Potential barriers to research were listed in the survey questionnaire, and respondents were asked to rate them on a scale from 0 ("not a barrier") to 5 ("a major barrier"). We analyzed these responses, grouping the top two rating grades as directly pertinent to their concerns (Figure 7). As a group, "clinical/teaching duties," "seed money," and lack of "protected time" were identified by the highest proportions of respondents (>30% for all). Protected time is the single most frequently expressed need by faculty who responded as either interested in doing or currently engaged in some clinical research. However, investigators with >60% effort devoted to research (and who are presumably funded extramurally) do not express this need. These latter "experienced" clinical research faculty identify other infrastructure needs such as seed money

FIGURE 7
Perceived Barriers to Research (all respondents, on a scale 0-5)



and better/more trainees. Not surprisingly, the lack of protected time or requirement for teaching or clinical activities was particularly acute in affiliate-based faculty with a limited research portfolio.

Though the barriers are challenging, these data can help to inform a discussion of various approaches to promote clinical research in collaboration with investigators based at the College and across a breadth of clinical departments. There is a robust—but fragmented—clinical research enterprise scattered throughout the affiliated academic health centers. While it is clear that not every institution has the infrastructure in place for all categories of clinical research, it is also clear (based on the faculty responses) that the existing resources are not widely available, especially to junior faculty and those who do not have a major role in clinical research.

Einstein-Directed Clinical Care Programs

The majority of Einstein's clinical education and care activities are carried out through the affiliated hospitals. However, the College has retained direct responsibility for two clinical care sites: the Children's Evaluation and Rehabilitation Center (CERC) and the Division of Substance Abuse (DoSA). Both CERC and DoSA represent outstanding, but currently underutilized, resources for translational and clinical research on important health issues that are prevalent at the local and national levels. An important aspect of this strategic plan is to identify ways to more fully integrate these programs into Einstein's research mission and agenda.

Children's Evaluation and Rehabilitation Center (CERC)

CERC's mission is to help children with disabilities reach their full potential and to support parents in their efforts to get the best care, education, and treatment for their children. As part of the Rose F. Kennedy Center for Research in Mental Retardation and Developmental Disabilities, the Center provides comprehensive evaluation, diagnosis and treatment services for infants, children, adolescents and adults who suffer from severe physical, developmental, and social-emotional disorders. These debilitating conditions—which include autism and autistic spectrum disorders, mental retardation, cerebral palsy, spina bifida, hearing impairment, and language and learning disabilities and other serious neurological problems—affect children's cognitive, emotional and social development and can significantly impact school readiness as well as the ability to function in society.

As one of the largest centers of its kind in the United States, CERC has a multidisciplinary professional staff that provides more than 58,000 diagnostic, therapeutic and related services to about 8,000 children and their families annually, while training close to 1,000 professionals each year. The primary population of CERC clients is children from the Bronx and surrounding areas who are at risk for having developmental disabilities because of both genetic factors and their exposure to multiple economic, environmental and social stresses. In addition, thousands of children from throughout New York State already diagnosed with developmental disabilities come to CERC to receive services. Among the many programs currently ongoing at CERC, three primary diagnostic and therapeutic programs include: 1) the Early Childhood Center, which treats young children (birth to age 5) who present with developmental delays coupled with social-emotional difficulties associated with environmental factors such as exposure to domestic violence, addiction and absent parents; 2) the Infant and Toddler Team (ITT), which provides family-based diagnostic assessments and individualized treatment plans for children ages birth to 3 who have, or are suspected of having, developmental delays. The ITT includes the RELATE Program, which provides evaluation and treatment for young children with autism and autistic spectrum disorders; 3) The Fisher Landau Center for the Treatment of Learning Disabilities, which since its advent in 1968 has been offering comprehensive services for infants, toddlers, school-age children, adolescents and adults with severe language and learning disorders.

Under the leadership of its new director, plans are underway for adding a clinical research component to CERC. This new clinical research program will aim to identify the causes of and develop innovative treatments for a broad spectrum of developmental disorders in children, including autism and autism spectrum disorders.

Division of Substance Abuse (DoSA)

DoSA and other substance dependency clinical programs are overseen by the Department of Psychiatry and Behavioral Sciences. DoSA treats adults who live or work in the Bronx that present with substance abuse addiction. Reliable diagnostic criteria and state-of-the-art assessment techniques are used to identify addiction characteristics and severity, screen and diagnose coexisting health and psychiatric conditions, and distinguish the most appropriate treatment path and level of care. Patients are provided with medical and/or behavioral interventions, psychosocial support, relapse prevention, and individual, family and group therapies aimed at management of addictions and improvement of the patient's health and quality of life. A unique feature of DoSA is that patients receive general health care through the program, offering opportunities not only for research to understand the causes of addiction and prevention and treatment strategies, but other aspects of health care that make for a substantial personal and societal burden.

Institute for Clinical and Translational Research (ICTR)

Over the last few years, the academic community in general—and NIH specifically—has reached consensus on the solutions for the challenges in clinical and translational research. These include:

- Developing a biomedical academic culture that emphasizes scholarship, coupled with a reward system that values membership in teams;
- Resource allocation in a centralized fashion, but that is responsive to divergent needs;
- Facilitation of research that bridges translational and clinical investigators.

The recently-announced "Clinical and Translational Science Award" (CTSA) model defined by the NIH Roadmap for Medical Research is part of its goal to re-engineer the clinical research enterprise along these lines. The CTSA calls for a transformative reorientation of both the infrastructure as well as the academic environment for clinical research. Einstein has operated an NIH-funded General Clinical Research Center (GCRC) that provides core services and facilities for patient-oriented research since 1963. In 1997, the GCRC program was reconfigured as a College-based operation under the philanthropic aegis of the Forchheimer Foundation. In 2006, 60 research protocols were underway in the GCRC. A second pediatric unit opened in 2006 in partnership with Montefiore Medical Center (MMC) to support research focused on children's diseases, and to complement resources for clinical research at the West Campus. Einstein launched its clinical research training program in 1998, and by 2006 its NIH-funded Master's degree granting program had become the focal point for developing the "pipeline" of new investigators, from a medical student M.D./M.S. program to a Ph.D. in Clinical Investigation granted by the Graduate School.

In response to the CTSA challenge, Einstein has established a new Institute for Clinical and Translational Research (ICTR) to integrate existing non-disease-oriented clinical research platforms into a seamless infrastructure for clinical and translational research. The ICTR oversees training and career development of investigators with an interest in clinical and translational research. Moreover, the ICTR formalizes a partnership between Einstein and MMC for the purpose of supporting clinical research and training. The College has committed resources and space for the development of the ICTR. In phase one, renovation of the Mazer Building will provide much-needed space to enhance the infrastructure for clinical research scholars, to house 10-15 new clinical investigators, and promote collaboration through the Institute.

The ICTR is a partnership with Montefiore Medical Center, but will extend its resources to all of Einstein's faculty. The Montefiore Medical Center provides comprehensive health care to the more than 1.4 million residents of the Bronx and southern Westchester County. Annually, the medical center and its network have more than 2 million outpatient visits and over $2 billion in revenues. The Einstein-Montefiore ICTR partnership facilitates access to clinically-important patient populations by Einstein researchers and provides expanded opportunities for Montefiore-based clinicians to initiate and participate in clinical research projects. In recent years, Montefiore has invested more than $140 million in medical information technology, including a networked out-patient and in-patient information system for the Medical Center and 19 primary care centers in the community. This database was intentionally built as a resource for research, enabling access to de-identified, aggregated clinical data that currently encompass over one million patients. A new Biomedical Informatics Network (BIN) is under development to allow the secure exchange of this and other datasets between the clinical program at Montefiore and researchers at Einstein. The BIN will create a new relational database environment for integration of clinical and scientific information.

A key feature of the ICTR structure is that ALL affiliate-based faculty can receive support, not just those based at the medical school or at MMC. The ICTR enhances the ability of each institution to recruit and retain highly qualified physician-scientists who are engaged in state-of-the-art translational and clinical research.

When fully-funded, the Einstein ICTR will offer multiple core services and facilities designed to break down barriers that often inhibit investigators' ability to translate basic discoveries into clinical applications. These resources enable researchers to more easily and efficiently perform clinical and translational research without the need to "reinvent the wheel" for every study. ICTR consultation services provide access to specialized expertise in biostatistics, trial/

study design, epidemiology, and bioethics. The Institute coordinates community engagement activities to facilitate study recruitment and retention in a manner that is sensitive to the needs of the community. Assistance with Institutional Review Board (IRB) regulatory matters is available. Finally, the ICTR helps coordinate early-phase therapeutics and diagnostics discovery and development, and awards pilot and collaborative grants to assist investigators in obtaining preliminary data for new research ideas.

By serving as a translational research "corridor" to resources throughout the college, the ICTR supports the goals of all science and technology theme areas represented in this strategic plan. For example, funds will be provided for shared facilities that include a Mass Spectroscopy Core for human research; the Moses Tower Cellular Therapeutics cGMP facility that interfaces with the goals of the stem cell research program; a Translational Genetics facility; MR imaging and spectroscopy; and a Biorepository for storage of blood and tissue samples to facilitate population-based studies. The Institute will enable widespread access to resources for proteomics, human genetics, and biomarker discovery in conjunction with development of the programs of the CGTM.

Novel translational research "incubators" are in development, such as a program to support the continuum of stem cell research from basic science to ethics. An incubator for statistical sciences will encourage research on new statistical methodologies that could be applied to clinical trials. A registry of research patient cohorts will enhance access to and analysis of datasets from completed and ongoing research studies. Finally, a major collaboration with MMC in biomedical informatics will foster research on clinical datasets created from electronic medical records of MMC patients.

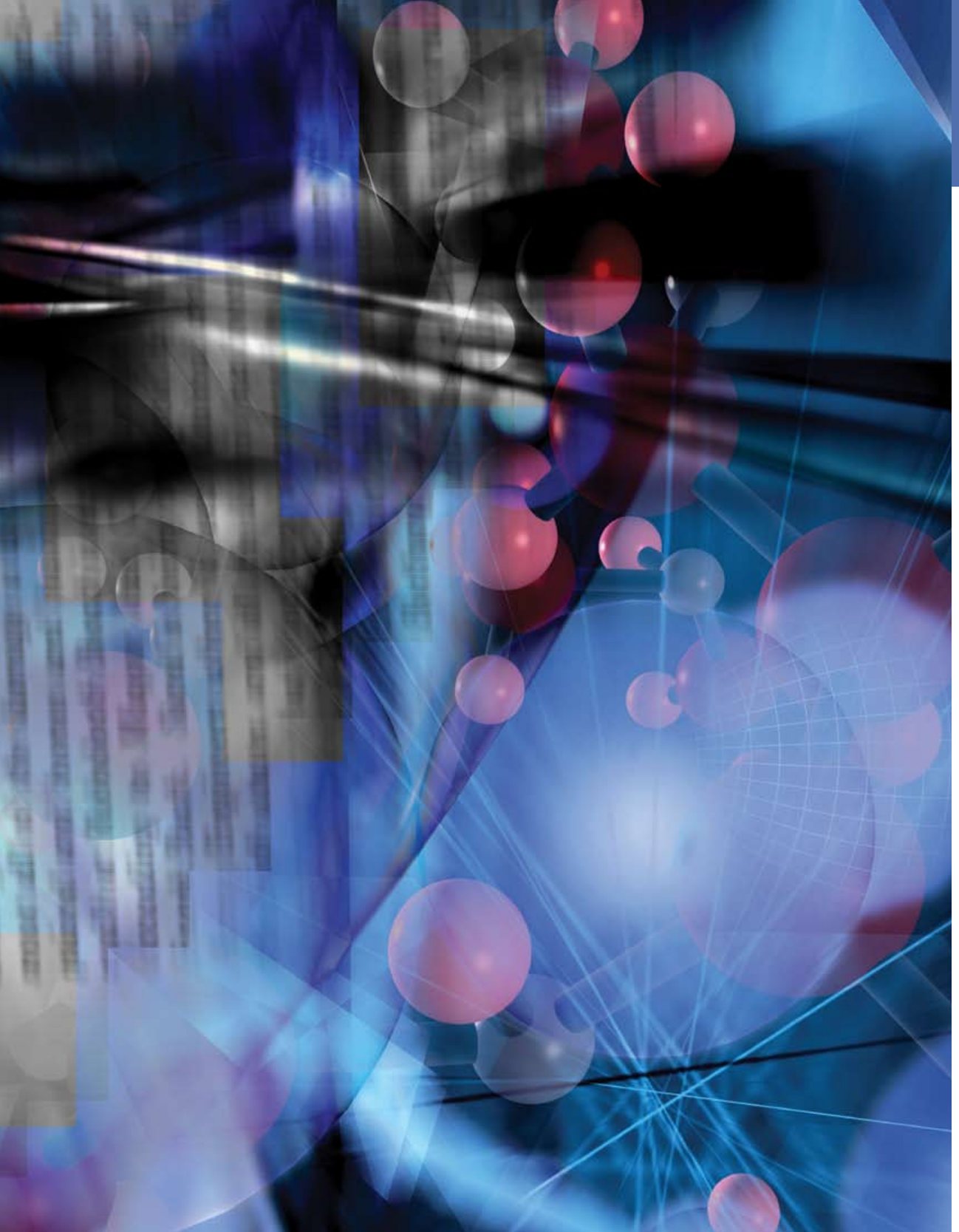
Clinical research resources continue to reside in many of the disease-oriented centers, departments, and affiliates. These programs synergize with the ICTR which bridges the various health-related programs. The Institute provides crucial support for Einstein participation in large, national, multi-center clinical research studies and trials, and enables long-term follow-up of patient cohorts for Alzheimer's disease, aging, diabetes, women's health, and other health issues. In addition, the ICTR will work with other clinical research support mechanisms, such as the Cancer Center's protocol review and oversight functions. The ICTR will provide a platform on which to build novel Einstein-wide efforts, including women and minority career and leadership development, nursing research and training, dental research training collaborations, and to foster the growth of already strong research programs in behavioral science to synergize with new opportunities in cancer, cardiovascular disease, and health disparities.

Clinical Research Education, Training, and Career Development

A principal focus of the ICTR is oversight of clinical training and career development programs. The NIH-supported Clinical Research Training Program (CTRP) is a 2-year program in clinical methodology that confers a M.S. degree in Clinical Research Methods upon completion. The CRTP offers a didactic curriculum, emphasizing epidemiology, biostatistics, study design, computer methods, and research ethics as well as a mentored experience in clinical research, leading to the preparation of a thesis. The program was recently expanded to include a new track granting a Ph.D. degree in Clinical Investigation. A research-oriented training program culminating in a Master of Public Health (M.P.H.) degree has been developed with the Ferkauf Graduate School of Psychology. Other educational opportunities, including certificate programs in research methods, bioethics, and community-oriented research, offer investigators the knowledge and skills to participate in clinical research.

The ICTR will permit expansion of the NIH-funded K12 program of mentored career development for clinical scientists in a multidisciplinary environment. This vital component of the Institute helps secure a "pipeline" of young physician-scientists engaged in clinical and translational research. Several members of the ICTR leadership themselves benefited from the formal mentoring available through the K12 program and successfully transitioned to independent faculty positions at Einstein upon completion.

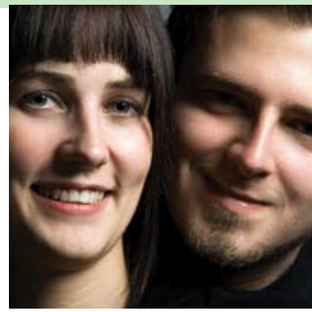
Advancing the Science and Technology of Research



Structural Biology and Proteomics

THE VISION

To develop state-of-the-art infrastructure that will strengthen Structural Biology resources and expertise at Einstein, maximize access to and use of this infrastructure by the Einstein research community, and leverage these resources to enhance the development of new therapeutics to treat human disease



The Challenge and Opportunity

Structural biologists map the architecture of individual proteins as well as multi-protein complexes and use that information to understand the structure, function, and dynamic interactions of those proteins and complexes. At atomic and molecular resolutions, structural data help scientists rationally design new molecules that selectively modulate the activity of particular proteins. Such inhibitors or activators serve as research tools that allow investigators to study protein activity in living cells or can, in some cases, be developed into new drugs to treat human disease in a targeted manner. The field of proteomics generates complementary data on the composition, assembly, and modification of proteins. Proteomics approaches are used to discover biomarkers that correlate with disease or identify new therapeutic targets.

Over the past 15 years, Einstein has made considerable investments in instrumentation and infrastructure to build a state-of-the-art program in structural biology with access to resources that span all biologically relevant resolution ranges from atomic to whole animal. Local infrastructure is available for nuclear magnetic resonance (NMR), x-ray diffraction, electron microscopy, molecular proteomics, and multiple spectroscopic techniques. Regional and national facilities provide unique opportunities in high resolution NMR and crystallography. Given this excellent program, Einstein is well positioned to continue exploiting the entire spectrum of structural information to advance understanding of fundamental biology and pursue novel clinical applications. However, all structural biology technologies require the generation of protein samples of sufficient quality and purity for analysis. *Protein production has become the rate-limiting step in the structure discovery and proteomics pipeline at Einstein that is a fundamental, early phase of therapeutic development.*

Essential Needs

The structural biology and proteomics pipeline has been an enormous success for those investigators who have protein production expertise. Others whose background and training do not include such capabilities or those who cannot bear the costs of establishing a protein expression and purification component in their own laboratories have suffered from the lack of a suitable centralized facility.

The establishment of an **Einstein Protein Production Facility** will serve the needs of the broad College research community and significantly enhance the utilization of existing resources for structural biology and proteomics. In addition, this resource will serve as an incubator for Einstein participation in large scale initiatives, such as NIH-sponsored programs for Structural Genomics of HIV-Host Interactions and Structural Genomics Centers for Infectious Diseases. The widespread impact of a Protein Production Facility cannot be overstated as, in addition to traditional research efforts, the generation of high quality protein tools is a frequent bottleneck for inhibitor screening, biosensor design, antibody generation, biochemical and biophysical analyses, as well as cell-based and whole animal studies. The Facility would support every area of basic and disease-oriented research at Einstein and is an essential resource for robust, in-house design and development of novel therapeutics.

The Einstein Protein Production Facility is envisioned as a resource that can provide investigators with a range of assistance suitable to their individual needs and expertise. Some investigators who have appropriate knowledge will be able to utilize the Facility's instrumentation directly. Others can request that the Facility perform each step of the protein production process, including cloning, expression, and purification. Varied demands related to the wide range of protein expression systems must also be accommodated. Some proteins can be produced in relatively simple bacterial systems, while others require sophisticated modifications that can only be achieved by production in more complex mammalian cells. Still other proteins are so toxic when made in large quantities that they must be produced in cell-free systems. The Facility will have the capabilities to support a variety of expression systems including cell-free, bacterial, yeast, insect, and mammalian. In addition, the Facility will archive important expression vectors and strains for the Einstein community and house standard instrumentation for cell harvesting and disruption as well as protein purification systems. An advisory committee composed of three or four faculty members would be responsible for administration of the Facility in consultation with a director and technical staff.

Mechanistic research to correlate protein mutations with complex *in vivo* phenotypes such as metastasis, immunity, cell motility, metabolism, or behavior is often hampered by the difficulty of genetically manipulating mammalian model organisms. Acquisition of **technology for the rapid generation of new mouse models** will accelerate Einstein's research programs in many areas. The ability to efficiently "knock-in" targeted mutations or "tag" proteins with biochemical markers *in vivo* permits detailed structure-function studies of complex biological processes. This allows researchers to exhaustively study specific proteins at every stage of development, in all cell types, and under various dietary and therapeutic regimens. In addition, the ability to conduct high-throughput "knock-out" experiments will accelerate the development of new mouse models of human diseases. Establishing advanced technologies for high-throughput manipulation of the mouse genome will leverage Einstein's already robust capabilities in proteomics, imaging, and other modalities and will support the College's efforts in the establishment and analysis of disease models.

An examination of commercially available drugs highlights the remarkable effectiveness of protein therapeutics for many human diseases, including Herceptin (breast cancer), EPOGEN (anemia), and Enbrel (rheumatoid arthritis, psoriasis). High-resolution structural data enable the design of protein reagents with enhanced properties that impact therapeutic efficacy. While the **development of protein therapeutics** is underway at Einstein on a small scale, further development of this program requires the capability to select molecules with enhanced affinity, specificity, and stability—expertise that does not presently exist at Einstein. These molecular evolution approaches, if available, would also impact imaging initiatives at Einstein, as a major effort is in progress to engineer novel proteins for cell-based and intravital imaging.

Achieving the Vision

Launching an Einstein Protein Production Facility requires:

- Instrumentation and infrastructure
- Laboratory space
- Ph.D. level director with experience in protein production for development and day-to-day management of the Facility

Implementation of a platform for rapid mouse model development involves:

- Infrastructure for high-throughput ES cell screening
- State-of-the-art technology for manipulation of the mouse genome
- Ph.D. level director with experience in mouse genetics.

Optimizing the development of protein therapeutics is a long-term goal that could eventually require:

- Recruitment of a tenure-track faculty member with expertise in one or more areas of molecular evolution (e.g., phage display, yeast cell surface display, mRNA display)

Einstein currently has state-of-the-art proteomics infrastructure for the characterization of protein mass, dynamics, and modification. However, this is an area of rapidly evolving technology and the College should be prepared to enhance this important translational capability as resources permit.

Applications to Human Health

Structural Biology and Proteomics approaches are universally applicable to basic and disease-oriented research programs. Examples of ongoing efforts illustrate the potential of these techniques for addressing critical needs in health and disease, including the development of new therapeutics.

Cancer: Researchers are using mass spectrometry to study the structural and dynamic changes that occur in microtubules upon binding the antitumor drug Taxol, a frontline treatment for breast, ovarian, and other cancers. This work has considerable clinical and prognostic implications as differences in microtubule composition appear to correlate with resistance to Taxol therapy.

Infection and Immunity: High resolution crystallography is revealing the structure of molecules involved in T cell immunity that represent outstanding targets to treat a range of diseases. Data from these studies are used to design variant molecules that are being examined in animal models with the goal of developing protein-based therapeutics for viral, bacterial, and fungal infections.

Diabetes, Obesity, and Other Metabolic Diseases: The technique of structure-based fragment assembly has enabled investigators to generate high affinity, specific inhibitors of PTP1b. This enzyme is involved in insulin resistance, making it a prime target for development of therapies for diabetes and obesity.

	Cancer	Infection and Immunity	Metabolic Diseases
Structural Biology	Structural basis of Taxol resistance	T cell based therapeutics	PTP1b inhibitors for diabetes and obesity

Imaging

THE VISION

To develop an integrated resource that will extend the resolution and interpretation of clinical imaging beyond that currently possible by enabling continuous imaging from nanometers to centimeters in living tissues

The Challenge and Opportunity

Imaging is a method of extracting information for all physical scales from single molecules to whole organisms, including information about the structure, conformation, and activity of the molecules present in the image. The establishment of a National Institute of Biomedical Imaging and Bioengineering in 2000 and the inclusion of imaging research as a key component of the current NIH Roadmap for Medical Research highlight the central role of this field in research on human health. A prime goal in imaging research is the development of multi-modal imaging resources that, by combining the capabilities of individual modalities, bridge the physical scales imaged by each, leading to increased resolution and clinical utility that far exceeds current practice.

Einstein has invested in significant expertise and infrastructure in the full range of imaging modalities covering all physical scales including: single molecule/structure (cryoelectron microscopy); single molecule/cell imaging (biophotonics); tissue microenvironments (biophotonics, PET, MRI); and organ function and architecture (PET, CT, MRI). Biophotonics research, the interrogation and manipulation of cellular and disease processes using photons, is underway in the Gruss Lipper Center for Biophotonics at Einstein. The Center has three components: faculty research driving invention and new imaging technology; the Innovation Laboratory for the development of new microscopes and related technology; and the Analytical Imaging Facility (AIF) that provides imaging services to Einstein researchers. The Gruss Magnetic Resonance Research Center (MRRC) provides facilities for whole body magnetic resonance imaging (MRI) of both humans and animals. Additional resources, including CT scanners and PET/microPET equipment, are available for clinical and research imaging in various sites across the Einstein campus and at the clinical affiliates. *The Biophotonics Center and the PET/MRRC represent significant resources that uniquely place Einstein at the forefront in the development of multi-modal imaging technology.*

Essential Needs

Currently, no other centers in the U.S. have the high, subcellular resolution capability *in vivo* represented by the Biophotonics Center, combined with a concomitant whole body imaging approach. Einstein has the opportunity to create the first unified, multi-modal **Integrated Imaging Resource** with continuous imaging from nanometers to centimeters in living tissue. This will generate the capability to associate molecular events with cellular and tissue changes and, thus, establish cause-and-effect relationships leading to disease. Components of the available imaging technologies will also be embedded within the Mouse Phenotyping Facility in the CGTM.

Using biophotonics approaches, researchers are now using single molecule imaging and intravital imaging (the ability to capture images in a live animal) in undissected living animals to identify tissue microenvironments that are responsible for normal physiology and progression to disease. These high resolution optical imaging methods make it possible to identify the cell types, signaling pathways, metabolic states, and tissue architecture that contribute to the microenvironment in health and disease. These features will be used as guides to develop markers and algorithms that allow the identification of the same microenvironments using MR, PET, and CT imaging—modalities that can be used clinically. Making this correlation between modalities requires the use of common animal models in experiments of registration, interpretation, and validation protocols. A collaborative team of faculty, engineering staff, and bridge postdocs and fellows will be needed to move the Integrated Resource into practice. When fully achieved, the Integrated Resource will impact research in multiple health-related areas such as prediction and detection of cancer metastasis, protein folding in neurodegeneration disorders, functional imaging in the brain, vascular abnormalities in acute and chronic sickle cell disease, and many others.

Achieving the Vision

Creating an Integrated Resource for imaging at Einstein requires:

- Faculty Recruitment
  - Biophotonics Center faculty
  - MRRC Director and magnetic resonance faculty
  - Faculty recruitment targeting fields such as data reconstruction/image analysis, radiation physics, CV/radiology imaging, MALDI-MS imaging, and cryo-electron microscope tomography
- Engineering and support staff
- Space
  - Second floor of the CGTM for planned Biophotonics Center expansion
  - Space to house small animal imaging modalities
- Equipment enhancements that may include technology such as specialized microscopes, magnets, cameras, FACS resources for eukaryotic cells and bacteria, and other state-of-the-art imaging equipment.

Applications to Human Health

Imaging research, covering the spectrum from molecules to whole organs, has wide-ranging applications to understanding and diagnosing human disease. Examples of ongoing imaging programs illustrate the translational power of these technologies.

Infection and Immunity: Einstein investigators are developing radiation-labeled antibodies, proteins, and other molecules for the purpose of imaging their distribution *in vivo* on a gamma camera (SPECT). Applications of this technique include imaging of aspergillus-specific antibodies to develop a diagnostic method of detecting aspergillus (fungal) infection in organ-transplant patients; imaging of organism-specific antibodies to detect *Cryptococcus neoformans* infections; and radioimmuno-imaging and therapy for human papillomavirus-associated cancers.

Diabetes, Obesity, and Other Metabolic Diseases: Developing non-invasive methods to assess beta cell mass in the natural history of diabetes is a critical target that would impact disease prevention, monitoring of immune system infiltration and inflammation, and monitoring of response to therapy. Evolving applications of PET and high resolution fluorine MRS technologies could be used to address this high priority clinical problem.

Reproductive Medicine and Health: Technologies for gene expression profiling and multi-photon based intravital imaging has allowed researchers to identify genes associated with invasive cancer cells in living breast tumors. These genes fall into well defined pathways that are coordinately regulated in metastatic tumor cells, revealing the pattern of an "invasion signature." Targets within these pathways are currently in retrospective studies of patients with breast tumors to investigate their diagnostic potential. These imaging technologies directly impact cancer and vascular research as well.

	Infection and Immunity	Metabolic Diseases	Reproductive Medicine and Health
Imaging	Biodistribution of infectious agents	Visualizing beta cell mass in diabetes	Invasion signature in breast cancer

Chemical Biology and Chemical Genomics

THE VISION

To promote robust and efficient translation of Einstein's basic research discoveries into clinical applications, including drug development, by establishing in-house resources for chemical library screening

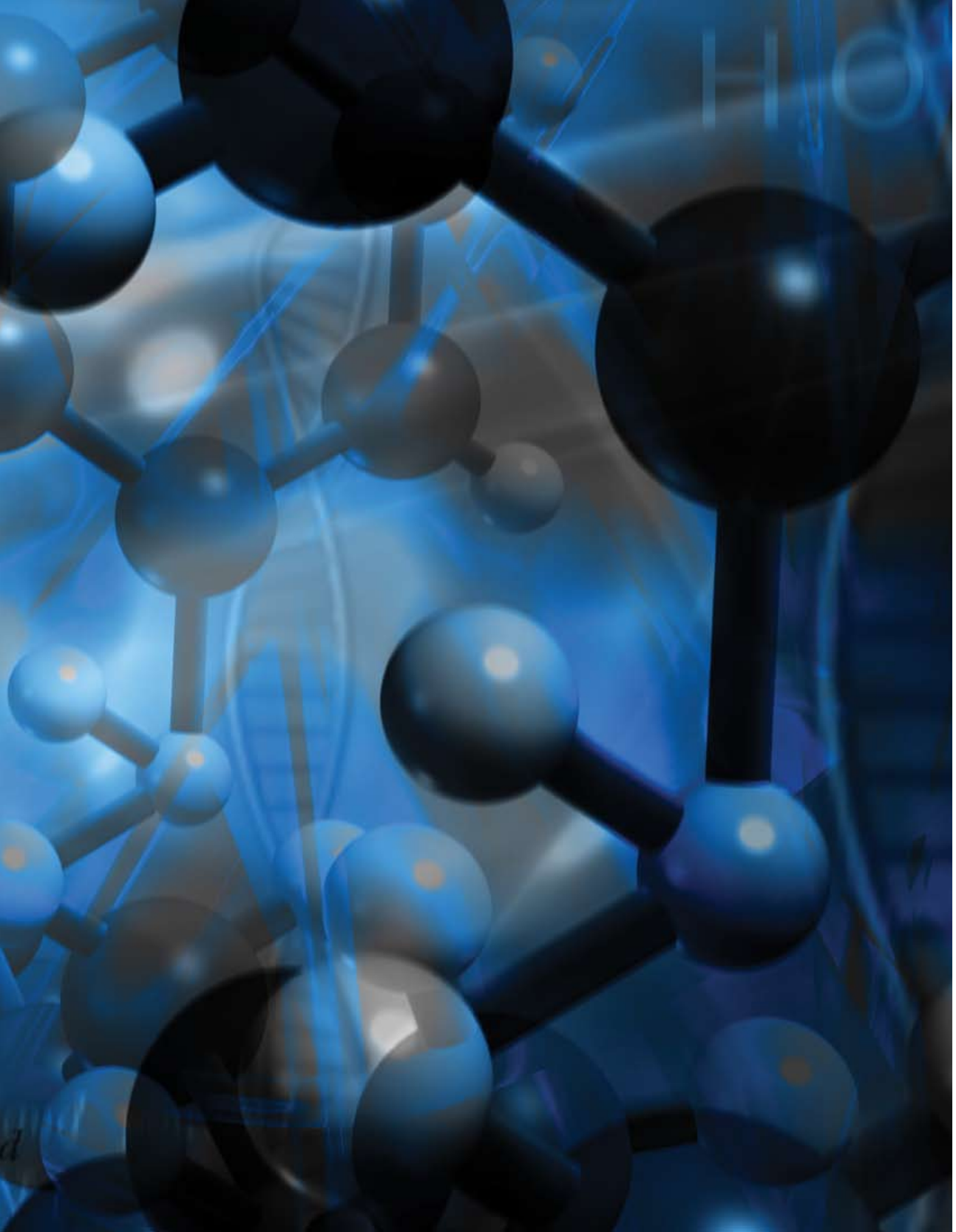
The Challenge and Opportunity

The fields of Chemical Biology and Chemical Genomics seek to discover, create and apply novel chemical tools to biological problems. The most well known application of chemistry in the biomedical sciences is the development of novel enzyme inhibitors or activators that can be developed into highly selective drugs to treat disease. Chemistry also provides the ability to design and construct molecules with unique properties such as: biosensors to probe disease-causing pathways; labs-on-a-chip to enable disease detection in the field; contrast agents for innovative diagnostic imaging technologies; inert materials to use as implants; and molecules that can direct stem cell differentiation or other biological processes. In short, chemistry offers the means to create new tools for fundamental research and to translate basic biomedical discoveries from that research into new opportunities for disease diagnosis, management, and cure.

The vast research infrastructure at Einstein supports active discovery of new targets for potential drug development. However, the existing chemical biology and chemical genomics programs, while innovative and productive, are limited in scope. Many Einstein investigators who want to identify an inhibitor of a newly discovered therapeutic target must look outside the medical center to academic collaborators in other institutions or to commercial screening sources. This can be a time consuming process and has implications for protection of Einstein's intellectual property. *The lack of a central, open-access resource for chemical screening at Einstein seriously impedes the ability to efficiently translate discoveries from the College's robust research effort into new therapeutic approaches.*

Essential Needs

An **Einstein Chemical Screening Facility** would address the needs of the faculty in several ways. First, it allows investigators to address problems that are otherwise intractable, such as identification of chemicals that can generate active proteins from defective genes—the chemical equivalent of gene therapy. Screening can be used to discover inhibitors for disease-causing proteins, a standard tool in the



drug development process. Chemical screening can help identify agents that generate a desired cellular behavior, such as reproducible differentiation of stem cells into a specific, mature cell type. Finally, agents that serve as adjuvants for known drugs, either by potentiating their action or limiting associated side effects, can be discovered through chemical screens.

Unlike many forms of analysis, chemical screening relies on assays that are unique to each investigator. In order to devise a useful screen, the screening specialist must work closely over an extended period of time with the investigator who devised the assay. Regional and national screening facilities require an application process, which can create long waiting periods. Commercial screening facilities generally do not allow for close communication between the investigator and the screening personnel and may also involve long wait times to gain access. An in-house Chemical Screening Facility will function as a walk-in service allowing for immediate access to equipment and expertise, faster results, and chemical libraries that would be unique to Einstein. Ongoing, direct interaction between the facility director and the principal investigator will make it possible to continually optimize the assay.

Initially, the Chemical Screening Facility will be "hands-on", where graduate students and postdoctoral fellows will perform the screens themselves. A doctoral level scientist and a technician will work closely with individual users while also maintaining instrumentation, chemical archives, and databases. Several different compound libraries will be maintained (mostly medium-throughput size of <10,000 diverse chemicals). Eventually, as more investigators utilize the Facility, it may be desirable to purchase larger libraries and high throughput robotic systems.

Achieving the Vision

Establishing a Chemical Screening Facility at Einstein requires:

- Instrumentation, chemical libraries, and databases
- Facility supervisor—this position could be filled by an investigator of any rank, from non-tenure track to full professor, who has the appropriate expertise to provide high-quality oversight and consultation with respect to the design and execution of screening projects
- Core laboratory space in the CGTM

In the long term, developing an effective chemical screening effort will rely on expanding the breadth of Einstein's Chemical Biology research program to include expanded chemical synthesis capability. Recruiting new faculty for the program cannot be accommodated within the current plan for the CGTM. However, there may be opportunities to house new Chemical Biology faculty in existing buildings to expand this important research program.

Applications to Human Health

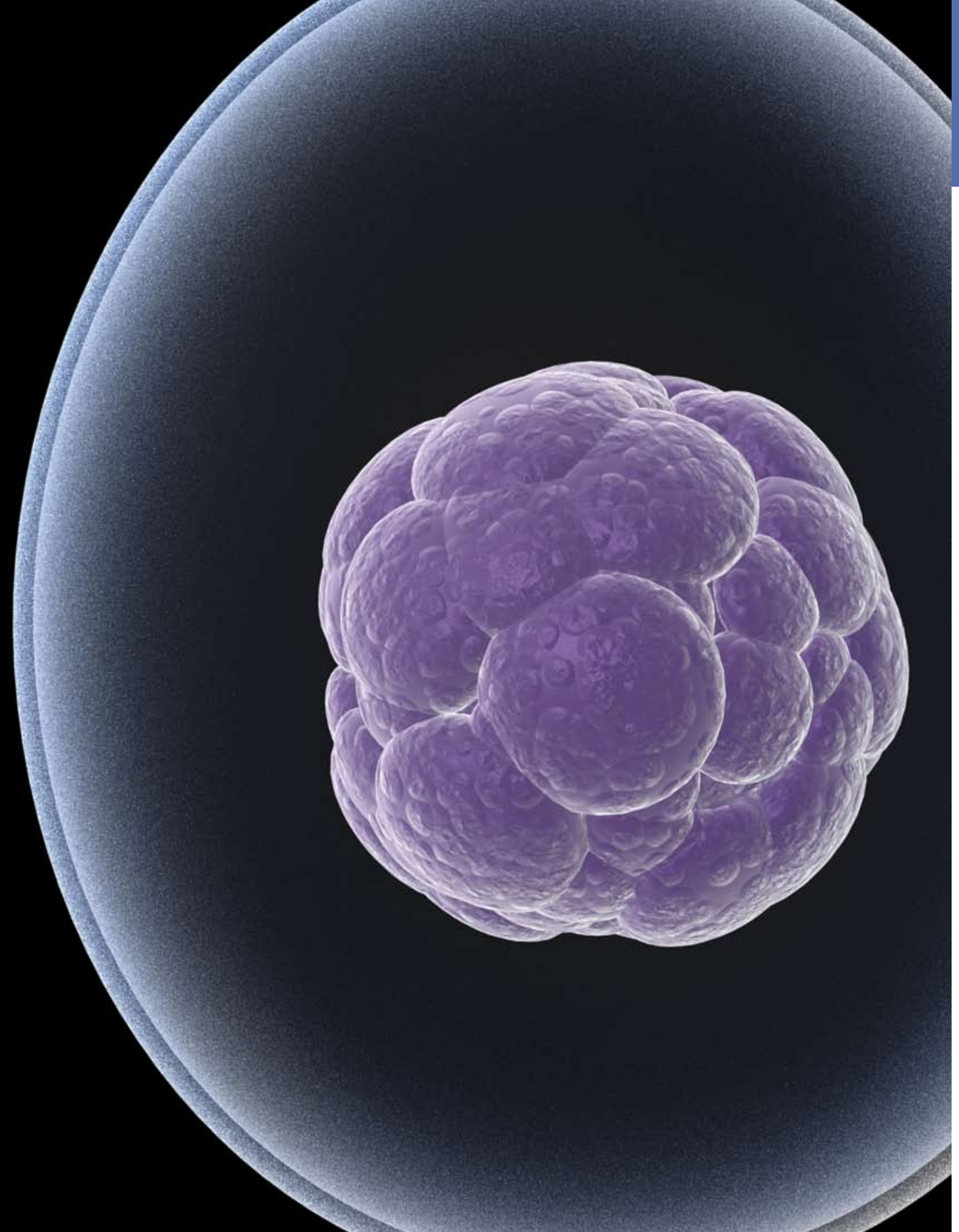
Chemical Biology and Chemical Genomics resources are widely applicable to all areas of basic science and disease-oriented research. Examples of the variety of topics that benefit from chemical genomics highlight the central role of this field in developing new research reagents and novel therapeutics.

Cancer: Einstein researchers studying a well validated protein involved in tumor metastasis, mts-1, have screened a library of FDA-approved drugs to identify the first known mts-1 inhibitors. These inhibitory agents are relatively modest in terms of potency, so chemical biology approaches will be needed to design, synthesize, and characterize more potent analogues that might be developed to treat metastasizing cancers.

Infection and Immunity: Natural Killer T cells (NK T cells) are an important component of the immune system that has been implicated in protection from infections and autoimmune diseases. KRN7000, a molecule that activates NK T cells, has been shown to delay or prevent the onset of autoimmune diabetes in a mouse model. By chemically modifying KRN7000, Einstein researchers were able to create variants that potently stimulate NK T cells, but in different ways compared to the original compound. These variants might have unique applications for treatment of certain autoimmune diseases, infections, or cancer.

Neuropsychiatric Diseases: Neural stem cells possess the capacity to differentiate into the three classes of cells that comprise the brain (neurons, astrocytes, oligodendrocytes). To date, researchers have been unable to identify conditions that would drive neural stem cells down one differentiation pathway to reliably produce a single cell type. A chemical library screen would facilitate the identification of molecules that promote one pathway versus the others.

	Cancer	Infection and Immunity	Neuropsychiatric Diseases
Chemical Biology/Genomics	Inhibitors of metastasis factors	Activators of Natural Killer T cells	Differentiation of neural stem cells



Stem Cells and Regenerative Medicine

THE VISION

To advance the use of stem cells for improving human health, obtaining new research tools for diagnosing disease, developing cell therapies, and thus positioning the College at the forefront of 21st century regenerative medicine

The Challenge and Opportunity

All cells in the human body can be traced back to a single cell, the zygote, formed by the union of an egg and sperm. As the zygote divides, the first few cells formed in the developing embryo retain the capacity to self-renew and to generate any cell in the body—characteristics that define "pluripotent" embryonic stem cells. In addition, throughout fetal and adult development, many organs or tissues maintain a supply of stem cells that can repopulate the tissue—for example, hematopoietic stem cells in the bone marrow continually produce different types of mature blood and immune cells throughout life. In recent years, science has increasingly recognized the potential of embryonic, fetal, and adult stem cells for understanding basic mechanisms of human biology and for developing novel organ/cell-replacement therapies and other translational applications to cure disease.

For more than 20 years, Einstein investigators have been instrumental in establishing the experimental basis for liver-directed cell and gene therapy. Indeed, the earliest studies of these therapies in people, which targeted the metabolic disorder of familial hypercholesterolemia, were based on translational work in animal models performed at Einstein. This and other successes stemming from Einstein research form a solid base of stem cell research that has major strengths in hematology, neurology, and liver. This strength was recognized by the award of an NIH-supported P20 Exploratory Center for Human Embryonic Stem Cells Research in 2005, one of the first such centers in the country. In 2006, Einstein joined the New York Stem Cell Foundation, which includes major academic centers in the New York City area, with the goal of advancing research in human embryonic stem cells (hESC). Finally, the Human Fetal Tissue Repository at Einstein, the only one licensed by New York State, acquires and provides human fetal tissue for research, including cell transplantation in patients. *Building on Einstein's unique resources and historical strengths, the time is ripe to create a coordinated, diverse, and translationally-focused stem cell research program that*

will harvest the potential of stem cells and regenerative medicine to improve human health and cure disease.

Essential Needs

Establishment of an **Einstein Institute for Stem Cells and Regenerative Medicine** will enable the realization of the vision for this area by consolidating, developing, and promoting stem cell efforts across the College. As a formal "home" for stem cell research, the Institute would support individual investigator research programs and facilitate the assembly of multidisciplinary team efforts to address major scientific goals. The Institute would increase communication and collaboration among basic and clinical scientists locally and with other institutions; manage and provide shared resources and technologies; and develop educational, enrichment, and training opportunities.

The Institute for Stem Cells and Regenerative Medicine would be built around five high-priority themes that would help Einstein maintain and expand its prominence in stem cell research:

- *Stem Cell Ontogeny*: Understanding the basic biology of stem cells during normal development is an essential foundation of stem cell research. Einstein stem cell investigators studying the development of human tissues are focused primarily on the fetal liver and pancreas, adult liver, fetal thymus, and fetal brain. Expanding research on human development into other critical organ systems would offer an opportunity to leverage existing programs in animal model systems and bolster the translational potential of Einstein research.
- *Stem Cell Identity and Self-Renewal*: The ability to maintain cultured stem cells in an undifferentiated state without oncogenic (cancerous) transformation is critical for both basic research and translational applications of stem cells. In addition, disease-specific research could be greatly enhanced by derivation of new hESC lines from appropriate donors—a line of research that is not currently eligible for federal funding. Promoting efforts in this area would help Einstein carve out a unique position in the stem cell research field.
- *Derivation of Differentiated Cells*: The potential of stem cells as tools to understand human physiology and to diagnose and treat disease has only begun to be tapped. Investigators are discovering methods to guide stem/progenitor cells down a pathway of differentiation to mature, specialized cells. New technologies, such as high-throughout assays and micro-bioreactors for cell culture studies, would help Einstein researchers accelerate their work on stem cell differentiation.
- *Endogenous Stem Cells*: In some organs—the brain, for example—transplantation of stem cells to repair damaged tissue may not be possible. In such cases, it may be more feasible to treat disease by activating stem cells that already reside in those organs. Identification of stem cell niches, understanding the signals that cause endogenous stem cells to mature into differentiated tissue, and developing new technologies to isolate stem cells residing in a variety of tissues are all areas that could be strengthened at Einstein.
- *Applications in Regenerative Medicine*: Einstein researchers are actively pursuing clinical development of cell and gene therapy using hESC, fetal and adult stem cells, and mature organ-derived cells, which have the potential to treat cancer, genetic disorders, HIV, hepatitis, and many other diseases. Much work remains to fully realize the potential of this research, including the development of noninvasive imaging assays to track transplanted cells and of preclinical animal models to test experimental therapies before moving into human trials.

Achieving the Vision

Establishing an Institute for Stem Cells and Regenerative Medicine requires:

- Recruitment or appointment of leadership and administrative staff
- Dedicated core facilities to facilitate stem cell research on multiple health and disease related topics. Each core facility would require a faculty or non-tenure track director, laboratory and office space in the CGTM or other building, and dedicated equipment.
  - Stem Cell and Manipulation Core to maintain undifferentiated stem cells and introduce new genes into stem cells
  - Dedicated FACS resource to characterize stem cells and isolate cell subfractions
  - Animal Xenotransplant Core for analysis of stem cells *in vivo*, development of clinical protocols, and repositing of unique animal models
  - Cell Banking Facility to cryopreserve and store clinical grade cell preparations under cGMP and GLP conditions
  - hESC Derivation Core for generating disease-specific cell lines
  - Cellular Therapeutics Laboratory to handle cells for clinical applications.
- New faculty recruitment in relevant areas such as biology of stem cells, generation of specific types of mature cells, and the role of endogenous stem cells in healthy and diseased tissues (hematopoiesis, liver, pancreas, cardiovascular, brain, and nervous system).
- Linkages between additional key programs, e.g., Reproductive Medicine and Health, to obtain materials for stem cell research, and the Institute for Clinical and Translational Research for facilitating the applications of stem cells in people, as well as partnerships with government, industry, philanthropic organizations or other institutions for regenerative medicine studies.

Applications to Human Health

The Einstein Institute for Stem Cells and Regenerative Medicine would immediately accelerate research in many areas relevant to human health and disease. The following examples that build on Einstein's existing stem cell research programs highlight only a few critical health issues that could be addressed by the Institute.

Cardiovascular and Blood Diseases: Investigators at Einstein have made progress in promoting differentiation of hESCs into red blood cells (RBCs). If cultured hESCs could routinely and reliably generate RBCs in large quantities, then blood supplies could be conveniently expanded into a product that would be safer and have fewer immunological problems than blood donated by people. Moreover, if therapeutic genes were introduced into RBCs, then it may be possible to obtain RBCs containing drug precursors or therapeutic proteins that would gradually be released into the blood stream. As mature RBCs live in the body for up to 3 months, this would offer new ways to correct protein deficiency diseases or coagulation disorders over prolonged periods. On the other hand, transplantation of hematopoetic or mesenchymal stem cells may help treat cardiovascular diseases, blood cancer, and HIV.

Liver Diseases: People with chronic hepatitis B or C constitute the largest group of liver patients, with 500 million people infected with HBV or HCV worldwide. Many of these patients go on to develop chronic liver failure that at present can only be treated with liver transplantation, a procedure that often fails in virally infected patients. Innovative approaches, such as the use of cells capable of resisting infection with hepatitis viruses or disrupting viral replication, offer powerful opportunities for early experimental studies to treat viral hepatitis, and eventually many other conditions. Einstein researchers are developing and testing fetal human liver stem/progenitor cells that have been manipulated with lentiviral vectors to express new genes that suppress HBV or HCV replication.

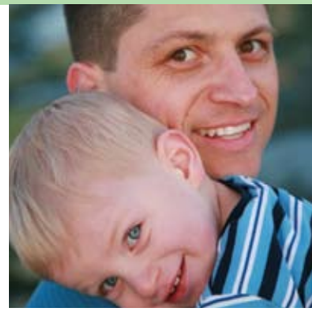
Neuropsychiatric Diseases: Using mouse model systems of Huntington's disease (HD)—a neurodegenerative disease that often does not manifest symptoms until the third or fourth decade of life—Einstein researchers have uncovered a series of developmental errors that affect three-dimensional patterning in the embryonic brain. Verification of these observations in related disease models and in human HD tissue samples would represent a major paradigm shift in understanding neurodegenerative diseases and would be a significant advance in developing therapies to combat these fatal diseases. To achieve this goal, Einstein researchers are interested in deriving hESC lines from healthy and HD embryos to perform detailed studies of molecular and developmental changes during stem cell maturation, as well as to identify novel targets for gene discovery and therapeutic applications.

	Cardiovascular Disease	Liver Diseases	Neuropsychiatric Diseases
Stem Cells and Regenerative Medicine	Unlimited supply of red blood cells	Cell therapy for Hepatitis B and C	Pathogenesis of Huntington's Disease

Human Genetics

THE VISION

To advance translational research at Einstein by facilitating the study of common diseases that result from genetic and environmental interactions, genomic variation, and epigenetic alterations



The Challenge and Opportunity

The normal functioning of genes is essential for the health of a cell and an organism. It is now recognized that most, if not all, human diseases have a genetic contribution. In some cases, the presence of the disease is almost completely accounted for by a mutation in a single gene, as represented by sickle cell disease. Other diseases such as diabetes and cardiovascular disorders have a more complex genetic contribution, and appear to be mediated by weaker mutations in a number of interacting genes. Even simple genetic diseases like sickle cell disease are influenced by other genes in the genome, altering the severity of the disorder.
The function of genes can be altered by mechanisms other than mutation. A gene that is switched off and is unable to become active when needed is as devastating for the cell as a mutation of the DNA itself. The switching on and off of genes is regulated by "epigenetic" mechanisms, which are increasingly recognized to be major influences on human diseases such as cancer.

The fields of human genetics and epigenetics represent an essential bridge between basic and clinical research. Genetics researchers can translate genes discovered in model organisms into studies of human disease. Conversely, clinicians who identify a new syndrome or a subclass of patients with differential disease course or response to therapy can use human genetics research to understand the basis of these observations. Newly identified genes or modifications can then be explored in model systems to understand disease and develop treatment strategies. Einstein has established a unique combination of state-of-the-art technologies for investigation of the entire set of genes in each individual genome that has allowed its researchers to develop robust programs on the genetic and epigenetic mechanisms of human disease. These programs provide a solid foundation for Einstein researchers to study diseases that manifest at birth or during childhood, as well as those that affect adults. However, the current effort is largely dispersed, with individual investigators required to expend considerable time and effort in establishing their own laboratory and clinical research systems to conduct genetics research.

To retain its competitiveness as a major biomedical research center, Einstein has a critical opportunity to develop a well coordinated, integrated program in human genetics and epigenetics research that will be a cornerstone of translational research at the College and promote research collaboration on diseases affecting the diverse populations of the Bronx and New York City, and by extension of the United States and other countries around the globe.

Essential Needs

An **Einstein Translational Genetics Center (TGC)** will provide needed intellectual, administrative, and physical infrastructure to establish a continuum between clinical investigators and basic research by enabling cohort studies. Cohorts for genetics research will, in particular, include patient populations in the Bronx and affiliated medical centers as well as others already under study. The TGC will partner with major basic science and disease-oriented research centers and programs at Einstein to investigate common diseases relevant to the local population (e.g., developmental delay/congenital disorders, aging, metabolic disorders, hematological diseases, cancer, others). Einstein has recently named a Director of the TGC and launched a recruitment effort to begin to expand this program.

A primary goal of the TGC will be to expand existing translational programs and facilitate new programs by providing intellectual infrastructure for genetic study design from inception to publication. An active consortium of faculty members with expertise in genetic diagnostics, family-based genetics, whole genome assessment, epigenomics, epidemiology, biostatistics, bioinformatics, and database design will be designated to work with individual investigators to formulate and design projects. The TGC will house several core facilities for administration, consultative services, specimen storage, and a range of analytic capabilities essential for human genetics research. Assembling the expertise and resources will require collaboration with other research support structures to avoid redundancies and inefficiencies.

The study of genetic and epigenetic factors is widely applicable across the spectrum of human health and disease. Three major scientific foci are envisioned in the initial development of the TGC. The Translational Epigenomics Program will determine the contribution of epigenetic regulation in normal development, cancer, and other diseases by building on existing studies on epigenetic changes in blood cell cancers. As with all human cancer, these diseases are highly heterogeneous, a feature which is mostly ignored by current therapeutic regimens. Understanding epigenetic differences among people with the same type of cancer has significant implications for the development of individualized diagnosis, prognosis, and treatment strategies. The Child Health and Disease Program will examine genetic modifiers and environmental factors that modulate the severity of single-gene disorders such as sickle cell anemia, prevalent in the Bronx, and genomic disorders and associated mental retardation/developmental delay, caused by structural rearrangements. The program will build on Einstein's strength in prenatal and postnatal genetics diagnosis, and complement existing research on a variety of conditions that affect child health, such as rhabdoid tumors, hearing impairment, Williams Syndrome, and velo-cardio-facial syndrome (VCFS). The Adult Health and Disorders Program will focus on understanding the genetic components of common adult onset diseases. Einstein has major research strengths in understanding the basis of longevity, genetic risks for development of late onset disorders in relationship to diabetes and metabolic disorders, and the genetic factors contributing to Huntington's Disease and other adult-onset diseases.

Achieving the Vision

Creating a Translational Genetics Center and establishing a critical mass of outstanding investigators in human genetics research requires:

- Resources to expand or create core facilities for essential services, including: administration; cell culture; genomics and genetics; epigenomics; genome imaging; gene therapy; and statistical genetics and bioinformatics.
- Technology
  - High-throughput DNA sequencing technology
  - Expanded resources for epigenomics analysis
  - SNP genotyping system; genome-wide analysis technology

Recruitment of a new Chair of the Department of Molecular Genetics: The person selected as the Chair may have personal expertise in any genetics-related field from basic research using model organisms through vertebrate models or human genetics; however, he or she will be expected to have a strong commitment to supporting and expanding human genetics research at Einstein.

- The new Chair will be responsible for recruitment of additional faculty in such areas as statistical genetics, epigenomics, complex genetics, and clinical genetics diagnostics.
- Space in the CGTM is allocated for new faculty recruitment as well as to house core laboratories for genetics research.

In the long term, it would be useful to develop a more coordinated organizational structure for enhanced access to vertebrate and invertebrate model organisms for genetic screens and functional studies. Overcoming barriers to the use of these models—including mice, zebrafish, yeast, fruit flies, and roundworms—is needed to support researchers who do not routinely use such models, but whose research would benefit from complementary studies in these alternate systems. Options for fostering model organism work within new or existing facilities and laboratories will be developed after the appointment of a Chair of Molecular Genetics.

Applications to Human Health

Genetic and epigenetic factors are central to understanding, preventing, diagnosing, and treating nearly all human diseases. Examples of Einstein research in this area illustrate the breadth of topics that can be studied through a robust Human Genetics research program.

Aging: By studying populations of individuals with exceptional longevity (>100 years old), researchers are teasing out genetic factors associated with successful aging. Genes that influence susceptibility to or protection from metabolic diseases appear to have a role in determining longevity and healthy aging.

Cancer: Research on epigenomic modifications in hematological malignancies (acute myeloid leukemia, lymphoblastic leukemia, lymphomas, and myelodysplasia) has enabled investigators to classify these patients into discrete subgroups based on molecular differences. The goal is to identify which subtypes are amenable to specific, targeted therapies, leading eventually to individually tailored therapy. Data from this program are expected to have an immediate impact on the medical care of cancer patients and to continuously feed back into new clinical trials.

Cardiovascular Disease: Einstein researchers are studying several congenital anomaly disorders, including two—Williams Syndrome and velo-cardio-facial syndrome (VCFS)—that are associated with congenital heart disease as well as cognitive disabilities and other health problems. These inherited disorders result from genomic deletions of up to several million DNA base pairs. Pinpointing the specific genes that are missing or defective in patients with these syndromes could provide insights into the basis of normal human cardiovascular and neurocognitive development as well as suggest new therapeutic options.

	Aging	Cancer	Cardiovascular Disease
Human Genetics	Metabolic genes in successful aging	Individually targeted therapy for cancer	Genetics of congenital disorders

Behavioral and Social Determinants of Health and Health Disparities

THE VISION

To create a seamless, interdisciplinary research environment that enhances investigator-initiated and collaborative social-ecological approaches to behavioral and social determinants of health and disease, with a focus on reducing health disparities

The Challenge and Opportunity

Scientists have long recognized that the traditional "nature versus nurture" debate offers a false dichotomy. Nearly every human condition results from complex interactions between biologic/genetic triggers and social-ecological factors, which encompass family interactions, community resources, social networks, gender and cultural norms, health behaviors, socioeconomic status, availability, cost and quality of health care, and many other issues. A key research challenge is to develop an integrated model that describes the dynamic relationships among these factors and their influence on susceptibility or resistance to diseases, and response to prevention or treatment. Elucidating these interactions is especially crucial in the Bronx populations, where social and ecological factors combine with genetic predispositions to produce severe health disparities that magnify the burden of disease.

Einstein has a longstanding commitment to the Bronx, which is the nation's poorest urban county and the third poorest overall. The recently awarded Hispanic Community Health Study (HCHS) is the most recent example of how Einstein has combined its pledge to improve Bronx health with cutting-edge, clinical research on fundamental questions of human health, disease, and disparities. The HCHS is an 8-year, NIH-sponsored study of social, behavioral, occupational, lifestyle and acculturation factors that influence risk for several conditions, including obesity, diabetes, and cardiovascular disease, in Hispanic adults of varying heritage (Puerto Rican, Cuban, Mexican, or Central American). Einstein's receipt of one of four national HCHS clinical centers illustrates the strength of social, behavioral, and epidemiologic research at the College and the unique opportunities afforded by the Bronx population. The HCHS and other social and behavioral studies are evidence of a critical mass of Einstein investigators in such disciplines as epidemiology, biostatistics, behavioral and social science. Einstein researchers benefit from excellent clinical information systems at major affiliated partners and a history of interdisciplinary collaboration. *Despite this interactive culture, substantial cultural barriers and gaps remain between departments and disciplines, which are especially severe between basic scientists and social/behavioral and epidemiologic researchers.*

Essential Needs

A cultural shift within Einstein to bridge the gap between disciplines can be achieved through several strategies. The first strategy is to demonstrate that social and behavioral

research is valued, so that its investigators can meet basic scientists on equal footing within the College. This could be manifested by support for development of more comprehensive research programs in the social and behavioral determinants of health and health disparities; be recognized in the number and size of recruitment packages for new faculty; and be rewarded through salary, space, and other tangible resources. In addition, social and behavioral content will continue to be integrated and expanded in the medical school curriculum.

A second strategy is to incentivize collaboration among existing social and behavioral researchers, who often work in isolation and in different departments. Bringing scientists together in formal and informal ways can create opportunities for new research, but a structure is needed to support this over time and across disciplines.

A third strategy is to support infrastructure to address questions that require basic and behavioral scientists to collaborate. One simple, but profound, theme that could be addressed in a coordinated manner is "why are poor people sicker?" This critically important question demands a multidisciplinary, translational approach that involves genetic and biomarkers research on predisposition to disease by race/ethnicity; epidemiological studies to identify risk factors; elucidation of the role of culture and literacy in developing interventions; clinical trials targeting prevention; and health services research on the role of access to, quality, and cultural competence of care.

A fourth strategy is to use existing opportunities to encourage collaboration among basic scientists and social/behavioral researchers. The NIH Roadmap for Medical Research has prioritized clinical and translational research that converts fundamental biomedical discoveries into improved human health. Translational research must take observations made in patient cohorts back to the laboratory to understand biological mechanisms and identify new therapeutic strategies. The Institute for Clinical and Translational Research (ICTR), will address some infrastructure needs to support such bidirectional translation. New and renovated space in the CGTM and other buildings provide an opportunity to recruit and retain essential faculty and to organize office space in ways that promote interchange and collaboration. The ICTR is an ideal venue to encourage behavioral and social science research, but an integrated behavioral and social science presence is needed to assure that the opportunities are identified and actualized.

Vigorous support for an interdisciplinary research environment will facilitate access to clinical and biological data and samples, including "cohorts" defined by clinical services, epidemiological studies, clinical trials, and public access/public health data. These resources should be linked when possible to serum, tissue, and genetic information in biorepositories and informatics databases. Expanding access to other clinical resources requires partnerships with the clinical affiliates and other Bronx-based entities. The cultural shift to support clinical and translational research would benefit from central infrastructure for clinical, behavioral and social science research.

The academic foundation for behavioral and social sciences, although strong, is fragmented by geographical and departmental barriers. Major strengths include the Division of Behavioral and Nutrition Research in the Department of Epidemiology and Population Health, the Department of Pediatrics, the Diabetes Center's Prevention & Control division, the Department of Family and Social Medicine, the Division of General Internal Medicine, and the School of Psychology. Existing expertise must be better coordinated to nurture the science base, build more synergistic research programs, and assist other researchers who would benefit from social and behavioral collaboration. A structure is needed to facilitate outreach to other fields, make best use of common resources and enhance training and career development of junior behavioral scientists. Creating an Institute of Behavioral & Social Science Research (IBSSR) would promote original basic and translational research and provide a means to integrate these disciplines, thus enriching all areas of research at Einstein.

Achieving Vision

Creating a supportive environment for multi-disciplinary behavioral and social science research focused on health disparities requires assessment and prioritization of the following programmatic and organizational elements, some of which are inherent in implementing the ICTR:

- Development of an academic infrastructure, such as the proposed IBSSR
- Faculty recruitment
  - Senior scientists in leadership roles to serve as leaders of affinity groups or themes, and in strengthening Centers' behavioral cores
  - Biostatisticians with expertise in behavioral and social science research
  - Faculty with experience in both basic and clinical research
  - Researchers who apply theories of behavior change to prevention and treatment (eg, obesity-related disciplines such as exercise physiology)
  - Cognitive psychology for basic decision-making research
  - Sociology and anthropology expertise
  - Expertise in community-based participatory research
  - Clinical addiction/mental health faculty with neuro-imaging experience
  - Faculty level evaluation expert to develop evaluation of educational, training, and research support programs
- Graduate students and postdoctoral fellows
  - An MPH program with Yeshiva University and the Graduate School of Psychology to provide research training at the public health intersection of chronic disease and behavioral science, and foster the development of non-MD behavioral science trainees and post-docs.
  - Additional NIH training grants (T32), including those with slots for clinical/behavioral trainees, could be coordinated at the IBSSR.
  - Translational Research Fellowships with graduate programs coupled to co-mentoring by senior faculty from different disciplines, at least one of which is clinical or behavioral science oriented.
- Support staff
  - A comprehensive and coordinated approach to data management to facilitate the conduct of clinical and population-based research, with units specific to research programs as well as centralized oversight to promote interoperability, collaboration, and quality control.
  - Outreach workers and translators to promote community engagement.
  - Centralized support for clinical trials including the management of regulatory concerns, negotiations with pharmaceutical companies, and assistance in patient enrollment and retention.
- Unified or contiguous space that is programmatically organized.
  - Physical space to promote synergy and integration within the IBSSR.
  - Fostering interests across disciplines requires "virtual space" communities for affinity groups, discussion groups/bulletin boards, and in-person meetings for presentations and grant development.
  - Community locations for patient recruitment, interviews, blood draws, and other needs common to clinical and population research would enhance the ability to perform population-based research recruitment.
- Core scientific facilities
  - Core services for clinical research consultation in the fields of statistics, study design, epidemiology, and ethics; integrated services for behavioral science design, methods, intervention development, and evaluation across social and ecological levels.
  - A data management facility with individual units in various programs under quality control supervision of a central unit.
  - A "cohorts registry" to provide access to data for hypothesis-driven data analysis and preliminary data analyses for grant applications.
- Patient populations
  - Establish partnerships for database sharing with community and/or private organizations such that mutual benefit occurs from having a major research institution in the Bronx.
  - Maximize the research potential of the MMC Clinical Information System and explore clinical data linkages with other affiliates.
- Infrastructure and organizational support
  - Cultural changes to encourage cross-disciplinary research, including reward structures that make this work respected and valued, such as special grant awards, and recognition for promotion/tenure.
  - Discussion of the challenges of balancing and complementing roles of departments, centers, and institutes and potential "affinity groups."

Applications to Human Health

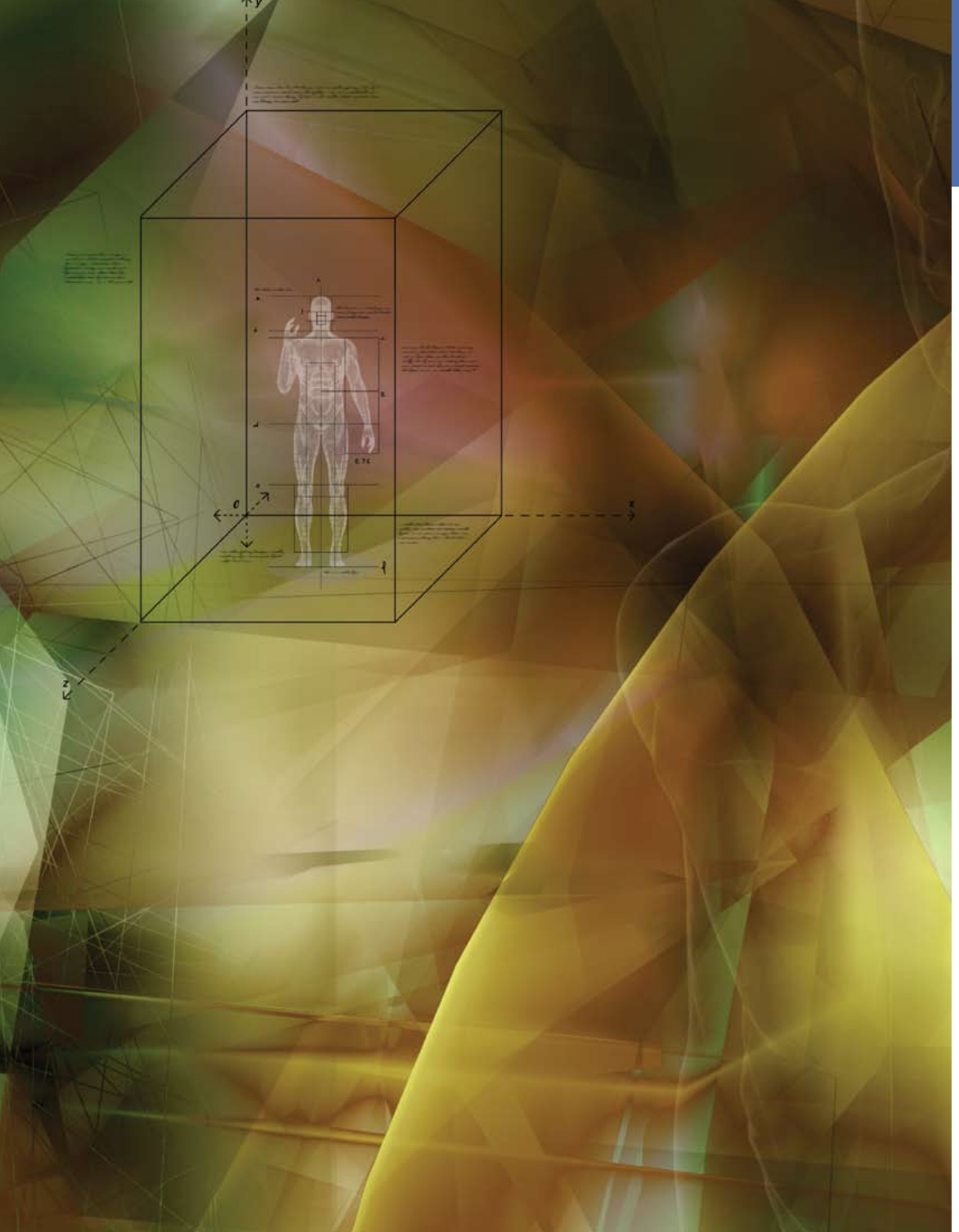
Behavioral and social science research impact all areas of human health and disease. These examples illustrate the diversity of questions that can be addressed by cross-cutting research guided by the perspective of these disciplines

Cancer: Although black women have a lower incidence of endometrial cancer than do white women, the mortality rate from this disease is higher among blacks than among whites. The disparity among women receiving comparable treatment for similar stage disease is higher for endometrial cancer than for any other tumor type. The Bronx provides an opportunity to examine the genetic, environmental, social/behavioral or health services causes of such disparities with multi-disciplinary teams of basic scientists, behaviorists, and population and health services researchers.

Cardiovascular Disease: The South Bronx has an excess of congestive heart failure, with hospitalization rates nearly twice the city- or state-wide rates. Poverty is the major factor associated with this disparity that produces a substantial burden of morbidity and mortality. Cross-cutting research opportunities include: clinical trials and translational studies of electrophysiology, pharmacotherapy, and surgical approaches to treatment; assessments of social and ecological factors contributing to poor outcomes, and outcomes/effectiveness research in clinical care programs.

Diabetes, Obesity, and Other Metabolic Diseases: Obesity, a significant public health problem in the Bronx as in much of the U.S., is influenced by race, ethnicity, income level, and education. A social-ecological framework of research can be undertaken to study individual, family, cultural, and community contributions to obesity. Important areas of investigation include: genetic and biologic factors, including gene-environment interactions; lifestyle and behavioral factors; cultural, social and community effects; nutritional causes and effects; and interactions among these issues.

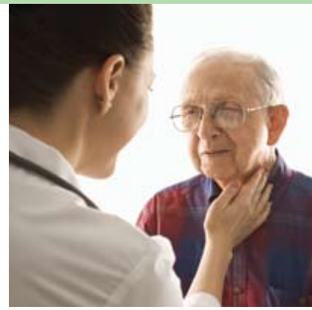
	Cancer	Cardiovascular Disease	Metabolic Diseases
Behavioral/Social/Disparities	Disparities in endometrial cancer death	Burden of congestive heart failure	Social-ecological factors in obesity



Computational Biology and Systems Biology

THE VISION

To advance our understanding of living systems by developing new approaches that combine theoretical and experimental methodologies to reveal the properties and functions of the component parts of biological systems and the higher level behavior of complex biological systems that emerges from the interactions of their parts



The Challenge and Opportunity

As technology becomes more sophisticated and knowledge about biology grows exponentially, traditional lines between scientific disciplines have begun to blur. Biological researchers now look to such fields as computer science, mathematics, engineering, and physics to answer fundamental questions. Computational Biology employs mathematical and physical theory to predict and analyze the components of biological systems. Examples include the theoretical study of enzyme function, the analysis of spectroscopic data from structural biology or imaging applications, prediction of protein structure, and dynamic interactions between neurotransmitters and their receptors. Systems Biology is the theoretical or experimental study of biological entities in their entirety. Examples include evolutionary theories, gene network interactions, immunologic networks, neural networks and behavior, and models of development. Though different in focus, a strong symbiosis exists between the two disciplines which penetrate almost all aspects of biological and biomedical research.

Einstein has established a presence in Computational Biology and Systems Biology through the philanthropically-supported Seaver Center for Bioinformatics. Four faculty members, recruited through the Seaver program, have been appointed in various academic departments. These faculty have initiated active, productive collaborations in basic and translational science with researchers throughout the College. The variety of topics being explored attests to the impact of these collaborations and includes: the activity of large protein complexes in cardiac muscle function; modeling the universe of three dimensional protein structure, function, and interactions; factors that control the hypermutation rate in genes that produce antibodies; and the neural processing of images and sound by the sensory systems. *However, the current program-based structure has not fostered the formation of a cohesive research effort among the computational and systems-oriented faculty or the development of an effective educational program in these areas at Einstein.*

Essential Needs

Scientific approaches used by the Seaver faculty to accomplish their diverse goals are remarkably similar. Creation of a Department of Computational and Systems Biology would

provide the necessary structure for meetings, seminar programs, course development and other connections to promote vital research interactions among the faculty. Moreover, a formalized departmental structure would place Einstein at the forefront of similar initiatives at other biomedical institutions. Through research and education, the department would advance understanding of living systems by developing new approaches that combine theoretical and experimental methods to explain the properties and functions of the components of biological systems and how higher level behavior of complex systems emerges from their interactions.

A new department would have the infrastructure, authority, responsibility, and accountability for achieving the complex task of integrating and coordinating research and education in these broad, dynamic fields. This would allow the development of a full educational and research program that would nurture students, postdoctoral fellows, and faculty who would have an international impact and add to the overall mission of the College. Further recruitment of outstanding faculty is more likely to be successful in the context of strong infrastructural support for their field of research that facilitates the development of collaborative Center grants and programs. Importantly, the CGTM offers the potential of locating computational, systems, and experimental scientists in physical proximity, a prime opportunity to foster interdisciplinary communication and collaboration.

Einstein does not currently offer comprehensive educational opportunities in the emerging disciplines of computational and systems biology, although some courses include sections on proteomics, bioinformatics, theoretical enzymology, and theoretical spectroscopy. Thus, an urgent need exists to educate students, fellows, and faculty alike on the role that systems level understanding and computation will play in many, if not most, research projects in the foreseeable future. It is essential that all in the Einstein research community understand and communicate with those whose expertise lies in computational and systems biology. Achieving such educational objectives may not be feasible without the organizational structure of a discrete department.

Achieving the Vision

Establishing a new department is not a trivial task and one that is made even more complex in this case by the fact that the fields of computational biology and, particularly, systems biology are relatively young. An advisory committee of Einstein faculty has been convened to further evaluate the most appropriate path for Einstein to pursue. This will be done in consultation with experts from external institutions. The charge to the committee is to:

- Evaluate the recommendation of the strategic plan working group to create a new department.
- If a department is recommended, define the mission and configuration of the department.
- If a department is not recommended, recommend an alternate structure and its mission.

Applications to Human Health

The tools of computational science and systems biology can be applied to a variety of biological problems from the quantum mechanics of biochemical reactions to models of development in complex organisms. The examples below only scratch the surface of how these disciplines can contribute to research on human health and disease.

Aging: Einstein researchers hypothesize that people with exceptional longevity have a genetic background that protects them against age-related diseases. Studies of the frequencies of genetic differences among different age groups serve as a starting point for elucidating the complex genetic networks responsible for longevity. Understanding the nature of and interactions among these genetic factors in age-related diseases will lead to new prevention and treatment approaches to lessen morbidity and mortality, and improve quality of life in the elderly.

Cancer: A variety of data sets have been assembled on the expression levels of 28,700 genes and other clinical characteristics of 30 patients with head and neck cancer. Using a systems biology approach to compare variations in cells that were "lymph node positive" versus "lymph node negative", researchers identified genes that are strongly predictive of the natural history of disease and response to treatment. This approach, which can be applied to many complex diseases such as other cancers or diabetes, will aid in the development of better diagnostic and treatment strategies for head and neck cancer

Neuropsychiatric Diseases: Nervous system diseases—for example, autism spectrum disorders or pediatric epilepsies—can often be classified into distinct diagnostic categories based on common features; yet, within each category there is a diversity of disease manifestations. Computational and systems neuroscience offer new approaches to unravel complex interactions within the neural network using genetic, epigenetic, behavioral, and other data from large affected populations.

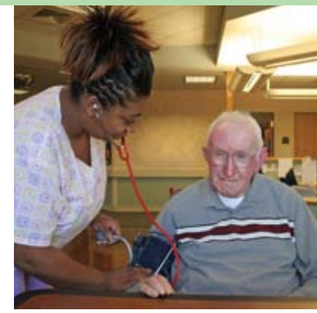
	Aging	Cancer	Neuropsychiatric Diseases
Computational/Systems Biology	Genetic networks in exceptional aging	Characterization of head and neck cancer	Etiology of complex diseases

Improving Human Health Through Research

Aging

THE VISION

To identify and prevent or delay the onset of chronic, debilitating, age-related diseases and promote healthy aging



The Challenge and Opportunity

In 2000, nearly 35 million individuals in the U.S. were 65 years of age or older, representing more than 12 percent of the population. By 2030, that number is expected to double to over 70 million people or 20 percent of the projected population. Likewise, the proportion of the population that is 85 years or older will grow dramatically from 1.5 percent in 2000 to 5 percent (21 million individuals) by 2050.* These statistics point to the urgent need for research on biological and behavioral factors that influence healthy aging. Innovative strategies that can reduce the burden of illness due to aging on individuals and the health care system are needed.

Einstein researchers have established a highly collaborative, multidisciplinary Institute for Aging Research to promote biological and clinical studies to identify factors associated with longevity and translate those discoveries into new approaches to prevent age-related disease and disability and promote active, healthy lives among older adults. Based on an assessment of current programmatic strengths and gaps, the Aging working group has articulated five major research goals to facilitate aging research at Einstein.

Major Research Goals

Genetics of Exceptional Longevity: To understand how genes influence lifespan, Einstein researchers have established a cohort of more than 350 individuals with exceptional longevity (~100 years old) along with more than 400 of their offspring between 60-85 years of age, and more than 500 unrelated individuals who are 60-95 years old. Research on this extraordinary group has already led to the discovery of several genes and other biological factors that are associated with increased longevity and lower rates of age-related diseases.

Longevity-related genes identified in this cohort must be validated in an independent population through a long-term epidemiological study. Once confirmed, these genes would represent targets for discovery and development of new drugs that can mimic their effects when used by individuals lacking a genetic pre-disposition to longevity and healthy aging.

New Treatments to Prevent the Metabolic Decline of Aging: The "metabolic syndrome" encompasses a variety of defects that are closely associated with age-related diseases, including abdominal obesity, type 2 diabetes, high blood pressure, blood lipid abnormalities, and heart disease. Einstein researchers are exploring the link between nutrient intake and metabolic defects

*Source: U.S. Administration on Aging

during aging through studies in animal models and human subjects. Both lines of investigation suggest that changes in biochemical pathways during aging make older individuals more susceptible to the effects of excessive nutrient intake that in turn lead to impaired metabolism.

An exciting observation that has emerged from this study is the discovery of the effect of humanin, a small protein (peptide) associated with early-onset Familial Alzheimer's Disease, on insulin action. Future research on humanin will aim to uncover the three-dimensional structure of the peptide, fully define its role in normal and disease physiology, and develop it as a target for drug development to combat age-related metabolic decline.

Early Diagnosis and Treatment for Alzheimer's Disease and Frailty: The Einstein Aging Study (EAS), which has been continuously funded for the past 12 years, aims to: identify the earliest cognitive, metabolic, anatomic, and neurologic markers that distinguish "normal" aging from dementia; define the natural history and risk factors for Alzheimer's disease and related dementias; and improve the ability to detect preclinical dementia at an early stage. Using a cohort of more than 1,000 Bronx residents over 70 years of age, Einstein investigators have described three stages in the evolution of Alzheimer's and shown that memory decline accelerates 7 years prior to a diagnosis of dementia. Several potentially modifiable risk factors for dementia and mild cognitive impairment have been identified, including low blood pressure, gait abnormalities, and participation in leisure activities.

To capitalize on the wealth of data available through the EAS, researchers are conducting clinical research studies on the structural, neurochemical, and immunologic changes in the brain at various stages of cognitive decline. This patient cohort puts Einstein in a unique position to make significant contributions to defining reversible risk factors and developing innovative strategies for prevention of age-related cognitive decline and dementia

Mechanisms to Delay Cellular Aging: Many age-related diseases, including Alzheimer's and Parkinson's diseases, result from a fundamental change in the way cells process proteins during aging. An Einstein researcher has identified an age-related defect in a mouse gene; when the defect is corrected, older animals exhibit improved protein processing and cellular function. Translating this finding into human elders will open up exciting new lines of investigation on longevity and common age-related diseases.

Einstein's strength in cell biology research puts the College in an excellent position to expand this topic into the study of multiple conditions affected by protein conformation changes and intracellular protein clearance, including neurodegenerative disorders, diabetes, cancer, and liver disease. Preclinical studies in animal models are planned to develop and test drugs that can repair age-related cellular defects.

Immune System Failure of Aging: Reduced immune function increases the burden of infectious diseases, cancer, and autoimmune diseases in the aged. A group of Einstein investigators studying changes in the immune system during aging has made discoveries on a molecular level that might explain the epidemiologic observation of increased fat mass and systemic inflammation during aging. These results position Einstein researchers to develop informative animal models that can be used to design and test new interventions aimed at reversing the immune defects of aging.

Intersection with the Science and Technology Areas

Aging research depends on many resources provided by the science and technology areas, including, but not limited to:

The genetics of longevity program and the Einstein Aging Study are generating massive amounts of genetic and biological data from these large cohorts of aging individuals. *Computational Biology and Systems Biology* and *Human Genetics* approaches can be applied to analyze high-throughput data from these studies to identify aging and longevity-associated genes and to identify all variations of these genes in the population.

Aging researchers are applying *Imaging* technologies from the microscopic level to track age-related changes in protein interactions and intracellular organization to whole organism imaging to visualize anatomic and functional changes in the aging brain.

Structural Biology techniques can be used to solve the three-dimensional structures of several peptides associated with longevity, cognitive function, or metabolism for the purpose of enhancing drug discovery. As described above, humanin, a protein found in the mitochondria that improves insulin sensitivity, is one target for structural research. Drugs that activate or mimic humanin could be used to treat the metabolic syndrome that is responsible for much morbidity and mortality in older adults.

	Aging
Computational/Systems Biology	Analysis of longevity genetic screening data
Human Genetics	Identification of age-related screening data
Imaging	Visualization of changes in cells and brain
Structural Biology	Three-dimensional structure of humanin

Cancer

THE VISION

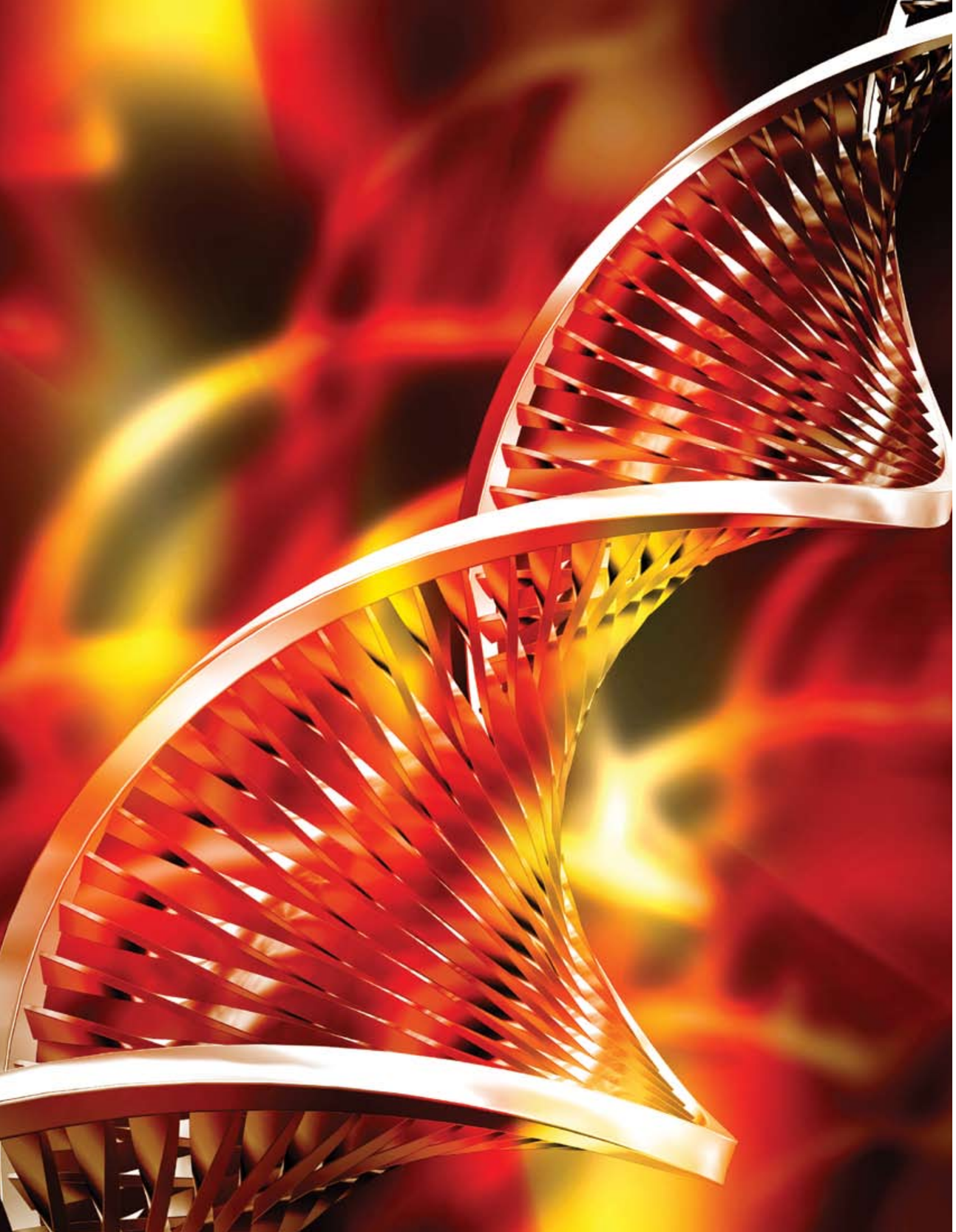
To strengthen research and technical capabilities at the Albert Einstein Cancer Center and link basic, clinical, translational, and population-based research in order to bring to fruition new, effective approaches to the prevention and treatment of cancer

The Challenge and Opportunity

Decades of biomedical research by scientists world-wide have greatly increased our understanding of the changes in normal cells that ultimately result in cancer. Knowledge of risk factors, prevention, screening, diagnosis and treatment of cancer has also improved. Prevention strategies such as smoking cessation or protecting skin from excessive sunlight reduce cancer risk. Screening methods like mammography and colonoscopy detect the beginning stages of cancer and allow early, curative interventions. Novel drugs, surgical techniques, and ways to deliver radiation that are targeted to specific vulnerabilities of cancer cells have enhanced outcomes and minimized toxicity. Nonetheless, more than a million Americans are diagnosed with cancer each year. One out of four deaths in the U.S. is caused by cancer—a rate that is second only to deaths due to cardiovascular disease. The National Cancer Institute (NCI) estimated the total economic burden of all cancers to be $190 billion in 2004.* Reducing this burden will require research to fill gaps in basic understanding and therapy of major cancers and, as importantly, translate current knowledge into prevention, early diagnosis, and treatment for all Americans.

In 1972, the Albert Einstein Cancer Center (AECC) was among the first research institutes in the U.S. to be designated and funded as a "Cancer Center" by the NCI. Since then, AECC has developed a broad range of innovative basic, clinical, population-based and translational research programs. Einstein researchers are deciphering the complex role of the immune system in the onset, progression, and therapy of cancer; studying chemical changes in DNA that cause cancer; and exploring how the tumor microenvironment influences the ability of cancer cells to invade and spread beyond the initial tumor site. Many studies utilize tissues obtained in the clinic in order to investigate abnormal processes directly in human cancers. New therapies emerging from basic science findings at AECC are being evaluated in advanced clinical trials at Einstein and elsewhere. Collaborating clinical and laboratory scientists focus on specific cancers such as leukemia and lymphomas, melanoma, colon, head and neck, and breast cancers to study basic biology, prevention, and treatment. These AECC programs

*Sources: Centers for Disease Control and Prevention; National Cancer Institute, Cancer Trends Progress Report – 2005 Update



constitute a solid foundation for dynamic research as new scientific knowledge and powerful technologies emerge. AECC's recent achievements reflect its unique ability to recognize and respond to the rapid pace of science in the 21st century.

Major Research Goals

Development of New Therapies: A major AECC goal is the translation of discoveries that emerge from basic laboratory studies into new cancer therapies. These opportunities are often related to the identification of a target that appears to drive the growth, replication, and survival of cancer cells. An x-ray structure of the target obtained in the AECC Structural Biology Core Facility enables the design of a potential chemical inhibitor. The inhibitor is tested, chemically modified, and validated in tumor cells growing in the laboratory and in animals. If these results are promising, the drug is evaluated for toxicity in animals before being tried in human patients. At any point following target identification and the development of a lead drug, these discoveries can be licensed to a pharmaceutical company which underwrites the high cost of clinical trials.

Development of a Cancer Clinical Trial Unit: Einstein has an active, though limited, phase I clinical trials program and a translational development program for experimental therapeutics. To break into the top tier of cancer clinical research institutions, the College needs a dedicated Cancer Clinical Trial Unit and a cadre of faculty recruits to perform high impact cancer trials with innovative therapeutic agents developed at Einstein and elsewhere. A partnership between Einstein and Montefiore Medical Center to establish this Unit would provide the research expertise as well as the physical space required to create a seamless interface between clinical research and patient care. Moreover, the Unit would capitalize on the state-of-the-art facilities for drug development through the planned chemical and structural biology programs.

Targeting the Immune System: A variety of cancer cell targets have been identified as candidates for drug development. Einstein researchers are developing a new structural and functional understanding of the immunological synapse—the interface and site of cross-talk between a T cell and a B cell of the immune sytem, integral to the production of antibodies. Some of these interactions could lead to tolerance—the ability of the cancer cells to evade the immune response. Developing drugs that block this interaction might restore normal immune mechanisms to attack and kill cancer cells.

In another approach, AECC scientists are developing antibodies to proteins within, or released by, cancer cells. Antibodies against melanin (a skin pigment) have been linked to a radioactive chemical for the treatment of malignant melanoma. Clinical trials with this novel drug will be initiated in 2007. Similar approaches are being used to target proteins produced by viruses in cancer cells. Antibodies directed to human papillomavirus proteins in cervical cancer are being evaluated in the laboratory.

Blocking Metastasis: Cancer cells often acquire the ability to invade surrounding tissues and blood vessels in order to metastasize or migrate away from the original site of development. Metastasis and the damage it causes, rather than the primary tumor which can often be removed surgically, is the usual cause of cancer-related death. Because most normal cells cannot migrate in this way, molecules that are unique to metastasizing cells represent prime targets for therapeutic intervention. Promising targets have come from AECC's unique studies on the propulsion machinery in malignant cells which, when blocked, prevent cancer cells from moving.

Tumor Microenvironment and Cell-Cell Interactions: Cancer cells are in constant communication with the surrounding milieu and subvert normal physiological processes to support tumor growth and metastasis.

For example, cancer cells send out signals that promote angiogenesis—the growth of new blood vessels that supply vital nutrients for tumor growth. Similarly, macrophages, that are normal components of the inflammatory reaction, are attracted to the tumor site where they, in turn, release factors that promote metastasis. Adipocytes (fat cells) in the tumor environment, in tissues like the breast, produce a factor that enables cancer cells to invade adjacent tissues. Understanding interactions between cancer cells and the surrounding tissue will enable Einstein researchers to develop drugs to manipulate this environment, halt or reverse tumor growth, and prevent metastasis.

Epigenetics of Cancer: Susceptibility to cancer can be traced in part to genetic factors that are inherited from our ancestors. However, cells can also undergo "epigenetic" changes due to environmental factors that modify DNA without changing the inherited gene sequences. Such modifications can trigger cancer or influence the natural history of disease or response to treatment. For instance, epigenetic changes to DNA can shut off the production of proteins (tumor suppressors) that block cell growth and tumor development. AECC researchers are focused on understanding the role of epigenetic changes in the development and progression of cancer and how this may be blocked by pharmacologic agents.

Population-based and Epidemiologic Research: Important clues regarding cancer causation come from studies designed to correlate the relationship among environmental exposures, exposure to infectious agents, diet, lifestyle factors, and the incidence of cancer. Important topics include: the relationship among obesity, diabetes, and cancer; identification of factors that predict risk of cancer in a high-risk population, such as characterization of benign breast tumors to predict which women are at high risk for subsequent development of breast cancer; and evaluation of which types of human papillomavirus infections of the cervix are likely to produce cervical cancer. In this way, risk factors can be identified and intensive, effective prevention measures can be designed and directed to the high-risk population. A major AECC goal is to build cancer epidemiological research through the recruitment of new faculty who are focused on viral-induced cancers and breast cancer. Initial successes in the area of obesity, energy metabolism, diabetes and cancer will be expanded and linked to research activities of the Diabetes and Aging Centers at Einstein.

Cancer Prevention: A major public health challenge in diminishing the burden of cancer is making available the benefits of what we already know about prevention, early diagnosis, and treatment to all Americans. There are large, medically underserved populations in rural and urban areas who are at high risk of cancer and have limited access to appropriate health care. One such area is the Bronx, where 75 percent of the population is African-American or Hispanic. Economic, social and language barriers impede the heath care of this population. AECC research will be directed to identifying factors that limit access of this population to medical care, and elements that put members of this population at high risk of cancer. In addition, initiatives will be designed to promote cancer prevention at behavioral and other levels and to evaluate the effectiveness of these interventions. This will require the development of an AECC Cancer Prevention and Behavioral Sciences program. These cancer-related activities complement existing Einstein programs for behavioral research in disease prevention with a special emphasis on the Bronx population.

Intersection with the Science and Technology Areas

Cancer research programs at Einstein rely heavily on access to the resources and expertise of the science and technology focus areas. Examples of intersection include, but are not limited to:

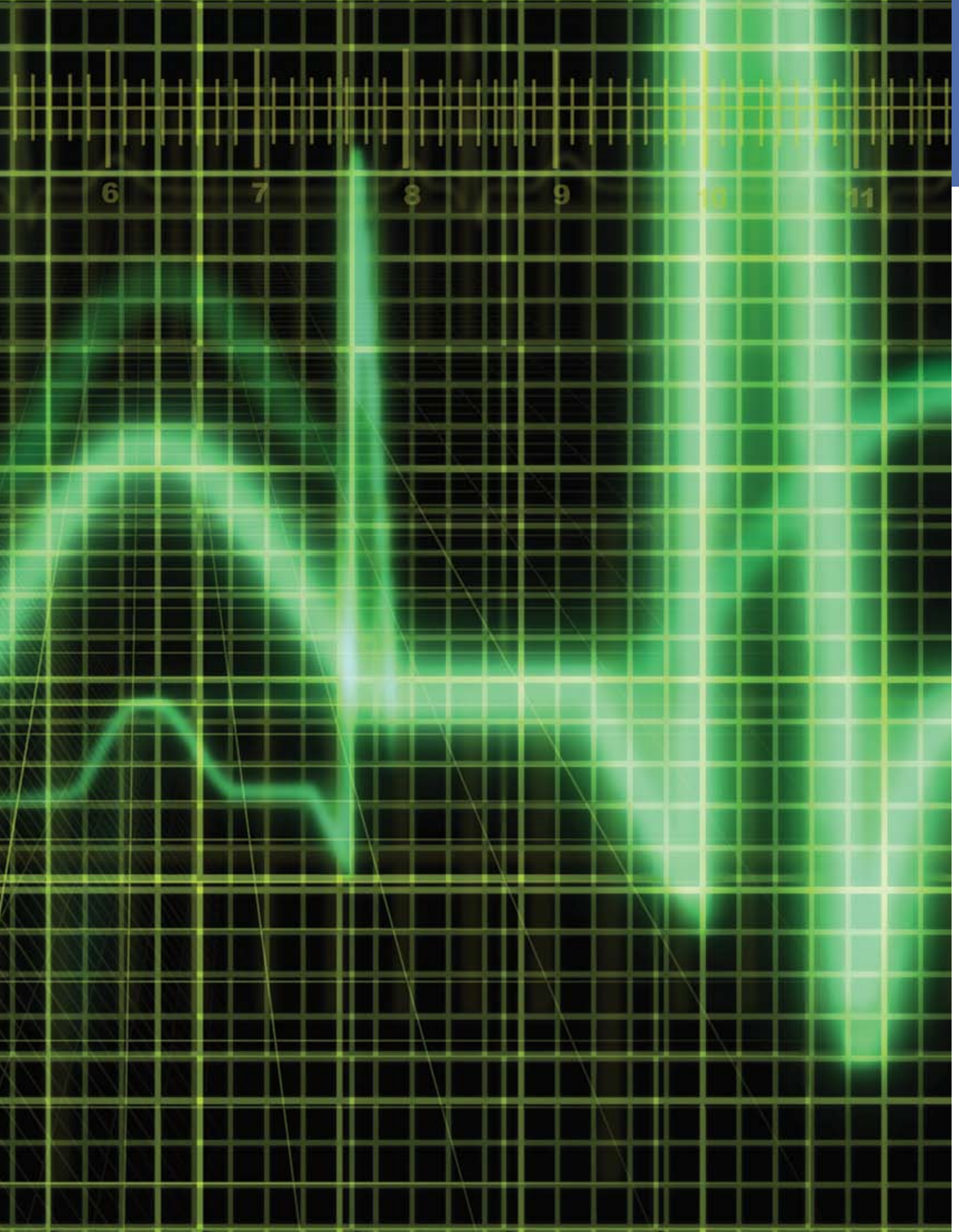
Increasing the health of the population is a major AECC goal that will be enhanced by increased collaborations between researchers focused on *Behavioral and Social Determinants of Health and Health Disparities* and their colleagues in other disease-focused centers at Einstein (AIDS, Diabetes, Aging, Neurosciences). These centers share common strategies in experimental design and analysis and their studies often use the same or overlapping populations. The ideal mechanism for bringing these investigators together is a common academic unit, which for cancer epidemiologists is the Department of Epidemiology and Population Health. Similarly, behavioral scientists require the recruitment of a critical mass and an academic base either within the context of a division in that department or some other entity. Populations derived from the Bronx and greater New York City areas are ideal for research on cancer-related behaviors, such as smoking, diet and obesity, and exercise and for studies on sexual- and blood-transmitted diseases associated with cancer. These initiatives are facilitated by well-established infrastructure such as the Bronx school clinics developed by the Montefiore Medical Center, the MMC health-care network and associated database, the NIH-funded Bronx Center to Reduce and Eliminate Ethnic and Racial Health Disparities, and the Bronx Alliance for Tobacco-Free Health.

When new cancer-specific drug targets are identified through basic research, *Chemical Biology* can be used to design new agents that selectively interact with the target. Many such leads have emerged from basic studies in AECC programs. In particular, radiochemistry strategies have been developed to link radioactive molecules to antibodies that selectively target specific types of cancer cells. Einstein researchers used this approach to develop an anti-melanin monoclonal antibody-linked radionuclide that is about to enter human clinical trials as a treatment for malignant melanoma, a highly virulent form of skin cancer.

Computational and Systems Biology is a rapidly evolving scientific discipline that has developed in response to new high-throughput instrumentation and technologies that offer the possibility of generating billions of bits of genetic and other information based upon studies on normal and malignant tissues. Strategies are needed to link this information with clinical and other data in order to derive valid correlations. These global approaches to information integration are required for transforming disparate data on epigenetic changes in DNA, gene expression patterns, and protein patterns (proteomics) into a cohesive, coherent picture that will inform physicians about cancer risk, natural history of malignant diseases, and the selection of therapeutic agents tailored to the needs of specific tumors in individual patients.

New *Imaging* technologies are vital to cancer research. A major thrust of AECC research is the development of mouse models of cancer. Documenting the initiation, sites of origin, and progression of these cancers requires the most advanced imaging technologies—including MicroPet/CT, ultrasound, multiphoton microscopy, and other technologies to monitor fluorescence—in the barrier facility where these animals are housed. These noninvasive approaches allow mice to remain alive while repeated measurements are made. Likewise, MRI imaging and spectroscopy in humans and animals at the Gruss Magnetic Resonance Research Center provides another method of visualizing tumor development, quantifying specific metabolic pathways and metabolites in living tissues, and monitoring the outcome of therapy in patients.

	Cancer
Behavioral/Social/Disparities	Cancer-related behaviors and risk factors
Chemical Biology/Genomics	Design of radiochemicals for cancer therapy
Computational/Systems Biology	Visualization of changes in cells and brain
Imaging	Visualization of the tumor microenvironment



Cardiovascular Disease

THE VISION

To discover underlying mechanisms, treatments, and preventive approaches for the most common and devastating cardiovascular diseases using an integrated, multidisciplinary approach employing cutting-edge technologies and capitalizing on the Bronx location

The Challenge and Opportunity

In 2003, more than 71 million Americans or one in every three adults were living with some form of cardiovascular disease (CVD) such as high blood pressure, coronary heart disease or stroke. CVD was the underlying cause of death in one of every 2.7 deaths in 2003 and has been the leading cause of death in the U.S. every year since 1900, with the exception of 1918. Strikingly, CVD accounts for more deaths each year than the next four leading causes of death combined and, in 2006, cost society an estimated $403 billion in direct and indirect expenses.*

Einstein researchers are committed to the development of a highly integrated, multidisciplinary investigational approach to answer fundamental scientific questions and translate new discoveries into clinical applications that can reduce the burden of CVD in individuals and the general population. The Cardiovascular Research Center provides a central hub to foster collaborations among investigators with diverse backgrounds and skill sets. The Cardiovascular Disease working group identified two major topics for which Einstein is poised to make significant contributions.

Major Research Goals

Heart Failure: Heart failure can arise from a variety of underlying causes including prior myocardial infarction, high blood pressure, valvular heart disease, congenital heart defects, drugs or toxins, autoimmune disease, or other triggers. Enlargement of the heart often precedes heart failure and sudden death due to arrhythmias is common. Despite the introduction of new drugs in recent years to treat this condition, the death rate from heart failure remains at about 500,000 individuals each year in the U.S.

With its current strength in myocardial biology research, Einstein has an opportunity to address major research goals related to heart failure: understand the molecular basis of heart failure; define mechanisms responsible for the growth, differentiation, and death of cardiac stem cells and heart muscle cells; investigate the role of cardiac hypertrophy in heart failure; and assess recovery of the heart

*Source: Heart Disease and Stroke Statistics–2006 Update. *Circulation*. 2006; 113:e85-e151.

in patients after mitral valve repair. Heart failure is a complex disorder that involves multiple molecular processes and cell types. However, technical advances, the development of suitable animal models and updated genetic and epidemiologic approaches make this topic ideal for productive collaboration among basic, translational, and clinical researchers.

Atherosclerotic Vascular Disease and its Sequelae: Atherogenesis is the formation of plaque in major arteries, often as a result of high blood pressure, high cholesterol, cigarette smoking, or diabetes. Sudden rupture of unstable plaque in a coronary artery can close off blood flow to the heart muscle, leading to a myocardial infarction or heart attack. Over one million Americans suffer a heart attack each year and 300,000 of those individuals die. Another 300,000 people die from strokes.

By building on the existing core group of vascular biologists, Einstein could position itself to make major contributions to research on the vascular events leading to atherosclerosis and the consequences of plaque instability that contribute to heart attack and stroke. Important questions to be addressed include: What are the molecular mechanisms of plaque instability? Can strategies be developed to preserve heart muscle during a heart attack? What are the mechanisms that control the growth of new blood vessels and how can these processes be manipulated to treat tissue damage caused by heart attack or stroke? Einstein researchers have access to cell systems, animal models, and patient populations that would facilitate research on this important health problem.

Intersection with the Science and Technology Areas

The cardiovascular disease research community at Einstein takes full advantage of the opportunities afforded by the science and technology theme areas. Examples of synergism include, but are not limited to:

In the U.S., women and certain racial/ethnic minorities exhibit profound disparities in terms of the development and treatment of cardiovascular disease. Interactions with the *Behavioral and Social Determinants of Health and Health Disparities* community will allow important questions about the morbidity and mortality of cardiovascular disease to be asked from a multidisciplinary perspective.

Interactions between cardiovascular researchers and the *Human Genetics* group are bidirectional. Genes found in human populations to modify risk for disease or response to therapy will inform mechanistic studies to understand the underlying processes and develop new, more effective drugs. In turn, observations made in cell or animal models will suggest candidate genes that can be validated in human genetic studies.

The full range of *Imaging* technologies is critical to cardiovascular research. Cellular imaging methods can reveal changes in mitochondrial function and other cellular processes in failing or diseased heart muscle cells. The intact human heart can be visualized in both the healthy and diseases states by a variety of modalities such as ultrasound, computed tomography (CT), and magnetic resonance (MR).

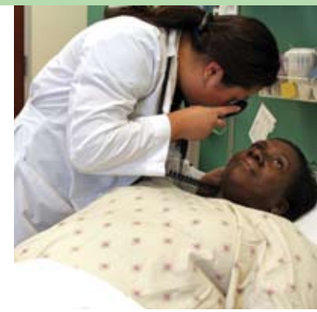
Cardiovascular researchers at Einstein have an exceptional opportunity to interact with the *Stem Cells and Regenerative Medicine* community to study ways of differentiating pluripotent stem cells into cardiac muscle cells that may have therapeutic potential.

	Cardiovascular Disease
Behavioral/Social/Disparities	Psycho-social factors of morbidity and mortality
Human Genetics	Genetic markers of risk or response to therapy
Imaging	Visualization of changes in cardiac cells and heart
Stem Cells/Regenerative Medicine	Differentiation of cardiac muscle cells

Diabetes, Obesity, and Other Metabolic Diseases

THE VISION

To prevent or reverse the current epidemic of diabetes mellitus, obesity, and related metabolic disorders



The Challenge and Opportunity

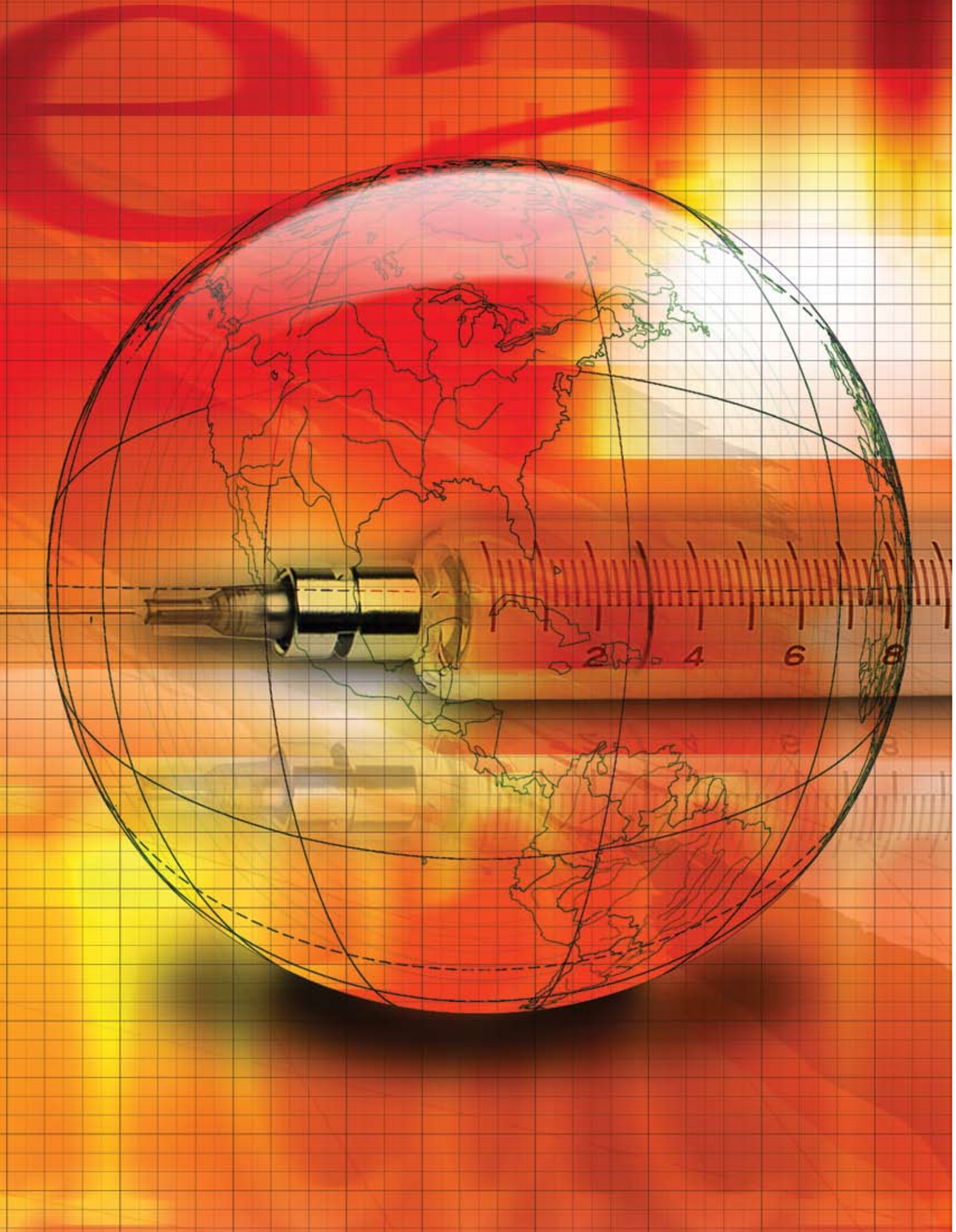
The epidemic of diabetes and obesity has been well documented. An estimated 20.8 million individuals—7 percent of the U.S. population—has some form of diabetes. Alarmingly, it has been predicted that one of every three American children born in the year 2000 will develop diabetes during his or her lifetime. The diabetes epidemic is not limited to the U.S., but is a global health threat affecting developed and developing countries alike. Similarly, obesity has become a significant and growing public health problem with two-thirds of American adults classified as overweight or obese. Obesity increases the risk for additional health problems such as diabetes, cancer, gallbladder disease, and heart disease. The economic costs of diabetes in the U.S. are estimated at $132 billion per year, while those of obesity and overweight are as much as $117 billion. Minorities disproportionately bear the burden of both diseases.*

For over 30 years, the Einstein Diabetes Research and Training Center has been a leader in basic and clinical research related to diabetes, obesity, and other metabolic diseases. As one of only five comprehensive diabetes centers supported by the NIH nationally, the Einstein DRTC is in an exceptional position to effectively translate basic science findings into clinical applications. The Bronx location provides access to a patient population that is greatly affected by the problems of diabetes and obesity, making this a vital area for Einstein involvement. The Metabolic Diseases working group identified research goals that would build on the College's foundation of excellence in diabetes and obesity research and be clinically relevant to the local and global communities.

Major Research Goals

Development of Type 1 Diabetes: Type 1 diabetes is an autoimmune disease that constitutes 5-10 percent of all diabetes cases. While not as prevalent as type 2 diabetes—the major form of diabetes linked to obesity—type 1 diabetes appears to be increasing in both U.S. and international populations. Because type 1 diabetes (formerly known as juvenile diabetes) often strikes during childhood, patients are faced with a lifetime of difficult disease management and the threat of long-term complications.

*Sources: Centers for Disease Control and Prevention, *National Diabetes Fact Sheet*, 2005; Weight Control Information Network



By harnessing its expertise in autoimmune disease, stem cell biology, and related research fields, Einstein is poised to make major contributions to the understanding and treatment of type 1 diabetes. Developing ways to identify T cells that are attacking the pancreas, would allow researchers to monitor at-risk individuals before diabetes onset and aid in the development of specific therapies to prevent or reverse type 1 diabetes. The vigorous stem cell research program could be expanded to study the differentiation of stem/progenitor cells into mature insulin-producing cells to replace those lost in type 1 diabetes patients.

Cellular Mechanisms of Obesity and Strategies to Prevent or Reverse Obesity: Body mass and composition are regulated by a complex interaction between the central nervous system and the rest of the body's tissues. Current approaches to controlling obesity—surgical, pharmacological, and lifestyle changes—are difficult to implement or only partially effective. Understanding how individual organs, such as the adipose tissue, skeletal muscles, and the liver, process nutrients might point the way to innovative therapies for obesity.

By expanding existing research programs on whole body metabolism to analysis of individual organs, Einstein has the resources to address this important issue in both animal models and human populations. In addition, examining the link between obesity and tissue-specific inflammation could lead to new understanding of the health consequences of obesity. Finally, genetic studies to identify inherited factors that make a person more or less susceptible to metabolic diseases are a first step toward the development of drug targets to treat obesity.

Insulin Resistance and its Clinical Sequelae: Insulin resistance causes considerable morbidity and mortality through its association with type 2 diabetes, obesity, high blood pressure, blood lipid abnormalities, cancer, Alzheimer's disease, polycystic ovarian syndrome, and a variety of other serious conditions.

Einstein researchers are at the forefront of diabetes and obesity research leading to the discovery, characterization, cloning, and therapeutic development of adiponectin, a hormone produced by fat tissue that links adipose biology, inflammation, and insulin resistance. Building on this strength, important research questions can be addressed such as the genetic basis of insulin resistance; epigenetic, environmental and psychosocial factors that affect metabolism; and the relative roles of high levels of glucose and insulin in mediating the damaging effects of insulin resistance.

Permanent Tissue Damage Caused by Diabetes and Obesity: The personal and public health care costs of diabetes, obesity, and other metabolic disorders are enormous. These diseases increase the risk of heart disease and stroke, kidney failure, blindness, and non-traumatic amputation, as well as critical and non-critical care hospitalization. Few effective therapies are available to prevent or reverse these serious long-term complications.

Culturally Sensitive Models for Diabetes Management: Despite the availability of therapies to effectively manage diabetes, a majority of patients with type 2 diabetes have not achieved metabolic control. Several behavioral factors may account for this disparity, including inconsistent medication intake, suboptimal diet, and lack of exercise. Researchers at Einstein have adopted a public health model, and have developed a bilingual, culturally sensitive, patient-centered telephone intervention specifically designed for use with underserved African American and Latino populations in the Bronx, which have the highest incidence of type 2 diabetes in New York City. Preliminary studies of telephone interventions conducted by the investigators have shown a clear connection between a culturally sensitive intervention approach and effectively facilitating lifestyle choices.

Intersection with the Science and Technology Areas

Achieving the important goals of diabetes and obesity research will require close interactions with the resources and expertise of the science and technology areas. Examples of intersection among these fields include, but are not limited to:

The increase in diabetes and obesity in the U.S. and globally is due in part to social and environmental changes such as the widespread availability of nutrient-dense foods and community environments that discourage exercise. Experts in *Behavioral and Social Determinants of Health and Health Disparities* will be needed on a wide range of issues related to diabetes and obesity. For example, the gene-environment interactions that predict an individual's susceptibility or resistance to these diseases are not well understood. The impact of social and behavior factors such as sleep deprivation, socioeconomic conditions, and availability of healthful foods and safe places to exercise must be explored. Importantly, the development of behavioral/lifestyle interventions that can stem the twin epidemics of diabetes and obesity are urgently needed.

At present, no safe methods are available to block the immune attack leading to type 1 diabetes. The tools of *Chemical Biology and Chemical Genomics* are needed to aid in the development of compounds that can interfere with the activity of T cells—the component of the immune system responsible for the autoimmune attack. Similarly, as the molecular pathways involved in the onset of obesity and type 2 diabetes are identified, library screening and chemical synthesis resources will be crucial to finding new drugs to manipulate these pathways and reverse disease.

Human metabolism is a complex process that involves many diverse organs (e.g. brain, pancreas, liver, nerves) and can lead to multiple disease manifestations (e.g. high blood glucose, high blood lipids, insulin resistance). *Computational Biology and Systems Biology* approaches will be invaluable in analyzing gene expression patterns in multiple tissues and developing an integrated, whole-body picture of metabolism in normal physiology and disease. These fields will be especially useful in understanding diabetic complications in which abnormal metabolism affects tissues like the eyes, kidneys, and sensory nerves.

Curing diabetes depends on finding a way to replace the insulin-producing beta cells in the pancreas that are destroyed in type 1 diabetes or die off in type 2 diabetes. The field of *Stem Cells and Regenerative Medicine* has the potential to achieve a diabetes cure by figuring out how to turn stem cells—which have the potential to become any cell type—into functional beta cells in a safe and reproducible manner. The stem cell field can also advance our understanding of fat cell biology and contribute to the search for obesity treatments.

	Metabolic Diseases
Behavioral/Social/Disparities	Environmental factors in diabetes and obesity
Chemical Biology/Genomics	New drugs for diabetes and obesity
Computational/Systems Biology	Metabolism in health and disease
Stem Cells/Regenerative Medicine	Replacement beta cells for diabetes

Infection and Immunity

THE VISION

To shift human biological research from organ concepts to a new focus on the human symbiont and associated systems

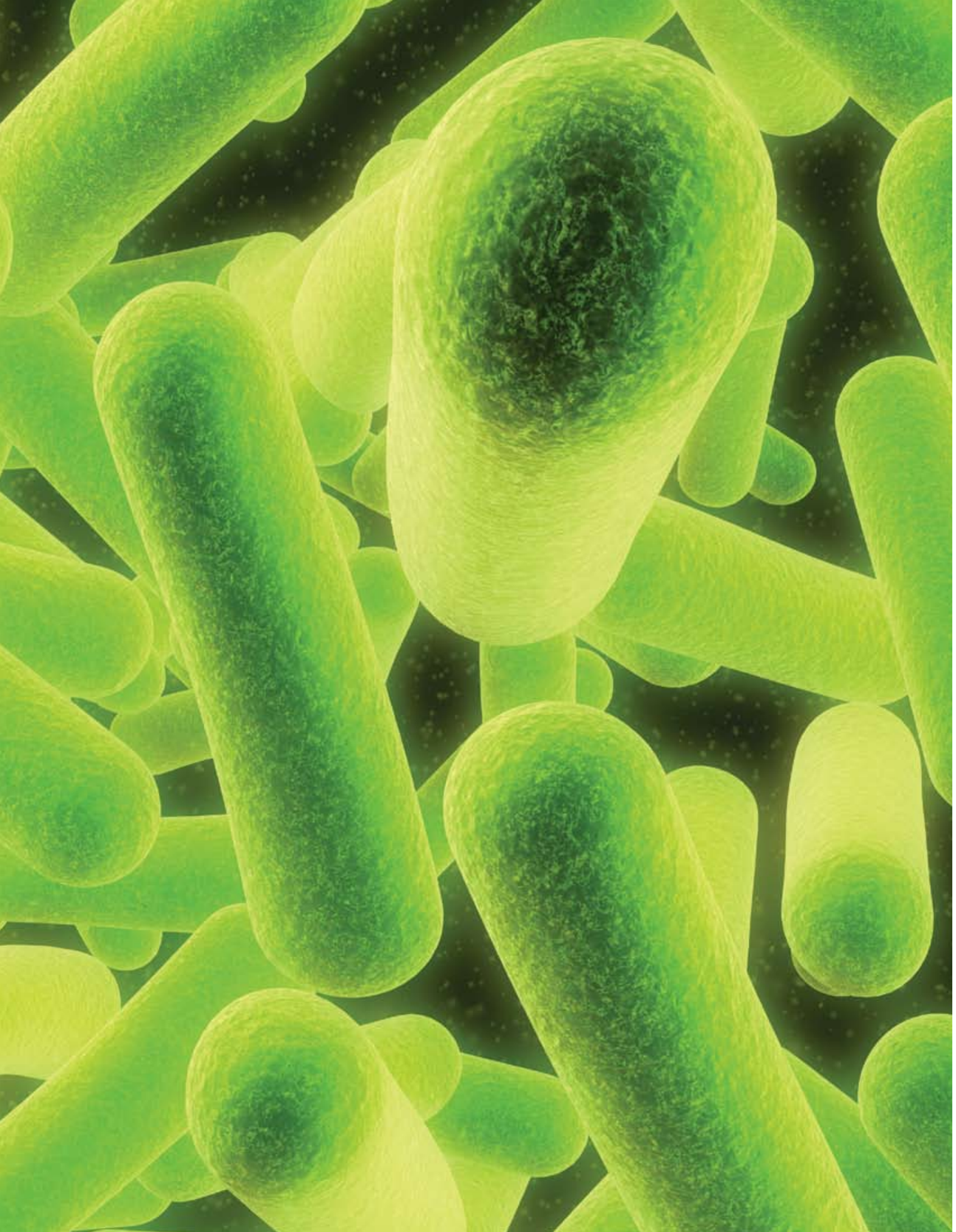
The Challenge and Opportunity

Shortly after birth, the human skin, intestinal tract and mucous membranes become populated with bacteria and other microbes that are essential to normal physiologic function. These microbes are often the first line of defense against disease and are required for proper development and health of the immune system. Throughout life, microbes in the body contribute to diverse processes—nutrition, mating choices, aging and many others. Conversely, most human diseases result from alterations in microbes associated with the body or a disruption in the immune response against these organisms. Infectious diseases caused by pathogenic microbes such as viruses or parasites—HIV/AIDS, hepatitis, and measles, to name just a few—may be most obvious examples of the effect of microbes on human health. However, researchers are finding microbes associated to some degree with most diseases. For example, infectious agents are associated with 45 percent or more of all cancers; even mental illness has been linked to infection in some cases.

Einstein is building on a long and productive track-record of research related to infection and immunity to understand how the immune system fails in disease and to use that knowledge to develop new therapies. This research field is especially critical considering the high burden of infectious and immune diseases, including HIV/AIDS, asthma, and allergies, in the south Bronx community. This major public health issue not only gives added urgency to Einstein's research efforts, but also provides the College's investigators access to a unique patient population for translational and clinical research. The Infection and Immunity working group articulated a series of research goals that would cultivate Einstein's existing strengths and accelerate its contributions to the field.

Major Research Goals

Diseases of Dysregulation of the Immune System: Many diseases attributed to microbes actually result from abnormal human immune responses triggered by microbial proteins. Further, research has revealed that chronic immune diseases such as asthma are caused or modified by human immune factors or interactions between the immune system and microbes. Hence, the investigation of allergic diseases and asthma interfaces with basic immunology, microbiology, and, to some extent,



rheumatology (diseases of the joints and connective tissue). Importantly, the course of allergic disease and asthma are affected by behavior and access to health care.

Einstein has outstanding strength in basic immunology and microbiology research. Researchers at Einstein are leaders in the characterization of immune molecules that play a critical role in activating or deactivating the immune response, which in turn synergizes with genetic factors in the development of allergic diseases or asthma. Moreover, Einstein investigators have made an important discovery that cryptococcal infection in an animal model predisposes the animals to the development of asthma. This observation, combined with the finding that most children in the Bronx acquire cryptococcal infections early in life, positions the College to make a seminal contribution to the field by linking early infection and the subsequent development of immune dysregulation leading to asthma. Pursuing this goal will require a multidisciplinary approach involving experts in immunology, microbiology, epidemiology, pediatrics, health disparities, and other relevant fields.

Vaccine Institute: Over the past several decades, the availability of vaccines against serious infectious diseases have dramatically changed the landscape of health and disease in the U.S. and worldwide. Morbidity and mortality from once common childhood diseases such as measles, diphtheria, and mumps, have plummeted. Vaccines have enabled the disappearance of smallpox and near eradication of polio worldwide. Yet, there are many infectious diseases for which no vaccines are currently available. Vaccine development is a funding priority of the National Institutes of Health (NIH) and private foundations.

Einstein has two vaccine efforts: development of a live, attenuated vaccine for tuberculosis which would be more effective than the currently available formulation; and the development of polysaccharide-derived vaccines for pneumonia, cryptococcal infections, and tuberculosis. Expansion of a vaccine development program at Einstein would represent a prime opportunity to foster bench-to-bedside translational research and to incorporate research on other organisms with local and global public health implications, such as HIV, hepatitis C, and malaria.

Genetic Basis of Susceptibility to Microbe-Induced Disease: Not everyone gets sick when exposed to a particular microbe. Biological differences, particularly genetic factors, significantly influence the likelihood for disease development. For example, individuals with a specific variation in the gene for a protein known as the "CCR5 receptor" are not susceptible to HIV infection. Developing a research focus on host susceptibility would foster multidisciplinary collaboration among Einstein experts in genetics, environmental sciences, behavior, health disparities, and immunology. Understanding individual susceptibility to disease is a necessary prelude to the development of "personalized medicine" approaches that seek to optimize therapies for individuals.

Mucosal Diseases: The mucosa is the critical barrier that separates the body from the outside environment and is the primary surface where the host meets most microbes. Numerous chronic diseases—ulcerative colitis, Crohn's disease, allergies, sinusitis, and others—arise from abnormal interactions between microbes and the immune system at the mucosa. In addition, the mucosa is the entry site for many disease-causing infectious agents, including HIV, hepatitis C, diarrheal diseases, and more.

The robust Einstein research programs in immunology and microbe research could be focused on understanding and treating mucosal diseases, which represent a significant public health problem across age, sex, and ethnic groups. The environmental and

emotional components of many mucosal diseases make this area ripe for collaboration with behavioral and social researchers.

Emerging Threats: The past few decades have seen the emergence and rapid, global spread of HIV, hepatitis C, SARS virus, influenza, and other microbes as major threats to human health. The use of anthrax in terrorism threats has shown the vulnerability of our society to biological warfare. The urgency of these potential threats has led to significant federal investment in research to combat emerging pathogens.

Einstein has a vigorous research effort devoted to basic and clinical research on these pathogens that is also linked to developing Global Medicine programs. In addition, research on emerging biological threats complements plans for construction of a Biosafety Level 3 Facility in the CGTM.

Immunopathogenesis and Treatment of HIV/AIDS: The Bronx is an epicenter of the HIV epidemic in the U.S. with one of the highest infection rates in the country. As a result, Einstein and Montefiore clinicians and researchers have been at the forefront of AIDS research and patient care since the emergence of the disease. Ongoing research projects range from basic science investigations of the mechanism of HIV replication to understanding the biology of pathogens associated with HIV infection to the development of novel therapies to treat HIV and HIV-associated microbes.

The Einstein/MMC Center for AIDS Research (CFAR) supports basic and clinical HIV/AIDS investigators. The diversity of research programs provides a critical mass of investigators to effectively translate findings from the bench into new clinical treatments for HIV/AIDS. Growth and development of the HIV research program ensures that the College can maintain its competitive status and continue to capitalize on access to the Bronx community and a long history of excellence in this field.

Intersection with the Science and Technology Areas

Each of the major goals for infection and immunity research are dependent on resources and expertise afforded by the science and technology programs. Examples of how these programs intersect include, but are not limited to:

Many infectious and immune-mediated diseases that are rampant in the Bronx—for example, HIV/AIDS, allergies, and asthma—are influenced by environmental and socioeconomic factors. The tools of *Behavioral and Social Determinants of Health and Health Disparities* research can be used to tease out the role of the environment and behavior in disease susceptibility and treatment outcomes. Behavioral research is also key to understanding factors associated with compliance in vaccine programs.

Chemical Biology and Chemical Genomics technologies can be applied to the development and testing of small molecules that can reverse dysregulation of the immune system or block infection by HIV or other microbes.

Understanding the correlation between the course of infectious disease and unique genetic markers in large patient cohorts will require the holistic perspective and creative mathematical approaches of *Computational Biology and Systems Biology* research.

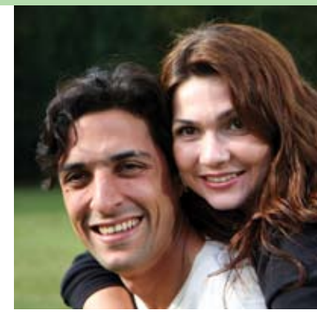
Structural Biology techniques will be used to solve the three-dimensional structure of proteins required for microbial infection or for normal immune system function. These structures can be used to design new drugs to mimic the protective immune effects. These fields will also intersect in the structural determination of the immunological synapse—the interface between T cells of the immune system and antigen-presenting cells that trigger an immune response.

	Infection and Immunity
Behavioral/Social/Disparities	Environmental and socio-economic factors
Chemical Biology/Genomics	New drugs for infectious and immune diseases
Computational/Systems Biology	Genetic determinants of infectious disease risk
Structural Biology	Immunological synapse discovery

Liver Diseases

THE VISION

To harness Einstein's significant and unique research strengths in basic liver biology and pathobiology to advance the diagnosis and treatment of liver diseases



The Challenge and Opportunity

Approximately 5.5 million people in the U.S. have been diagnosed with chronic liver disease or cirrhosis (fibrosis of the liver) and another 20 million have gallbladder disease. Together, chronic liver disease and cirrhosis are the 12th leading cause of death and account for $1.6 billion each year in economic costs. When liver cancer and gallbladder disease are factored in, the costs of liver disease rise to $10 billion per year. The underlying causes of liver disease include such diverse triggers as infectious agents, inherited factors, impaired metabolism, alcohol, and environmental toxins. Rates of viral liver disease and liver cancer are increasing in the U.S. and internationally. Although more than 5,500 liver transplants are performed each year in adults and children with end-stage liver disease, more than three times that number—17,000 patients—remain on a waiting list.*

For more than 30 years, the Marion Bessin Liver Research Center at Einstein has been at the leading edge in research on basic liver biology and pathobiology. To enhance the impact of this research program on public health, Einstein investigators must find ways to translate basic science discoveries into clinical research that will impact the prevention, diagnosis and treatment of liver diseases. The Liver Diseases working group identified key research goals that represent promising targets for clinical translation and that synergize with the development of a Liver Transplant Program at Montefiore Medical Center.

Major Research Goals

Cell and Gene Therapy for Liver Diseases: While liver transplantation is an effective treatment for some patients, whole organ transplantation involves major surgery and is limited by the shortage of available organs. The development of liver cell transplantation techniques could provide a safer, less expensive alternative that could use stem/progenitor cells to restore liver mass and function. Introducing specific traits into such cells before transplantation by targeted gene therapy could provide a means of repairing genetic defects in the liver.

*Source: National Institute of Diabetes and Digestive and Kidney Diseases, Action Plan for Liver Disease Research, 2004.

Einstein investigators have successfully used fetal liver stem/progenitor cells to replace a third of liver mass in normal adult rats—a level of repopulation that would be sufficient to treat most liver diseases. In addition, analogous cells from human fetal liver have been isolated and expanded in the laboratory. These fundamental advances will enable Einstein researchers to engage in clinical studies, in collaboration with Montefiore, to repopulate the liver in human patients undergoing radiation therapy for certain types of liver cancer or metastasis. Gene therapy approaches will be used to reverse inherited diseases such as Crigler-Najjar syndrome, Wilson's disease, lysosomal storage disorders, and others.

Hepatocyte Lipid Accumulation and the Development of NASH: The prevalence of nonalcoholic fatty liver disease (NAFLD), already among the most common liver diseases in the U.S., is expected to rise even further due to the increase of major risk factors for this condition, including diabetes and obesity. NALFD starts with fat/lipid accumulation in liver cells and often progresses to nonalcoholic steatohepatitis (NASH), a chronic liver disease characterized by liver injury and inflammation.

Einstein researchers have considerable opportunities to expand on current basic science studies to define the basic mechanisms of NAFLD and NASH and develop new therapies to treat these debilitating diseases. New animal models of steatohepatitis are needed to better understand the molecular mechanisms of disease. The role of genetic factors and metabolic abnormalities must be understood. Biomarkers that signal progression from NAFLD to NASH are needed.

Mechanisms of Liver Cell Injury and Death: The goal of treatment for any chronic liver disease is to halt liver failure that results from loss of hepatocytes, the cells that make up 60-80 percent of the liver mass. To achieve this goal and develop more effective therapies, it is necessary to understand the mechanisms of hepatocyte injury and cell death.

Current Einstein efforts on the mechanisms of toxin and fat induced liver injury and processes of cellular injury could be expanded to include drug, immune-mediated, and viral forms of hepatocyte injury. Critical areas of study include understanding the role of the innate immune system in liver injury, the development of animal models of drug toxicity, and the characterization of signaling pathways that promote or prevent cell death. Such research would generate fundamental insights into the mechanisms of liver injury that will be essential for future drug development.

Liver Regeneration, Hepatitis Viruses, and Liver Cancer: The liver is unique among solid organs in its capacity to regenerate in response to liver injury or loss of as much as two-thirds of its cell mass. Researchers are looking for ways to harness this regenerative ability to stimulate regeneration for cell-based therapy without increasing the risk of liver tumors and, conversely, to inhibit cellular proliferation when treating liver cancer.

Einstein researchers are attacking this problem from a variety of angles, including the study of cell cycle regulators in hepatocyte regeneration, identification of chemicals that stimulate regeneration, evaluation of protein changes associated with the initiation or progression of liver cancer, and the use of selective irradiation and cell transplantation to stimulate proliferation and restore liver mass. Research in this area could be fostered by expanding efforts to define the role of microRNAs in liver biology, development, metabolism, cancer, and infection by hepatitis viruses. The potential clinical applications of microRNAs will accelerate the translation of basic research findings into strategies that could directly benefit patients. Moreover, the further development of preparative hepatic irradiation techniques could increase the feasibility of stem cell transplants as a therapy to restore liver mass and function.

Drug Transporters and Hepatotoxicity: Most drugs that are used for non-liver diseases

are removed from the blood by the liver, broken down, and then excreted through the digestive system. Toxicity of these drugs in the liver cells—hepatotoxicity—is the most common reason for withdrawal of clinically effective drugs. Genetic differences make some patients more or less susceptible to drug-induced toxicity.

A new division of Hepatology in the Department of Medicine will facilitate clinical research in the field of clinical liver disease. For example, a team of Einstein investigators have reported major advances in the identification and molecular understanding of cell membrane transporters that carry drugs and other toxins into hepatocytes. Although much has been learned about these fundamental processes, little is known about individual variations in drug transport or metabolism that regulate toxic reactions to drugs, a significant clinical problem. Research is needed to identify the genetic polymorphisms or other biological mechanisms that predict which patients may be at risk from the administration of specific drugs.

Intersection with the Science and Technology Areas

Liver disease research benefits from interactions with a variety of science and technology areas that include, but are not limited to:

Human Genetics resources facilitate the discovery of genetic factors that influence susceptibility to drug-induced toxicity, a major clinical problem limiting the use of otherwise effective drugs in some patients.

Molecular *Imaging* tools can be used to visualize "receptor-mediated endocytosis"—the process by which many toxins, viruses, and peptides enter liver cells. Studying this process in detail will permit identification of regulatory elements that could be targets for drug discovery.

Close collaboration with the *Stem Cells and Regenerative Medicine* community is critical to the development of hepatocyte cell therapy for liver disease. Indeed, ongoing studies of fetal liver stem/progenitor cells are expected to lead in the near future to early stage clinical trials in human patients with liver cancer.

Proteomics techniques from the *Structural Biology* field enable researchers to analyze changes in protein expression and modification that correlate with initiation or progression of liver cancer. The changes represent possible biomarkers to enhance early diagnosis and targets for new drugs that can readily distinguish between normal and carcinogenic cells.

	Liver Diseases
Human Genetics	Genetics of drug-induced liver toxicity
Imaging	Receptor-mediated endocytosis analysis
Stem Cells/Regenerative Medicine	Cell transplant therapy for liver disease
Structural Biology	Protein changes in liver cancer

Neuropsychiatric Diseases

THE VISION

To define disease pathogenesis, prevent disease, and promote cures by exploiting endogenous neural stem cell repair mechanisms, emerging genetic and epigenetic reprogramming and recoding strategies and innovative pharmacogenomic tools

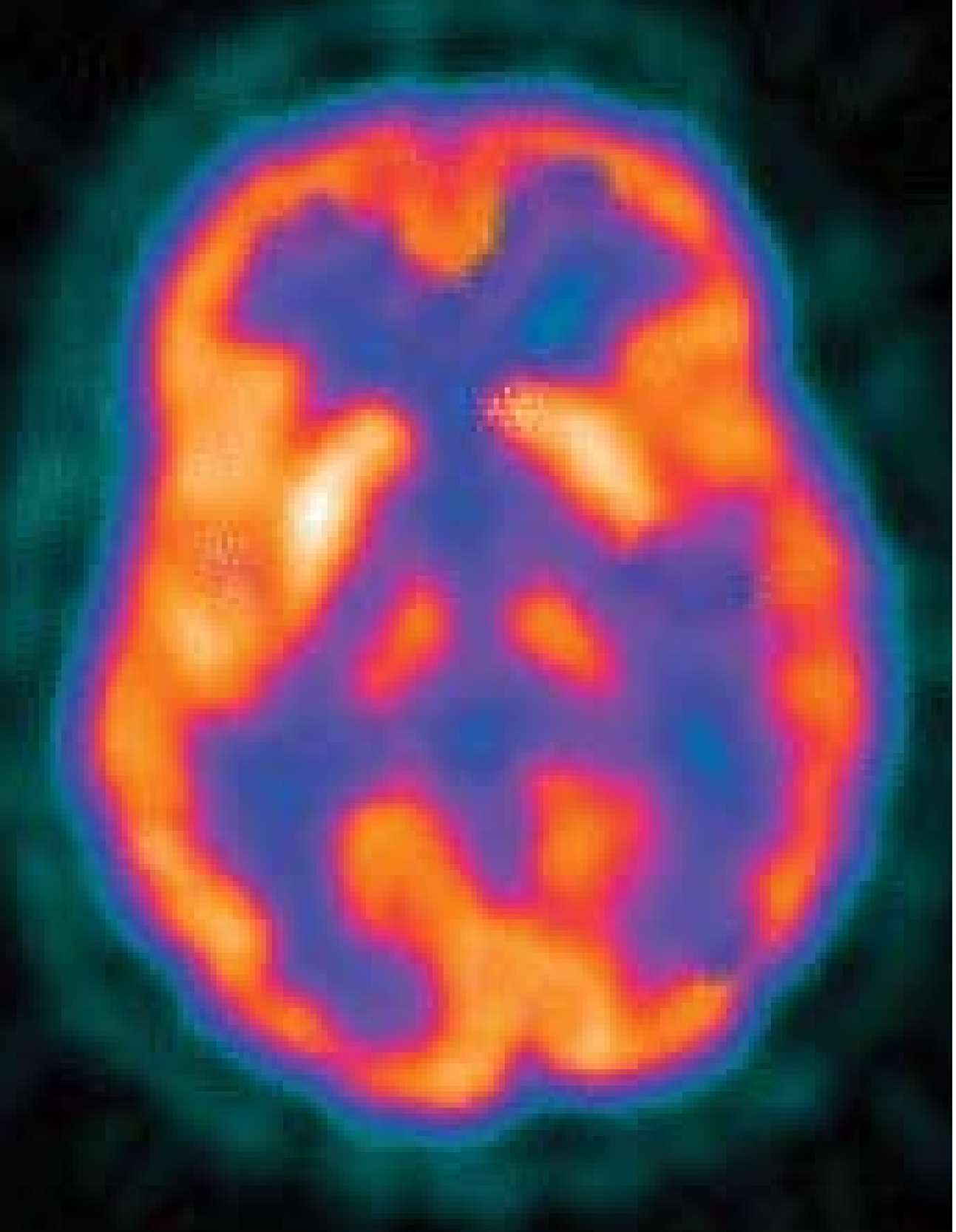
The Challenge and Opportunity

Neuropsychiatric diseases comprise a stunningly diverse range of conditions that affect every age group, socioeconomic class, and racial/ethnic group. The National Institute for Neurological Disorders and Stroke lists well over 400 rare and common neurological diseases that are included in its research mission.*

Neurological diseases can begin during development and childhood (autism spectrum disorders, learning disabilities, mental retardation); appear during adulthood or in the elderly (Parkinson's disease, Alzheimer's disease and other dementias, Huntington's disease); or result from injury (brain/head trauma, spinal cord injury) or disease (complications of diabetes or HIV/AIDS). Some diseases affect primarily the brain (epilepsy, schizophrenia, bipolar disease), neuromuscular system (amyotrophic lateral sclerosis (ALS), multiple sclerosis, dystonias), or other organs. Infections or cancers of the brain and nerves throughout the body can occur. Individually and collectively, these diseases exact a heavy personal and societal toll in terms of medical costs, societal stigma, and quality of life.

Einstein has established multiple clinical and research programs that propel its efforts to understand, prevent, treat, and cure neuropsychiatric diseases. The Children's Evaluation and Rehabilitation Center (CERC) and the Clinical Genetic Screening and Counseling Program provide interdisciplinary clinical care and clinical genetics resources in the areas of mental retardation, early-stage autism spectrum disorders, attention deficit hyperactivity disorders, learning disabilities and epilepsy. The Kennedy Center for Research in Mental Retardation and Developmental Disabilities serves as an important bridge linking basic science, translational research, and clinical research in neurodevelopmental disorders. Human tissue banks for the study of neurodegenerative diseases provide unique resources for translational research. With these and other resources representing a strong base on which to build, the working group defined several key opportunities for advancing Einstein research on neuropsychiatric diseases.

*Source: http://www.ninds.nih.gov/disorders/disorder_index.htm



Major Research Goals

Alterations in Neural Cell Patterning and Specification in Neurodevelopmental Disorders: Development of the central nervous system is a complex, carefully orchestrated process that is still poorly understood in mammals, including humans. Researchers have not yet identified which points along the pathway go wrong in specific neurodevelopmental disorders like autism or mental retardation. Gene-environmental interactions appear to contribute to neural development in both normal and pathologic states. In addition, many of these disorders are characterized by dysfunctions in multiple brain systems, further complicating the analysis of the underlying developmental errors.

A primary goal of neuroscience research at Einstein is to develop a more complete understanding of the basic mechanisms of the neural development pathway and how key transitions along that path give rise to individual developmental disorders. The program can expand on existing research strengths in three-dimensional patterning of the neural tube, specification of stem cell generating zones, neural subtype identity, and other critical areas to address this fundamental research question.

Susceptibility to Late-Onset Neuropsychiatric Disorders: During development, the nervous system must pass through critical—but poorly understood—phases that set up appropriate cell identity, patterns of connectivity among the nerves, functional properties, and environmental responsiveness. Alterations in these phases may impart susceptibility to the later development of diseases characterized by degeneration of the nervous system (e.g. Parkinson's, ALS) or psychiatric illnesses due to physiologic defects (e.g. schizophrenia, bipolar diseases).

To tackle this important issue, researchers are defining critical periods during embryonic development, early childhood and adult life, and aging as well as identifying the gene-environmental interactions, epigenetic events and other developmental mechanisms that characterize each of these stages. In addition, it will be necessary to map early developmental periods that are essential for later developmental stages and adult functions.

Endogenous Surveillance and Repair in Neurological Disorders Characterized by Alterations in Neural Cell Identity and Connectivity: The mechanisms of immune surveillance and self-repair in the nervous system are poorly understood and, thus, impede our understanding of the causes and developing new treatments for certain neurological disorders. Immune system dysfunction is a hallmark of diseases that include multiple sclerosis, cancer, and infections. Disorders resulting from impaired nerve connectivity, such as brain trauma or spinal cord injury, are compounded by the inability of the central nervous system to repair itself.

Einstein researchers are pursuing a multidisciplinary approach to understand the role of innate and adaptive immunity, genome integrity, RNA/DNA editing, and protein folding and turnover in neural surveillance. In addition, research on the mechanisms of neural repair will make it possible to selectively activate regional stem cells for tissue remodeling, reconstitution of neural circuits, and reestablishment of normal cognitive, behavioral, motor, and sensory functions.

Neurological Disorders Characterized by Disruption of Neural Network Plasticity and Brain Homeostasis: A well-functioning nervous system maintains balance or homeostasis despite being faced with continual internal and external stressors. Moreover, the nervous system is highly adaptive and capable of remodeling neural networks first established during development. The inability to maintain the coherence of this neural network can result in a broad spectrum of neurological disorders.

A key research challenge is to develop a molecular and systems understanding of local and global changes in neural network wiring and the inability of compromised neural circuits to maintain the plasticity or flexibility of the nervous system. Harnessing stem cells to remodel neural network connections will provide new therapeutic strategies to restore normal functions.

Psychiatric and Behavioral Science Opportunities: Remarkable advances in brain sciences promise to reduce the burden of mental illness and behavioral disorders through research. The World Health Organization reported that mental disorders comprise four of the top five sources of premature death and disability in 15-44 year olds in developed countries. Schizophrenia, bipolar disorder, depression, autism, and other mental disorders are serious, often life-threatening illnesses for which we need reliable diagnostic tests, new treatments, and effective strategies for prevention. Neuroscience offers the opportunity for advances for these disorders. As with other illnesses, progress in mental disorders requires an understanding of environmental as well as genetic factors.

Intersection with the Science and Technology Areas

Neuropsychiatric research requires multidisciplinary approaches to both analyze the details of developmental stages and network connectivity and to create a holistic understanding of the complex nervous system overall. Examples of intersections between this field and the science and technology areas include, but are not limited to:

The development and ongoing remodeling of the central nervous system is extremely complex with respect to both time and space. This complexity demands a *Computational Biology and Systems Biology* approach to analyze: mechanisms involved in normal and abnormal developmental processes; neural network functions that mediate critical period transitions and alterations in those functions that contribute to neuropsychiatric diseases; and roles of protein-protein interactions, protein folding and degradation, and protein synthesis in nervous system health and disease.

Neuropsychiatric disorders are influenced by genetic and epigenetic factors, many of which have not been identified. A vigorous *Human Genetics* research program is needed to discover genes and epigenetic mechanisms that affect developmental diseases; modify disease onset, progression, or response to therapy; or impair neural network plasticity and balance. Finding genes involved in neuropsychiatric disorders will accelerate the design of new therapies to prevent or reverse these often devastating and incurable diseases.

Loss of specific neural cell types—for example, dopamine-producing cells in Parkinson's disease—or gaps in the neural network as in a spinal cord injury characterize many neurological disorders. Research in *Stem Cells and Regenerative Medicine* offers the opportunity to replace missing cells and restore health if stem cells can be differentiated into mature, highly specific neural cell types. Stem cell research in neurology has the added challenge that the complex three-dimensional architecture of the nervous system will be extremely difficult to restore by common transplantation techniques even after stem cell differentiation mechanisms are developed. For this reason, neuroscience researchers must focus on identifying endogenous neural stem cell zones and learn how to activate these cells in the body to directly repair damaged tissue.

Many neurodegenerative diseases result from improper protein folding, degradation, interactions, or modifications. *Structural Biology* methods are essential tools for identifying the precise protein defects that characterize disease—for example, the role of abnormal beta-amyloid folding in Alzheimer's disease. This field can also help in the analysis of molecular complexes involved in critical periods of neural development or regeneration.

	Neuropsychiatric Diseases
Computational/Systems Biology	Understanding neural network complexity
Human Genetics	Genetic and epigenetic causes of neural complexity
Stem Cells/Regenerative Medicine	Activation of endogenous neural stem cells
Structural Biology	Protein defects in neuro-degenerative diseases

Reproductive Medicine and Health

THE VISION

To create a national program of excellence for research on the influence of reproductive hormones on susceptibility to disease, course of disease and treatment outcomes

The Challenge and Opportunity

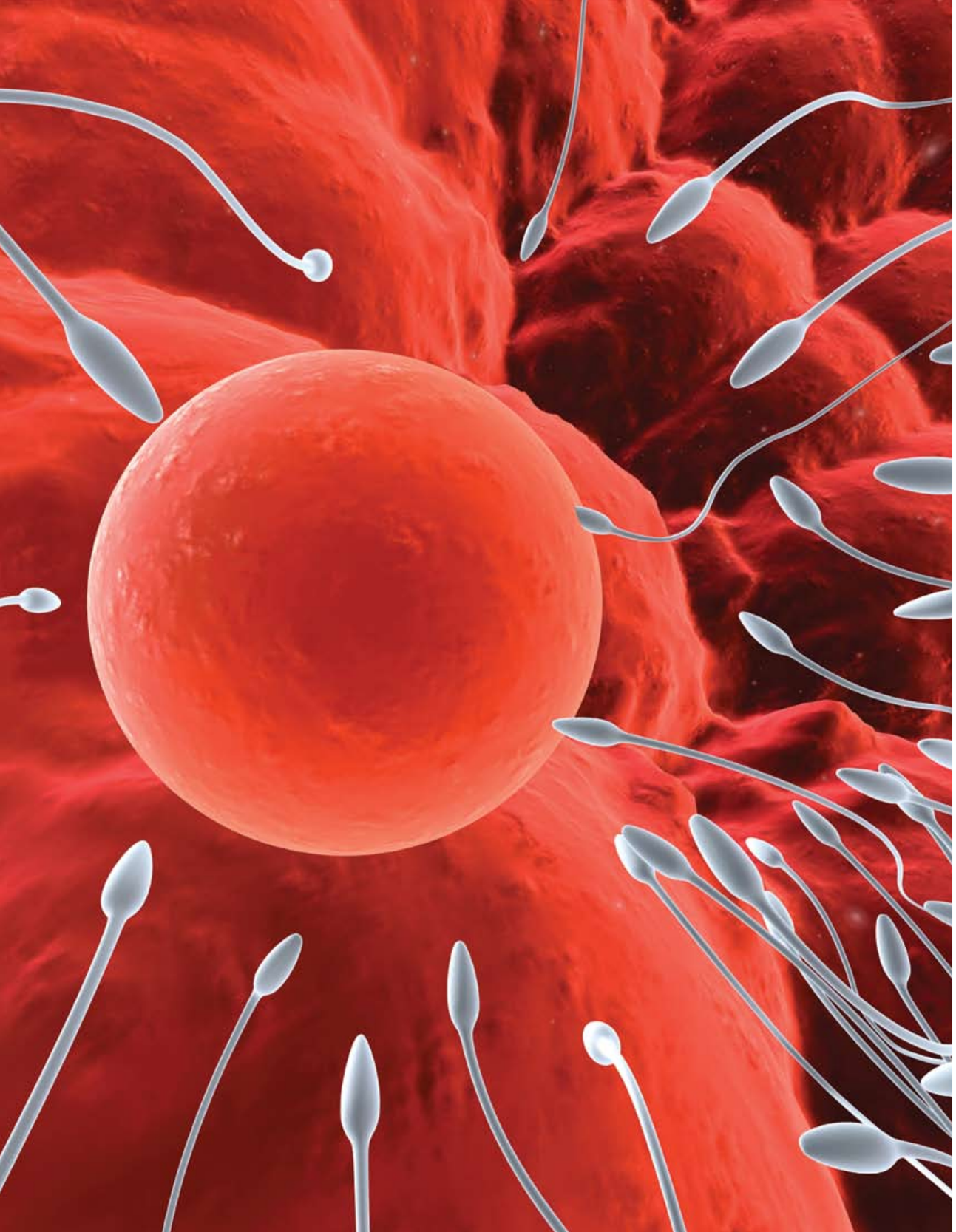
The influence of reproductive hormones is more obvious in women than men due to the dramatic alterations in these hormones over the course of a woman's lifespan (i.e., pregnancy and menopause). Reproductive medicine encompasses cancers that are unique to women (cervical, uterine, ovarian) or that disproportionately affect women (breast); conditions for which large sex-based disparities in prevalence or burden have been documented (e.g., depression, drug abuse, domestic violence); and conditions in which sex hormones have a major impact on susceptibility, course of disease, or response to therapy (e.g., cardiovascular disease, certain infections). Many of these issues related to women's health, obstetrics and gynecology, and gender-based medicine are highly prevalent in the local Bronx community.

The existence of an Office for Research on Women's Health at the NIH highlights the national commitment to research on women's health and sex-based disease. Einstein has a small, but productive, research base in reproductive medicine and health that actively participates in national, multicenter clinical research studies on women's health. The Center for Reproductive Biology brings together investigators with a shared interest in research on the regulation of the female reproductive system. The working group proposed major scientific opportunities that, if pursued, would expand on this solid base of reproductive medicine and health research at Einstein.

Major Research Goals

Contraception, Fertility/Infertility, and Menopause: Understanding the basic biology of human reproduction is central to the prevention of unwanted pregnancy and the elimination of involuntary infertility, a disorder that affects 15 percent of the adult population. Menopause happens to all women who live long enough to reach this milestone and increases risk for a number of diseases.

Einstein researchers have an opportunity to make significant contributions to the understanding of basic sex hormone action and mechanisms that control reproductive processes at various stages of the female reproductive cycle. A large, excellent clinical program for infertility diagnosis and treatment, a clinical program for prevention of unwanted pregnancy, and participation in large research programs



on menopause (WHI, SWAN) all position Einstein researchers to jumpstart a basic science effort in this field.

The Intrauterine Environment (Pregnancy and Pregnancy Outcomes): Genetics can now be used to diagnose disease before implantation of an embryo. Research on human embryonic stem cells has led to the identification of early expression of genetic diseases that appear later in life. Intriguingly, conditions such as adult obesity and metabolic syndrome, neurodegenerative diseases, and liver regeneration may all involve intrauterine exposures that initiate irreversible changes in cellular function that manifest as disease in adulthood.

Research to understand how processes go awry in early development will lead to the development of new prevention strategies. Resources exist at Einstein to begin to address the fundamental role of the intrauterine environment in pregnancy, pregnancy outcomes, and adult diseases. Clinical prenatal counseling, prenatal diagnosis, and preimplantation genetics programs are in operation. The In Vitro Fertilization program is set to provide materials for research on human embryonic stem cells. Another major factor influencing pregnancy outcome is the timing of childbirth. Preterm birth, the leading cause of perinatal morbidity and mortality, is highly prevalent in the Bronx community and an important target for Einstein research.

Sex-Based Diseases: Numerous diseases afflict women disproportionately or differently compared to men, including certain cancers, neuropsychiatric disorders, obesity, and some social/behavioral problems. In addition, the reproductive hormone environment constitutes a key risk determinant in diseases such as cardiovascular disease, viral infections, and autoimmune diseases. For example, cardiovascular disease takes an accelerated course with worse outcomes as women age.

Einstein investigators are studying the role of reproductive hormones in HIV infection in both men and women and in human papillomavirus infection which can lead to cervical cancer. By collaborating with Einstein's disease-oriented programs, researchers can address questions such as the relationship between obesity, hormones, and female cancers, the hormonal basis of endometrial proliferation and cancer, the differential effects of metabolic syndrome in women, or the causes of increased risk for adverse consequences of substance abuse and mood disorders in women.

Gynecologic Oncology and Immunology: Einstein has developed several areas of leadership in the field of Women's Health. A notable success of Einstein research was the establishment of the human papillomavirus (HPV) as a major cause of cervical cancer. This paradigm-shifting discovery ultimately led to the development of a commercially-available HPV vaccine that has the potential to eliminate most cases of cervical carcinoma. Einstein scientists also played a pivotal role in the discovery of Taxol, an agent that disrupts cell structure and is now a mainstay in ovarian cancer treatment.

Building on these successes, Einstein researchers are now examining the role of obesity, growth factors, and sex steroids on carcinogenesis, with an emphasis on women's cancers of the breast, ovaries, cervix, and endometrium. In addition, the role of the immune system in cancer progression is a critical area of study. Einstein investigators are using a mouse model of breast cancer to examine how certain immune cells promote tumor survival, growth, and progression to malignancy. Understanding the biological regulation of these processes will allow researchers to design novel approaches for cancer therapy.

Interaction Between Hormones and the Nervous System: Women's health research is a particularly fertile ground upon which Einstein investigators have built collaborative partnerships. For example, research on the cellular and molecular mechanisms

of steroid hormones intersects with how neuronal signaling is regulated, as well as with nutrient sensing and reproductive function. Conversely, other collaborations examine the role of hypothalamic dysfunction in female reproductive senescence, or mechanisms of how hormones provide neuroprotection against brain injury.

Intersection with the Science and Technology Areas

Achieving the scientific vision of *Reproductive Medicine and Health* research relies on robust interactions with the science and technology fields. Opportunities for intersection with these resources include, but are not limited to:

Sex-based health disparities result not just from biological processes that affect women and men differently, but also from societal and environmental factors that impact access to care and discrimination in healthcare delivery. The *Behavioral and Social Determinants of Health and Health Disparities* field can help address these and related issues. The social causes and health disparities that contribute to the rate of preterm birth in the Bronx and the health disparities in disease susceptibility and treatment in women of different social/ethnic backgrounds are just two examples of critical research questions that can be addressed.

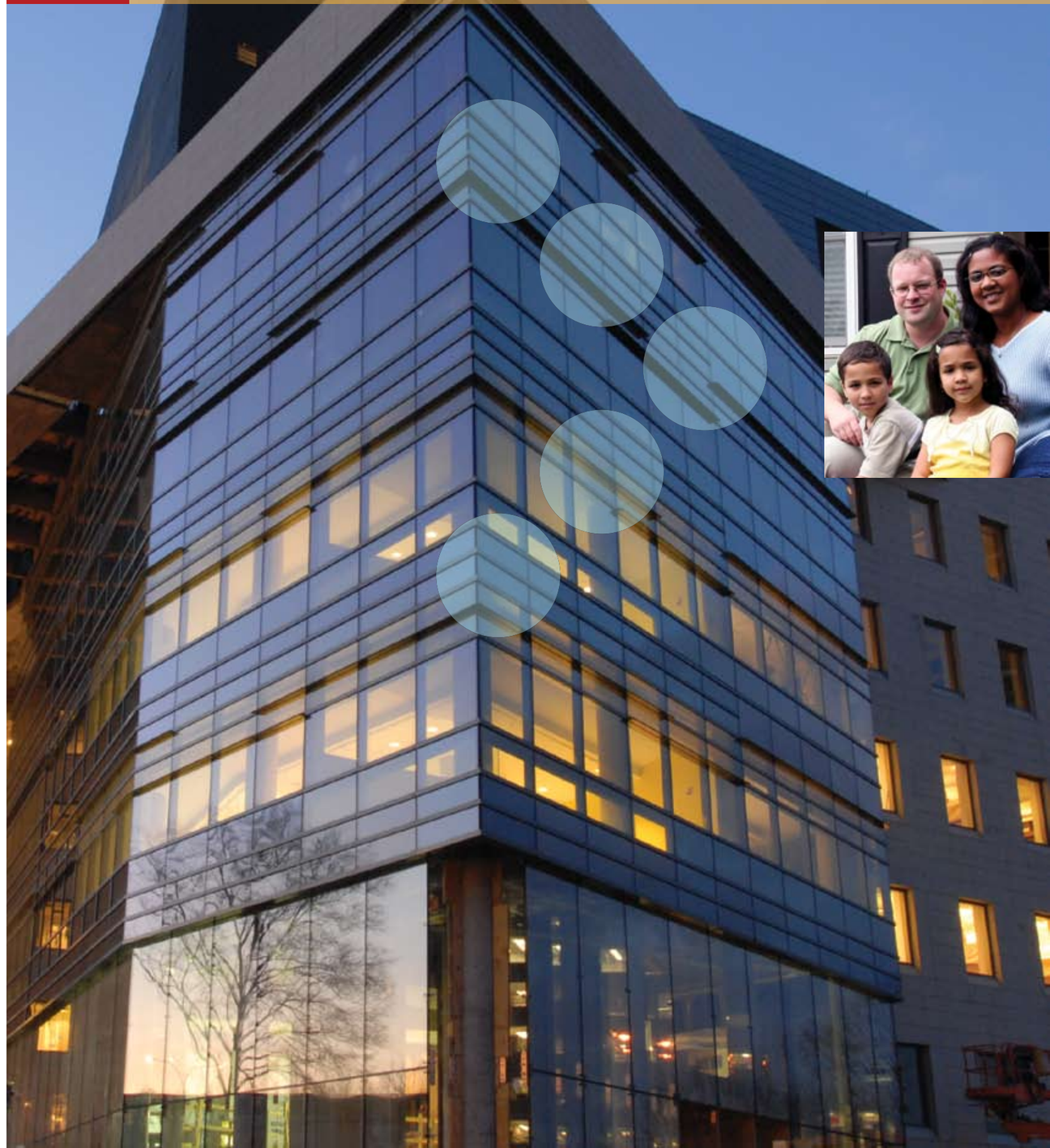
Treatment of menopausal symptoms suffered a setback with the discovery that hormone replacement therapy, used by millions of women to alleviate hot flashes and other symptoms, may increase the risk of developing certain diseases (e.g., cardiovascular disease, breast cancer). *Chemical Biology and Chemical Genomics* strategies are needed for the design and development of new treatments for menopausal symptoms and other targets in reproductive medicine.

Reproductive medicine poses special problems in *Imaging*. The ovary resides within the bony pelvis, making it inaccessible by modalities such as MRI. The placental interface is a dynamic structure that is technically difficult to approach. Knowledge of the molecular signature of metastasizing breast cancer cells has allowed Einstein researchers to develop imaging techniques that may have diagnostic potential in human breast cancer. New and innovative methods for imaging cellular effects of hormones on small blood vessels would be a major advance for early diagnosis of heart disease in women. Brain imaging in response to hormones from puberty through aging are needed. Einstein has access to clinical cohorts that can support the development of improved imaging technologies in this field.

Research on reproductive health and disease synergizes strongly with the field of *Stem Cells and Regenerative Medicine*. A strong stem cell program will facilitate research on early human development, a first step in understanding fetal origins of adult disease and developing strategies to prevent diseases before they begin.

	Reproductive Medicine and Health
Behavioral/Social/Disparities	Disparities in healthcare access and delivery
Chemical Biology/Genomics	New treatments for menopausal symptoms
Imaging	New ways to visualize ovaries and placenta
Stem Cells/Regenerative Medicine	Fetal origins of adult diseases

Realizing the Vision for the Future of Einstein Research

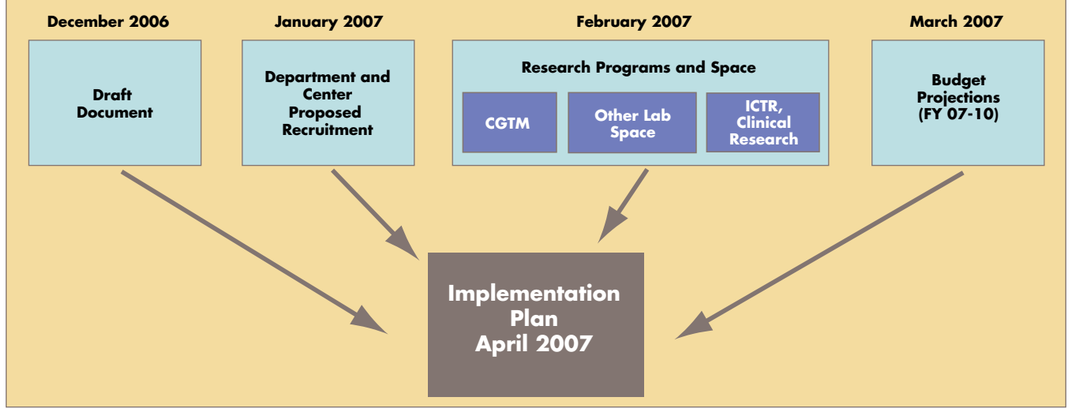


The Einstein Strategic Research Plan builds on our tradition of fundamental research excellence, partnership opportunities with our major academic medical center affiliates, and our unique position in the Bronx community. The planning process has evolved over the past nine months from the initial stages of assessing the current infrastructure and scientific and clinical talent pool, to defining the specialized personnel and programs required to engage new challenges in human health, including the departmental and center plans for the future and the space and financial resources needed (Figure 8).

This section outlines a growth trajectory to create the environment that will allow investigators to engage in science at all levels, from the bench to the bedside, and from the clinic to the community. At the same time, this plan will position Einstein for new initiatives to deliver the breakthroughs in basic science that will have an impact on the prevention and treatment of disease.

For the research enterprise to continue to grow, the current and projected fiscal responsibilities must be considered in order to prioritize our investments. Prior to the development of this plan, Einstein benefited from the doubling of the NIH funding for biomedical research programs from 1999-2003 (Figure 9). However, as annual NIH budget spending has leveled off—and NIH budgets are projected to fall between 1% and 2% for the next 2-3 years—the College must expand its base of non-NIH resources, especially in the philanthropic arena. A major concern in this budgetary climate will be to ensure that bridging funds sustain investigators—especially new investigators—and their critical research programs. The recent Congressional Joint Funding resolution provides $28.9 billion for NIH in FY2007, an increase of $620 million (only 2.2 percent) over FY2006. It is clear that the NIH alone cannot support biomedical research growth. The addition of new space will be fundamental to growth in this changing climate, and must be coupled with approaches to optimize research space productivity.

FIGURE 8
Strategic Research Plan Timeline



Implementation in the Michael F. Price Center for Genetic and Translational Medicine (CGTM)/Harold and Muriel Block Research Pavilion

The CGTM—both its facilities and its intellectual and human capital—will be a resource for the entire College of Medicine. The CGTM's programs will be integrated with research in basic science departments and all the health-related focus areas with proactive approaches to expanding upon and facilitating new interactions and collaborations, ensuring that the College community will have a major stake in its success.

A major focus of this Strategic Research Plan is populating the CGTM with faculty investigators, trainees, cores, and shared facilities in 100,000 net square feet of program space. The projected initiation of this process will begin in late 2007; in early 2008 we will begin to implement the other cores and shared facilities to be housed in the CGTM. Specialized facilities will comprise 28,300 net square feet (Figure 10).

The CGTM will house approximately 40 principal investigators (it should be noted that the precise number will depend on the scope of each program and the seniority of recruited faculty). The proposed distribution of space for investigators and facilities provides the optimal flexibility going forward. Thus, 50,000 net square feet of investigator space is allocated to the Strategic Research Plan theme areas (Figure 11). In addition, 22,000 net square feet is devoted to common space, including a 100 seat auditorium on the first floor.

Implementation in Facilities Other than the CGTM

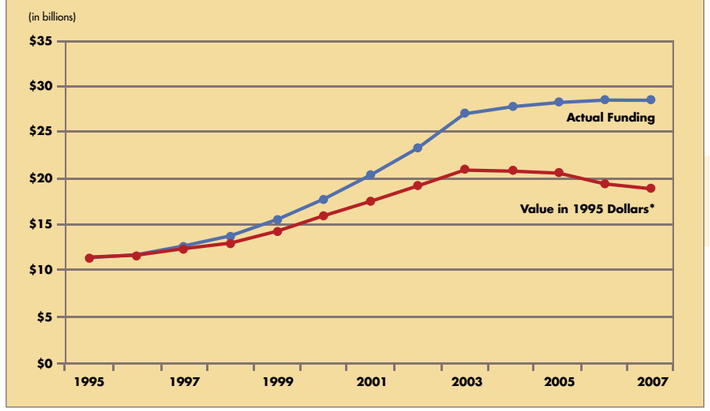
Through strategic allocation of resources by the College and its affiliated medical centers, other new space will become available to house research faculty and staff. This includes an additional 15,000 net square feet of office space in the Mazer Building at the East Campus, all of which will be devoted to the Institute for Clinical and Translational Research and related programs, including centralized biostatistics and biomedical informatics. This space will also permit the location of investigators and other clinical research staff in space that does not require wet-bench laboratory facilities.

In addition, existing Einstein laboratory research space in Forchheimer, Chanin, Ullmann, and Kennedy will require ongoing renovation and reconfiguration as the back-filling of vacated space permits programmatic alignments, expansion of existing programs, and incremental space for successful investigators. At Montefiore Medical Center, several Einstein wet bench research laboratories exist at the West Campus (Moses Storage Building). Short-term plans for 2007-2009 also include creation of a 2-story vivarium at the Moses Research Tower and a Cellular Therapeutics stem cell facility at the Moses Research Tower. Finally, the Magnetic Resonance Research Center will require investments in leadership, new imaging faculty, and hardware to provide a first-class resource for magnetic resonance imaging for human and animal studies.

Over the past several years the College has leased 10 acres of land from the City of New York which has provided space for the construction of the CGTM. As part of this agreement, Einstein will ultimately take ownership of the Van Etten Building, a 350,000 square foot building dating to 1952, small parts of which are currently available for lease by the College. In addition, the College is actively negotiating with the City for an additional 6 acres of property adjacent to student housing and fronting on Eastchester Road. These acquisitions present the College with a historically unprecedented opportunity to envision what a rational plan for campus expansion could look like.

The College is committed to hire a major architectural planning firm that specializes in university planning to work with faculty and administration to develop a 10-year master facilities plan. This plan will consider our needs for expanding clinical research, providing additional housing for newly recruited students, post-docs and faculty, new amenities for the College community, and long-range contemplation of the best sites for future research laboratory construction.

FIGURE 9
NIH Funding History, FY 1995-2007



Source: National Institutes of Health
*Reflects inflation based on the Biomedical Research and Development Price Index

FIGURE 10
Specialized Scientific Facilities in the CGTM

Floor	Facility	Net Square Feet
Basement	Mouse Barrier (8400 cages) Transgenic/Gene Targeting Small Animal Phenotyping/Imaging	12,300 1,500 700
1	Histopathology Small Animal Phenotyping/Imaging	1,800 1,400
2	Imaging Innovation Laboratory Satellite Analytical Imaging	1,600 600
3	Protein Production	2,100
4	Translational Genomics	2,100
5	Chemical Screening Bio-Safety Level 3	2,100 2,100

FIGURE 11
CGTM Investigator Space

Floor/Wing	Research Theme Area
1 West	Stem Cells, Liver
2 West	Biophotonics
2 East	Cancer, Women's Health
2 Southeast	Computational and Systems Biology
3 West	Cardiovascular, Genetics
3 East	Diabetes and Obesity
3 Southeast	Computational and Sytems Biology
4 West	Human Genetics
4 East	Human Genetics
4 Southeast	Computational and Systems Biology
5 West	Infection and Immunity
5 East	Infection and Immunity
5 Southeast	Computational and Systems Biology

Initially, this facilities plan will concentrate on the best use of the Mazer and Van Etten buildings and make recommendations as to their rehabilitation. They will then concentrate on our current and future research and educational needs, insuring that a carefully planned stepwise use of facilities and space is developed that is rational, cost effective and esthetically pleasing. This firm will interview faculty and administrative leaders at all levels to define the programmatic needs that will drive the planning process.

New and Enhanced Research Programs

The growth of the research enterprise will be matched by the growth of basic and translational research at both ends of the spectrum. These objectives are best met by enhancing opportunities for collaborative teams of scientists and clinicians. These teams can a) provide broad training for a range of young investigators, b) leverage common resources and skills, c) speed the transfer of new findings from bench to bedside, and *vice versa*, and d) enable nimble course corrections as specific research fields and funding opportunities demand. In addition to the wide array of existing Einstein Centers and Institutes (Figure 1), several ***new entities built largely upon existing faculty expertise*** are in the planning or early implementation phase:

- Einstein Institute for Stem Cells and Regenerative Medicine
- Division of Translational Genetics (Department of Molecular Genetics)
- Division of Bioinformatics (Department of Epidemiology and Population Health)
- Institute for Vaccine Research and Training
- Einstein-Montefiore Cardiovascular Research Center
- Institute for Behavioral and Social Science Research
- Institute for Clinical and Translational Research
- Department/Center/Institute for Computational and Systems Biology
- Yeshiva University and Ferkauf School of Psychology Institute for Public Health Sciences
- Integrated Imaging Resource

The scope of future prospects in clinical and translational research is extensive, and will offer opportunities to build novel programs with direct linkages to the new faculty to be recruited. New ***research teams*** that are evolving within Einstein- or affiliate-based clinical programs include

- The Children's Evaluation and Rehabilitation Center
- Center for Autism
- Liver Transplant Program
- Radiation Biology and Cancer Therapy
- Montefiore-Einstein Stroke Center
- Substance Dependence Programs
- Cancer Clinical Trials Center

Enhancing the Infrastructure for Science

The goals of this plan cannot be carried out without attention to administrative organization and infrastructure. Specifically, these considerations are crucial for facilitating interactions and creating synergies among faculty and between departments and centers.

Administrative Initiatives

- Review of criteria for promotion/faculty reviews (empowering a broad range of faculty to ensure academic advancement in the context of team science)
- Administrative structure, including an Assistant Dean for Scientific Resources (organizing the College to better meet the needs of the scientific community)
- Faculty development, including focus on women and minorities (building career and leadership opportunities within Einstein and its affiliated academic medical centers)
- Enhanced communications (breaking down academic research silos)

Infrastructure Initiatives

- Funding for Bridging Postdoctoral Fellows (capitalizing on collaborative research opportunities)
- Pilot funds to support innovative, cross-disciplinary research (Dean's discretionary fund, leveraging Center-based pilot funding, etc.)
- Research IT infrastructure and support (collaborating with Yeshiva University to build a 21st Century research technology platform)

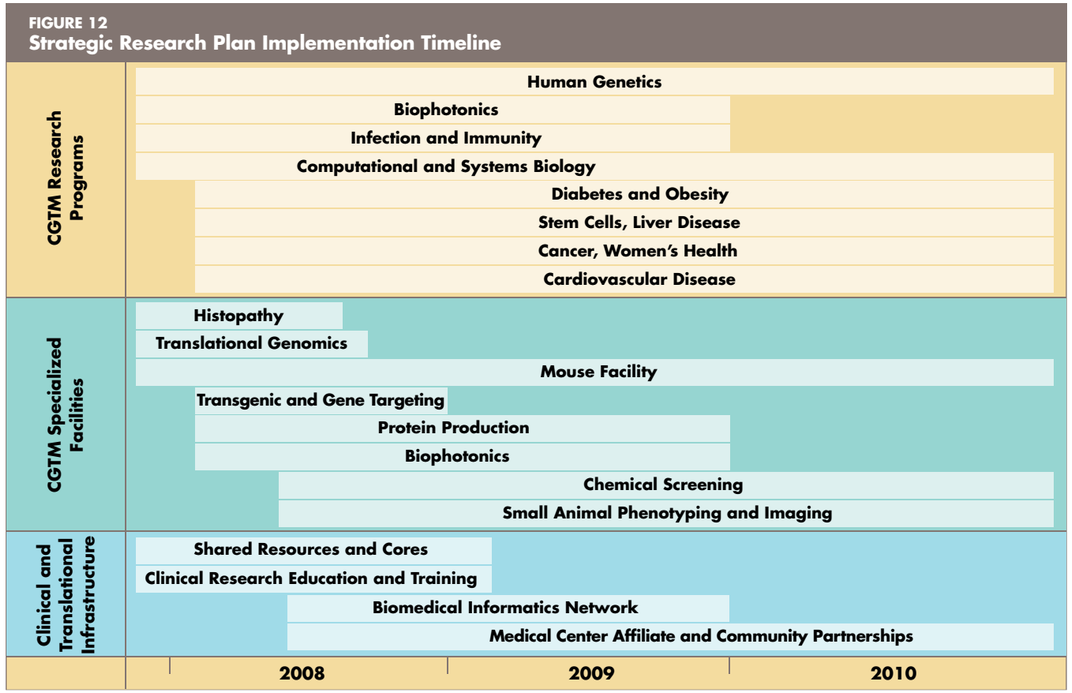
Implementation Phasing and Timeline

Figure 12 represents the timeline for implementation of many of the specific objectives of the Strategic Research Plan. The bars denote the anticipated interval between initiation and completion of a specific target. It should be noted that many aspects of the Plan will require recruitment and reconfiguration within the existing 300,000 net assignable square feet of research space outside the CGTM. Since this Strategic Research Plan is dynamic and will change as we go forward, we expect to map out new timelines as circumstances develop.

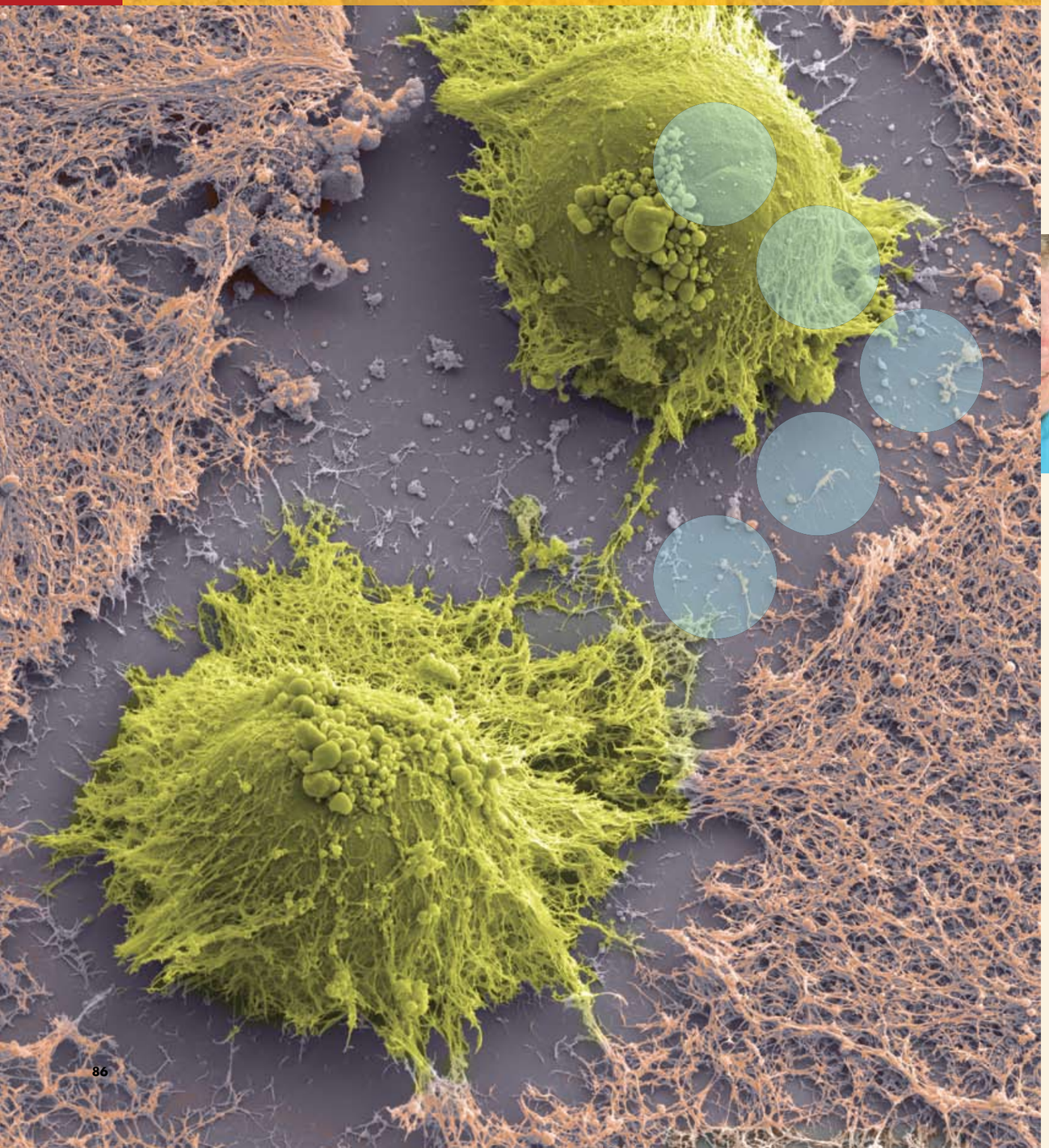
The Strategic Research Planning process has engaged a wide range of the Einstein faculty and administration (see Appendix). Our ultimate strength resides in the human and intellectual capital of the faculty who are dedicated to pushing the boundaries of knowledge. Expansion of the faculty base will prioritize commitments to departments and centers, as well as to the explicit goal of recruiting approximately 40 new investigators for the CGTM. The shared facilities of the CGTM will serve the broad research community, and offer avenues of innovation in developing diagnostics, new drugs, and disease prevention strategies. In parallel, additional new faculty will be integrated within departmental and center space as it becomes available, and within the new locations outlined above. We also recognize the emerging needs for research in areas that provide new prospects, together with new leadership that is recruited for existing departments, divisions, and centers.

Prioritization of the many top-tier initiatives outlined in this plan will require consideration of available funds, space, and the timing of the recruitment of new faculty. This plan is therefore not fixed and immutable. Going forward, this Plan will be adjusted in order to continue Einstein's leadership in biomedical research. Achieving these goals will require strategic partnerships with our affiliated medical centers, with regional, national, and international academic collaborations, with the philanthropic community, and with industry. Finally, we must continue to engage the public—and particularly the people of The Bronx—in our pursuit of improving human health and reducing the burden of disease.

FIGURE 12
Strategic Research Plan Implementation Timeline



Strategic Research Plan Contributors



©Andrew Paul Leonard

Allen Spiegel, MD
The Marilyn and Stanley M. Katz Dean
Professor of Medicine and of Molecular Pharmacology

Working Group Leaders

Steven Almo, PhD
Professor of Biochemistry and of Physiology & Biophysics

Julia Arnsten, MD
Associate Professor of Medicine, of Epidemiology & Population Health, and of Psychiatry & Behavioral Sciences

Leonard Augenlicht, PhD
Professor of Medicine and of Cell Biology

Nir Barzilai, MD
Professor of Medicine and of Molecular Genetics
Ingeborg and Ira Leon Rennert Professor of Aging Research

Aviv Bergman, PhD
Professor of Pathology

John Blanchard, PhD
Professor of Biochemistry
Dan Danciger Chair in Biochemistry

Eric Bouhassira, PhD
Professor of Medicine and of Cell Biology
Ingeborg and Ira Leon Rennert Professor of Stem Cell Biology and Regenerative Medicine

Edward Burns, MD
Executive Dean
Professor of Pathology and of Medicine

Arturo Casadevall, MD, PhD
Professor and Chair of Microbiology & Immunology
Professor of Medicine
Leo and Julia Forchheimer Chair in Microbiology and Immunology

John Condeelis, PhD
Professor and Co-Chair of Anatomy & Structural Biology

Donald Faber, PhD
Professor and Chair of Neuroscience
Florence and Irving Rubinstein Chair in Neuroscience

Norman Fleischer, MD
Professor of Medicine
Jacob A. and Jeanne E. Barkey Chair in Medicine
Director, Diabetes Research & Training Center

I. David Goldman, MD
Professor of Medicine and of Molecular Pharmacology
Susan Resnick Fisher Academic Chair in Brain Cancer Research
Director, Albert Einstein Cancer Center

Harris Goldstein, MD
Assistant Dean for Scientific Resources
Professor of Pediatrics and of Microbiology & Immunology
Director, Einstein/MMC Center for AIDS Research

Sanjeev Gupta, MD, MBBS
Professor of Medicine and of Pathology

Meredith Hawkins, MD
Associate Professor of Medicine

Susan Horwitz, PhD
Distinguished Professor and Co-Chair of Molecular Pharmacology
Distinguished Professor of Cell Biology
Rose C. Falkenstein Chair in Cancer Research

Richard Kitsis, MD
Professor of Medicine and of Cell Biology
Dr. Gerald and Myra Dorros Chair in Cardiovascular Disease

David Lawrence, PhD
Professor of Biochemistry

Paul Marantz, MD
Associate Dean for Clinical Research Education
Professor of Clinical Epidemiology & Population Health and of Clinical Medicine

Mark Mehler, MD
Professor and Chair of Neurology
Professor of Neuroscience and of Psychiatry & Behavioral Sciences
Alpern Family Foundation Chair in Cerebral Palsy Research

Bernice Morrow, PhD
Professor of Molecular Genetics
Sidney L. and Miriam K. Olson Chair in Cardiology

Charles Rubin, PhD
Professor and Co-Chair of Molecular Pharmacology
William S. Lasdon Chair in Pharmacology

Nanette Santoro, MD
Professor of Obstetrics & Gynecology and Women's Health
Associate Professor of Medicine

Matthew Scharff, MD
Distinguished Professor of Cell Biology and of Medicine
Harry Eagle Chair in Cancer Research/National Women's Division

Victor Schuster, MD
Professor and Chair of Medicine
Professor of Physiology & Biophysics
Ted and Florence Baumritter Chair in Medicine

Steven Schwartz, PhD
Professor of Physiology & Biophysics and of Biochemistry
Director, Seaver Program in Bioinformatics

Peter Selwyn, MD
Professor and Chair of Family & Social Medicine
Professor of Epidemiology & Population Health, of Medicine, and of Psychiatry & Behavioral Sciences

David Shafritz, MD
Professor of Medicine, of Cell Biology, and of Pathology
Herman Lopata Chair in Liver Disease Research
Director, Marion Bessin Liver Research Center

Arthur Skoultchi, PhD
Professor and Chair of Cell Biology
Judith and Burton P. Resnick Chair in Cell Biology

E. Richard Stanley, PhD
Professor and Chair of Developmental & Molecular Biology
Renée E. and Robert A. Belfer Chair in Developmental Biology

Pamela Stanley, PhD
Professor of Cell Biology
Horace W. Goldsmith Chair

Daniel Stein, MD
Associate Professor of Medicine

Sylvia Wassertheil-Smoller, PhD
Professor of Epidemiology & Population Health
Dorothy and William Manealoff Foundation and Molly Rosen Chair in Social Medicine

Other Faculty

Myles Akabas, MD, PhD
Professor of Physiology & Biophysics, of Neuroscience, and of Medicine
Director, Medical Scientist Training Program

E. Stephen Amis, Jr., MD
Professor and Chair of Radiology

Ruth Angeletti, PhD
Professor of Developmental & Molecular Biology and of Biochemistry

Joseph Arezzo, PhD
Professor of Neuroscience and of Neurology

Anthony Ashton, PhD
Assistant Professor of Cardiothoracic Surgery

Stephen Baum, MD
Professor of Medicine and of Microbiology & Immunology
Chair of Medicine, Beth Israel Medical Center

Laurie Bauman, PhD
Professor of Pediatrics

Eran Bellin, MD
Associate Professor of Clinical Epidemiology & Population Health and of Clinical Medicine

M. Donald Blaufox, MD, PhD
Professor and Chair of Nuclear Medicine
Professor of Medicine and of Radiology

Henry Bodenheimer, Jr., MD
Professor of Medicine

Michael Brenowitz, PhD
Professor of Biochemistry

Michael Brownlee, MD
Professor of Medicine and of Pathology
Anita and Jack Saltz Chair in Diabetes Research

Robert Burk, MD
Professor of Pediatrics, of Microbiology & Immunology, of Obstetrics & Gynecology and Women's Health, and of Epidemiology & Population Health

Streamson Chua, Jr., MD, PhD
Professor of Medicine and of Neuroscience

Christopher Cimino, MD
Assistant Dean for Educational Informatics
Professor of Clinical Neurology

Ana Maria Cuervo, MD, PhD
Associate Professor of Anatomy & Structural Biology, of Medicine, and of Developmental & Molecular Biology

Brian Currie, MD
Vice President and Senior Medical Director, Montefiore Medical Center
Assistant Dean for Clinical Research at Montefiore Medical Center
Professor of Clinical Medicine and of Clinical Epidemiology & Population Health

Mark Czaja, MD
Professor of Medicine

David D'Alessandro, MD
Assistant Professor of Cardiothoracic Surgery

James David, MD
Associate Dean for Students
Associate Professor of Clinical Psychiatry & Behavioral Sciences

Peter Davies, PhD
Professor of Pathology and of Neuroscience
Judith and Burton P. Resnick Chair in Alzheimer's Disease Research

Teresa DiLorenzo, PhD
Associate Professor of Microbiology & Immunology and of Medicine

Francine Einstein, MD
Assistant Professor of Obstetrics & Gynecology and Women's Health

Mark Einstein, MD
Assistant Professor of Obstetrics & Gynecology and Women's Health

Harry Engel, MD
Associate Professor and Interim Chair of Ophthalmology & Visual Sciences

Anne Etgen, PhD
Professor of Neuroscience, of Psychiatry and Behavioral Sciences, and of Pediatrics

Todd Evans, PhD
Assistant Dean for Graduate Studies
Professor of Developmental & Molecular Biology
Director, Sue Golding Graduate Division

Mary Fabry, PhD
Professor of Medicine

Andras Fiser, PhD
Assistant Professor of Biochemistry

John Fisher, MD
Professor of Medicine

Eugene Flamm, MD
Professor and Chair of Neurological Surgery
Jeffrey P. Bergstein Chair in Neurological Surgery

Dorothy Frenz, PhD
Professor of Otorhinolaryngology–Head and Neck Surgery and of Anatomy & Structural Biology

Marvin Fried, MD
Professor and Chair of Otorhinolaryngology–Head and Neck Surgery

E. John Gallagher, MD
Professor and Chair of Emergency Medicine
Professor of Medicine and of Epidemiology & Population Health

Mark Girvin, PhD
Professor of Biochemistry

Richard Gorlick, MD
Associate Professor of Pediatrics and of Molecular Pharmacology

John Greally, MB BCh, PhD
Assistant Professor of Medicine and of Molecular Genetics

Peter Gregersen, MD
The Feinstein Institute for Medical Research, North Shore – Long Island Jewish Health Institute

Susan Gross, MD
Associate Professor of Clinical Obstetrics & Gynecology and Women's Health and of Clinical Pediatrics

Chandan Guha, MBBS, PhD
Associate Professor of Radiation Oncology

David Hall, PhD
Professor of Neuroscience

Victor Hatcher, PhD
Associate Dean for Continuing Medical Education
Professor of Biochemistry and of Medicine
Director, Office of Research and Sponsored Programs, Montefiore Medical Center

Lawrence Herbst, DVM, PhD
Associate Professor of Pathology and of Microbiology & Immunology

Andrea Howard, MD
Assistant Professor of Epidemiology & Population Health and of Medicine

William Jacobs, Jr., PhD
Professor of Microbiology & Immunology and of Molecular Genetics
Investigator, Howard Hughes Medical Institute

Linda Jelicks, PhD
Associate Professor of Physiology & Biophysics

Shalom Kalnicki, MD
Professor and Chair of Radiation Oncology

John Kane, MD
Professor of Psychiatry & Behavioral Sciences and of Neurology
Chair of Psychiatry, North Shore – Long Island Jewish Health System
Dr. E. Richard Feinberg Chair in Schizophrenia Research

Robert Kaplan, PhD
Associate Professor of Epidemiology & Population Health

Zaven Kaprielian, PhD
Professor of Pathology and of Neuroscience

T. Byram Karasu, MD
Professor and Chair of Psychiatry & Behavioral Sciences
Dorothy and Marty Silverman Chair in Psychiatry

Mimi Kim, ScD
Professor of Epidemiology & Population Health

Robert Klein, MD
Professor of Medicine and of Epidemiology & Population Health

David Lefer, PhD
Professor of Medicine and of Pathology

Jack Lenz, PhD
Professor and Interim Chair of Molecular Genetics
Professor of Microbiology & Immunology

Richard Lipton, MD
Professor of Neurology, of Psychiatry & Behavioral Sciences, and of Epidemiology & Population Health
Lotti and Bernard Benson Faculty Scholar in Alzheimer's Disease

Robert Lummis, PhD
Assistant Dean for Information Technology
Associate Professor of Neuroscience

Sridhar Mani, MD
Associate Professor of Medicine and of Molecular Genetics
Miriam Mandel Faculty Scholar in Cancer Research

Robert Marion, MD
Professor of Pediatrics and of Obstetrics & Gynecology and Women's Health
Ruth L. Gottesman Chair in Developmental Pediatrics
Director, Children's Evaluation and Rehabilitation Center

Thomas McDonald, MD
Associate Professor of Medicine and of Molecular Pharmacology

M. Diane McKee, MD
Associate Professor of Family & Social Medicine

Ari Melnick, MD
Assistant Professor of Developmental & Molecular Biology and of Medicine
The Diane and Arthur B. Belfer Faculty Scholar in Cancer Research

Irwin Merkatz, MD
Professor and Chair of Obstetrics & Gynecology and Women's Health
Chella and Moise Safra Chair in Obstetrics & Gynecology and Women's Health

Robert Michler, MD
Professor and Chair of Cardiothoracic Surgery

Solomon Moshe, MD
Professor of Neurology, of Pediatrics, and of Neuroscience

Ronald Nagel, MD
Professor of Medicine and of Physiology & Biophysics
Irving D. Karpas Chair in Medicine
Director, Bronx Comprehensive Sickle Cell Center

Charles Nordin, MD
Professor of Medicine
Chair of Medicine, Jacobi Medical Center

Robert Ostfeld, MD
Assistant Professor of Medicine

Laurie Ozelius, PhD
Associate Professor of Molecular Genetics

Philip Ozuah, MD, PhD
Professor and Chair of Pediatrics
Professor of Family & Social Medicine

Roman Perez-Soler, MD
Professor of Medicine
Chair of Oncology, Montefiore Medical Center

Liise-anne Pirofski, MD
Professor of Medicine and of Microbiology & Immunology
Selma & Dr. Jacques Mitrani Chair in Biomedical Research

Jeffrey Pollard, PhD
Professor of Developmental & Molecular Biology and of Obstetrics & Gynecology and Women's Health
Betty & Sheldon Feinberg Senior Faculty Scholar in Cancer Research

Steven Porcelli, MD
Professor of Microbiology & Immunology and of Medicine
Murray and Evelyne Weinstock Chair in Microbiology and Immunology

Michael Prystowsky, MD, PhD
Professor and Chair of Pathology

Chaim Putterman, MD
Associate Professor of Medicine and of Microbiology & Immunology

Thomas Rohan, MD, PhD
Professor and Chair of Epidemiology & Population Health

Luciano Rossetti, MD
Professor of Medicine and of Molecular Pharmacology

Denis Rousseau, PhD
Professor and Chair of Physiology & Biophysics

Jayanta Roy-Chowdhury, MBBS
Professor of Medicine and of Molecular Genetics

Rachel Saunders-Pullman, MD
Assistant Professor of Neurology

Philipp Scherer, PhD
Professor of Cell Biology and of Medicine

James Scheuer, MD
Professor of Medicine

Ellie Schoenbaum, MD
Professor of Epidemiology & Population Health, of Medicine, and of Obstetrics & Gynecology and Women's Health
Director, Clinical Research Training Program

Vern Schramm, PhD
Professor and Chair of Biochemistry
Ruth Merns Chair in Biochemistry

Edward Schwartz, PhD
Professor of Medicine

Gary Schwartz, PhD
Professor of Medicine and of Neuroscience

Jeffrey Segall, PhD
Professor of Anatomy & Structural Biology

Harry Shamoon, MD
Associate Dean for Clinical and Translational Research
Professor of Medicine
Director, General Clinical Research Center

Dennis Shields, PhD
Professor of Developmental & Molecular Biology and of Anatomy & Structural Biology

Nicholas Sibinga, MD
Assistant Professor of Medicine and of Developmental & Molecular Biology

Robert Singer, PhD
Professor and Co-Chair of Anatomy & Structural Biology
Professor of Cell Biology and of Neuroscience

Richard Smith, MD
Associate Professor of Clinical Otorhinolaryngology - Head and Neck Surgery and of Clinical Surgery

Edmund Sonnenblick, MD
Distinguished Professor of Medicine
Edmond J. Safra Republic National Bank of New York Chair in Cardiovascular Medicine

Joseph Sparano, MD
Professor of Medicine and of Obstetrics & Gynecology and Women's Health

David Spray, PhD
Professor of Neuroscience and of Medicine

Bettie Steinberg, PhD
Professor of Otorhinolaryngology–Head and Neck Surgery and of Microbiology & Immunology
Dean, North Shore - Long Island Jewish Graduate School of Molecular Medicine
Chief Scientific Officer, Feinstein Institute for Medical Research

A. Hal Strelnick, MD
Professor of Clinical Family & Social Medicine
Assistant Professor of Epidemiology & Population Health

Howard Strickler, MD
Professor of Epidemiology & Population Health

Kevin Tracey, MD
Professor of Microbiology & Immunology

Alda Tufro, MD, PhD
Associate Professor of Pediatrics and of Developmental & Molecular Biology

Joe Verghese, MBBS
Associate Professor of Neurology
Louis and Gertrude Feil Faculty Scholar in Neurology

Vladislav Verkhusha, PhD
Associate Professor of Anatomy & Structural Biology

Elizabeth Walker, PhD
Professor of Medicine and of Epidemiology & Population Health

Jonathan Warner, PhD
Professor of Cell Biology
Joseph and Gertrud Buchler Chair in Transgenic Medicine

Louis Weiss, MD
Professor of Medicine and of Pathology

Rachel Wildman, PhD
Assistant Professor of Epidemiology & Population Health

Ian Willis, PhD
Professor of Biochemistry

Allan Wolkoff, MD
Professor of Medicine and of Anatomy & Structural Biology
Director, Belfer Institute for Advanced Biomedical Studies

Staff

Margaret Arnim
Administrative Director, Institute for Clinical and Translational Research

Ana Cioffi
Administrator, Neurology

Michelle Cissell, PhD
Consultant

Emanuel Genn
Associate Dean for Business Affairs

John Harb
Assistant Dean for Scientific Operations

Charles Hathaway, PhD
Director, Office of Grant Support

Julia Herrick
Assistant Dean for Research Development

Tonya Johnson
Program Administrator, Office of Clinical and Translational Research

Justine Levin-Allerhand, PhD
Director, Corporate and Foundation Relations

Barbara Levy
Assistant Dean for Academic Affairs

Shelly Motzkin
Assistant Dean for Academic Administration

Richard Seither, PhD
Associate Director for Administration, Albert Einstein Cancer Center
Senior Associate of Medicine

Richard Zaiff
Assistant to the Associate Dean for Business Affairs