



Revised draft: May 21, 2008

SCHOOL OF MEDICINE STRATEGIC PLAN 2008

EXECUTIVE SUMMARY

The School of Medicine is recognized as a leader in medical education and a national force in the discovery of new knowledge in the basic and translational biomedical sciences. The ultimate goal of our collective effort is to improve human health and alleviate disease at the level of the individual, community, nation and ultimately, the world. We are committed to excellence with our activities in order to train future leaders in humanistic and compassionate clinical care and cutting edge biomedical research. By building on our current strengths and strategically investing in emerging areas we will enhance our national and international stature as a research-intensive medical school. To achieve our goals we will continue to cultivate an environment of collegiality, diversity and respect among faculty, staff and students.

A primary mission of the School of Medicine is education. The newly revamped Western Reserve2 medical curriculum emphasizes independent active scholarship and research prowess to position our students to face existing, and anticipate future, challenges in clinical care and humanistic medicine. Through a continuing and transparent process of self-assessment and re-evaluation of our educational mission we will refine our curriculum to meet the needs of our students. Our student applicant pool has increased dramatically in recent years. We need to maintain this trend and retain our ability to attract the brightest and best students through both fiscal and intellectual support. The success of the Western Reserve2 curriculum depends upon continued investment by all faculty and staff.

The School of Medicine aspires to be a top ranking research-intensive School that fosters the next generation of leaders in the basic, translational and clinical research community. To achieve this goal the School recognizes that it must retain and promote its existing strong faculty to leadership positions as well as recruit the very best faculty from national and international sources. Retention and recruitment of world-class faculty is a high priority dependent upon several parameters noted below.

There must be a strong, talented graduate student pool. Traditionally, the School of Medicine has relied heavily on graduate students to drive the research enterprise. While standards have been maintained and the diversity of our students has increased in recent years, we need to enroll adequate numbers of excellent students to keep our programs vital. Changes in admission procedures and tuition coverage are needed to ensure the success of all aspects of graduate education and the research endeavor.

The School recognizes the need for state of the art infrastructure and research platforms to support the research mission. The benefits of outstanding core facilities are wide-ranging and invaluable. Continued support of current facilities and future investment in informatics and computational cores are necessary to maintain a competitive position for the institution. Strong administrative support for the grant application process as well as grants management and its associated administrative requirements (Technology Transfer, Human Resources for student/faculty) is essential for an organization as focused and dependent on research as the School of Medicine. Strengthening these functions is fundamental to our continued success.

The School realizes the need to capitalize more effectively on the expertise of its clinical affiliates. The School was recently awarded an NIH Clinical and Translational Science Award (CTSA) to develop as a center of excellence in translational research and interdisciplinary learning by expanding multidisciplinary biomedical research programs. This award should enhance our clinical and research programs in the School of Medicine,

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along with our partner academic institutions and hospitals. Developing effective and mutually acceptable terms of engagement with our clinical affiliates is critical to fulfilling our potential in clinical and translational research.

As an integral component of the overall educational and research mission of Case Western Reserve University, the School of Medicine will enhance human health through interdisciplinary programs that build on the strengths of the School in concert with those of the other Schools and the College of the University.

MISSION STATEMENT

The School of Medicine is dedicated to enhancing human health. This mission will be accomplished through excellence in medical education, biomedical research and clinical care. Above all we are committed to state of the art educational pedagogy utilizing integrative approaches. Our educational experience engages unique emerging technologies. The fundamental underpinning of our work is the creation of new knowledge. Our unique history has and will foster the training of unique individuals as humanistic physicians. These activities occur within the regional environment and incorporate a global influence.

VISION STATEMENT

The vision for Case Western Reserve University's School of Medicine aspires to develop national and international leaders in compassionate clinical care, biomedical research discovery and scholarly endeavors.

SCHOOL OF MEDICINE GOALS

Our mission will be pursued by making progress and meeting benchmarks toward achieving the following goals:

1. Providing innovative and nationally recognized educational programs for medical students and for graduate students.
2. Promoting research discovery and fundamental knowledge that leads to improvement in clinical care.
3. Nurturing outstanding and creative scholarship among our academic communities.
4. Maintaining and enhancing the School's national and international stature as a research-intensive medical school.
5. Achieving a diverse and culturally rich faculty, staff and student body that reflects the community of the future.
6. Providing the infrastructure and technologies necessary to achieve excellence in research, education and clinical training.
7. Align the research excellence in the School with the outstanding clinical programs in our hospital affiliates to accelerate therapeutic development and promote the economic and social well being of our community and region.
8. Promoting clinical excellence among our affiliated care givers by recruiting and retaining the best physicians inspired by new therapeutic advances.
9. Establishing a culture of self assessment with the flexibility for strategic realignment.

Potential steps to achieving the above goals:

- Attract the top ranked incoming medical students and graduate students that are the most sought after in subsequent academic, clinical and business placement.
- Develop and maintain effective cross- and inter-disciplinary research programs that can compete with the best in class for external resources.
- Participate in interdisciplinary research efforts within and outside the School of Medicine as well as programs at a national and international level.
- Have the financial means, intellectual environment and physical infrastructure to attract and retain top-tier faculty that have national and international stature in their field.
- Establish an efficient and effective intellectual property and technology transfer program that will allow the School of Medicine to form effective partnerships with biotechnology and pharmaceutical companies. The

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School of Medicine needs to be an institution with which commercial biomedical companies want to do business.

- Create an outstanding infrastructure and opportunities for creativity in informatics science that are required for cutting edge research in the School of Medicine and other Schools and the College in the University at large.
- Have more responsive and collaborative School of Medicine and University administrative support for research that is devoted to a shared vision of excellence.
- Attract the brightest and best graduate students in sufficient numbers to drive the research programs and develop a financial plan for maintaining and expanding a vigorous graduate education.
- Increase the breadth of financial support through increased endowment and a concerted effort in philanthropic investment.

STRATEGIC ASSESSMENTS

OVERVIEW: Approach to the Strategic Planning Process in the School of Medicine

Given the complexity of its mission, the participation of several hospital partners in education and research and the large number of students, faculty and administrative staff in the School of Medicine, nine task forces charged with defining goals and challenges in the following activities were organized: Medical Education; Graduate Education; Academic Structure; Research with an emphasis on a) Research Infrastructure, b) Research Priorities and Opportunities, c) Clinical Interface with Basic Research; Hospital Affiliates; International Programs; Interdisciplinary Programs (within the SOM and with other administrative units in the University). Membership of these committees included senior faculty, administrative staff, and students where appropriate. Each task force met several times from December 2007 through March 2008, and produced a written document that was reviewed and discussed at meetings convened by a “Task Force Leadership Committee.” Members of this committee included the chairs of the nine task forces above and two co-chairs that included the SOM Vice-Dean for Research and one senior faculty member. The Dean attended meetings of the leadership/oversight committee and various task forces whenever possible.

A brief summary of the strategic planning goals and challenges identified by each of the task forces is presented in this **Overview** section. The following section – **Issues, Goals, Strategies and Metrics** – highlights the main elements of the strategic plan in the context of the SOM, the University and the University Circle Community.

Medical Education Task Force

The task force emphasized the importance of maintaining and enhancing the high national reputation of the School of Medicine curriculum in medical education, beginning with the “Western Reserve” curriculum in the 1950’s and continuing with the “Western Reserve2” curriculum that has been implemented in the past 1-2 years. The “Western Reserve2” curriculum emphasizes interdisciplinary medical education, small group problem-based learning, individual learning and scholarship that is to last a lifetime. New research and scholarship learning experiences are to include production of a thesis with a faculty mentor and the establishment of joint degree programs, e.g. MD-JD, MD-PhD (other than the NIH funded MSTP), MD-MBA, MD-MPH. The challenges to the full implementation and success were noted to include a) sufficient scholarship funds to recruit the best students in an environment where our peer Schools of Medicine have substantially greater endowments to provide financial aid, b) lack of sufficient financial support to compensate faculty for participation in medical student education, especially in the clinical area where business and administrative pressures limit the time physicians can spend in educational activities relative to clinical service, and c) the inferior physical facility for medical student education relative to our peer institutions. Priorities for the strategic planning were to develop financial and scholarship incentives for participation of faculty in medical education, programs to reinvest basic scientists in medical education objectives, consideration to develop a cadre of “Master Teachers” and creation of a “Center for Medical Education.”

Graduate Student Education Task Force

The task force strongly felt that a high quality doctoral student and post-doctoral program was essential to maintaining and enhancing the competitive edge of a research intensive medical school. In particular, it was deemed essential that American students from outside the Midwest and international students were needed to increase the pool of talented trainees. Sustainable financial mechanisms are needed to support this mission. The task force concluded that existing mechanisms of financial support needed to be expanded and increased through philanthropy and endowments. For example, based on the number of R series NIH grants at the SOM (N = 345 in 2007) and assuming that it takes on average 5 years to obtain the PhD degree, 68 incoming doctoral students per year are required to achieve one student per R grant. This number is well above the total of 47 graduate students who matriculated in 2007. To address this challenge, the task force proposed that fundamental changes in the way tuition is paid be considered, e.g. creation of a tuition waiver system based in the Dean's office and a substantial increase in the endowment support for trainees. To execute these and related curricular changes needed to recruit outstanding graduate students, it was recommended that greater administrative support for graduate student education be provided. The success of this effort was considered essential and a critical determinant of local efforts to develop the biotechnology industry and its role in the economic revitalization of Cleveland and the Northeastern Ohio community.

Academic Structure Task Force

The task force recognized the changing character of medical research and education that placed high premium on interdisciplinary activities that cross traditional departmental and administrative structures. One example pertinent to this reality is the concept of a "Center" that facilitates interdisciplinary education and research that are now the "norm" at some of our highly regarded peer Schools of Medicine, e.g. systems and computational biology, health and disease at the molecular, individual and population level. At the same time, we want to allow for the flexibility to respond quickly to opportunities that arise from new initiatives supported by NIH or private philanthropies, e.g. gene-environment interactions as determinants of complex human health problems such as infectious, cardiovascular, and metabolic disorders, and the impact of ecological degradation on human health. Academic career path development of faculty and students whose primary "identity" is in a Center vis-à-vis traditional Department was recognized as a new challenge faced by Case Western Reserve as well as other Universities. Means of addressing these challenges include encouraging meaningful joint faculty appointments across units in the School of Medicine and throughout University, the establishment of Centers when external funding and scientific rationales for such exist and more transparent definitions of paths to tenure and promotion to encourage faculty participation in interdisciplinary research and education.

Research Infrastructure Task Force

The School of Medicine has risen to the top ranks of American medical schools with respect to NIH funding. In order to maintain and improve its position, the SOM must continue to recruit and retain top-flight faculty and the best medical and graduate students. Recent experience has shown that investment in instrumentation infrastructure and faculty with expertise to apply the related technologies to research are required to achieve excellence. For example, the Center for Proteomics and the Center for Imaging Research have catalyzed cutting-edge interdisciplinary research programs across many departments within and outside the SOM. This momentum will however be lost if new investments are not made and existing programs are not provided with sufficient support. The long-term view realizes that investments made in tough times can have a very high return on investment. To facilitate continuing development of infrastructure and determine the optimal distribution of resources to this goal, the task force recommended a) the establishment of an office of the Vice Dean of Research to have authority and responsibility for coordinating development of institutional research core facilities and to assist the Research Committee in evaluating research proposals and, b) developing metrics to evaluate the immediate and long-term impact of cores in enhancing our research mission.

These metrics should include:

1. The number of investigators served.
2. New funding that depends on the core.
3. Financial self-sufficiency with subsidy for the SOM.

4. New technologies implemented by the core.
5. Ensure lack of duplication or more efficient information provision.
6. Provision to sunset core.

The office of the Vice Dean has been established and is actively pursuing these tasks. Areas of recent investment such as the improved animal facilities, clinical and translational research support from the CTSA, imaging and proteomics, and a microarray facility are now beginning to pay off as faculty from the School of Medicine and other units in the University take advantage of them to promote research and attract external funding. Gaps that need to be addressed in the near future were noted to include computational and informatics resources, faculty in the search for the new chair of the Department of Epidemiology and Biostatistics, and better coordination of structural biology activity across departments and administrative units. Related to non-research infrastructure, the task force received significant feedback from faculty that purchasing, grants administration, human resources and other administrative activities are not operating with the level of service orientation and efficiency appropriate to a modern research enterprise. For example, it is believed that many policies are implemented without regard to the needs of the “customer.” It was recommended that the Dean appoint a new standing committee composed of faculty and administrative staff to provide a venue to address problems in a systematic way.

Research Priorities and Opportunities Task Force

The task force sought the input on research priorities by soliciting written proposals for areas of emphasis and investment from the faculty in the SOM. Emphasis was placed on programs that promoted interdisciplinary activity within the SOM, linkages with the clinical affiliates and with other Schools in the University as well as innovative programs that built on existing areas of research strength with a high likelihood of funding from external sources.

Five central themes emerged: Metabolism and Disease, Cancer, Infection and Inflammation, Cardiovascular Health and Disease and Neurosciences linked directly to the Health alliance identified at the level of the University (Figure 1).

These five themes intersect at multiple levels and provide an intellectual basis for the vast majority of ongoing research in the School Of Medicine and its clinical affiliates. In addition, these broad research areas provide a framework in which more specialized programs as well as technical and core facilities can flourish and reach appropriate target faculty. A further 7 specialized research areas were identified as warranting strategic development including: Population and Public Health, Centers for Membrane Biology, Sleep Research, Systems Medicine,

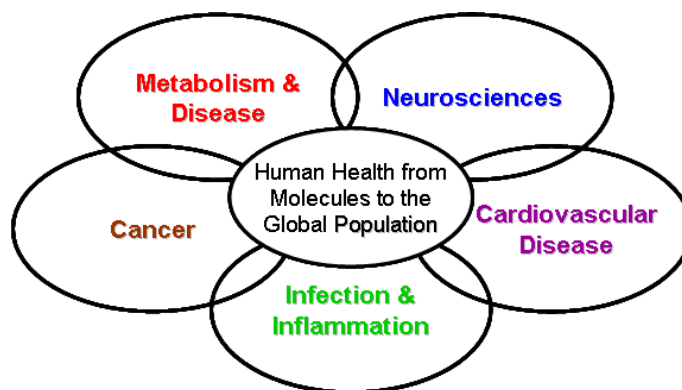
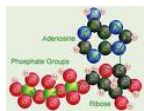


Figure 1: Five Central Themes of SOM

Translational Therapeutics and Informatics, Biomedical Engineering and Imaging. The intersection of these emerging programs with the major themes is shown in Figure 2. Each theme and emerging program is outlined below and detailed in the Appendix. It is important to recognize that these priorities do not signify a lack of continuing commitment to support other ongoing basic and translational research programs in which the School and its hospital affiliates have already established a record of excellence. It is anticipated that all areas of the School’s research will benefit from strategic investment in the integrated themes.



Theme one: Metabolism and Disease

One of the most troubling developments in US health care over the past decade has been the rapid increase in prevalence of obesity and type 2 diabetes. Since 1980, the number of Americans suffering from diabetes has doubled to more than 20 million, and that number is projected to double again by 2025. Particularly ominous is the recognition that diabetes, obesity and metabolic syndrome cluster together, predisposing patients to future diabetes, cardiovascular disease, and kidney failure. Together, they contribute to the escalating fiscal costs of health care and, via their effects on vascular disease, to the burden of patient suffering in the US.

Building on our existing strengths we propose to develop a Center for Metabolic Diseases that will focus on the triad of diabetes, obesity and metabolic syndrome (hypertension, hyperlipidemia, and insulin resistance). The goal is to build an integrated program providing; a) encouragement of innovative and relevant investigations by young researchers, b) cross-fertilization and dissemination of ideas, and c) translation of promising therapeutic approaches identified in animal studies into clinical research and community-based translation. This effort is to be interdisciplinary and will include members of Case Western Reserve University and UH Case Medical Center.

There will be 3 primary research groups representing the major research areas pertaining to diabetes and obesity: ***(1) complications and consequences, (2) metabolism and nutrition, and (3) control and prevention.*** Each of these groups each will interact with a translational group to extend the basic research into the clinic and back again, and to initiate community-based intervention research. The basic science groups will interact with other scientists and core facilities on campus (including Immunology, Neuroscience, Genetics, Stem Cell and Regenerative Medicine Center, Proteomics Center, Mouse Metabolic Phenotyping Center, Cleveland Center for Structural Biology, Microarray Core, Transgenic Animal Core, Functional Imaging Core, Bioinformatics Core, Systems & Computational Biology Cores) to facilitate state-of-the-art basic research related to diabetes, obesity and metabolic syndrome.

The study of lipid metabolism, obesity and metabolic syndrome are underrepresented in Cleveland, but enhancing these research areas would provide critical expertise necessary to develop ways to treat or inhibit these conditions in the community. It would have the additional benefit of helping to integrate metabolism, mitochondria, complications, cancer, and sleep investigators together. This will be our first priority for additional recruits. Other areas of need or where existing strengths should be enhanced are in the areas of (1) cardiovascular disease due to diabetes/obesity/metabolic syndrome, (2) the interface between neuroscience, the gut, exercise physiology, and appetite control, (3) fetal programming and imprinting by diet, and (4) the role of the intestinal microbiome in development of obesity and diabetes, and in regulation of glycemic control.



Theme two: Cancer

The Case Comprehensive Cancer Center provides a nexus for coordinated interdisciplinary research into all aspects of cancer. Today, 235 faculty of CWRU and UHCMC coordinate research efforts in nine scientific programs, representing the Schools of Medicine, Engineering, Arts and Science, Social Work, Nursing, Dentistry and has consulting interactions with the schools of Law and Management. The Cancer Center is closely aligned with the Ireland Cancer Center, the Neurologic Institute, Rainbow and Children's Hospital and the Ferchill Pediatric Brain Cancer Institute of University Hospitals Case Medical Center, and the CTSC, the Center for Clinical Investigation, each of the Departments of the School of Medicine and the Department of Biomedical Engineering and the Center for Stem Cell and Regenerative Medicine. The Center supports 17 shared resources that facilitate cancer research across these schools and institutions and is the epitome of transdisciplinary, translational research that includes and takes advantage of all corners of the University.

The cancer center has 2 overarching goals:

- 1) Reinvest in and promote cancer research throughout the academic community
- 2) Reinvest in University Infrastructure

Cancer Center members benefit from complex infrastructure technologies including the Imaging Center, the Proteomics Center, the computational and informatics expertise of the Departments of BME and EECS, and the

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Animal Resource Center as well as the emerging programs in discovery therapeutics, membrane biology, clinical investigation, systems biology and informatics, and greater emphasis on the disciplines of neurosciences, metabolism and disease, vascular diseases, and genomics. There are nine scientific programs in the Cancer Center each with opportunities for development and expansion.

Cancer Genetics:

This program is focused on discovering new cancer-associated genes that are critical to pathogenesis, etiology and progression of cancer, which can be used for early diagnostics, new therapeutic targets and animal validation models. Patient and family cohorts with colon cancer, esophageal cancer, breast cancer and brain tumors provide a unique resource for cancer causing gene discovery. Our expertise in RNA biology provides a unique platform for integrated research. Recruitment in cancer pathology, genetic epidemiology, large database genomics of cancer, computational genomics and translational research oncologists, a cancer biorepository imaging and informatics is needed.

Molecular Oncogenesis and Cancer Biology:

This program spans cancer oncogenes; signaling; cancer migration and invasion; drug discovery based on novel cancer targets; DNA repair and chromatin structure; nuclear receptors in cancer; cell death and autophagy; RNA cancer biology; transcription control in cancer; cancer vascular biology; inflammation, infectious malignancies and immunity; and cancer structural biology. Recruitment includes investment in disease based scientific discovery and newer technologies focused in cancer including proteomics, RNA biology and human tumor screening, target identification and therapeutics development of new cancer treatments, imaging, and molecular imaging of aberrant cell functions.

Stem Cell Biology, Cancer Stem Cells and Therapeutics:

This initiative is part of the CWRU Center for Stem Cell and Regenerative Medicine (CSCRM). New initiatives will develop a gene-function based analysis of stem cell proliferation and differentiation in the study of cancer stem cells. Recruitment leadership for stem cell therapeutics will be coordinated between the UHCMC, ICC and CWRU SOM, pediatric stem cell therapeutics, cancer stem cell expertise and embryonic stem cells through the Department of Genetics. Other initiatives will include establishing an embryonic stem cell core facility; a program in developmental and embryonic stem cell biology through the Department of Genetics; increased use of the Imaging Center and the Animal Facility for human/mouse chimeric animals to evaluate stem cell biology; and use of cancer stem cells to define the transformation of normal to malignant stem cells.

Cancer Developmental Therapeutics and Imaging:

This initiative will be focused on drug action and new cancer targets for therapeutic imaging of tumors; drugs and treatment responses including anti-angiogenesis; and drug discovery based on anti-cancer targets. This is an internationally recognized program with expertise in drugs and imaging technology targeting DNA repair, anti-angiogenesis, signaling and receptor kinases and apoptosis. Pharmacokinetic analysis of clinical samples during early drug development and clinical trials can be done within the Cancer Pharmacology Core. Enhancing capabilities to conduct innovative clinical research through the resources of the CTSC, UHCMC, ICC, and the Center for Clinical Investigation will benefit this program. Key needs are to develop a drug screening capability based on targets identified by CWRU investigators using s-RNA; in silico and actual drug screening, coupled with cancer imaging; and high throughput target and drug screening in conjunction with BME and the Center for Imaging and a proposed center for therapeutics.

Cancer Disease Oriented Research:

The Cancer Center has prioritized for expansion: GU Malignancies; Colon Cancer; Breast Cancer; Lung Cancer; Brain Tumors; Melanoma and Leukemias and Lymphomas. Reinvestment in these disease areas by the SOM and UHCMC ICC will enable the multi-investigator teams to seek larger grants. Additional recruitments will support laboratory-based research and clinical and translational research including cancer pathologists, immunologists and scientists interested in signaling, structural biology, membrane biology, drug discovery, pharmacology, etc. These groups will also benefit from biorepositories of these tumors and in proteomic and genomic capability to evaluate lead targets and pathways in specific tumor cohorts.

Cancer Prevention and Control, and Population Research:

Members of this program focus on cancer etiology, epidemiology, early detection and prevention and practice and community intervention. Current focal areas include:

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- Gene – environment interaction for colon, prostate, glioma, and breast cancers;
- Quality improvement interventions for preventive service delivery in primary care settings using the Practice-Based Research Network (PBRN);
- Cancer screening and early detection.

New initiative in chemoprevention will use recognized targets for cancer initiation to develop and implement long term intervention studies to reduce cancer rates in high risk populations. Access to the web based family cancer history record tool, GREAT, will help identify high-risk groups in the population. Survivorship based research will examine the acute and chronic effects of cancer therapy and proactively manage long term follow up of late effects, secondary malignancies and psychosocial aspects of treatment.

Key needs include: recruitments into the areas of Cancer Epidemiology, Health Behavior Change, Tobacco research, Interventional practice based science, Biomarker applications in the clinical setting; Population-based wet lab and space for long term storage of biorepository material.

Cancer and Aging:

The two major themes of this program include analysis of the impact of the basic mechanisms of aging on cancer etiology, biology, as well as the tolerance to treatment and psychosocial impact of aging on the treatment and outcome of cancer. This is one of only two Cancer and Aging programs approved by the NCI. Members study animal models of aging and cancer, the role of DNA repair in aging, the impact of co-morbidities on treatment and treatment tolerance and late effects in older patients with cancer, as well as psychosocial aspects of cancer on older individuals. Additional recruits in epidemiology and outcomes research, social work, nursing, basic science of aging and clinical management of older patients with cancer are needed.

Cancer Immunology, Inflammation and Infection:

Focus on cancers related to inflammation, immunity, and infection. A number of cancers are caused by infections with RNA or DNA viruses and others are promoted by altered immune response to infection and chronic inflammation. This new initiative links infectious malignancies with cancer immunology and cancer immunotherapeutics and takes advantage of the strong components of immunology, infection and cancer biology at Case. This provides the opportunity to develop an internationally recognized program in Cancer Immunology and Infection. Areas to develop include HIV-associated malignancies and cancers related to HPV; Hepatitis C; EBV lymphomas; helicobacter; and the impact of altered immunity and chronic inflammation on malignancies. Recruits that cut across disciplines include immunology, infection with links to the CFAR, links to the Center for Imaging, the CSCRM for cell therapy and BME for managing vaccine development/delivery. These will need support for mouse models to be used in studies of complex genetics, environmental exposures and infection, and improved nanotechnology for vaccine development and delivery.



Theme three: Neurosciences

The major goal of the development of The Integrated Neurosciences Research Program is to align neuroscience research into 6 major programs: 1) Basic neuroscience; 2) Neuro-degeneration; 3) Neuro-Oncology; 4) The Neurovascular Unit; 5) Sleep and Circadian Biology; 6) Visual science research. Programmatic alignment will facilitate growth and integration between the Case Western University School of Medicine, the Neurological Institute of University Hospitals, and affiliated institutions. Current neuroscience research strengths exist in distinct programs that span the spectrum from the basic sciences to studies of nervous system pathophysiology to disease specific therapeutics. Synergy between these independent groups will be achieved by forming an integrated neuroscience research program in which leaders of basic and clinical sciences cooperatively plan, consolidate and develop interdisciplinary programs. These leaders will be brought together in an executive committee to meet quarterly and identify areas ripe for development. Recruitments into the neurological sciences will be coordinated and leveraged across programs. A foundation of outstanding cell and molecular neuroscience, coupled with new leadership in the clinical sciences of the Neurological Institute creates current opportunity for development.

Basic Neuroscience Research Program:

Understanding normal brain function and how this is altered by disease, injury, or environmental factors is one of the most exciting frontiers in science today. The Neurosciences Department currently has an intellectual framework focused in three major areas:

1. Development of neural circuits

The Neurosciences Department will capitalize on its expertise in cell and molecular studies with new programs aimed at understanding how genetic and epigenetic factors interact to build and maintain complex neuronal networks to generate behavior. New recruitments will combine modern molecular genetics with cellular, behavioral, and imaging approaches to identify causal links between gene function, circuit development, synaptic function, network activity and physiology. This theme in neurodevelopmental disorders links to investigators and clinicians in psychiatry, neurosciences, genetics, pediatrics, and cognitive science to create cross-disciplinary programs and funding initiatives involving faculty at CWRU, University Hospitals and affiliated institutions.

2. Neural Function/Systems Neuroscience

Normal brain function emerges from the organized patterns of activity in large populations of cells that are interconnected through specific neural circuits. Understanding how these neural circuits develop, operate, and govern behavior is a major focus of the Neurosciences Department and investigators across campus. This systems neuroscience group synergizes with new initiatives in systems biology with the overall the goal of applying quantitative approaches to biological problems. Cross institutional working groups have nucleated between basic neuroscientists and investigators in Biomedical Engineering, Cognitive Science, Biology, and the functional electrical stimulation (FES) group at the VA.

3. Neural Plasticity and Repair

Understanding the response of the nervous system to injury and disease is critical for the development of new therapeutic approaches to repair neurological damage. Building on existing strengths in spinal cord injury, demyelinating diseases and ischemic insults and the Center for Translational Neuroscience, additional investments in this area would provide a nucleus for the development of substantive interactions with the Neurological Institute Centers as well as provide expertise in cellular neurosciences to complement the device technology being developed in the Department of Biomedical Engineering.

Neurodegenerative Diseases Research Program:

Neurodegenerative diseases, including Alzheimer's (AD), Parkinson's, (PD) Transmissible Spongiform Encephalopathy's (TSEs), tauopathies, and Amyotrophic Lateral Sclerosis (ALS) represent some of the most significant causes of disability and exact a very substantial economic toll in the US. Substantial investment is needed to re-establish our historical strength in Alzheimer's Disease related research in the areas of the basic neurobiology of the disease as well as clinical management. In addition, it is important to establish laboratories with translational projects (e.g., drug discovery, early biomarkers) that will intersect with the Neurological Institute clinical programs and the Center for Memory and Cognition. This will require investments at the senior faculty level and include clinical investigators interested in translational research, as well as basic scientists. It is anticipated this strategic investment will make the institution competitive for re-establishment of an NIH-funded ADRC that will require coordination between the School of Medicine and University Hospitals and its affiliates.

A strategic priority in TSE-related research is to ensure continuation of national prominence for a Program Project and National Prion Diseases Surveillance Center beyond the current cycle ending in 2012. This will require resources for recruitment of faculty and develop further strength in early non-invasive diagnostics. A strategic initiative is to expand the CWRU/NI programs to other neurodegenerative diseases such as Parkinson's disease and other movement disorders (e.g., Huntington's) Expansion of these programs requires resources for recruitment of both basic and physician scientists and promoting interactions between neurology and neuroimaging investigators.

Neuro-Oncology Research Program:

A clear program in Neuro-oncology translational research will capitalize on the major strengths of the Neurological Institute, University Hospital-Case Medical Center (UHCMC), Rainbow Babies & Children's Hospital (RBCH), Ferchill Brain Tumor Center (FBTC), Case Comprehensive Cancer Center (CCCC), the Center for Translational Neuroscience (CTN), the CWRU/UH Center for Imaging Research (CIR) and the Center for Stem Cell and Regenerative Medicine (CSCRM). The mission of the program will be to leverage new

understanding of the molecular basis of cancer of the brain and spine to optimize personalized treatment of patients with a focus on the molecular classification, imaging and validation of treatment response and outcomes. With its focus on translational therapeutics this program will facilitate interactions and collaborations between clinical and academic investigators. A unique opportunity is afforded in the Neurological Outcomes Core within the NI that coordinates data collection on outcomes within the Case Comprehensive Cancer Center, and integrates activity across many units. The Neurological Outcomes Core will be housed within the Center for Clinical Investigation as part of the NIH Clinical and Translational Science Award (CTSA) and would facilitate collaborations between colleagues at MetroHealth Medical Center, Cleveland Clinic and Case Western Reserve University School of Medicine. To take advantage of these opportunities requires recruitment in translational neuro-oncology faculty to lead, coordinate and focus the emerging program.

Neurovascular Unit Research Program:

Stroke is a major cause of death and disability in the United States and the School of Medicine, University Hospitals and their affiliated institutions have strength in the areas of cerebrovascular biology and diseases. The Cerebrovascular Center within the NI established one of the first integrated clinical stroke systems and recently has been strengthened through the recruitment of several internationally recognized clinical faculty. The Neurovascular Unit research program will take advantage of these new recruitments to develop a multi-investigator research program in the areas of basic and translational neuroscience related to the neurovascular unit and disorders of the brain. Goals of the program will be to develop new treatment strategies to decrease the morbidity and mortality due to stroke and other cerebrovascular diseases as well as understand the role of the neurovascular unit in neurodegenerative conditions and neuro-oncology. Program expansion to address vascular/endothelial biology, imaging and animal modeling approaches, as well as translational aspects in drug development are needed. The development of expertise in the cerebrovascular unit will leverage emerging and ongoing programs in a number of departments in addition to neurology, neurosurgery and neuroscience. These include BME, Radiology, Genetics, Nutrition, Epidemiology and Physiology.

Mood and Neurodevelopmental Disorders Research Programs:

The Department of Psychiatry has existing strengths in the Mood Disorders program including the Bipolar Research Center. In addition, programs in child and adolescent psychiatric conditions and studies of the geriatric population provide a unique “across the lifespan focus”. Interdepartmental collaborations with investigators in Biostatistics/Epidemiology, the Mandel School for Applied Social Sciences, Psychology and Pediatrics add depth and breadth to the program. Three specific areas have been targeting for further development:

1. Pre-clinical Infrastructure

Recruitment of mid-level investigators with complementary scientific foci would benefit existing programs including bipolar diseases and child psychiatry. Such recruits could focus on pharmacology, genetics or neuroimaging.

2. Clinical Program in Substance Use Disorders

Building on the existing Addiction Recovery Program, recruitments would broaden the base of research. Clinical services now offered include comprehensive addiction psychiatry assessments, ambulatory detoxification, several levels of care including partial hospitalization, intensive outpatient programs, aftercare counseling, medication assisted therapies for opioid dependence (buprenorphine), and consultation to general hospital patients. The creation of this clinical infrastructure has laid the groundwork for a parallel research infrastructure which would serve as a nucleus for translational science.

3. Expansion of the Bipolar Disorders Center

The development of a vibrant and sustainable program will be greatly enhanced through the support of research training fellowships. Industrial support has been garnered that supports training in adult fellows but is not applicable for child or geriatric training fellowships. Support for an initiation of this program would be leveraged into federally supported programs with increases in the number of funded training faculty developed through the training program.

Sleep and Circadian Biology

As discussed under the Sleep and Circadian program, there is considerable expertise at the SOM in clinical and epidemiologic sleep research. However, this program has not realized its full potential because of lack of a cadre of scientists investigating basic mechanisms of sleep and circadian biology. There is currently no representation in

the Neuroscience Department in these rapidly advancing fields. This represents a major gap in the portfolio given recent major advances in circadian biology, including identification of central and peripheral “clock” genes and proteins, many believed to be important in a range of homeostatic and disease mechanisms, including cell division and tumor genesis and metabolism. The proposed program will expand the Sleep Research Program to include scientists in circadian biology, integrate these activities into the basic Neuroscience Program and Neurological Institute, as well as interface with the Cardiovascular and Metabolic initiatives.

Visual Sciences Research Programs:

Research in the visual sciences at CWRU has been orchestrated through the Visual Sciences Research Center (VSRC) whose mission is to promote the understanding of the eye and visual system, including extraocular muscle function, biochemical aspects of lens pigmentation, and immune responses in the eye. Future expansion will concentrate more on underlying causes of clinical disease and blindness, especially retinal disorders such as Acute Macular Degeneration, Retinitis Pigmentosa, Diabetic Retinopathy and Glaucoma. Expansion will be targeted to 4 distinct areas:

1. Retinal function disorders

Age-related macular degeneration (AMD) and Retinitis Pigmentosa are among the most devastating causes of blindness. Expanding this program will include programs aimed at further understanding angiogenesis associated with the wet form of AMD.

2. Blindness associated with Aging and Diabetes

The systemic metabolic disorder, diabetes, is widespread in the USA and the incidence is increasing rapidly. Diabetes exerts one of its most harmful effects upon the retina. Building on existing expertise an extensive program in glaucoma will be developed with appropriate recruitment.

3. Visual impairment and blindness due to infectious diseases, immune responses and inflammation

Infectious diseases are a major cause of blindness worldwide, and include corneal infections (keratitis) caused by viruses, bacteria, fungi and parasites, and retinopathy caused by the protozoan *Toxoplasma gondii*, which infects over one billion people worldwide. Inflammation is involved a number of diseases such as atherosclerosis and rheumatoid arthritis. Ocular diseases indicating a role for inflammation include diabetic retinopathy and AMD. Future recruits will expand this area.

4. Molecular epidemiology of blinding diseases

Genetic dysfunction is becoming increasingly central in ocular diseases. The recent discovery of two genes that mediate risk to patients with AMD has stimulated additional programs. Genes are being mapped for AMD, diabetic retinopathy, age related cataract, Fuchs’s dystrophy and keratoconus. The location of genes for these diseases will form a cornerstone for visual research in the School of Medicine.

The proposed neurosciences research program will identify, prioritize and integrate translational neuroscience research between the School of Medicine, the Neurological Institute of University Hospitals and their affiliated institutions. This collaboration provides a unique opportunity for multidisciplinary translational neuroscience research that will enhance our ability to compete for external funding and enhance our national reputation in neuroscience research. This program will also link to other major themes of strategic development in the School of Medicine including Cancer, Metabolism and Infection and Immunity and Cardiovascular Disease.



Theme four: A program in Infection and Inflammation

The goal of the program is to promote basic, translational and clinical research concerned with the molecular biology, immunology, evolution, and population dynamics of the microbial biosphere as it relates to human health. Despite remarkable advances in the development of antimicrobial drugs, infectious diseases continue to be responsible for millions of deaths, serious medical complications, and enormous social and economic challenges at a global level. It is only by developing a thorough understanding of the biology of pathogenic microbes, of mechanisms of resistance in their hosts, and how these two interact during infection that new antimicrobial drugs, vaccines and improved strategies for prevention and treatment of infectious diseases at an individual and population level can be achieved. Currently over 170 faculty at CWRU have their primary research, education and/or clinical interest in this area, making infection and immunity perhaps the largest

“unrecognized” programmatic area in the University.

Case has a national reputation for international research in infectious diseases of major public health impact in the developing world with formal relationships between CWRU and Makerere University in Kampala Uganda that helped to escalate the level of TB and HIV care and prevention in Uganda as a model for the developing world. Currently there are programs in tuberculosis, HIV, malaria, helminthiases, dengue, Japanese encephalitis, viral hemorrhagic fevers, and dengue in Uganda, Zimbabwe, Kenya, Brazil, South Africa, Papua New Guinea, Ethiopia, Philippines, and Morocco.

We propose formation of an interdisciplinary program on “Biology of Infection and Host Immunity” that will be distinguished through an integrated and interdisciplinary approach to basic and human-oriented research and education on pathogens of international health importance and their interactions with host immunity. It will blend the intellectual cultures of basic microbiological and immunological research typically funded by the NIH with epidemiology, public health, and population-based and clinical operational research studies represented by the Centers for Disease Control and Prevention and philanthropies such as the Gates Foundation. There are no comparable programs within other major research-oriented universities in the United States.

The program will undertake the following goals:

- **Create novel interdisciplinary educational and research programs for undergraduate, MD and PhD students.**
- **Provide multidisciplinary research opportunities for undergraduates, graduate students, postdoctoral fellows and residents.**
- **Promote partnerships with private industry and government.**

To achieve these goals the program will undertake:

1. Creation of a central data and project management core.

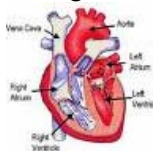
A core that meets GCP requirements and that is open to the entire CWRU community for local clinical studies and trials in infectious diseases.

2. Creation of a central coordinating core for international infectious disease research.

The core will encompass not only IRB and regulatory matters but also project, data and sample repository management. This core will build on existing infrastructures in the TBRU and the Center for Global Health and Diseases.

3. Improved containment and imaging facilities for research on animals carrying infections.

Initial academic initiatives include focusing on cancer virology, the development of an integrated program in antibacterial resistance and microbial population and a center for microbial genomics. The program would serve as a focus for research on infectious agents considered to be agents of bioterrorism and emerging pathogens that are threats to public health nationally and internationally. The program would act as a catalyst for a University-wide program concerned with public policy aspects and ethical, legal, and sociological aspects of bioterrorism and infectious diseases of public health significance. Knowledge generated within the Program will ultimately be used to formulate national and international strategies to prevent, interrupt, and or even eradicate select infectious diseases. Conversion into public health action will be facilitated by interactions with bioethics, nursing, management, social sciences, and health care economics and delivery.



Theme five: Cardiovascular Health and Disease

The goal is to create an institute that integrates the School of Medicine and School of Engineering to promote and expand research, innovation and development in cardiovascular disease. Cardiovascular disease accounted for 36.3% of all 2,398,000 deaths in 2004, or 1 of every 2.8 deaths in the United States. The associated morbidity and mortality explains why CVD is the largest market opportunity within the health care sector, estimated at more than \$420 billion in the US alone. Case Western Reserve University is uniquely positioned to fulfill the needs of modern biomedical research, development and innovation. The proposed **Case Cardiac Institute of Technology and Innovation (CITI)** will provide the organizational structure to integrate and promote translational research and dovetails well with the goals of the recently acquired Clinical and Translational Science Award (CTSA).

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The Department of Macromolecular Science and Engineering would be among the founding partners to establish the CITI as a truly interdisciplinary enterprise. The main goal of the CITI is to promote and integrate multidisciplinary approaches to research and innovation in CVD. The CITI will actively pursue external government funding opportunities, particularly through the Ohio Department of Development as well as funding from philanthropy, industry partners, technology transfer agreements. Financial independence is anticipated by Year 3. Other metrics of success are as follows: 1) increase extra-mural funding dedicated to CVD research within CWRU, 2) Increase in the number of patent applications, and 3) Increase in the number of start-up companies and commercial products created. These endpoints will be assessed 5 years after the creation of the CITI.

Together these major themes will help to link the majority of ongoing and new research programs in the School of Medicine to promote human health from molecules to the global population. They will be linked to emerging programs as shown in Figure 2 below.

The identification of major themes and new areas of strategic development do not imply that there will not be continued investments in existing areas of strength that are critical to maintain the vitality of the research program. Indeed, the programs outlined in this strategic plan are dependent on existing areas of strength in the basic and clinical department and centers.

	Metabolism & Disease	Cancer	Neurosciences	Infection & Inflammation	Cardiovasc. Disease
Population & Public Health	★ ★	★ ★ ★	★	★ ★ ★ ★	★ ★ ★
Membrane Biology	★	★ ★	★ ★ ★	★ ★ ★	★ ★
Sleep Research	★ ★	★ ★	★ ★	★	★ ★
Systems Medicine	★ ★ ★	★ ★	★ ★ ★	★ ★	★ ★ ★ ★
Therapeutics & Informatics	★ ★ ★	★ ★	★ ★	★ ★ ★	★ ★
Biomedical Engineering	★ ★	★ ★	★ ★ ★ ★	★	★ ★
Imaging	★ ★	★ ★ ★	★ ★ ★	★ ★	★ ★

Figure 2. Substantial interactions occur between each of the major themes as well as with all the emerging programs.

STRATEGIC PROGRAMS FOR DEVELOPMENT IN THE SCHOOL OF MEDICINE

Development of a Program in Population Health and Personalized Medicine

a) Genetics and Genetic Epidemiology: This program will integrate appropriate research and training activities in two academic programs at Case SOM to provide greater continuity and synergies across the spectrum of molecular, statistical and epidemiological methodologies, and create greater opportunities for bidirectional translational research (animal ↔ human), as well as a new focus on personalized medicine. Current approaches to complex diseases call for the inclusion of molecular techniques and animal experiments as components of genetic epidemiological studies. Conversely, genetic and genomic animal studies may generate large amounts of data that require application of sophisticated statistical and techniques traditionally housed in genetic epidemiology groups.

The development of Case as a leader in Personalized Medicine, which is currently a nascent but hugely promising area, will require close interaction between individuals with expertise in modeling data and genotyping to identify clinically important genetic variants as well as understanding of clinical, pharmacological and functional consequences of such variants. Thus, programmatic coordination and integration should enable close

SOM Strategic Plan - Draft

interactions among clinical genetics, basic genetics, genetic epidemiology and genetic statistics that will enhance the scope and competitiveness of grant proposals and broaden the spectrum and quality of training in genetics and genetic epidemiology. The proposed program reflects the complexity and quantity of data often needed to assess the genetic etiology of complex diseases, the current blurring of lines separating genetics from genetic epidemiology, the increasing competitiveness of grant applications that require bi-directional translational components, and the need to provide a fuller spectrum of training opportunities to graduate students.

b) Community and International Health: The focus of this entity will be to support and further catalyze research aimed at understanding, at a population level, the determinants of health and disease, as well as to develop and evaluate approaches for disease prevention and health promotion. Areas of foci will include research on health disparities; and behavioral; social and environmental risk factors, with research that includes community interventions and urban and international population health studies. In addition, this entity will serve as the academic home for epidemiologists with expertise in study design, survey methods, sampling, and risk assessment, with training programs that include a MPH and MS/PhD in epidemiology.

c) Quantitative Health Sciences: This entity will create a home for researchers with interests in developing and applying methodologies for managing, analyzing, and modeling data of all sorts. Thus, this entity will provide an academic home for statisticians, biostatisticians, computational scientists, informatics scientists, and system biologists. This entity will encourage joint appointments of faculty from other schools as well, such as Engineering.

d) Clinical and Translational Investigation: This will be the academic home for the CTSC, as proposed in the CTSA application, engaging clinical investigators and physician scientists in clinical and translational research, with a focus on clinical trials (T1, T2, T3) and outcomes research (i.e., those areas that are patient – vs. population – focused). This entity will also develop and support postgraduate training programs in Clinical Investigation distinguished by a focus on the clinician investigator and team science. This academic program will offer a highly integrated clinical research practicum (patient mentored research) coupled with selective course work on key competencies in clinical investigation as well as training programs for clinical research for the entire research team. The entity also will provide “consulting” services in statistical, data management, regulatory issues and study design through an extensive “concierge” service and Core Services.

Development of the Center for Membrane Biology

The activities of the center for membrane biology will have wide ranging interactions across SOM and University. For example, a large and increasing number of diseases are linked to specific types of membrane proteins while normal cell function is critically dependent on membrane protein function since most signal transduction processes are initiated at the membrane and many pathological processes occur and evolve because of mutations in membrane proteins or alterations in their regulation and function.

The further development of the recently formed *Center for Membrane Biology* (CMB) will foster multidisciplinary collaborations directed at fundamental experimental issues as well as develop world-class facilities for the study of membrane proteins. The CMB will require investment to expand the institution’s technical capabilities in 2 critical areas:

(1) Enhance the technical capabilities already present at Case SOM in high resolution structural biology including expansion of expertise in NMR, mass spectrometry, X-ray crystallography, and atomic force microscopy. Introduce into the Institution instrumentation for high-resolution cryo-electron microscopy and electron crystallography, including 3D reconstruction capabilities and add expertise in solid-state NMR and molecular dynamics.

(2) Establish a Core Laboratory for the large-scale recombinant expression, purification, and functional analysis of membrane proteins and for their robotic protein crystallization. Both initiatives are being developed cooperatively by the Departments of Pharmacology and Physiology and Biophysics. The core facility will collaborate with engineering faculty to develop high-throughput screening approaches and implement sophisticated technologies for assessing the function of membrane proteins in living cells.

Success of the CMB will be gauged by attainment of several important milestones within the first five 5 years after its initiation in addition to continued excellence in published research:

SOM Strategic Plan - Draft

1. Award of grants for instrumentation and the subsequent development and management of access to that resource.
2. Establishment of a Membrane Protein Expression, Analysis, and Crystallization Core facility and integration of the core with the nascent protein expression and crystallization facilities in the departments of Pharmacology and Physiology & Biophysics.
3. Submission and award of a training grant.
4. Completion of faculty recruitment in the areas outlined above.
5. Award of at least one NIH research grant to each recruited faculty member and documentation of a significant number of new NIH or other research grants to existing CMB members enabled in part by the CMB and new facilities.
6. Evidence of multiple new collaborations between existing and/or recruited faculty for the study of novel membrane proteins.

Sleep and Circadian Research Program

Sleep disorders, including obstructive sleep apnea (OSA), insomnia, periodic leg movements, and narcolepsy, and disorders associated with insufficient and poor quality sleep, affect approximately 50 million Americans and are associated with substantial morbidity. There are over 30 Case faculty members from over 15 departments/schools whose research involves sleep science. A 2006 review of federal funding in sleep identified Case within the top 10 best NIH-funded sleep research institutions. The current portfolio includes extensive collaborations across many disciplines, including engineering, epidemiology, pediatrics, genetics, radiology and physiology, which extends across Departments and Schools. Nationally, Case is especially known in the areas of public health, clinical trials, and genetic epidemiology of sleep disorders. Case serves as the Sleep Reading Center for major NIH funded studies, playing a leadership role of the performance and analysis of polysomnograms from over 20,000 research participants in studies performed from national and international clinical sites. Case is the site of the only family based genetic epidemiological study of sleep apnea in the world. Sleep training is supported by a NIH research training award as well as an ACGME approved clinical sleep fellowship. However, growth of this program is limited by the absence of researchers in circadian biology and relatively few faculty investigating molecular mechanisms underlying sleep disorders.

This proposal will form a Sleep Research Center, the goals of which are:

- Position the Center for designation as a Center of Excellence, integrating clinical, training and research opportunities across disciplines in sleep medicine.
- Position the Center as an IOM model Type 3 center that:
 - Develops a center for public health education, training for clinical care and research, and integrates patient-oriented, basic, and translational research and clinical care.
 - Serves as a Regional Coordinating Center for education, training, mentoring, clinical trials, and large scale population genetic studies in sleep medicine.
- Serve as a model clinical-academic program for Case Medical Center and for multidisciplinary clinical and translational science complementing goals of the newly funded CTSA.
- Increase NIH funding with PPG and other center grants, particularly focused at building stronger interdisciplinary programs that extend the strong epidemiological observations to clinical trials and to the laboratory, including linking mechanistic, genetic and clinical studies in areas such as:
 - Insufficient Sleep and Cardiovascular Risk
 - Insufficient Sleep, Hypoxemia and Cognition and Behavior
 - Obesity, Metabolic Dysfunction, and Sleep Disorders (potentially including psychiatric diseases)
 - Intermittent Hypoxemia, Mortality and Bone Disease
 - Social Stress, Urban Health and Sleep and Health Outcomes
 - Understanding the role of sleep and circadian rhythm disorders across the age continuum, spanning in-utero, early life, adult, and senescence, and the impact of circadian biology on disease susceptibility and treatment of cancer and metabolic disorders

SOM Strategic Plan - Draft

- Expand existing training programs to provide trainees from multiple sub-specialties and across Departments and Schools to interact in cross-disciplinary training opportunities, including accessing the wealth of data from large scale epidemiological research, large genetic assay data, and system biological expertise. To develop the potential of this program will require significant investment in a number of sleep related areas.

Systems Medicine

Systems Medicine represents a new scientific discipline of increasing importance to Biology and Medicine. This new science attempts to understand the integration of these pieces into networks, complexes and the biological organizations critical to cellular and organism function. Systems Medicine is key to understanding the function of complex biological systems, to understand their normal development, to understand their transition to abnormal or disease states, and to discover innovative modalities for treating and preventing disease.

This proposal outlines a plan for expansion of research and education programs in Systems Medicine and related areas at the SOM. Overall, there are four major areas that will be developed as part of this proposal or in coordination with other major initiatives:

1. Systems as they relate to organ function and physiology
2. Systems of molecular interactions at the cellular and sub-cellular level
3. Computational biology, bioinformatics, and related quantitative health sciences
4. Education and training programs to develop the next generation of scientists

Goal 1: Enhance programmatic efforts in Systems Medicine areas related to organ and molecular systems to promote existing strong programs and enhance existing departmental efforts in this area.

Goal 2: Develop a world-class faculty and infrastructure for Bioinformatics, Biostatistics, Medical Informatics, Systems Analysis, and Computational Biology.

Goal 3: Enhance educational opportunities in Systems Medicine within the graduate programs of the School of Medicine.

These educational activities will provide glue to cement the existing and the emerging collaborations in terms of a unique student cohort that will move seamlessly between laboratories across the campus. With a foundation of world-class research and a record of innovative and often revolutionary educational programs, this program will accelerate our contributions to Systems Medicine as we train a new generation of biological and biomedical researchers.

Translational therapeutics and computational informatics

This proposal outlines a plan to establish a *Center for Translational Therapeutics and Chemical Biology* (CTTCB) that will bring medicinal chemistry and screening expertise to biological targets of therapeutic relevance. The CTTCB will develop an integrated “Bench-to-Bedside and Bedside-to-Bench” approach to understand and treat disease. The “Bench-to-Bedside” paradigm will create dedicated and multidisciplinary teams composed of synthetic chemists, assay development, and profiling scientists to streamline molecular agents through the drug discovery and development process. In the “Bedside-to-Bench” paradigm, results generated from clinical-based studies will be used to develop new agents and strategies in patient care. Emphasis will be placed on developing a “personalized medicine” approach, i.e. using genetic and proteomic information to rationally develop effective and safe therapeutic modalities on patient-by-patient basis. Four (4) major initiatives will be developed within this proposal and/or in conjunction with other strategic programs:

Initiative 1: Enhance and establish programs linking basic science with clinical outcomes by developing resources and technologies to generate/characterize chemical libraries, identify lead compounds, and convert lead compounds into drug-like entities. Synergy will be developed with other proposed initiatives including infectious disease, cancer biology, membrane biology, and metabolic and neurological disorders.

Initiative 2: Enhance and establish programs applying clinical-based information to rationally develop new therapeutic agents and treatment strategies. A “personalized medicine” approach will be developed by integrating genetic, epigenetic, proteomic, and metabolomic information. Synergy will be generated from existing Centers (Cancer, Proteomics, etc.), Departments (Genetics, Nutrition, Pharmacology, etc.) and other proposed initiatives (Systems Medicine Initiative and Bioinformatics/Computational Biology).

SOM Strategic Plan - Draft

Initiative 3: To enhance educational opportunities in areas associated with Translational Medicine and Chemical Biology within the graduate and medical programs of within the University. To obtain additional funding from foundations and national funding sources (NIH, NSF) through training grants.

Initiative 4: Enhance the University's ability to generate composition of matter and intellectual property on several chemical entities having clinical utility. By licensing agents and/or creating new biotech companies, the CTTCB will provide opportunities to generate more revenue from industry as well as funding from foundations and national sources.

This strategic plan proposes the development and maturation of a number of additional centers and programs. It is recognized that as medicine develops emerging technologies and research foci replace existing approaches. In order to allow new investment the School of Medicine will need to sunset less current centers and programs. The School currently has in excess of 53 centers and opportunities for consolidation and closing centers should be considered in the development of research programs. It is proposed that centers be critically reviewed after 5 years and only maintained if a persistent need is clearly identified.

Biomedical Engineering in the School of Medicine

Few programs in the university bring together the breadth of interdisciplinary research and teaching opportunities across our institutions as Biomedical Engineering. Medical research in cardiac disease, neuroscience, and cancer are coupled with advanced concepts in instrumentation, materials science, computation/modeling and imaging; with the current NIH and institutional focus on translational research, establishing the first ever links between BME and the SOM (a joint department of the Schools of Engineering and Medicine since its Charter in 1968) will provide significant yet previously unrealized synergies. Collaborations across the university to Physics, Biology, Mathematics, Computer Science, Mechanical Engineering, Macromolecular Science, and Chemistry are unique opportunities for impact in the SOM in biochemistry, genetics, proteomics, cancer and imaging (and others) which already are vital or are emerging. Together these provide unsurpassed opportunities to not only leverage prior institutional investments, recent awards like the CTSA and institutional strengths in areas like proteomics, genomics, structural biology, systems engineering, macromolecular sciences and cognitive sciences, but also to create a compelling engine for discovery on both research and teaching fronts. The mission to translate these to patient care is ensured by the word “medical” in the department’s name.

	Computing and Sensing	Imaging (including nanotechnology)	Tissue Engineering BioMaterials	Neural Engineering
Cancer	X	X	X (agents, therapeutics)	
Neuroscience				Z
Cardiac	X		X	
Proteomics Genetics	X	X (agents, therapeutics)		
Other	X (Systems Biology; Metabolic Models)	Z	Z	

Z = ongoing recruitments in BME for positions in the School of Engineering
X = potential recruitments in BME to new positions in the School of Medicine

Future SOM recruitments will be strategically linked to ongoing investments to ensure coordination of recruitment and allocation of space and to synergize collaboration and impact. Since its inception, BME faculty members have been the top research

Figure 3: Recruitment coordination in Biomedical Engineering

performers in CSE in general, and new BME CSE faculty would be recruited with the same expectation. With the growing emphasis in translational research at NIH, this represents a unique opportunity to develop relationships and research program in basic science departments in the SOM and opportunities with clinical researchers at UHC and other strong regional institutions.

New recruits in the SOM (X's above) would provide unique opportunities for computational modeling in

cancer and proteomics/genomics to add synergies to emerging plans in Systems Biology. Imaging faculty in cancer (contrast agents) would complement recent recruits. A neuroimaging researcher would complement recruits in fMRI and radiochemistry to provide new research in structure/function relationships via diffusion tensor MR imaging foci imminently translatable to humans and applicable to programs in the Neurological Institute. Bioelectricity provides unique opportunities to complement structure/function research. Tissue/Materials research in cancer would complement existing strengths by exploring new nano-drug delivery vehicles for cancer and cardiovascular diseases. Further, recruits in FES/Neural engineering will complement recent investment in the Center for Translational Neuroscience, the Neurological Institute and the well-established FES program at Case.

The Case Center for Imaging Research

The Case Center for Imaging Research was conceived with the purpose to advance our understanding of biology and medicine through noninvasive in vivo investigation of normal and pathologic processes. Initial University and Hospital investments to form the center have been effectively leveraged, and allowed the center's impact to grow exponentially. This growth has included key recruits in areas of basic science discovery through molecular imaging to clinical translation. These have positioned the Center to be a recognized leader in imaging sciences. This developmental track allows imaging to impact each of the primary disciplines identified as School of Medicine themes. Specifically, imaging research has had major impacts in the fields of metabolism, cancer, neuroscience, infection and inflammation, and cardiovascular disease. For example, Case Western has pioneered the field of interventional MRI. These studies have also impacted the greater N.E. Ohio area by prompting a startup company, Interventional Imaging Inc. Many of Case faculty discoveries have been or are currently being translated into the clinical arena for cardiovascular imaging and provide unique insights into the structure, function, and energy balance following infarction. A further development is in the area of molecular imaging technology that allows tumor margins to be identified in breast and brain cancer to facilitate improved surgical removal. The formation of Akrotome Imaging Inc., a fledgling startup, has arisen from this research. The Case Center for Imaging Research has also developed projects across many other disciplines such as neuropsychology, infectious diseases, and the development of radionuclides for assessment of various metabolic processes including Alzheimer's disease and multiple sclerosis diagnosis and non-invasive assessment of cancer therapeutics. Each of these initiatives is detailed in the appendix entitled "The Institute for Imaging Life" and completes a research portfolio that spans a continuum from basic to applied imaging research. These initiatives and continued focus on imaging will ensure that Case Western continues *leading* the cutting-edge.

Clinical Interface with Basic Research Task Force

The School is committed to developing a research portfolio that is aligned with the strategic clinical initiatives of our Hospital affiliates. The CTSA and the emphasis on translational research is one example of such alignment. Other areas include investment in cardiovascular research, major projected investments in Pediatrics and commitments to invest in the Neurological Sciences to support and enhance the Neurological Institute. Continued investment in Cancer research will maintain strong leverage between clinical and basic science programs.

The task force largely considered issues regarding mechanisms to promote optimal interactions in research activity between faculty with primary appointments in departments with major activities in the affiliated hospitals (University Hospitals-Case Research Institute, MetroHealth Medical Center, and the Veterans Administration Hospital) and those based at the SOM. The importance of this interface is evident in clinical research activities and education involving the recently funded CTSA grant, training of physician scientists, clinical trials involving human research subjects, and scholarship and career promotion of faculty with primary appointments in clinical departments. The complexity of this interface is enormous given the different mechanisms of faculty support among the various hospitals and the recent institution of a mechanism of a dual source of salary for faculty at University Hospitals (University Hospitals Medical Group paymaster) who at the same time are funded by NIH (CWRU paymaster). Issues of benefits, tuition support for children, etc. are considered particularly important in this context. The task force recommended convening clinical research committees at each affiliate, development of a physician-investigator development fund, establishing a Clinical

SOM Strategic Plan - Draft

Interface Advisory Board to address issues of salary cap, clinical reentry, and identifying mechanisms of promoting research between hospital-based departments and SOM-based departments.

Hospital Affiliates Task Force

Among a wide ranging menu of options for improving collaborations among the hospital affiliates of the SOM that were discussed, a few were of greatest interest. These included recommendations that 1) affiliates' representatives should meet quarterly with the Dean to create an ongoing forum in which collaborative efforts can be discussed; 2) developing a unified approach to clinical rotation evaluations for medical students; 3) mechanisms of improving the Mt. Sinai Skills and Simulation Center collaboration; and 4) establishing smooth mechanisms to assess faculty and resources at the affiliates to respond to rapid turnaround of RFA's available to CTSA participants. This task force continues to be active.

International Programs Task Force

The SOM has been at the forefront of externally NIH-funded biomedical research and bioethics concerned with international health for the past several decades yet has not achieved substantial philanthropic or internal University support for these activities. Many of the students who matriculate at the SOM cite "international health" activities as one of the main features involved in their decision. It is especially important that the challenge of reducing the fragmentation of various international programs be confronted now, given the increasing attention to the "internationalization" of health problems and the recognition that leading American universities need to offer students and faculty a global perspective on research, education and service. The task force recommended a series of goals that included 1) stimulation of research by providing seed funding for international projects that addresses diseases of poverty; 2) initiation of applications across departments that incorporate operational research with basic or molecular research, e.g. molecular epidemiology of emerging infections; 3) a University-wide "Global CTSA" that would provide a mechanism for public-private partnerships for development of novel and cost-effective control methods for diseases of poverty and health problems that affect disenfranchised groups such as women and children in the developing world.

Interdisciplinary Programs Task Force

This task force sought input from Chairs and Directors of departments and centers in the SOM, affiliated hospitals, Deans of other schools in the University and selected individuals known to have an interest and expertise in interdisciplinary collaboration. Town hall meetings were held to solicit additional comments and stimulate discussion on this issue. After identifying "successful" interdisciplinary efforts, e.g. systems biology, functional electrical stimulation, medical entrepreneurship, center for imaging research, etc., there was consideration of expanding programs based on existing islands of excellence and expertise, anticipated interests of our future students and funding opportunities. These included expanded and better university-wide coordination among efforts concerned with Children's Health, Mind and Brain, Nanotechnology/Nanomedicine/Nanotoxicology, Biomedical Engineering and Infectious Disease. Challenges to implementation and the success of efforts include breaking down financial and administrative barriers to collaboration across the various schools of the University, reducing impediments to faculty career promotion for those who participate in interdisciplinary efforts and promoting and facilitating interdisciplinary activities among the various schools of the University.

ISSUES, GOALS, STRATEGIES AND METRICS: for the Strategic Plan of the School of Medicine

Issue 1: A primary mission of the SOM is to educate future physicians and biomedical scientists

Goal: Create an environment that attracts the highest quality medical and graduate students and post-doctoral fellows that are competitive with our peer research-intensive medical schools.

Strategies:

- a. Fully implement and modify the "Western Reserve2" curriculum according to student and faculty feedback
- b. Continue to enhance and support the office of graduate student education

SOM Strategic Plan - Draft

- c. Develop mechanisms and financial incentives for excellence in teaching of medical and graduate students through student evaluations
- d. Increase the amount of endowed funds to support medical and graduate student education
- e. Create incentives for faculty participation and excellence in medical student and graduate student education
- f. Integrate more optimally the educational experience of Master's degree students with those of M.D. and Ph.D. students

Metrics:

- a. Placement of graduating medical students in high quality residency programs, including those at hospital affiliates of our peer institutions
- b. Feedback from medical students who matriculate in 2007 through 2011
- c. Success in increasing the endowment for medical student and graduate student financial support
- d. Increase in the number of graduate students from academically excellent undergraduate schools
- e. Attraction of top international students to our graduate education and research programs
- f. Placement of graduate students obtaining the PhD degree in highly respected post-doctoral fellowships
- g. Interdisciplinary education activities and "core courses" across the University that are sustainable with high levels of student satisfaction
- h. Continuing success of the SOM NIH-funded Medical Scientist Training Program (MSTP) through tracking of publication and placement
- i. Evaluation of the new MD-PhD program in clinical research, biostatistics and epidemiology and engineering supported by CTSA
- j. Implementation of the goals of the CTSA, CTSTP and continuation of the K12 program jointly run by SOM and the CCF Lerner College of Medicine
- k. Improvement in the physical facilities for small group discussion and medical student education
- l. Implement a tracking system for MDs and PhDs to identify metrics of successes (# in Best Doctors, Faculty positions, Research Awards, Certifications etc.)

Issue 2: A primary mission of the SOM is to conduct cutting-edge biomedical research

Goal: Increase our national reputation for excellence in biomedical research

Strategies:

- a. Continue to recruit and retain outstanding biomedical scientists to basic science departments and centers in the SOM and departments that are supported by the Case Research Institute
- b. Increase the endowment to support research at the School of Medicine
- c. Provide appropriate and transparent financial and space incentives for excellence in research and sustaining extramural support
- d. Utilize the Center and other innovative organizational structures to enhance interdisciplinary research within and outside the School of Medicine and University Circle institutions that conduct research, e.g. Cleveland Museum of Natural History
- e. Improve the research infrastructure in order to facilitate biomedical research goals, particularly with respect to animal facilities, computational and informatics expertise and hardware, structural and systems biology, high-throughput genomics and biostatistics, and informatics
- f. Recruit an increased number of high quality graduate students to participate in the research of funded investigators
- g. Successful applications for new and retention of existing NIH-funded training grants
- h. Award for success in research excellence in interdisciplinary activity by achievement of tenure and promotion of academic rank

Metrics:

- a. Number of research publications in high impact biomedical journals
- b. Service and membership of our faculty on NIH and other granting agency study sections

SOM Strategic Plan - Draft

- c. Election of our faculty to membership on prestigious national organizations such as the National Academy of Sciences and the Institute of Medicine
- d. Representation of our faculty at highly respected national and international scientific meetings, e.g. Keystone conferences, Cold Spring Harbor meetings, Gordon conferences, etc.
- e. Retention of highly regarded senior faculty, especially those who have demonstrated sustained extramural funding ability
- f. Recruitment of junior faculty who achieve >70% salary support from external sources after receiving start-up support from the SOM that covers the first 3-5 years after initial appointment at the Assistant Professor level
- g. The number of newly endowed chairs for research-intensive faculty
- h. Increasing the national ranking of the SOM in terms of NIH-funded research dollars
- i. Establishment of interdisciplinary research programs that become self-sustaining after appropriate seed support from central administration
- j. Enhancement of the biotechnology effort in the University Circle community that can be quantified by the number of newly established and sustained business ventures in this area, number of patents, licensing agreements, and patent income

Issue 3: A mission of the SOM is to serve the community and broader society through promotion of health of the individual and population

Goal: Promote student and faculty participation in local, national and international service in health care delivery and research

Strategies:

- a. Participate vigorously in medical student programs concerned with health issues of the poor in Cleveland, nationally and internationally
- b. Increase the gender and racial diversity of our faculty
- c. Sustain, with University support, a Global Health curriculum that brings together students from the various schools in the University for a common experience that highlights the importance of interdisciplinary approaches to addressing human health and disease in our society and globally
- d. Encourage and reward faculty participation in programs intended to promote health careers of students from the Cleveland community, e.g. John Hay High School program in the sciences supported by the Cleveland School System
- e. Continue to support and expand summer research programs and experiences for minority high school students in the Cleveland area
- f. Continue the emphasis on excellence in programs and courses concerned with humanitarian emergencies that occur during periods of war and natural disasters

Metrics:

- a. Number of faculty and students participating in health care service or research involving disadvantaged and disenfranchised populations, comparing the present number to that in 2010-2011
- b. Development of a set of core courses on the major human health issues that involve joint participation by faculty from the School of Medicine with faculty from the College and other Schools of the University
- c. Recruitment of high quality undergraduate, graduate and professional students to the University on the basis of their participation in the faculty activities in community education and service
- d. Quantification of the number of women and minority on our faculty, especially those successfully progressing upward in academic rank and assuming leadership positions