Executive Summary of School of Medicine Strategic Plan and The Institute for Genome Sciences and Policy

Introduction and Goals:

The Duke University School of Medicine has the interconnected missions of the discovery of new knowledge, the education of physicians and other health care providers, and the provision of quality health care. Its scientists, teachers and clinicians rank among the leaders in their fields, and its outstanding programs draw students, trainees, and patients from around the world. While we are pleased that the School of Medicine enjoys the reputation that it does today, we believe our educational and research programs can be stronger. Clearly we cannot rest on past accomplishments; just maintaining our current status will require a level of investment in our academic programs comparable to that of our peer institutions.

This is a particularly good time for the School of Medicine to consider an aggressive agenda to enhance its academic programs for the following reasons:

1. Biomedical research over the past 25 years has made extraordinary progress, and the opportunities for fundamental discovery and application of this knowledge to improve the well being of mankind have never been greater. We are indeed embarking on a new century that will likely see biology and medicine supersede the natural sciences as the frontier for unprecedented breakthroughs.

2. Funding for biomedical research from both the public and private sector is experiencing record rates of growth. The NIH budget is on track to double over the next five years from what it was only two years ago. As biomedical research matures and practical applications increase, investment opportunities from the private sector are increasing in parallel with funding from the public sector.

3. As the wealth of the nation has grown during the current economic boom, more individuals and foundations are able to and want to contribute to worthwhile causes. Improving the health of mankind is a strong interest of philanthropists.

4. The products of this investment in research will lead to improved health.

Thus, the opportunity to strengthen the academic programs of the School of Medicine would seem to be very good over the next five to ten years. By taking advantage of these opportunities, it should be possible to strengthen not only academic programs within the School of Medicine but across the entire...
Internal and External Environments:

Undeniably, we face considerable challenges in delivering the quality of care made possible by the last 25 years’ worth of discoveries, in transmitting this explosion of new information to students and trainees, and in exploiting this knowledge to develop new approaches to patient care, given shrinking clinical margins. Teaching hospitals have been and continue to be particularly hard hit by the Balanced Budget Act of 1997, which slashed Medicare reimbursements and lowered payments from the government for physician training. By 2002, according to a study by the Association of American Medical Colleges (AAMC), these cuts will cost the average teaching hospital a total of about $43 million and could drive up to 40 percent of them into the red (US News & World Report March, 2000). Simultaneously, physician and hospital reimbursement for patient care is declining as a consequence of the movement to managed care, and the ability of practice plans and teaching hospitals to subsidize the academic mission is falling precipitously. Reliance on clinical margins is no longer a viable mechanism to support the academic mission of medical schools.

In many regards, these are the best of times for academic medicine. Basic biomedical and clinical research have yielded extraordinary new opportunities to improve health care, funding for medical research is growing at an unprecedented rate, and rapidly expanding philanthropic and private sector donations for medical initiatives have reached unparalleled heights. Major international initiatives such as the Genome Project have created a virtual revolution in biology and medicine. The NIH budget is on course to double over what it was only a few years ago. Philanthropy and private sources of funding have never been so plentiful.

Duke is as well or better positioned than most institutions to respond to this environment, but we need to make aggressive commitments to our academic programs -- commitments at least comparable to those of our peers. A recent survey of top schools’ investments in new programs and facilities showed many institutions planning to expend well over $200 million in the next five years. If we seize the opportunities available in a cogent and timely manner, our School of Medicine will be able to continue making seminal contributions to the foundations of biomedical knowledge, enhance training opportunities for the next generation of academic leaders and healthcare providers, and improve the quality of health for people around the world.

The core mission of a research-intensive university, such as Duke, is the development and dissemination of new knowledge. We must maintain strong research programs to develop new knowledge, and we must maintain superb training programs for MD’s and PhD’s to ensure critical dissemination of that knowledge. Equally important is a vigorous, high-quality patient-care program, which is both a source of knowledge and a focal point for the application and dissemination of new knowledge. Success in attaining this mission depends on the collective body of scholars in the School of Medicine, i.e., the faculty, students, and trainees. This community of scholars is a most prized possession, and it needs constant encouragement, nourishment, and investment for both sustenance and growth.
In assessing the current status of the School of Medicine (SOM), each of the three primary missions has been evaluated: education, research, and clinical programs. Correspondingly, plans have been developed to improve the quality of these programs and position us to take advantages of the favorable environment to further develop our academic programs.

**Education:**

By almost all measures, the Duke University School of Medicine stands among the top tier academic medical centers in the country.

- Our School of Medicine has ranked from 3rd to 6th in the *U.S. News & World Report* for the past five years. This year’s *U.S. News & World Report* shows Duke's reputational rank by leading institutions in the country: number three by academics and number two by residency directors.

- Our medical and graduate students’ superior academic credentials indicate our success in recruiting some of the most capable minds in the country -- individuals who are also extraordinary in their personal attributes and commitment to improving the health of society. The School of Medicine was ranked 6th in the 1999 US News and World Report Medical School rankings.

- Our post-graduate medical programs and post-doctoral PhD programs also engage many of the best and the brightest. Students choose Duke because of our academic and clinical reputation.

- Over 20% of our graduates remain in long term academic positions, with only Harvard, Johns Hopkins, University of Chicago and Yale having greater success in this area.

The medical school has several significant needs to preserve the high quality of its educational programs and matriculates. First, the curriculum needs to be updated. Second, the physical facilities are outdated and unable to accommodate the educational technology that is part of a modern medical curriculum. Both will need resources and planning immediately.

**Research:**

Our research programs in the School of Medicine are very strong but can be improved.

- Duke has the nation’s strongest clinical research and clinical trials program; the quality of work and attraction of extramural funding performed in the Duke Clinical Research Institute and other parts of the school is unparalleled by any other academic medical center in the country. This year our total corporate gifts are up 35% to $11,880,063 and commercial research revenues are almost $100 million.

- Our basic research programs are highly regarded as well, usually ranking among the top 10 institutions in NIH funding and in the AAMC evaluation.
of funding per principal investigator.

- National academic recognition of the faculty is a measure of the quality and reputation of the faculty. There are 20 faculty members from the School of Medicine in the Institute of Medicine (IOM) and 20 in the National Academy of Sciences (NAS).

- While overall NIH support of medical schools grew an unprecedented 15.1% last year, Duke grew at 7.2%. Our research strategy must include an aggressive plan for growth that will ensure our continued tradition of basic and clinical research excellence and help us pursue additional funding.

Clinical Programs:

Our clinical programs enjoy a strong reputation and rank among the top tier in the country.

- Our faculty are recognized as superb clinicians. Every year we are well represented in The Best Doctors in America.

- Our Medical Center has been consistently ranked among America’s best medical centers by U.S. News & World Report for the past ten years.

- Duke Hospital has ranked from 4th to 5th in this evaluation system over the last five years and the best medical graduates in the country select Duke for their clinical training.

We have the opportunity to focus our research efforts to directly impact on the care of patients and to continue our national leadership in patient care.

Principles, Goals, and Major Initiatives

For the past two years, the School of Medicine has undertaken a strategic planning process involving all departments. In partnership with other schools in Duke University, a number of new strategic alliances have been forged and are part of the major initiatives described here. Those specific plans involving education will be developed at a later date, but several major initiatives have been launched to support the academic and educational programs of the School of Medicine:

- The Nanaline Duke Scholarships, a full-tuition merit scholarship program, attracted eight students with outstanding academic records and extraordinary leadership potential. Additional scholarships will be needed to limit medical school debt and permit us to continue a tradition of need-blind admissions.

- Expansion of advanced degree programs has been started so that more students can pursue dual degree training and broaden the areas available for advanced study. Many of these students will become the next generation of leaders and scholars.
• A Curriculum revision has been initiated that holds significant promise for enhancing the intellectual experience of our medical students. Funding for this is needed.
• The Center for Multicultural Affairs is enriching the diversity of our medical school. Plans for a new Center for Complementary and Alternative Medicine presents the opportunity to evaluate and implement new therapeutic strategies in the Duke University Health System.
• A new Program in Professionalism was launched to provide our students with the skills required to become not only outstanding physicians but also caring practitioners who see their patients as fellow human beings who happen to be ill.
• Formation of the Center for Chemical Biology has already strengthened ties between faculty in the medical school in arts and science departments.
• A new Department of Biostatistics and Bioinformatics has been approved and is being developed.
• A new Center for the Study of Medical Ethics and Humanities is already providing new opportunities for scholarship and leadership in these areas.

The strategic plan was built on the premise that new interdisciplinary research programs are necessary to enable this community of scholars to generate and disseminate knowledge effectively, and to translate this information into new diagnostics and therapeutics. Prior initiatives such as the Comprehensive Cancer Center, the Center for the Study of Aging and Human Development, the Center for Human Genetics, the Center for Structural Biology, the Center for Chemical Biology, the Center for Medical Ethics and Humanities, and the Center for Brain Imaging and Analysis have catalyzed interdisciplinary collaborations and benefited faculty across the entire school.

Duke University School of Medicine has one of the strongest clinical research programs in the country, and the Duke Clinical Research Institute is a model for interdepartmental and interdisciplinary work. Recent studies have demonstrated that the practice of medicine is not as well founded in the body of sound scientific principles as it can or should be. There is a national mandate to establish which practices and therapies lead to the best clinical outcomes and to develop systems that ensure this knowledge is utilized to provide the most effective and efficient care possible. The Duke Clinical Research Institute is ideally situated to lead a major program in evidence-based medicine to not only conduct clinical trials but also evaluate patient outcomes in a variety of settings. In addition, the DCRI will be a partner in the development of clinical trials leading from efforts in the IGSP and the beneficiary of infrastructure and scientific support in the Department of Biostatistics and Bioinformatics.

The School of Medicine of Duke University also has a long and successful history of building interdisciplinary, interdepartmental basic science research teams. With the sequencing of human, bacterial and yeast genomes has come the genomic revolution that has changed the way biomedical research is performed and has spawned a myriad of new technologies. The development of genomic technologies (the analysis of the genetic material at an entire genome level), functional genomics (the analysis of gene expression at a genome scale), and proteomics (the study of proteins at a genome scale) have created enormous opportunities to make rapid progress in solving societal health problems such as cardiovascular diseases, cancer, infectious disease,
neurodegenerative diseases and environmental toxin-induced diseases, to name a few. Coupled with unprecedented support of biomedical research from government and private foundation sources, these scientific breakthroughs now provide Duke University with an extraordinary opportunity to develop new and visionary programs that will bring investigators together from throughout Duke University to form new multidisciplinary research teams.

In the spring and summer of 2000, 16 departments and 7 centers or institutes within the Medical Center contributed 5-year strategic plans to the Dean of the School of Medicine. Since Dr. Holmes’ departure from Duke in September 2000, a committee has catalogued all departmental, center and institute interests, being mindful of collaborative opportunities with other schools in the University, and then sorted them into the five most common areas of interest:

- Cancer Genetics/Genomics
- Cardiovascular Genetics/Genomics
- Microbial Pathogenesis and Host Disease/Vaccines
- Neuroscience and Brain Imaging
- Environmental Health Science and Toxicology

These areas were chosen both because many of the proposed new initiatives naturally fit into these categories, and also because these areas are of common interest to investigators associated with other schools of our University in addition to investigators in the Medical School. Technologies associated with genomics and proteomics will permit us to explore each of these areas in novel ways.

A major criterion for selection of the new initiatives is that they all fit programmatically into the broad plans envisioned for the Institute for Genome Science and Health Policy (ISGP). This committee endorsed the original plans of Dr. Holmes for ISGP wherein ISGP is comprised of five infrastructure centers: The Center for Models of Human Disease, the Center for Human Genetics, the Center for Genomic Technology, the Center For Bioinformatics and Computerized Biology, and the Center for Genome Policy, Law and Ethics. In addition to these Centers providing infrastructure, our planning effort has also envisioned area-specific "Centers/Institutes of Excellence" in areas similar to those listed earlier: cardiovascular disease, cancer, host defense/microbial pathogenesis/vaccines, neurobiology and environmental health/toxicology. They will be described in detail later in this plan.

A. The Duke Institute of Genome Sciences and Policy

The Duke Institute of Genome Sciences and Policy was conceived as a bold plan to develop the infrastructure and research programs that will have the capacity to take advantage of the phenomenal advances resulting from the completion of the human genome as well as various other genomes. Considerable planning and development has already begun within the general context of the IGSP. The five primary Centers have been identified, Directors or interim directors identified, and activities have been initiated in several instances. For instance, the Center for Human Genetics is fully operational with a permanent Director in place: the Center for Genome Technology is well underway with an initial investment for infrastructure and faculty recruitment and now outside funding beginning to support growth. To date, the School of Medicine has committed approximately
$32 million in faculty and programs that directly impact the IGSP activities.

A unique aspect of the Duke initiative is the integration of activities that span the entire University, ranging from the studies of human genetics and mouse models for disease within the Medical Center to bioinformatics and policy studies in the Arts and Sciences component of the University. Moreover, although the Center for Genome Technology was initially developed as a Medical Center initiative, it is anticipated that critical future development will involve programs in engineering and chemistry. This integration of activities across the campus is a major strength of the Institute, providing the opportunity to bridge programs in a way not possible in most other instances. But, this integration also presents a significant challenge in coordinating the planning of the Institute and also defining the resources that will be necessary to build the initial infrastructure of the Institute.

Herein we propose an outline plan for the development of resources to create the Institute of Genome Sciences and Policy. In so doing, we have detailed the scope and infrastructure envisioned for each of the five primary centers of the IGSP, including the necessary space, operating resources, resources for recruitment of directors, and plans for faculty recruitment.

The Medical School will invest approximately $130 million in the IGSP over the next five years, including a number of important initiatives that are already under way. This investment will provide much of the necessary support for the further development of the Center for Human Genetics as well as the majority of support for the Center for Human Disease Models and the Center for Genome Technology. In addition, School of Medicine support for the new initiative in Bioinformatics and Biostatistics will provide a significant finances for the new Center for Bioinformatics and Computational Biology. Nevertheless, to fully achieve the goals of the IGSP, as well as to create the opportunity that will attract a major figure to direct the Institute, additional investment will be required to bring the plan to fruition.

On the following pages, we have detailed the scope and plans for each of the primary Centers of the IGSP as well as the resources anticipated to be needed to bring these plans to reality. We have also detailed the sources of School of Medicine funds that will be directed to each initiative and the proposed University co-investment in the IGSP. These investments would be funded from 2000-01 through 2003-04. Finally, we have also described the resources necessary to allow the recruitment of an overall Director of the IGSP. The details of the organizational structure are described below.

Director of the Institute of Genome Sciences and Policy

Resources to support the recruitment of a Director of the IGSP

- Space: build-out of 1st floor of Genetics Building. Approximate cost $5 million.
- Director recruitment: endowed chair ($2 million)
- Quasi-endowment: $10 million

Total cost: $52 million
B. Center for Human Genetics

Program description:

The Center for Human Genetics has been created by the Medical School to provide core resources and expertise in study design, databasing, family and patient ascertainment, and statistical and molecular analysis necessary to carry out large scale genetic analysis of human patient populations. The CHG is divided into two primary cores: the Family Ascertainment, Genetic Epidemiology, and Informatics Core, headed by Dr. Margaret Pericak-Vance, and the Genomic Research Laboratory Core, headed by Dr. Jeffery Vance. The CHG will focus on diseases that are common in the general population, have an established genetic component, and are of significant public health concern. Understanding the underlying complicated genetic basis will ultimately allow identification of environmental influences and help to develop individualized plans for treatment and/or prevention, with efforts directed at pharmacogenetic applications.

Current status:

The CHG is highly successful and has achieved national status under the direction of the Vances. The Medical School has committed approximately $5 million to the CHG for program development.

Resources to support the future development of the Center for Human Genetics:

- Program development commitment to current director ($4.9 million)
- Program development: recruitment of 3 new investigators into the Center. Approximate cost of $2.25 million for start-up.

Total cost: $ 37.1 million, including $4.9 million already committed

C. Center for Models of Human Disease

Program description:

Duke University Medical Center has committed to the establishment of a Center for Human Disease Models, as a key component of the Institute of Genome Sciences and Policy, to provide the core infrastructure that will allow large-scale mutagenesis coupled with the ability to establish efficient and high-throughput phenotypic screens. We also believe that we can create a Center with a unique concept that will distinguish Duke from other such ventures. In particular, we propose to integrate the activities of the Center with the broader program of the IGSP and in particular, to synergize with the activities of the Center for Human Genetics. In practice, we propose to develop the equivalent of a clinical infrastructure for the mouse to enable collaboration with a variety of genetics efforts at Duke that can create a program that is unique in its ability to focus on the identification and understanding of disease-causing genes.

Current status:

The Medical School and University have received Trustee approval to begin work on the new CMHD building at an estimated construction cost of $41 million ($31 million for the Medical School’s 3 floors and $10 million for the University’s...
Programs have been initiated that focus on the development of mouse models for drug addiction (M. Caron), heart failure (H. Rockman), and hypertension (T. Coffman).

**Resources to develop the Center for Models of Human Disease:**

- Space: Construction of the new 121,000 sq.ft. building. Approximate cost - $41.1 million for Medical School, including operating subsidy of $9.7 million. Program development: Recruitment of 4 new investigators into the Center. Approximate cost of $3 million for start-up.
- Program development: funds currently committed ($3.4 million)
- Director recruitment: Endowed chair ($2 million); start-up funds ($3 million)
- Quasi endowment: $10 million program development fund

Total cost: $62.5 million

**D. Center for Genome Technology**

**Program description:**

The Duke Center for Genome Technology was established in 1999 as a resource for the development of advanced technologies for genome analysis. The Center for Genome Technology is the home for investigators actively engaged in the development of new and novel approaches to genome analysis through technology enhancement and development. In addition, the Center also provides support for Duke investigators in the application of these technologies for their research. The Center has developed the infrastructure and expertise for a range of activities including large scale DNA sequencing, DNA microarray analysis for high-throughput measures of gene expression, and SAGE analysis for comprehensive determinations of transcriptional programs. The generation of the massive data sets from sequencing and array analysis, which represents the power of these approaches, also creates entirely new challenges with respect to data analysis. As such, the development of the Center for Genome Technology has proceeded in close association with the Duke Center for Bioinformatics and Computational Biology.

**Current status:**

The Medical School’s Department of Genetics is serving as the start-up point for this Center, providing space as well as initial faculty appointments. The Duke Endowment has committed $3 million to the School’s initial infrastructure requirements. Several major programs have now developed within the Center with one now receiving outside funding (NIDDK) and proposals for the other two pending. The programs include:

- Duke/NIDDK Functional Genomics Center
- Duke Cardiovascular Genetics Program
- Cryptococcus DNA Sequencing Project

The School also receives approximately $1 million per year in Howard Hughes funding ($4.3 million over 5 years) for investigators involved in genetics-related
research.

**Resources to develop the Center for Genome Technology:**

- Space: Construction of 25,000 sq.ft. in the proposed 120,000 sq.ft. IGSP building, Approximate cost $35 million (for the building).
- Program development: Recruitment of 4 new investigators into the Center, in addition to the Director. Approximate cost $3 million for start-up.
- Program development: funds currently committed ($4.7 million)
- Director recruitment: Endowed chair ($2 million) and start-up funds ($2 million)
- Quasi endowment: $10 million program development fund

Total cost: $ 21.7__ million (excludes cost of IGSP building)

**E. Center for Bioinformatics and Computational Biology**

**Program description:**

A major impact of the revolution in genome analysis is the generation of massive quantities of data - rather than studying the impact or role of single genes, or a few genes, one now can study thousands of genes simultaneously. The power of such a high-throughput technology is the ability to generate tremendously complex data from which patterns can emerge that will tell us something about the disease, or the organism. This will be expanded to the study of other aspects of gene function, including the determination of the complement of proteins in the cell, modifications in these proteins, and predictions of how amino acid sequence determine protein structure. This explosion in data presents tremendous opportunities for extracting information from these complex datasets, dependent on the methodologies of statistics, computer science, and mathematics. Our ability to develop new programs that build a bridge between traditional analytical disciplines such as mathematics, statistics, computer science and the genome analysis component of the new biology will be an absolutely essential part of the success of the IGSP.

**Current status:**

The Center for Bioinformatics and Computational Biology, in collaboration with the Center for Genome Technology, has sponsored an initiative to develop a University-wide graduate program in Bioinformatics and Genome Technology (BGT). The initial aim is to allow students from any existing graduate program to attain a Certificate in the program. This program began with this fall semester of 2000 and it is already very clear that the demand is high – most of the courses initially offered have been vastly oversubscribed. We also believe that moving rapidly to establish such a program will help galvanize Duke faculty to become actively involved in developing graduate activities in BGT and related areas.

**Resources to develop the Center for Bioinformatics and Computational Biology:**

- Space: Approximately 10,000 sq.ft. in the proposed 120,000 sq.ft. IGSP building, Approximate cost $35 million (see Center for Genome
F. Center for Genome Ethics, Law, and Policy

Program description:

The Center for Genome Ethics, Law, and Policy will provide the infrastructure for faculty to develop programs that address the political and ethical consequences of the advances in genomic sciences. Accompanying the advances in the revolution in genomics will be equally complex and significant problems of addressing the way that society deals with them. The availability of detailed genetic information regarding an individual's state of health, and more importantly, an individual's future potential for disease, will be of great value to those that provide employment and insurance coverage. The challenge for society and the individuals that will lead us into the next century will be how to make use of these advances, to benefit the well being of the individual, while protecting the privacy of the individual.

Current status:

The development of the Center is in the planning stage. Currently includes E. Kiss (Director of Kenan Center), P. Cook (Sanford Public Policy), and members of the Center for Medical Ethics (J. Sugarman) within the Medical Center.

Resources to develop the Center for Genome Ethics, Law, and Policy:

- Space: Space to be determined within the proposed 100,000 sq.ft. IGSP building.
- Program development: Recruitment of new investigators into the Center.
- Director recruitment: Endowed chair ($2 million) and start-up funds
- Initial computational infrastructure: To be determined.
- Quasi endowment: To be determined.

Total cost: to be determined ($2.3 million already committed by SoM)

IGSP Area-specific "Centers/Institutes of Excellence"

Following this framework for the IGSP, we present the five major areas of research opportunity that derive from the School of Medicine strategic plans together with descriptions for how each of these areas of focus will integrate with the infrastructure of
the IGSP and with programs from within the University.

A. Cancer Genetics/Genomics

The Medical Center and Cancer Center leadership recognize the importance of and opportunities for advances in the understanding of cancer through the application of genetic and genomic analysis to enhance cancer diagnosis, prevention, treatment, and drug development. Opportunities to enhance clinical evaluation and treatment are illustrated by current examples of genetic characteristics of tumors in leukemia and breast cancer predicting a poor prognosis and the necessity for more intense therapy. Recent advances in the use of gene expression analysis, using DNA microarrays as well as SAGE analysis, for more precise characterization of tumor phenotypes offers the promise of developing molecular phenotypes that predict clinical outcome.

It is apparent that the application of genetic and genomic technologies of the characterization of tumor oncogenes and cellular mechanisms of resistance will continue to lead to improvements in treatment. In addition to genetic alterations intrinsic to tumors, it is also clear that inherited variation in genes encoding drug metabolizing enzymes can alter the pharmacokinetics of the chemotherapy agents used and for clinical responses in these patients. The fact that these same enzymes also metabolize the hormonal agents used for the treatment of breast cancer emphasizes the potential importance of pharmacogenomics in the treatment of cancer patients.

Integration with the IGSP and other University components:

This "area center of excellence" within ISGP will contribute to the activities of both the Center for Human Genetics and the Center for Human Disease Models. Three faculty would be recruited in the development of the Center for Human Genetics, two within the newly created Division of Human Genetics and one in the Department of Genetics. One of the faculty recruited to the Division of Human Genetics would be recruited as Chief of the Division. Space would be provided within the Center for Human Genetics facility. The Division of Human Genetics together with the Center for Human Genetics would establish a translational laboratory for genetic screening for disease predisposition genes for human disease.

We also envision at least one additional recruit into a Cancer Genetics Program to be in the area of mouse genetics, developing mouse models for human cancers. This recruit might likely be appointed within the Department of Genetics.

This area will depend on genome technology developments that will be focused in the Center for Genome Technology and that will involve interactions with individuals in medical school departments but also the School of Engineering and the Department of Chemistry. In addition, bioinformatics activities focused in the Center for Bioinformatics and Computational Biology that will include investigators from ISDS, Computer Science, and Mathematics will be a critical component of these activities.

Resources to develop the Center: $4.5 million.

B. Cardiovascular Genetics/Genomics
Program Description: Duke has a long and rich history as a leader in cardiovascular medicine. The cardiology clinical database accumulated over the past twenty five years, and now enriched by the programs of the Duke Clinical Research Institute, represents a major and unique resource for cardiovascular studies, particularly those that apply genomic analyses for the identification of genes that affect disease onset and progression. Likewise, the School has strengths in basic studies of cardiovascular function and signal transduction pathways, along with the mouse model systems for the study of vascular function. With the recent recruitment of Dr. Pascal Goldschmidt, a premier geneticist, to head the Division of Cardiology and organize the Cardiovascular Center for Genome Sciences (CCGS), Duke is now poised to bring this array of resources and strengths into full force.

The focus of the center will be on the identification of gene variants that account for an increased susceptibility for common forms of heart disease, such as coronary artery disease and atrial fibrillation. The focus of most cardiovascular genetic programs in the past was on the identification of loci within the human genome that harbor rare mutations capable of driving infrequent disease processes. Our goal is quite different. We are looking for subtle variations in multiple genes, which as an aggregate create susceptibility for common forms of heart disease. Such effort requires the availability of high throughput technologies for the study of gene expression, the discovery of single nucleotide polymorphisms (SNPs), and genotyping experiments on very large cohorts. Not only are we searching for patterns of gene expression or gene variants that can help with risk stratification of our patients, but we also plan to use the information to select and target therapeutic strategies (pharmacogenetics). The type of approaches that will be implemented to achieve our goal will include the study of aging of cardiovascular tissues, in terms of gene expression and epigenetic alteration. As aging is a key determinant for the development of chronic diseases like atherosclerosis and atrial arrhythmia, its mapping will provide great insight into the genetic makeup of the susceptibility for these disorders. Another way to identify culprit modifiers will require genetic studies on animal models (mostly in the mouse) relevant to cardiac illnesses. The discovery of variants for key modifiers as well as generation of proof of concept via large genotyping experiments illustrates other methods that allow breakthroughs in cardiovascular genome sciences.

Integration with the IGSP and other University components:

The overall program for the Center for Cardiovascular Genetics will be very tightly integrated with the infrastructure of the IGSP. The analysis of vascular tissue to identify the gene expression patterns, critical to the discovery of the genes that impact on disease, is dependent on the newly developing genomic technologies of DNA microarray analysis fostered by the Center for Genome Technology and the Center for Bioinformatics and Computational Biology, Center for Ethics and the Center for Ethics, Law, and Policy. A particularly unique aspect of the Duke initiative in genomic studies, will play a critical role in the debate as to how this information is put to use through the development of genetic tests that identify an individual’s susceptibility to disease.

Need for program enhancement and development:

- We anticipate that a $5 million investment in this program, in
addition to approximately $4.7 million currently committed, will be critical to bring the program to a critical level so that competition for significant outside funding can be successful. The IGSP plan includes $4 million of this proposed new funding; another $1 million remains to be identified.

C. Microbial Pathogenesis and Host Defense

Program Description:

The last decade has seen the emergence and spread of a host of new infectious disease entities with serious consequences, and the CDC has started a journal called "Emerging Infectious Disease". The Duke Human Vaccine Institute was formed in 1993 to oversee the interdisciplinary interdepartmental development of programs/investigator teams to facilitate the development of vaccines for infectious diseases (HIV, malaria, TB, Hepatitis C), autoimmune diseases (Juvenile Onset Diabetes) and various cancers. Funding of this initiative will serve to develop programs in microbial pathogenesis at Duke, reinvigorate HIV research, begin a Hepatitis C pathogenesis and vaccine development program, and, as well, begin vaccine programs in malaria, tuberculosis, and juvenile onset diabetes.

In addition, an existing fungal pathogenesis group led by Joe Heitman in Genetics and John Perfect in Medicine, focus on the study of Cryptococcus neoformans pathogenesis, has become the premier group of its kind that combines clinical, molecular biology, and genetics expertise to the study of Cryptococcus. With the arrival of Fred Dietrich and the establishment of a major genome-scale DNA sequencing infrastructure, the group is poised to take the fungal pathogenesis program to an even higher level and to serve as a paradigm in the further development of pathogenesis programs at Duke.

The opportunity for development of these areas of excellence is further enriched by the recent decision to re-focus the Department of Microbiology on the development of programs in microbial pathogenesis. Thus, the ability to expand the initiatives described above can and should be in synergy with the plans for new development of Microbiology.

Human Vaccine Institute. The Duke Human Vaccine Institute (HVI), under the direction of Dr. Barton Haynes, is a multidisciplinary entity dedicated to performing the basic and clinical research required to make vaccines that will prevent and/or treat human diseases. Three types of diseases are amenable to vaccination: infectious diseases, autoimmune diseases, and cancer. A major goal of HVI is to bring new understanding to disease pathogenesis, new technology to vaccine development, and to develop new ways to treat and prevent infectious diseases, autoimmune diseases and cancer that are exportable to underdeveloped countries around the world.

Success in creation of the Human Vaccine Institute will be interactions with faculty from the Schools of Medicine, Law, and Bioengineering, and Departments of Mathematics and Chemistry, and Law, and Programs in Genetics, Ethics, and Public Policy. The Duke HVI will be "an area center/institute of excellence" in the ISGP, and as such, will comprise the programs for Host Defense/Microbial Pathogenesis Genome Sciences in ISGP.
Opportunities of the Duke HVI include platform technology discovered by the HVI investigators on how to make "adjuvants" or helper molecules for vaccines, such that powerful adjuvants are available for formulation with the Duke AIDS vaccine, and vaccines for a number of infectious diseases, as well as for a vaccine for juvenile onset diabetes. Duke scientists have been working on a vaccine for HIV, and vaccines for cancer for 15 years, and coupled with the new technology available, are poised to solve the most difficult problems and are primed for success. This effort is led by Barton F. Haynes, MD, an internationally known leader both in HIV vaccine development and in the study of the human immune system, who brings investigative talent and administrative leadership to the HVI.

**HVI Priority Programs for the Next 5 Years in Vaccine Development**

- **HIV-1.** The main priority of HVI is to develop a practical vaccine for HIV-1 infection.
- **Hepatitis C.** This is a rapidly spreading pathogen. Investigators will be recruited in the pathogenesis of Hepatitis C to make a Hepatitis C vaccine.
- **Mycobacterial diseases.** Investigators will be recruited in the pathogenesis of mycobacterial diseases, to begin a program in development of a vaccine for TB. TB is the most common disease world-wide, and a vaccine is desperately needed.
- **Parasitic diseases.** Investigators will be recruited to form a major program in parasitic disease vaccine development. These diseases include malaria, schistosomiasis, and filariasis.
- **Genomics and proteomics.** Investigators will be recruited for identification of both host and pathogen genes involved in host pathogen interactions. From this program will come a myriad of protein and gene candidates to target for manipulation of the immune system.

**Additional priority area candidates are:**

- Cytomegalovirus and *chlamydia pneumoniae*. These vaccines could be of use for prevention of heart disease and Alzheimer’s disease.
- For an autoimmune disease vaccine, the first priority will be a vaccine to prevent juvenile onset diabetes.
- For a cancer vaccine, Duke HVI members will focus on platform technologies including RNA transfection of dendritic cells for inducing immune responses to a myriad of tumor antigens as is being led by Dr. Eli Gilboa.
- A program will be begun with the School of Engineering to develop new microbiocides for sexually transmitted diseases—a desperate need to improve world health.
- A program will be begun with the Sanford School of Public Policy, the Kenan Program in Ethics, and the Schools of Law and Business to understand the policy, ethical and legal issues related to health care and vaccine rationing, trials and financing in order to ultimately learn the best and most cost-effective ways to provide vaccines and therapies to those who need them world-wide.
- **Fungal pathogenesis program.** One already well established program in microbial pathogenesis focuses on the molecular basis for...
pathogenesis of Cryptococcus, a particularly important pathogen in immunocompromised individuals. The opportunities in Cryptococcus are particularly attractive, in part due to the wealth of scientific investigation at Duke, and in part due to the fact that there is wide interest, particularly at NIH, in now focusing a concerted genomics effort on this organism including the determination of the complete genome sequence. This is a very multidisciplinary group involving clinical investigators in Medicine (Perfect, Cox, Alspaugh) and basic science investigators in Genetics (Heitman, Dietrich), Microbiology (Mitchell, McCusker), and Biology (Vilgalys).

Integration with the IGSP and other University components:

The Duke Human Vaccine Institute proposes to be the premier vaccine development group in the US and be dedicated to making practical, cost-effective vaccines for world-wide use. Success of the Duke Human Vaccine Institute will require close interactions and inclusions of existing and new faculty from multiple schools at Duke. The overall program for the Human Vaccine Institute will be integrated with the infrastructure of the IGSP. It will utilize the Center for Genome Technology and the Center for Bioinformatics and Computational Biology in IGSP. A program is planned in microbiocide development with the polymer group in Engineering and Bioengineering. Pathogenesis of microbial agents and animal models of cancer and autoimmune will be studied in the Center for Models of Human Disease. Disease predisposition genes to TB and other infectious agents will be mapped in the Center for Human Genetics. Social and ethical issues of vaccine use will be studied in collaboration with the Center for Ethics, Law and Policy. Collaborations have already begun with Tim Haystead of the Center for Chemical Biology in the Department of Pharmacology and Cancer Biology to use combinatorial chemistry and proteomics screening techniques to identify targets for malaria and other pathogen vaccine development.

Need for program enhancement and development:

- Although funding for ISGP will provide considerable infrastructure support for HVI efforts, and it is anticipated that outside funding from NIH and private sources will be available to support much of the ongoing work of the program, it is important for institutional funding of HVI for faculty recruitment, and to support the development of malaria, Hepatitis C and other vaccine development working groups, as well as to support the Cryptococcal pathogenesis working group.
- We anticipate that over the next 5 years, 5 new faculty will need to be recruited for HVI, and as well, funds for expanding ongoing efforts is needed in order for HVI investigators to be competitive for outside funding. These efforts will require $4 million for faculty recruitment and $1 million for programmatic development. The IGSP plan includes $2 million for the HVI; $3 million needs to be identified. These funds would allow for the recruitment of 3-5 thought-leaders as program leaders and for the rapid application of genomics and proteomics technology to vaccine development for 3-4 infectious agents and juvenile onset diabetes.

D. Neuroscience and Brain Imaging
Program Description:

With the development of the Department of Neurobiology into one of the premier neuroscience units in the country, together with the success of the Center for Human Genetics in the study of neurogenetic disorders, including the discovery of APOE-4 genes that predispose to Alzheimer’s disease, Duke has moved to become a national leader in neurobiology research. The Program for Neuroscience, centered in the Department of Neurobiology as well as the Division of Neurology in the Medical Center, is now growing to include the Center for Cognitive Neuroscience and the Brain Imaging and Analysis Center. Inclusion of the Center for Cognitive Neuroscience (CCNS) under the direction of Ron Mangum has greatly enhanced the opportunities for both classroom and laboratory training in Cognitive Neurosciences. Although Ron Mangum has only been at Duke two years, he clearly has the energy and vision to create a very strong program in Cognitive Neurosciences that will dovetail with the mainstream neurobiology that we now offer to graduate students. The program in Brain Imaging and Analysis Center (BIAC) under Greg McCarthy has now been running for three years, and has also rapidly grown to represent strengths that augment our ability to train our graduate students in this aspect of basic research and clinical neuroscience. The CCNS offers no specific graduate program at present, and will depend on a strong collaboration with Neurobiology and BIAC over the next few years to generate a cohesive program for students specifically interested in this dimension of neuroscience. The same situation applies to BIAC.

Brain functions are affected by genetic actors, by developmental and aging processes, and by interactions with the environment - both social factors as well as physical insults to the brain. The major target areas that are likely to be funded by NIH as per their strategic plan include: normal brain processes; the contributions of developmental and aging processes to brain and behavior and to neurological and behavioral disorders; brain organization and function, how these go awry in mental and neurological illness, and how they are affected by treatment; the role of genes in brain and behavior and in vulnerability to and protection against mental and neurological illness; interactions of the environment with brain and behavior and the role of environment in neurological, mental and behavioral disorders; the interactions of behavior with biological, social, and developmental factors and the effects on adaptive and maladaptive functioning; brain and behavioral processes in cognition and emotion. plasticity and neuronal repair.

E. Environmental Health Science and Toxicology

Program Description:

With the assistance of the late Dr. Charles Putman, Vice-Provost for Research Development, Barton Haynes (Chair of Medicine) and Norm Christenson (Dean of the Nicholas School of the Environment) created a Center for Toxicology and Environmental Health. They then recruited Dr. David Schwartz, the premier lung toxicology and environmental health geneticist in the US to Duke as Chief of the Pulmonary and Critical Care Medical Department and to be the Director of an interdepartmental center. Duke is poised to take a leading role in the growth of environmental programs that tap into the resources and expertise of investigators throughout the campus.

This opportunity is further enhanced by the development of genomic technology
within the IGSP that has now provided the infrastructure for building programs in environmental genomics. With this infrastructure, and the expertise in environmental science, Duke is in a strong position to partner with the NIEHS to meet the goals of the Environmental Genome Project.

The theme of the Center is to understand the effect of environmental exposures and global climatic changes on human health. This will be accomplished by establishing an interdisciplinary Center that encourages the use of complementary biologic systems (humans, mice, drosophila, worms, and zebra fish) to investigate the role of genetic susceptibility in the pathogenic response to environmental toxins and global climatic changes. This approach will enable us to develop and investigate environmental models of human disease that represent biologically unique gene-environment-pathophysiological phenotypes. Environmental exposures and genetic engineering will be used to examine pathogenic mechanism that are relevant to environmental lung disease, neurodegenerative diseases, and developmental disorders.

The recent advances in human and molecular genetics has provided an unparalleled opportunity to understand how genes and genetic changes interact with environmental stimuli to either preserve health or cause disease. Our rapidly changing global environment as well as space and exploration highlights the importance and urgency of this research program. The proposed Center will build on the strengths of investigators in the School of Medicine, the Nicholas School of the Environment, the School of Law, the Pratt School of Engineering, the Divinity School, and the Arts and Sciences College to create a multi-disciplinary program focusing on the genetic factors that underlie susceptibility/resistance to environmental stress. The Center will serve as a technical and scientific resource to advance the understanding of environmental genetics for the state, region, nation, and international community.

**The Center For Toxicology and Environmental Health** will be an "area center of excellence" within the IGSP, and will include four scientific cores (pulmonary biology, neurotoxicology, developmental biology, and bioethics) and six research facilities (exposure assessment, disease modeling, climate sciences, gene discovery, bioinformatics and biostatistics, and training). This Center will interface with the other Centers in the IGSP through joint scientific ventures and by working with the other Centers to recruit faculty, allocate space, identify equipment needs, and train students and faculty. It will interact extensively with each of the centers in IGSP.

**Need for program enhancement and development:**

The Center for Environmental Health and Toxicology will need institutional support to become sufficiently functional to compete for grants from NIEHS and the EPA as well as the NSF. In addition new faculty and new cores within the center need to be funded. There will be at least three new faculty recruited, as well as programmatic support needed for the cores listed above. We anticipate that **$4 million** are needed for faculty support and **$1 million** needed for core programmatic support. $3.7 million of this proposed program is described in the IGSP Plan for Environmental Genetics. An additional $1.3 million needs to be identified.

**F. Protein Analysis Infrastructure**
We anticipate that the critical infrastructure to support much of the activities of these programs will be provided by the development of the Institute of Genome Sciences and Policy. In particular, the further development of resources for human genetics, the development of facilities for mouse models, the genome technology infrastructure, and programs in bioinformatics will be critical for these scientific initiatives. But, we also recognize that one area critical for much of this work is currently under-developed and must be enhanced. This involves the proteomics core activities that provide state-of-the-art capability for protein analysis. We are fortunate to benefit from the recruitment of Dr. Tim Haystead into the Center for Chemical Biology and the Department of Pharmacology and Cancer Biology. Haystead brings enormous talent and expertise to the analysis of proteomes and the application of novel protein detection technology that will enormously enhance the activities of these programs. But, this enterprise must also be further developed enhanced in order to meet its full potential.

We propose that the proteomics program directed by Tim Haystead should be further developed within the context of the Center for Chemical Biology with this Center potentially becoming one of the key infrastructure Centers of the Institute of Genome Sciences and Policy. Further development of the Center for Chemical Biology will provide the technologies to advance proteomics at Duke University, development that will enhance programs outlined here but also a variety of other programs in both the School of Medicine and the University. As such, this will require the combined involvement of the schools of Medicine and Arts and Sciences and Engineering that will include investigators in Engineering, Chemistry, Bioinformatics/Biostatistics and Pharmacology.

Given the relationship of technology development in both the Center for Genome Technology as well as the Center for Chemical Biology, and the close interaction of both of these activities with the Bioinformatics programs, it might be most advantageous to locate the technology development components of the Center for Chemical Biology within the proposed new IGSP building together with these other two Centers.

The Center for Chemical Biology will bring two novel and advanced proteomics technologies to work in two project areas.

- **Proteome profiling of normal and diseased tissues**: It is now generally recognized that the underlying molecular mechanisms that cause cancer, diabetes and hypertension all involve inappropriate protein phosphorylation. When these protein modification data are combined with protein identification, it will be possible to connect the phosphoproteome directly to the genome and in doing so enable us to define the molecular mechanisms that underlie human diseases such as cancer, diabetes and hypertension.

- **Proteome mining: drug and target discovery en masse.** The proteome mining technology Tim Haystead has developed at Duke represents a paradigm shift that will revolutionize drug discovery. Briefly, the technology utilizes affinity arrays containing natural ligands to maximally extract all novel drug components from large combinatorial chemical and phage display peptide libraries as well as to identify their physiological targets en masse. The technology is unique in that it combines the power of combinatorial chemistry with state of the art microsequencing and the Genome projects. The targeted genomes in this project will be those of the Malaria organism and the host human genome, with the aim of discovering new anti-malarial agents and developing a vaccine for malaria in...
collaboration with investigators in the Human Vaccine Institute. These projects are predicted to have massive humanitarian impact in the third world. To put proteome mining into effect at Duke we require the combined efforts of chemists, engineers, clinicians, immunologists, cell biologists, and bioinformatic/biostatisticians.

In addition, the activities of the Center will further enhance technology development and research activities in several addition ways including novel chemistry and engineering development. Also the Center is seeking expertise to develop new sequencing algorithms for automated protein sequencing by mass spectrometry and Edman sequencing.

Summary

The Duke School of Medicine proposes to initiate six interdisciplinary, interdepartmental initiatives over the next 5 years in **Cancer Genomics**, **Cardiovascular Genomics**, **A Proteomics Technology Center**, **the Human Vaccine Institute**, **Programs in Neurobiology and Environmental Health and Toxicology**. Funding these initiatives will enrich the infrastructure for all Duke University Programs, and position Duke to research national preeminence in genomic and proteomic biomedical research. The highly integrated nature of all six of these programs will reaffirm the School of Medicine’s progress to full integration with schools and programs university-wide. Moreover, Duke investigators will be well-positioned for the future to be world leaders, and to compete for sponsored research support in order to develop new drugs, vaccines and diagnostic tools for society’s major problems.

Investments Needed For The Strategic Agenda

A Sources and Uses Document has been developed which outlines the investments needed in faculty and programs to achieve the goals described above and the sources of the funds for these initiatives. This document also includes investments committed to existing as well as new programs.

In addition to these investments in people and programs, a commitment has been made by the School of Medicine to establish a Center for Human Disease Models through construction of a 121,000 gross square foot addition to the current vivarium. A commitment has also been made to construct a new 130,000 gross square foot building to house the Center for Human Genetics and incremental wet and dry laboratories for other programs. Assuming the Institute for Genome Sciences and Policy (IGSP) continues on its present course, it is anticipated that an additional 120,000 gross square foot research building will be needed within the next four years to accommodate this initiative. While the IGSP is a university-wide initiative, the SOM hopes to be a major contributor and beneficiary of the IGSP. To accommodate these two centers, the IGSP and the incremental faculty and staff related to these programs, it is anticipated that 1,200 new parking spaces will be needed.

In addition to this new construction, the Nanaline Duke research building is in need of significant renovation. We anticipate renovation of this building in two to three phases, beginning in 2002. Upgrades to the second floor of the CARL Building, General Clinical Research Center, and several other SOM buildings are anticipated in the next five years.

Recognizing the opportunities for growth in biomedical research and the potential for
new sources of government and non-government funding, we anticipate that a fourth new research building of approximately 200,000 gross square feet will likely be needed sometime after 2005. Funding for this potential building need has not yet been identified.

**Summary of Proposed New Facilities**

– Center for Human Genetics

$30__ million, 130,000 GSF, 75,000 NSF

– Center for Human Disease Models (construction cost only)

$31__ million, 121,000 GSF, 70,000 NSF

– Renovate existing space, i.e., Nanaline Duke Building and other buildings

$54__ million, (known projects in long term financial plan, including the Nanaline Duke renovation. Additional renovation needs have not yet been determined and funding has not yet been identified beyond the planned $54 million).

– New Biomedical Research Building (IGSP)

$35__ million, 120,000 GSF, 70,000 NSF

– New parking structure

$10__ million, 1,200 cars (part of the construction cost will be recovered over time via parking fees)

**Summary of Projected Return on Investments:**

- **Advanced degrees earned by over 50% of medical students**

- **Enhanced research funding**
  - Funding per Principal Investigator: top 5 in AAMC ranking
  - NIH ranking: 11 to 6

- **Enhanced faculty recognition**
  - 5 new members elected to National Academy of Sciences
  - 8 new members elected to Institute of Medicine

- **Enrichment of academic programs in other schools in the University**

**Financial Planning**

Financing will be a challenge, but through conservative planning it should be possible to
make the investments needed to keep Duke among the top academic medical centers in the nation. Financial support from the Duke University Health System and the Private Diagnostic Clinic is and will continue to be important, but market forces limit this source of revenue. Our clinical faculty is working harder than ever to maintain clinical revenues, and this source of support for academic programs is not envisioned to increase. Our current faculty is quite productive in securing extramural funding, but we believe we can do better and have projected an increase in grant support that should be attainable, if they are provided the appropriate infrastructure support from the School. Additional external funding must be identified to implement this strategic plan. Sources of additional external funding include the growing NIH budget, industrial partnerships, venture capital, intellectual property, and philanthropy obtained through the current University-wide campaign.

The entire strategic planning initiative – faculty recruits (4 chairs, 15–20 tenure track faculty per year, and 5 incremental faculty per year), programs (Advanced Degree, DCRI, IGSP, Integrative Biology, Bioengineering, and Translational Medicine), and facilities (two new centers, renovations of existing space, new research building, and parking structure) – are estimated to cost approximately $450 million. The funding sources for these proposed investments will be the Long Term Financial Planning Reserves of the School of Medicine (including the Health System transfer), University funding of $60 million or more, anticipated major gifts for the IGSP building and specific IGSP programs.

Implementation of this strategic plan must be done in conjunction with academic initiatives being developed in other schools and critically important is a tight interface between this plan for the School of Medicine and that being developed by the Duke University Health System. The mission of the SOM is inextricably linked to that of DUHS. Not only does the SOM receive most of its investment capital from DUHS, it must have access to the diverse patient population provided by DUHS to carry out its clinical teaching and research missions. Much of the support which the clinical faculty generate to cover their salaries also requires that DUHS continue to be successful.

As reviewed in the introduction to this document, the SOM faces many challenges but there are extraordinary opportunities as well. We believe that a strategic plan along the lines described in this document will enable Duke University School of Medicine to not only maintain its current preeminent position among academic medical centers in the world but to enhance its contributions and the stature of this University as one of the leading research-intensive institutions of higher learning in the country.