

BACKGROUND

1. Historical Perspective: The Mount Sinai Predoctoral and Postdoctoral Training Program in "Mental Retardation and Developmental Disabilities" began under the directorship of Dr. Kurt Hirschhorn (1967-1977) and is currently in its 35th continuous year of NIH support, under the directorship of Dr. Robert J. Desnick (1977-present). The training program was initially provided through the Division of Medical and Molecular Genetics at the Mount Sinai School of Medicine, which then became the Department of Human Genetics in 1993. The Mount Sinai School of Medicine has continued to undergo remarkable progress in the development of research and clinical programs, as well as in faculty recruitment. This has had an important, positive impact on the recruitment and training of our predoctoral and postdoctoral fellows. For example, in the past five years, Mount Sinai has seen the completion and full occupation of a new research facility, the East Building, and the development of extensive new core and animal facilities to support the expanded research. This has led to the addition of over 100 new faculty in our School of Medicine. There have also been sweeping changes in the medical school and graduate school curricula, an affiliation with New York University, and the development of multidisciplinary training programs designed to take advantage of the new research initiatives. Mount Sinai now ranks 24th in NIH research funding among 124 medical institutions. The training program in "Mental Retardation and Developmental Disabilities" has benefited substantially from these developments, particularly the recruitment of many new research faculty who are eager to train students and who are employing state-of-the-art technology to investigate critical scientific questions related to the molecular basis of mental retardation and developmental disabilities, developmental neurobiology, and molecular-based therapies.

2. Training History and Synopsis of the Current Program: The Program Director and many of the faculty have had long and successful experiences in training predoctoral and postdoctoral fellows in human genetics, biochemistry, molecular biology, neurobiology, and related fields. Currently, our training program has 11 predoctoral and 33 postdoctoral (14 M.D., 15 Ph.D., and 4 M.D./Ph.D.) fellows. Although the number of highly qualified applicants for predoctoral and postdoctoral positions has decreased nationally in past years, there has been a recent upturn in quality domestic applicants to Mount Sinai. We have been able to recruit outstanding trainees, in part due to our geographic location, well-known faculty, and excellent track record. We anticipate an increasing number of qualified applicants will enter our MRDD training program, particularly since advances in molecular and clinical genetics and neurobiology have made such important progress in delineating the etiologies of MRDD. In addition, we expect that the recruitment of Dr. Frederick Suchy as the Chairman of Pediatrics (Dr. Kurt Hirschhorn stepped down after 25 years as Chair), and the addition of several other outstanding new faculty to our training program will attract even more outstanding applicants. In the past four years alone, 25 new faculty appointments have been made in the Department of Human Genetics and the Institute for Gene Therapy and Molecular Medicine, bringing additional expertise in genomics (Drs. Diaz and Martignetti), gene delivery systems (Drs. Branch, Linden and Snoeck), structural biology and proteomics (Drs. Bromme, Aggaral, Wong and Zhou), as well as immunologic correlates of gene therapy (Dr. Jonathan Bromberg) and stem cell biology (Drs. Keller and Snoeck). Currently, there are 32 primary and 11 secondary faculty in the Department of Human Genetics, 10 primary and 12 secondary faculty in the Institute for Gene Therapy, and 16 primary and 12 secondary faculty in the Fishberg Center for Neurobiology.

In the past, more than 100 predoctoral students were supported by this grant and most have gone on to academic positions. In addition, more than 100 postdoctoral fellows have been supported and many now hold positions at various ranks including professorships, division chiefs, and chairmanships. Therefore, this training program has produced numerous, qualified researchers and physician/scientists with genetics expertise in the area of mental retardation and developmental disabilities.

3. Institutional Commitment to Training: The Mount Sinai Medical Center has a long and distinguished tradition of excellence in clinical and basic research, as well as in education and training. In 1963, the Board of Regents of New York State chartered The Mount Sinai School of Medicine. After affiliation with the City University of New York (CUNY) in 1968, the Mount Sinai School of Medicine established the Graduate School of Biological Sciences, which administered the Biomedical Sciences Doctoral program under the aegis of CUNY. This affiliation with CUNY provided access to a full range of university facilities, courses in diverse disciplines, and important faculty and graduate student support. More recently, in 1999, the Mount Sinai-New York University (NYU) Health Care System was established, and the Mount Sinai School of Medicine relinquished its CUNY affiliation and became affiliated with NYU, as a completely separate medical school within the same university as the

NYU School of Medicine. Today, all predoctoral students at Mount Sinai receive their Ph.D. degree in Biomedical Sciences from the "Mount Sinai School of Medicine of New York University". The administration of the Mount Sinai Ph.D. program (e.g., recruitment, admissions, course curriculum, etc) continues to remain entirely at the Mount Sinai School of Medicine, although the academic benefits from the NYU affiliation have been considerable. These include: i) the development of multi-institutional training programs; ii) an integrated and funded (P20) program in computational biomedicine that involves numerous members of Mount Sinai's Graduate Faculty in a joint program with the stellar mathematics faculty of the NYU's Courant Institute; iii) a relationship between faculty in Mount Sinai's Biophysics, Structural Biology, and Biomathematics training program with the excellent faculty in chemistry and physics at NYU Washington Square; and iv) the development of an interdisciplinary program in functional genomics between the Institute for Genomic Sciences at Mount Sinai (see below) and faculty in the Departments of Biology and Anthropology and the Courant Institute at NYU Washington Square. It should also be noted that Mount Sinai School of Medicine has retained important ties with CUNY, (e.g., with its Engineering program) and continues to be highly interactive with other institutions such as the Museum of Natural History and New York Botanical Gardens in support of specific programs in genomics and in tissue-based research.

Since 1968, over 300 students have earned Ph.D. degrees from our Graduate School. Our predoctoral trainees receive their Ph.D. degrees in Biomedical Sciences with specialization in areas such as Human Genetics, Neuroscience, Molecular Biology, Cell Biology, Physiology and Biophysics, Molecular Pathology, Pharmacology, Biochemistry or Biomathematics. Mount Sinai provides a major proportion of the Biomedical Sciences intramural fellowship support, offers a full range of graduate courses, including all required and many elective courses, and provides the amenities of student life on the Mount Sinai campus. Currently, 190 students are enrolled in the predoctoral program of the Graduate School. In addition, in the early 1970's the Graduate School of Biological Sciences and the Medical School instituted an M.D./Ph.D. program that has continuously received NIH Medical Scientist Training Program awards since 1977. This highly competitive program has graduated 85 students, and currently has 57 students enrolled in its rigorous research training program. The Mount Sinai School of Medicine and the Graduate School of Biological Sciences also provide specialized clinical and basic science training to over 330 MD and PhD postdoctoral fellows, many funded by various NIH and Foundation training grants.

4. Expansion of the Basic Science Programs at Mount Sinai: Consistent with the strong tradition of research and training at Mount Sinai, and recognizing the critical necessity of collaboration between the clinical and basic sciences, the Dean of the School of Medicine has made a major commitment during the past decade to further the development and growth of the basic sciences in the Medical School. Recognizing the essential roles of molecular biology, neurobiology and immunology in providing the foundation for medical progress in the 1990's and into the 21st century, the School of Medicine created Centers of Excellence for basic research in 1988 which included: The Fishberg Research Center of Neurobiology (Dr. John Morrison, Director), The Brookdale Center for Molecular Biology (Dr. Paul Wasserman, Director) and the Center for Immunobiology (Dr. Lloyd Mayer, Director). These Centers were further complemented by the establishment of the Institute for Gene Therapy and Molecular Medicine (Dr. Savio Woo, Director), the Institute for Computational Biomedicine (Dr. Harel Weinstein, Director), the Ruttenberg Cancer Center (Dr. Stuart Aaronson, Director), and the Department of Human Genetics (Dr. Robert Desnick, Chairman). Moreover, in recognition of the essential role of computational resources in the future of clinical and basic medical sciences (e.g., DNA informatics, linkage analysis, structural biology), the Institute for Genomic Sciences was recently established and is directed by Dr. Robert Desnick. These initiatives provided resources for the renovation of space and development of core facilities, including construction of a Good Management Practice (GMP) facility for the support of research projects focused on the development of molecular therapeutics. The establishment of these new programs has fostered an even greater interaction between the clinical and basic science faculty leading to numerous cross faculty appointments between Departments and Centers, and strong collaborations between physician/scientists and basic scientists that will facilitate translational research efforts.

Thus, Mount Sinai's academic mission has been continually fostered by a commitment to the growth of its biomedical research establishment. This commitment has been demonstrated by the completion of the East Research Building in 1996 which provided 225,000 sq ft of additional laboratory space, and afforded the opportunity to recruit over 100 new faculty, many of whom have been added as preceptors for this training program in such areas as structural biology, neurobiology, gene therapy, human genetics, signal transduction, bioinformatics, immunobiology, stem cell biology and developmental biology. Indeed, the success of its faculty recruitment and its increasing prestige as a

Medical School and premiere research institution, led Mount Sinai to formulate and adopt a new Strategic Plan in 1999. The centerpiece of this plan, which has been approved by the Trustees, is the construction of a new Translational Research Building which has been designed to provide the ideal setting for bringing scientific developments from the bench to bedside and back. The building will house an outpatient Clinical Research Center, imaging and large animal research facilities, and extensive laboratory space. To maximize interactions among clinical and basic investigators, each basic laboratory floor will also contain workspace and offices for clinical investigators. These changes should continue to significantly impact on our ability to recruit outstanding trainees to our programs.

5. Establishment of the Institute for Genomic Sciences: Pertinent to this application, in 2001 Dr. Robert J. Desnick was appointed the Director of the newly established Institute for Genomic Sciences. This institute was created in anticipation of the impact that the post-genome era will have on biomedical research, and will facilitate the study of genes and the function of their protein products in health and disease. This Institute will support basic and translational research in comparative functional genomics, human molecular evolution, predisposition/susceptibility to pathogens, pharmacogenetics, the identification of genes underlying common diseases and complex traits, and in particular, genes involved in MRDD. Such studies will involve the interaction of scientists and physicians in many disciplines including computational biology, molecular genetics, neurobiology, psychiatry, structural biology and medicine. The Institute will be composed of current faculty and newly recruited individuals who will have membership in the Institute, and a primary appointment in a Department or Center. New faculty will include genetic epidemiologists, pharmacogeneticists, complex trait experts, and molecular evolutionists. Important interactions will be established with the faculty and programs of our Institute for Gene Therapy, the Rutenberg Cancer Center, and the recently established Institute for Computational Biomedicine. In addition, to enhance the Institute's research and educational programs, adjunct appointments have been offered to faculty with genomics expertise in the Courant Institute and the Departments of Anthropology and Biology at New York University, at the American Museum of Natural History, and at the Biology Department at University College London. The Institute will sponsor a monthly seminar series, a monthly "Research in Progress" seminar, and a graduate survey course in "Genomic Science", and more advanced courses in specific topics in genomic sciences. Graduate training in genomic sciences will be in conjunction with the predoctoral program in "Genetics and Genomic Sciences", and other graduate programs in the Graduate School of Biological Sciences at Mount Sinai (see below). The Institute's mission will focus on basic and applied research in genomics and genomic medicine. Specifically, the Institute will conduct: 1) research to identify individual genes, determine the function of their protein products, and elucidate how they interact in executing simple and complex biologic processes; 2) applied research to identify the genes involved in common diseases and complex genetic traits for the development of improved diagnostics and rationally designed novel therapies; and 3) research focused on the ethical, social and legal implications of genomic science.

6. Establishment of the Institute for Computational Biomedicine: The Institute for Computational Biomedicine (ICB) was established within the Mount Sinai School of Medicine in 2000. The faculty of the Institute engages in research and education in Bioinformatics and Computational Biology. The ICB is designed to foster interdisciplinary activities in all areas of modern biomedicine, to which it will bring approaches from applied mathematics, computer science, and computer-based technologies. The ICB promotes core research in bioinformatics, computational biology, and applied mathematics that is directly related to biomedical research and translational aspects in medicine. In addition, it is involved in the development of novel computational research tools in bioinformatics, computational biology, modeling and simulation of integrative biological systems (macromolecular systems, cells, tissues, organs and entire organisms). This institute assists our MRDD faculty and trainees in many aspects of their research, and provides numerous educational opportunities in computational biology and bioinformatics.