

The Skirball Institute of Biomolecular Medicine: An Infant among Giants

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The New York University School of Medicine has a long and proud history of accomplishment in research, education, and patient care. It counts among its graduates Dr. Walter Reed, the conqueror of yellow fever, and Drs. Jonas Salk and Albert Sabin, who developed vaccines for the prevention of poliomyelitis. In the 1960's and 70's, its faculty, with Severo Ochoa in Biochemistry, Lewis Thomas in Medicine, and Howard Green and Baruj Benacerraf in Pathology was renowned worldwide. Notable among its post-doctoral students at that time were Marianne Grunberg-Manago, Charles Weissman, and Piet Borst.

Recognizing the growing importance of basic research, the School of Medicine, under the leadership of its dean, Dr. Saul Farber, set out nearly a decade ago to again enhance its basic biomedical science program and to bolster its support of research. The resulting Skirball Institute adds a new expanded, strongly interdisciplinary dimension to the connection between molecular biology and medical research. The Institute's name derives from the Skirball Foundation, which was established in 1950 and contributed the original installment of the endowment for the institute. Mr. Jack Skirball, a rabbi from Philadelphia, resigned from the rabbinate and became a successful film producer, which led to the establishment of a foundation in his name.

The Skirball Institute of Biomolecular Medicine opened its doors in October 1993, with its first recruits joining the institute during 1994. The Institute (Fig. 1), encompassing 60,000 square feet of laboratory space divided over four floors, focuses mainly on basic research but provides both core facilities and interaction between the clinical disciplines and the activities in basic science at the New York University Medical Center. With a strong awareness that most medical breakthroughs originate in basic research, the medical center has allocated considerable re-

sources to developing a state-of-the-art, modern, interdisciplinary research unit right in the center of the medical school environment.

A decision was made to focus the research effort at the Institute on three programs devoted to Developmental Genetics, Molecular Pathogenesis, and Molecular Neurobiology. Each of these research programs contains two senior scientists functioning as coordinators for the programs and seven to eight junior faculty recruited at the level of assistant or associate professor. One floor has been reserved for Structural Biology, including crystallography, and to groups devoted to technological developments in protein and DNA chemistry. Units for high resolution electron microscopy, confocal, ultrasound, and MRI microscopy, as well as biocomputing have also been included on this floor. These groups directly interact through collaborative projects with the faculty in the Skirball Institute and with several scientists in the basic science and clinical departments of the medical center for which these resources are essential.

The Institute is governed by a Steering Committee selected from representatives of the medical school faculty in both the clinical and basic sciences, with the dean of the Medical School participating in the meetings. In addition, the recruitment as well as the evaluation of the research progress is governed by a Scientific Advisory Board of highly respected scientists from within the United States. As of Spring 1997, 30 principal investigators have been recruited from the outside to the Skirball Institute of Biomolecular Medicine. The programs for Developmental Genetics and Structural Biology are now fully occupied. Additional positions are available in Molecular Neurobiology and Molecular Pathogenesis, and we are currently completing the last recruitment drive to fill the Institute. When complete, the Institute will house around 40 investigators, 140 postdoctoral fellows, and 80 graduate students, and sufficient technical and administrative staff to fulfill its mission. We contemplate a total budget of around \$20 million per

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FIG. 1. The Skirball Institute of Biomolecular Medicine.

annum at steady state, of which at least 70% must be secured through outside federal or foundation support.

Collaboration and interaction is a founding principle of the Skirball Institute. All equipment that can be shared must be shared, and interdisciplinary interaction between several different technical skills is the principle for the recruitment to the different programs. Twice a month, the Skirball Institute lunch lectures (SKILL), in which the postdocs and students discuss their research with all scientists in the programs present. The core facilities are now fully operational, with shared equipment for peptide synthesis, DNA and protein sequencing, biocomputing, electron microscopy, imaging, and confocal microscopy. Facilities for embryonic stem (ES) cells and transgenic mice are also available.

Some notable breakthroughs have already emerged, such as Dr. Steven Burden's analysis of the important molecular interactions in the development of the synapse between nerves and muscles, which also involves a molecule identified in his laboratory. Dr. Dan Littman, coordinator of the Molecular Pathogenesis Program, has located two important receptors by which HIV is taken up by T-lymphocytes and macrophages. In the Developmental Genetics Program, Dr. Alexandra Joyner has found, together with Dr. Cindy Loomis from the Department of Dermatology, a new role for the engrailed gene in signaling the dorsal-ventral axis in limb development. Dr. Dan Turnbull, together with Drs. Gordon Fishell and Alexandra Joyner, has taken advantage of high-resolution ultrasonography, developed at the Skirball Institute in the Structural Biology Program, to perform for the first

time microinjections of cells and retroviruses directly into early mouse embryos in utero. In the Structural Biology Program, Dr. Stevan Hubbard has contributed an elegant and thorough analysis of the tyrosine kinase domains in both the insulin and the FGF receptors. While joining the Skirball Institute, Dr. Ruth Lehmann reported on a new gene critical for germ cell development, and Dr. Joel Belasco identified new RNA binding domains in the HIV Rev protein.

The challenge of creating a state-of-the-art interdisciplinary center right in the midst of a classical medical school, with its traditional department structure, has been successfully met in the establishment of interactions that are closer than those in many other newly formed biomedical institutes. Each recruit at the Skirball Institute receives a primary appointment in one of the existing departments and a secondary appointment and laboratory space in the Skirball Institute. In our current recruitment effort we support the interdisciplinary principle by, for instance, bringing together experts from cell biology, immunology, bacteriology, and virology into the Molecular Pathogenesis Program, so that the research environment is truly interdisciplinary, but the assignments of the individual investigators' primary appointments respect the natural department borders. The Developmental Genetics Program likewise covers expertise in *Drosophila*, zebrafish, frog, and mouse systems. The group leaders thereby interact with their department for graduate and medical school teaching, but profit from an interactive environment and all the core facilities at the Skirball Institute.

The precise contributions that molecular medicine will make for humankind in the future cannot be predicted, but if the past is prologue, then the ceaseless progress of scientific research tells us that molecular medicine might help to find remedies for many diseases that now have none, will prevent disabilities that are now unavoidable, and will ease pain that must now be endured. Many of

these advances, unforeseen and unimaginable today, will begin by creative insight and collaborative efforts by teams of biomedical researchers. The New York University School of Medicine has developed the Skirball Institute to strengthen its base in biomolecular research and might, thereby, be in a favorable position to provide remedies for several debilitating diseases in the future.