1982

The Rockefeller University Hospital: Environment for Discovery

The Rockefeller University

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A NEWCOMER to The Rockefeller University campus on Manhattan's upper East Side would have some difficulty identifying the Hospital. Only the decorative use of the caduceus on the red brick exterior furnishes a clue. Otherwise the Hospital shares the architectural features of the older buildings on campus, built in the opening decades of this century after the founding of the University in 1901 as The Rockefeller Institute for Medical Research. The Hospital's physical integration into this compact cluster of buildings is symbolic of its traditionally close relationship to the institution as a whole, one of the few in the world today engaged exclusively in scientific research and graduate education in the biomedical sciences and in related behavioral and physical sciences.

A Pioneer in Biomedical Science

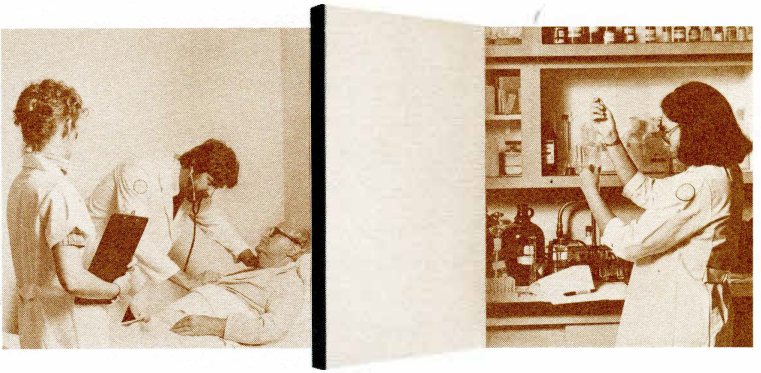
The Rockefeller Institute was established by John D. Rockefeller, Sr., in response to the pressing need for biomedical research facilities in this country. At that time, young American physicians bent on scientific careers went to Europe to obtain laboratory training. The objective of the new institute was to benefit mankind through basic research and its application to the understanding, treatment, and prevention of disease. In carrying out that objective, The Rockefeller has been a major force in bringing the United States to the forefront of the biological and medical sciences. It has also served as a model for the establishment of similar research centers. From its beginnings, scientists have been attracted to the institution from all parts of the world, and many young M.D.'s and Ph.D.'s have come here for advanced training. In 1954, the Institute became a graduate university, and the first Ph.D. degrees were granted in 1959. In 1965, its name was changed to The Rockefeller University.

Compared to general purpose universities, this insti-

tution is modest in size. Its 15-acre campus is the base for a scientific community of about 1,450 people—250 regular faculty, 200 postdoctoral fellows and research associates, 100 graduate students, and a staff of about 900, including laboratory technicians, nurses, instrument makers, electronics specialists, and other supporting and administrative personnel.

A Wide Freedom of Inquiry

The University has an administrative structure built around more than 50 laboratory groups, a few comprising a single scholar and the rest ranging from groups of 3 to more than 35 persons, including students. Although the laboratory groups represent a great diversity of scientific fields, from theoretical physics to behavioral science, individual investigators are encouraged to cross disciplinary lines and pursue overlapping interests with their colleagues in other groups. There are no traditional departmental boundaries. Rockefeller scientists enjoy a wide freedom of inquiry and set their own research goals. Out of this unique organization has come a series of achievements that, directly or indirectly, have benefited the lives of people throughout the world and have influenced the development of some of the most important fields in the life sciences.



THE ROCKEFELLER HOSPITAL has the same organizational flexibility as have the other University laboratories and, since 1910 when its doors were first opened to patients, it has operated in exactly the same spirit. Rufus Cole, its first director, insisted that the Hospital should be staffed by full-time salaried physicians working in their own laboratories, but strongly supported by and free to collaborate with the other institutional laboratories. Cole believed the real purpose of a research hospital was to attempt to understand the normal physiological characteristics of human beings, in order better to analyze the derangements that occur in disease. In 1910, these were original concepts: The Rockefeller Hospital was the first clinical research institution where human disease could be studied and treated in a setting of rigorous, scientific inquiry.

This unique approach to clinical research made the Hospital the pacesetter in revolutionizing academic medicine in America. Its impact was critically important in upgrading medical education at a time when many medical colleges were no more than trade schools. Most of the medical school leaders who moved for reform had served "apprenticeships" in clinical research at The

Rockefeller Hospital. For seven decades, successive generations of clinical researchers have come to the Hospital for advanced training and have moved on to influential positions in other institutions.

In the 1950s, the 40-bed Hospital served as an organizational model for the federally supported Clinical Center, with 500 beds, that was established by the National Institutes of Health in Bethesda, Md., as well as for the smaller clinical research centers set up, with federal funding, by more than 80 American medical schools.

Between Medicine and Biology

Infectious and nutritional diseases, which were the predominant lethal or crippling illnesses at the turn of the century, were a major focus of concern in the creation of the Hospital. Since then, the Hospital has stood at the gateway between medicine and biology. The basic, as well as the clinical, knowledge that has come from the research at the Hospital has dramatically demonstrated the importance of the direct study of disease in human beings.

Often the observation of disease led to a clearer understanding of life processes; out of this, such new scientific disciplines as genetics, cell biology, and immunology have emerged and reached their present major status. For example, the nature of bacterial virulence, a matter of continuing concern to the clinical investigator, spurred pioneering experiments in biochemical genetics, and an important discipline was born. Similarly, the prevention of infectious disease was the clinical objective that promoted the development of immunology; this led, in turn, to the discovery of a host of immune-based disorders. In still another area, the clinical study of pulmonary and kidney failure resulted in the invention of many basic, now-indispensable tools of biochemistry.

Perhaps the most dramatic example in the Hospital's

Entrance to the Hospital.

history of how the combination of basic and clinical research can produce results useful to the practicing physician and may also result in basic discoveries that significantly expand our understanding of the mechanisms of life is the work of Oswald T. Avery. He and his gifted associates were investigating the chemistry of the pneumococcus, causative factor of lobar pneumonia, when they demonstrated for the first time that DNA is the genetic material. Their finding, published in 1944, has been considered the central discovery of twentieth-century biology.

Focus on Clinical Investigation

Today The Rockefeller University Hospital is the largest and the only private facility in the country that is devoted exclusively to clinical investigation. Its staff consists of about 10 percent of the University's senior faculty members and their colleagues. The 40-bed unitlogs about 9,000 inpatient days each year, as well as an additional 5,000 outpatient visits. The patients are drawn not only from the New York metropolitan area but also from other states and other countries.

All patients receive the most modern medical care, without charge, during often lengthy stays for research on and care of their illnesses. Many patients keep in touch with the Hospital after their release, either as outpatients or through their own physicians. Like the faculty of the other University laboratories, faculty members at the Hospital hold full-time salaried appointments and do not charge professional or laboratory fees to patients. Though The Rockefeller Hospital carries out many of the conventional medical functions of patient care common to all hospitals–and prides itself on the high quality of that care–these activities are conducted strictly in the context of its primary scientific mission.

JUST as the interests of the University have broadened and deepened in all branches of the basic life sciences, so too has the research program of the Hospital acquired new dimensions. Like their predecessors, today's investigators, inspired by the concept of human disease as a general biological problem, are looking ever more deeply into organic structure and function, while at the same time seeking to integrate their findings into the "ordered complexity" of animal physiology and chemistry.

The disorders under study today can be divided into two broad categories–immunology and metabolism. The largest percentage of bed use in the Hospital is devoted to research on rheumatoid arthritis, systemic lupus erythematosus, and other collagen diseases; problems of cholesterol metabolism; acute and chronic glomerulonephritis; obesity; and diabetes. Dermatologic disorders and endocrine-related cancer have recently been added to the list of chronic disabling diseases under study. The Hospital laboratories also are engaged in research on rheumatic fever; a variety of genetic disorders, including the porphyrias; problems of alcoholism, drug addiction, and nutrition; and clinical pharmacology. A recent and

Campus in spring.

growing interest is in the area of biochemical toxicology and the impact of environmental chemicals on man.

Investigators in the Hospital frequently join forces with other scientists on campus on work that demands a multiplicity of professional skills. In turn, basic research programs with potential clinical implications draw upon the resources of the Hospital when appropriate.

Need for Clinical Researchers

In recent years, there has been a declining interest in clinical research among medical students and graduates in this country and in most of the western world. If the trend is not reversed, the growth of medical knowledge in the next generation will be seriously impaired. A key step toward the solution of this problem is to provide assured opportunities and financial support to gifted young physicians, thus encouraging them to consider careers in clinical investigation as an alternative to medical practice.

Exposure to outstanding physician-scientists, to a discipline that applies the analytical powers of the modern sciences to disease problems, and to an atmosphere of collaborative research between basic scientists and clinicians is critical to the development of a new generation of clinical investigators. The Rockefeller Hospital offers such an environment. It is seeking to recruit outstanding young physicians who are completing their residency programs and are prepared to join the Hospital staff in order to train themselves for careers in the clinical sciences.

The Right Environment

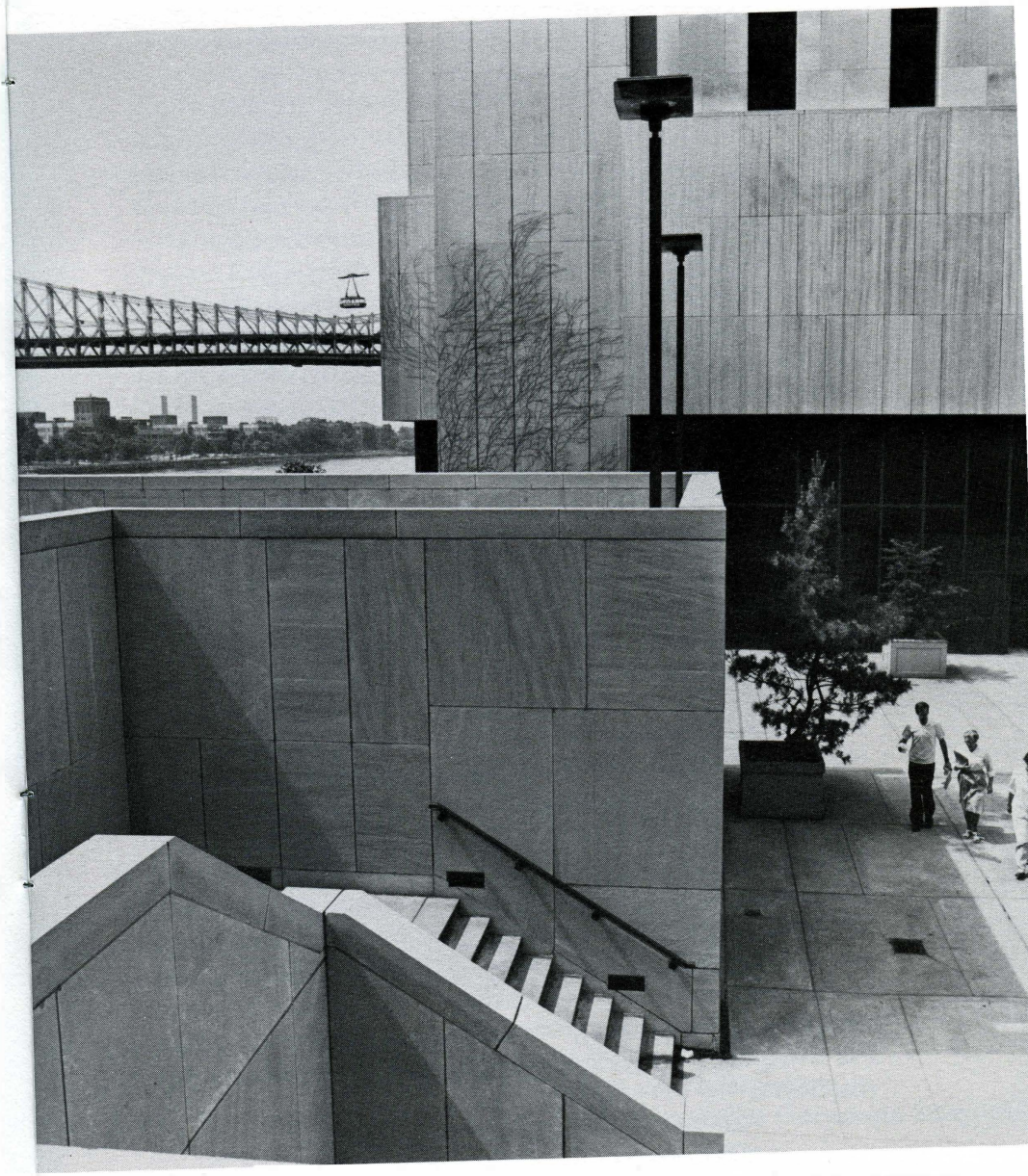
To a select group of such young men and women, The Rockefeller Hospital offers full financial support, including salary and laboratory facilities, for three or more years. These Clinical Scholars are given faculty appoint-

ments and become full colleagues in the Rockefeller research community. Every effort is made to house them near the campus, situated in one of the most coveted neighborhoods in New York City.

Young researchers find an unusually rich range of personal and professional associations open to them within an institution where almost all of the disciplines contiguous to medicine are represented. They share in the intimacy and administrative simplicity that are among the great strengths of the University and its Hospital. They find colleagues willing to open their laboratories to visitors; to expose their ideas to the scrutiny of other investigators; to give assistance; and to debate, persuade, and teach. These associations are further enhanced by ties, formal and informal, that link the University to its immediate neighbors, The New York Hospital-Cornell Medical Center and Memorial Sloan-Kettering Cancer Center, as well as to other medical institutions in New York City. To all this must be added the best of music, theater, ballet, art, spectator sports, and recreational facilities of all kinds–virtually at the doorstep of the University.

Learning by Experience

When Clinical Scholars join a laboratory group at the Hospital–even if they have had little previous laboratory experience–they quickly become familiar with the basic research disciplines of that group. In the first year or so, they are guided toward a research goal of their own; but within the very flexible framework of the group they have considerable freedom of choice. They learn by experience (since there are no formal courses) to recognize investigative challenges, to frame important questions, and to design meaningful experiments and perform the laboratory work required to answer those questions. At least 80 percent of their work day is spent in the labora-



Tower Building plaza with Queensboro Bridge in background.

tory. The remainder is devoted to the care of their research patients.

This division of time points up the real strength of the clinical research programs at the Hospital. First, the scientists are not burdened by responsibilities for formal teaching, ward service, or administration. Second, each investigator can study patients on the metabolic ward for extended periods without any demand for tightly structured protocols, because it is the tradition at the Hospital to study small numbers of patients in great detail. Third, the clinical situation guides the nature of the questions asked and the manner in which the answers are sought; the discoveries that result are a measure of the ingenuity of the investigator. Having demonstrated mastery of the discipline of patient-oriented research, the trained investigator becomes much sought-after in academic medicine.

A National Resource

For more than 70 years, the Hospital has served as a national resource in the study of human disease. It has shown itself capable of adapting effectively to a changing scientific, academic, and social environment. Its original purpose not only remains valid but, in fact, is even more important now as federal funding for clinical research declines. To ensure against the uncertainties of federal grants, The Rockefeller University is now engaged in a ten-year development program to broaden its base of private financial support. One of the fruits of this effort is the funding by the University of the Clinical Scholars program and other major projects designed to strengthen the Hospital's remarkably productive environment for discovery.

Bacteriology and Immunology

This laboratory, headed by Professor Emil C. Gotschlich, has spent more than three decades in seeking a greater understanding of the host's relationship to infectious agents and the diseases they produce. Among the diseases under study have been those in which an established relationship to a known microorganism has been demonstrated as well as those diseases in which a presumed microbial agent might be involved. In the former category has been a study of post-streptococcal sequelae as well as group B infections of the newborn. Knowledge of many of the structures and functions of hemolytic streptococci has been elucidated. Also, a genetic marker in rheumatic fever and a nephritogenic protein unique to nephritis strains have been discovered, and the host's immune response to microbial infections in these disease states has been described. Of equal importance has been the elucidation of the role polysaccharides of the meningococcus play in immunity to these infections with the development of active vaccines against the group A and C meningococcus.

Among the diseases in which a presumed infectious agent may play a role are rheumatoid arthritis and multiple sclerosis. In the former, evidence has accrued indicating a possible relationship between bacterial mucopeptide antigens and the disease state. In multiple sclerosis, the evidence is inconclusive, but suggests that a prior viral event coupled with abnormalities in immunoregulation might trigger a neurological lesion.

Current activities of the laboratory include exploration, in experimental models and in man, of the relationship of microbial antigens to rheumatoid arthritis. In rheumatic fever, the role of the genetic marker in the immune response to streptococcal antigens is being explored. In glomerulonephritis particular emphasis is being placed on the role of a nephritogenic protein in acute nephritis as well as on pathological mechanisms involved in the development of chronic glomerulonephritis. Neuroimmunological studies are concentrated on the role of cellular and humoral regulatory mechanisms in multiple sclerosis and on a better definition of the role CNS antigens play in chronic neurological diseases. Concomitant with these studies of pathogenesis is the continuing basic exploration of bacterial virulence factors important in the prevention of known infectious diseases.

Biology of Addictive Diseases

The laboratory of Dr. Mary Jeanne Kreek is engaged in the study of the disposition and physiological effects of addictive agents, particularly alcohol and narcotics. The goal is to determine factors that contribute to the initiation and perpetuation of addiction, and influence treatment.

Current studies focus on the possible roles of chronic liver disease, prevalent in addicted patients, and of altered endocrine and neuroendocrine function, either drug-induced or spontaneous, in the occurrence of recidivism following achievement of the drug-free state and in the initial development of addiction. Using various technologies, this laboratory has made the first documentation of clinically significant interactions between a narcotic and any other drug, the initial clinical and laboratory discovery of the effects of chronic opioid administration on enhancing albumin synthesis, and the first demonstration that the liver acts as a reservoir for storage and release of long-acting narcotics.

In 1964, Professor Vincent P. Dole, Dr. Marie Nyswander, and Dr. Kreek introduced pharmacological maintenance treatment of narcotic addiction with methadone, an orally effective, long-acting narcotic. Studies conducted at The Rockefeller University Hospital showed that such treatment prevents narcotic abstinence and drug-seeking behavior and restores patients to a functional state. Other studies have shown that chronic methadone treatment is medically safe. Studies of the role of ACTH, beta-endorphin, and other hormones in narcotic abstinence and in drug-seeking behavior of drug-free narcotic addicts and alcoholics are in progress. Also being explored is the role of endogenous opioids in the normal physiological control of intestinal motility and in motility disorders.

Cellular Physiology and Immunology

This laboratory is concerned with the roles of leukocytes and their products in inflammation, infectious cellular immunity, and cancer. Headed by Dr. Zanvil A. Cohn, it includes among its faculty Drs. Marcus Horwitz, Carl Nathan, Nadia Nogueira, William Scott, Samuel Silverstein, Ralph Steinman, and Jay Unkeless. It is well known for structural and functional analyses of murine macrophages, their secretory products, and the properties of their membranes in pinocytosis and phagocytosis. Dendritic cells, which play essential roles in T-cell stimulation and transplantation immunity, were first purified in this laboratory.

In the last five years the scope of the laboratory has expanded to the study of human cells and diseases, opening up opportunities for investigations integrating laboratory and clinical research. Methods have been developed to purify and culture monocytes and dendritic cells from human blood and tissues, and to isolate their plasma membrane proteins and receptors using monoclonal antibodies. Major disease-related areas under study include:

a) The role of activated macrophages in host defense against tumors, Legionnaires' disease bacteria, leprosy, and *Trypanosoma cruzi*.

b) Tumoricidal and microbicidal properties of reactive oxygen metabolites (hydrogen peroxide, superoxide anion), and antioxidant defenses of normal and malignant cells.

c) Monocyte- and macrophage-derived arachidonic acid metabolites (prostaglandins, leukotrienes) in immediate hypersensitivity and immune suppression.

d) Biochemistry and functional properties of Fc and complement receptors.

e) Differentiation of mononuclear phagocytes.

f) Production of lymphocyte-activating factors by human dendritic cells, and the functions of dendritic cells in inflammation and arthritis.

In conjunction with the appropriate divisions at The New York Hospital-Cornell Medical Center, this laboratory maintains Fellowship Training programs leading to Board qualifications in Infectious Diseases and Hematology-Oncology.

Cutaneous Biology and Investigative Dermatology

Professor D. Martin Carter, formerly at Yale University, has established new laboratories at The Rockefeller to explore fundamental mechanisms operative in disabling skin diseases.

His laboratory group has been studying the relative contributions of genetic and environmental influences on such cutaneous functions as aging and skin cancer. The environmental factors that damage DNA are of special interest, and include photo injury by ultraviolet irradiation of various wavelengths and by UV irradiation combined with such phototoxic drugs as psoralens and chlorpromazine. Proliferative cellular responses have been characterized in cultured cutaneous fibroblasts exposed to psoralens and long-wave UV light. The role of pigment as a defense has been demonstrated in cells and in skin, and photomediated stimulation by psoralens of pigmentation by way of tyrosinase activity also has been demonstrated. Further enhancement of photomediated cellular damage by changes in temperature and atmospheric oxygen tension are under investigation. Cytogenetic consequences of photomediated psoralen-DNA damage have been characterized. Sister chromatid exchanges (SCEs) have been shown to develop after *in vitro* exposure to psoralens and light, and the influences on SCEs of DNA binding, K_m, and DNA-cross-linking potential of various psoralens have been shown. The capacity of cutaneous cells to repair psoralen-DNA damage is being studied, using cells from normal persons and from those who are suspected of having heritable heightened susceptibility to DNA damage.

This group was among the first to use psoralens and long-wave UV irradiation to treat patients with psoriasis. By carefully monitoring psoralen blood levels, it has been possible to modify photo-treatment times to match maximum skin photosensitivity. Clearer understanding of psoralen metabolism is the result.

Endocrinology

This laboratory was only recently organized by Professor Jack Fishman, but the research it is engaged in is a continuation of work which has been going on for the past 25 years. The focus of interest is on the biology of the steroid hormones, with particular emphasis on their role in human physiology and pathophysiology. The laboratory has pioneered in the characterization of the biosynthetic and metabolic pathways of the steroidal hormones in man and has been instrumental in establishing that their metabolic transformations are not solely catabolic in nature, but that the biological properties of the metabolites are of major consequence in the expression of hormone action. In the course of these studies, entire new categories of natural steroids have been identified, among them the catechol estrogens and the cortoic acids. The former are now known to exhibit unique central properties and are under intensive examination for their role in the control of pituitary hormone release in the human. The differential biological properties of steroid metabolites give emphasis to the changes in their formation that are associated with certain diseases. The existence of specific and distinct perturbations of steroid hormone metabolism have now been documented in several diseases.

Investigations are also concerned with the impact of diet, drugs, and other environmental agents on hormone biotransformation in man, in the expectation that changes in the latter are responsible for some of the physiological effects of these factors. The role of estrogen metabolism in human reproduction and its involvement in the etiology of breast and endometrial cancer are also under intensive study.

The clinical investigations have their counterpart in laboratory studies directed at the biochemical mechanisms of hormone biosynthesis and transformation, and at the nature of their biological action in appropriate target tissues, including the central nervous system.

Human Behavior and Metabolism

The laboratory of Professor Jules Hirsch and colleagues utilizes the findings of behavioral science, metabolism, and endocrinology to understand the nature of human obesity and the manner in which man and animals control food intake and energy metabolism. This laboratory has pioneered in the demonstration that obese subjects, even after reducing their weight, show persistent abnormalities in adipose cellularity, with an excess number of small adipocytes when compared to nonobese subjects. The reduced obese also show behavioral abnormalities which resemble those described in starvation. Studies now in progress utilize subjects in the Rockefeller Hospital and in its outpatient departments, as well as a variety of animal models of obesity maintained in the Laboratory Animal Research Center at The Rockefeller University.

Present areas of investigation include:

a. Taste in three-day-old infants. The development of sweet taste in man and its relationship to food intake and body size.

b. Adipose tissue metabolism, studied *in vitro* with adipose tissue aspirates. The effect of cell size on sensitivity to lipolytic agents.

c. Changes in hypothalamic-pituitary function as a result of weight loss. Measures of TSH and ACTH, as well as insulin, growth hormone, and cholecystokinin, in man and experimental animals.

d. The effect of lipectomy, high caloric intake, and early infantile feeding on the cellularity and behavior of obese and normal rodents.

Studies currently beginning are the effect of diet and adipose tissue composition on serum lipid level and on immune function, and the effect of weight reduction in man on thermogenesis and autonomic function.

Lipid and Lipoprotein Metabolism

This laboratory, initiated in 1952 by Professor Edward H. Ahrens, Jr., has engaged in studies of lipid and lipoprotein metabolism in man: effects of various dietary fats on plasma lipid and lipoprotein levels, milk fat composition, erythrocyte lipids, and adipose tissue composition; effects of carbohydrate/fat exchanges on plasma lipids; absorption of fat by the intestine; mechanistic studies of lipid-lowering drugs. These studies depended on the development and refinement of new methods for use with patients as well as in the laboratory, including the first application of gas-liquid chromatography in this country; the measurement of intestinal lengths under physiological conditions; the sampling of adipose tissue by needle aspiration; the measurement of biliary lipid flow rates; and the introduction of orally fed liquid formulas for research.

For the last 15 years, this group has focused on sterol metabolism in man. By developing and refining the sterol balance technique and by combining it with studies of isotope kinetics, it has become possible to measure the key regulatory factors governing the movement of cholesterol in, through, and out of the body, and thus to understand the mode of action of dietary and drug interventions aimed at reducing plasma and tissue lipid levels. These studies have demonstrated that individual patients respond very differently to diet/drug challenges. Present efforts of the laboratory are directed mainly to measuring the precision of feedback control of cholesterol synthesis in large numbers of outpatients, in order to tailor the management of hyperlipidemia to the pathogenetic defects in each person.

The laboratory also is engaged in studies of cholesterol synthesis in mononuclear cells and in the intestinal mucosa; in defining the kinetics of mevalonate metabolism in man and in laboratory animals; in studies of sterol metabolism in patients maintained solely by total parenteral nutrition; and in a wide variety of functional studies of changes in membrane fluidity effected by the feeding of saturated and polyunsaturated fats.

Medical Biochemistry

The objective of this laboratory, established in 1971 by Professor Anthony Cerami, is to apply the knowledge of chemistry to understand the pathogenesis of diseases and to develop drugs to treat them. The major areas of research are diabetes and aging, parasitology, and genetic diseases.

The purpose of the diabetes research is to ensure understanding of the biochemical mechanism of the disease's many sequelae and to develop ways to prevent these complications. Studies on the biochemical basis of the sequelae have led to the concept that glucose can chemically react with body proteins in a nonenzymatic manner, and that the higher the glucose concentration, the greater the reaction. As a result of these findings, the degree of carbohydrate control can be monitored in diabetic patients. This is accomplished by assessing the amount of sugar-hemoglobin component (hemoglobinA_{1c}), which in turn gives a measure of the previous month's integrated blood glucose concentration. A method of measuring glyco-peptides found in urine has been developed. As a result of studies on nonenzymatic reactions, the concept of a delivery system capable of supplying insulin to the body as a function of glucose concentration was developed, and a practical apparatus is in progress.

Significant work has been done on cataract formation and peripheral neuropathy, the two major complications associated with diabetes, and an increased amount of reaction of glucose with important proteins in both the lens and peripheral nerve has been found.

New drugs have been found for the parasitic diseases trypanosomiasis, leishmaniasis, and filariasis. An in-depth study of host-to-parasite response is of prime importance in understanding the basic disease processes.

Pharmacological agents for treating genetic diseases have been emphasized in this laboratory. New agents for sickle-cell anemia, thalassemia, and cystic fibrosis are now being evaluated.

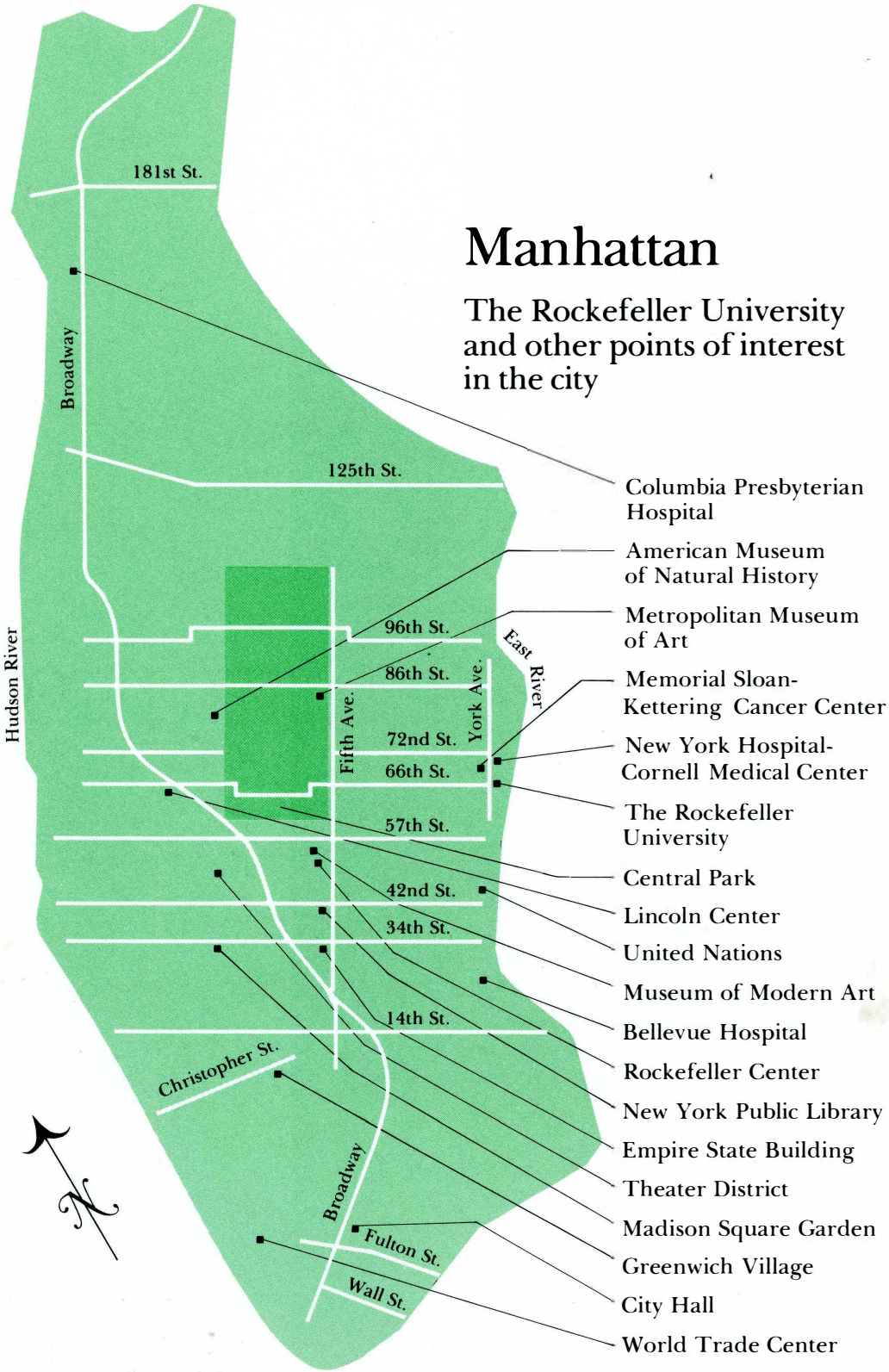
Metabolism-Pharmacology

The laboratory of Professor Attallah Kappas focuses on biochemical and clinical problems involving the oxygen-binding pigment heme; the pathways by which it is synthesized and degraded; and the various roles which heme plays in cellular metabolism and the biotransformation of such natural and foreign chemicals as hormones, drugs, and environmental pollutants.

The main diseases under intensive investigation are the human porphyrias, which, in one form or another, result from genetic aberrations in activities of the various enzymes in porphyrin and heme production. Certain acquired disorders of heme metabolism, such as metal poisoning, and some drug intoxications are also being studied. The general approach is to examine — at the biochemical level and in a number of tissue-culture or animal-model systems — the factors that regulate heme and heme-protein (cytochrome P450) metabolism, and to translate the findings of such studies to the human situation when that is feasible and useful.

Laboratory investigations relevant to the main interests of the group include the manner in which metals regulate the degradation of heme in tissue-cultured liver cells and in the organs of whole animals; the adaptations which take place *in vivo* to protect against the detrimental effects of environmental chemicals, especially trace and heavy metals; means for controlling the activity of heme-pathway enzymes in order to achieve selective biological effects involving heme synthesis or degradation; and the development of sensitive analytical methods for analysis of all products and intermediates of the heme pathway. Thus, application of these methods to diagnostic use in humans can be achieved, utilizing the smallest possible biological samples.

A newly developing interest of the laboratory group is the role of nutritional factors in regulating drug, hormone, and other chemical biotransformations.


Manhattan
The Rockefeller University and other points of interest in the city
181st St.
Broadway
125th St.
Hudson River
96th St.
86th St.
Fifth Ave.
York Ave.
East River
72nd St.
66th St.
57th St.
42nd St.
34th St.
14th St.
Christopher St.
Broadway
Fulton St.
Wall St.
N
Columbia Presbyterian Hospital
American Museum of Natural History
Metropolitan Museum of Art
Memorial Sloan-Kettering Cancer Center
New York Hospital-Cornell Medical Center
The Rockefeller University
Central Park
Lincoln Center
United Nations
Museum of Modern Art
Bellevue Hospital
Rockefeller Center
New York Public Library
Empire State Building
Theater District
Madison Square Garden
Greenwich Village
City Hall
World Trade Center