Creating a Tradition of Biomedical Research

Contributions to the History of The Rockefeller University

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Darwin H. Stapleton

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Chapter 2

Institutionalizing Excellence in Biomedical Research: The Case of The Rockefeller University

J. Rogers Hollingsworth

Professor of History and Sociology, University of Wisconsin–Madison, Madison, WI

Introduction

The goal of this essay is to explain why more major discoveries occurred in biomedical science at Rockefeller University than at any other research organization during the twentieth century. Why would this small organization in New York City—unknown to millions of Americans—have performed better on this criterion than such renowned organizations as Harvard, Yale, and Stanford universities in the United States; Cambridge and Oxford universities in Britain; and the Pasteur Institute in Paris? And why is Rockefeller credited with more major breakthroughs in biomedical science than all the German Kaiser-Wilhelm and Max-Planck Institutes combined? (See Appendix I for a definition of major breakthroughs in biomedical science and Appendix II for Rockefeller scientists who made major breakthroughs.)

There is no single answer to such a complex problem. To address it requires a theoretical framework to explain how the structure, culture, and leadership patterns of research organizations interact with their changing environment so that they can continuously have radical innovations; in this case major discoveries in biomedical science.[1] Several themes in the recent literature on organizations and radical innovations are relevant if we are to understand what occurs in a research organization over a long period of time. First, it is important to comprehend how changes in the environment of an organization influence changes in the organization itself. Second, if an organization is to make radical breakthroughs time and time again, it needs to be ambidextrous in its internal operations: both taking the necessary incremental steps so that strategy, structure, leadership, and personnel are linked to one another in a fairly harmonious fashion on a day to day basis; and having leadership with the capacity to take the radical or revolutionary steps to look beyond the present so that the organization can quickly adapt to significant changes in the environment. Throughout the twentieth century Rockefeller University has been ambidextrous and highly adaptive to its environment, often pursuing both incremental and radical changes simultaneously.

An organization accustomed to delicately balancing its components cannot lightly alter them, lest its operating system be endangered. Change in organizational strategy, structure, and leadership styles is often unwelcome, even resisted, inasmuch as it requires moving away from norms, habits, and conventions that previously had been effective. In fact, much of the success of the University over the last century in making major breakthroughs occurred because of its ability to carry out these dual activities: to maintain its established practices at high levels of performance and to look beyond the immediate future to make radical changes in its practices.

The achievements of Rockefeller are uncharacteristic of research organizations across the globe. Most organizations tend to experience a great deal of inertia, generally failing to make radical changes as environments change. Even organizations that have performed well have a tendency to congeal in self-congratulation, to idealize their own practices to such an extent that they do not adequately modify themselves in response to environmental change.

But research organizations that successfully adapt to their changing environment, and in the process make fundamental breakthroughs across long periods of time, have particular structural attributes. A recent study of research organizations in Britain, France, Germany, and the United States demonstrates that major discoveries throughout the twentieth century tended to occur in an organizational setting in which there was a high degree of interaction among scientists in diverse fields, and a high degree of flexibility in the organizational structure allowing it to adapt quickly to new trends in science. Over time, biomedical knowledge has become increasingly more complex (involving both multiple fields of knowledge and greater depth), but if research organizations are to make major discoveries, it is imperative for them to incorporate scientific diversity and depth in such a way that scientists can interact with intensity and frequency across diverse fields. However, as research organizations add greater scientific diversity and depth, it is important that these parts remain well-integrated and not isolated from one another; otherwise, there will not be the requisite horizontal communication with frequent and intense multidiscipline interaction.[2]

Increases in scientific diversity and depth, if not properly managed, can ultimately limit the capacity of a research organization to make major discoveries. As research organizations increase in diversity and depth, there is a tendency for them to become larger, more differentiated, less integrated, and less flexible. These changes in turn are usually accompanied with increases in hierarchical coordination, bureaucracy, and organizational rigidity with negative consequences for scientific research and discovery.

Successful research organizations credited with several major discoveries have had a distinctive style of leadership, that is, leaders who have had (1) a strategic vision for integrating diverse areas and for providing focused research; (2) an ability to facilitate obtaining funding; (3) a capacity to facilitate the provision of rigorous criticism of science but within a nurturing environment; and (4) an ability to recruit sufficiently diverse personnel so that research groups are constantly aware of significant problems. Leaders who exhibit all of these qualities also have tended to be so well versed in the past accomplishments of their organizations that they have a high capacity to articulate their cultures. At the same time, they have tended to be versatile in those areas of science just emerging on the horizon, giving them a good sense of the direction in which the organization should move. In short, the distinguished leader is one who cannot only bring about dovetailing between the existing culture and competence of the research organization and new fields of science, be sensitive to the traditions of the organization, and be highly supportive of what the organization is doing in the short-term, but also be a visionary and risk-taker capable of moving researchers into unknown areas. As long as a research organization is relatively small, it is feasible for the very rare and talented individual to have the ambidexterity to play these seemingly contradictory roles. However, as the organization increases in size and complexity, it becomes ever more difficult for a single individual to embody all of these traits.

The discussion that follows develops these themes. It focuses on the changes within the Rockefeller University in response to changes in its environment, and on the strategy, structure, leadership, and personnel of the organization as it has attempted to adapt to alterations in twentieth century science.

There was no steady state in any of these trends. The leaders of Rockefeller have not always correctly understood and responded to the changes in the external environment. They have not always anticipated the major institutional and scientific patterns of change, nor has the organization always had the same level of excellence in its flow of ongoing work. Nevertheless, the University has been more successful in meeting all of the aforementioned challenges than any other research organization, and this is the key to understanding why it has performed so well in having so many major breakthroughs in biomedical science.

Institutionalizing a Culture of Excellence

To understand the origins of the Rockefeller Institute for Medical Research, we need to recognize that in the latter part of the nineteenth century, the United States lagged far behind the frontiers of biomedical science as they existed in Europe, especially in Germany. Throughout the nineteenth century, the United States lacked high standards in biomedical science and did not provide high-quality training for young scientists and physicians. Most medical schools had few if any laboratories, they were rarely affiliated with hospitals or universities, and their capital outlays were generally quite small.[3] Of course, some schools were better than others, and a few Americans made contributions to medical knowledge; but overall even the best medical schools and centers for research in the United States were inadequate. Among the best were those of the University of Pennsylvania, the University of Michigan, and Harvard, Yale, and Columbia universities. Although by 1900 they were progressing in basic science research, the training and research at each of these schools fell far short of the best medical advances of the time. Germany had become the center for scientific medicine in the late nineteenth century, and more than 15,000 Americans went there between 1870 and 1914 to study the medical sciences. In the history of American biomedical science, few things are of greater importance than the traveling of this generation of Americans to Germany, especially in the 1870s and 1880s. They brought back what they found, and it was these European institutions and ideas that ultimately revolutionized science and clinical medicine in the United States.[4]

All of this must be set in the context of the major institutional changes taking place in the United States during the last half of the nineteenth century. There was literally a transformation in the American economy, which produced unprecedented wealth in America. John D. Rockefeller Sr., the wealthiest of all Americans and one of the great entrepreneurs of American capitalism, believed that his capacity to make money was ". . . a gift from God . . . to be developed and used to the best of our ability for the good of mankind. I believe my duty is to make money and still more money and to use the money I make for the good of my fellow man according to the dictates of my conscience."[5] To assist in his philanthropic activities, Rockefeller Sr. chose Frederick T. Gates, a Baptist minister, who quickly immersed himself in understanding Rockefeller's business and philanthropic affairs.

In 1897, Gates submitted a proposal to Rockefeller in which he argued that although various departments of natural sciences had been generously endowed in various American universities, medicine, because of the commercial orientation of medical schools, had not been well supported. As a result, medical research was in a poor condition in America, usually conducted by practitioners who could, at best, steal a short time from their private practices. He argued that medicine could hardly hope to become a science until research was properly endowed and dedicated scientists were permitted to have uninterrupted study and investigation, completely independent of clinical practice. To achieve these ends, he proposed the establishment of a research institute. With John D. Rockefeller Jr., a new graduate of Brown University, Gates developed a wonderful working relationship in managing Rockefeller philanthropic affairs in general, and more specifically, in the development of a biomedical research institute.[6]

As both men quickly realized that they needed the advice of people with a rich knowledge of medical science, they gathered a distinguished group. Rockefeller Jr. consulted with his family physician, Dr. Emmett Holt, renowned pediatrician and author of the leading textbook on pediatrics; Christian Herter, a well-known scientific investigator who had established his own private laboratory in New York City for his research in biochemistry, pharmacology, and bacteriology; William H. Welch, the dean of the Johns Hopkins Medical School; Hermann M. Biggs, head of the Division of Bacteriology of the New York City Department of Health; T. Mitchell Prudden, professor of pathology at the Columbia University College of Physicians and Surgeons (who had known Welch since their student days in Germany in the 1870s); and Theobald Smith of the Harvard Medical School, the leading American bacteriologist of the day and a former student of Welch. Welch suggested the addition of his former student at Johns Hopkins, Simon Flexner—then professor of pathology at the University of Pennsylvania. And in 1901, these people became members of the board of directors of the Rockefeller Institute for Medical Research.[7]

Each had training in pathology, and each believed that the best strategy at the time for attacking disease was by using the tools of bacteriology. Each also thought that it was only a matter of time before physiology and chemistry would have to be integrated with bacteriology in order to advance knowledge of diseases. Despite common elements in their scientific backgrounds, the group represented diversity in experience, which in the long-term was to prove valuable to the Rockefeller Institute. Herter had extensive experience in research and in clinical practice; Holt in hospital clinical practice; Biggs and Smith had backgrounds in public laboratories; and Smith, Welch, Prudden, and Flexner were researchers in university medical schools. From the very beginning, there was an extremely high level of trust among these men, and this was extremely important in understanding the early success of the Institute.

Perhaps the most important contributor to the success of the Rockefeller Institute was William H. Welch, who had already been instrumental in establishing Hopkins as the premier medical school in North America. The more Welch reflected on the idea of an institute, the more he was intrigued by its potential, so when he was pressed by Rockefeller Jr., Gates, and the small group of scientific advisers, he agreed to serve as president of the new institute's board, a position he held for thirty-two years. The choice of Welch as president is indicative of the capacity of the Rockefellers to recruit excellent people to implement their programs. Some have argued that Welch had more influence in developing the biomedical sciences in the United States than anyone else in American history. In addition to serving for more than three decades as president of the Board of the Rockefeller Institute, he served as president of the American Association for the Advancement of Science, the National Academy of Sciences, the American Medical Association, the Association of American Physicians. In addition, he was a member of the Board of Trustees of the Hooper Foundation for Medical Research at the University of California, San Francisco, one of the key individuals in establishing the National Research Council, and a member of the Board of Trustees of the Carnegie Institution in Washington (1906–1934) and Chairman of its Executive Committee from 1909 to 1916. As a key figure in these organizations, Welch had frequent and more contact with the elite in all fields of American science than anyone else.[8] The Rockefellers could not have made a better choice than Welch to steer the initial board of the Rockefeller Institute. He had an excellent comprehension of the direction in which biomedical science was moving, high visibility and legitimacy in American science, and outstanding judgment about the type of scientists and the specific scientists whom the Institute should recruit.

One critical decision was what kind of organization Rockefeller Institute should be. Because of their academic backgrounds, Welch, Prudden, Flexner, and the other scientific advisers tended to think the new organization should be linked to an existing university. However, the Rockefellers and Gates were insistent that there be no formal link with a university. The idea of the Rockefeller organization, as conceived by the Rockefellers and Gates—laymen who had become sensitive to the shortcomings of the existing medical establishment—was that biomedical knowledge could not be substantially advanced until an organization existed with proper endowment, and with qualified scientists with adequate salaries, independent of both private medical practice and university teaching, devoting full time to research.[9]

Welch proposed Simon Flexner to be the first director. Here, too, a better choice could hardly have been made. Flexner, the fourth of five children, was born to Jewish parents in Louisville, Kentucky and grew up in semi-poverty, after his father died prematurely. Shortly after receiving a medical degree from a local school in Louisville, he went to Johns Hopkins—but not as a regular medical student—where he became associated with Welch. Quickly, the breadth of his education increased. He went to Europe in 1892 and studied in some of the great laboratories and later worked in the laboratory of Jacques Loeb at Woods Hole. Slowly, Flexner was integrating medical and biological science, so that by the time he became the director of the Rockefeller Institute he had demonstrated that he was a creative and productive scientist, capable of absorbing and integrating new and complex ideas, and with the capacity to develop and implement new research programs and to operate on many fronts at once.[10]

Flexner's Vision

As the first director, Simon Flexner left an indelible mark on the Institute. As a result of his achievements and efforts, the expectation developed among the trustees of the Rockefeller organization that it should be headed by an individual who had a strategic vision for integrating scientific diversity, who could create an organizational environment that blended criticism and nurturing, who had the capacity to recruit personnel alert to significant problems and able to solve them, and the ability to secure funds. Not all subsequent heads of Rockefeller lived up to the leadership standards that Flexner epitomized, but these are the ideals by which successive leaders have been evaluated.

Although the Koch Institute in Berlin and the Pasteur Institute in Paris were founded around great scientists and their research, the Rockefeller organization under Flexner's leadership became a new kind of research organization that from its beginning emphasized diversity in the biomedical sciences. Instead of being focused on a specific area of science, the Institute pursued research in multiple areas of the biomedical sciences. Biomedical science was changing very rapidly by the time the Rockefeller Institute was established. Because bacteriology had become closely linked with pathology, and both fields were becoming more closely related to discoveries in organic and physical chemistry, as well as physics, a broad conception of biomedical science was the guiding philosophy of the Institute from the beginning. As

Flexner internalized a great deal of scientific diversity, perhaps it was almost intuitive on his part that he would recruit a staff that reflected a good bit of scientific diversity.

The recruiting of a high level staff proved to be very difficult. Most senior professors in leading American medical schools viewed the Rockefeller Institute as a high risk "up-start," and they were unwilling to leave the security of their permanent positions. Most young people, hoping for careers at established universities, also viewed the Institute with some suspicion. For some years, there had been vicious attacks in the press by Henry Demarest Lloyd, Ida Tarbell, and others against "Rockefeller money" and the Standard Oil Trust, and by the time of planning for the Institute much of the nation's press was hostile to the Rockefellers.

Many medical practitioners perceived the scientific agenda of the Institute as an assault on their legitimacy, and indeed, the dominant tone of the medical profession of New York City was quite hostile to basic biomedical research.[11] Young scientists were frequently warned to stay clear of the Institute. Both Peyton Rous, a future Nobel laureate from the Institute, and Jacques Loeb, one of the most important scientists in the history of the Institute, had initial reservations about going there because they feared they might not have freedom to conduct their research.[12]

Flexner thought it necessary to recruit at least a few experienced scientists, not only young people. Because senior university professors were unavailable, many tended to view initial scientific staff he gathered as a "motley group."[13] Most had outstanding ability, but were uninvolved with established American universities and academic disciplines, which proved to be a blessing in disguise. For the most part, the earliest appointments were opportunistic and personalistic in nature. Flexner placed considerable emphasis on recruiting scientists whose origins were in different cultural areas and who worked in different scientific areas (e.g., Alexis Carrell from France; Karl Landsteiner from Austria; Hideyo Noguchi from Japan; Phoebus Levene and Samuel Meltzer from Russia; and Jacques Loeb, Leonor Michaelis, and Max Bergmann from Germany). Several were of Jewish origin in an era of strong anti-semitism. Almost every one of these scientists internalized cultural diversity in his own cognitive makeup, which increased the potential for crossing scientific disciplines. Feeling an affinity for others who crossed academic discipline boundaries, the early appointed scientists established and reinforced a culture based on broad, interdisciplinary approaches to scientific problems.

From the beginning, the Institute did not organize the production of knowledge around academic disciplines, which was the usual practice in major universities. In organizations in which academic disciplines were dominant for organizing and coordinating the production of knowledge, there was a tendency to recruit specialists in disciplines, scientists who by definition internalized less scientific diversity (and often, less cultural diversity). The distinctive Rockefeller recruitment of scientists socialized in several cultures, subsystems, disciplines, or working environments meant the presence of a staff with more potential to acquire new styles of thought and scientific competence. From the outset, the Institute was a place where there was a willingness of scientists to participate in multiple scientific worlds simultaneously, fostering the cross-fertilization of ideas and the opportunity for communication across diverse fields of research. These conditions facilitated the development of the hybridization of ideas that over time leads to scientific creativity, sudden insights, and the opening of novel pathways to difficult problems.

As a research organization, the Institute had several distinct advantages over most teaching institutions. Most teaching organizations attempt to present an entire field of knowledge to their students and find it awkward to neglect certain subfields. They tend to recruit people not so much because of their research excellence but because of the necessity to cover a particular area of knowledge. Unlike a university, a research institute has no obligation to cover an entire field of knowledge, and it can be very opportunistic in terms of the fields on which research is undertaken. It can neglect or pursue fields, can recruit scientists solely on the basis of their ability to attack selected problems, and it has the flexibility to move into new areas with considerable rapidity. Moreover, the Rockefeller Institute had the luxury of being able to recruit scientists of excellence even if they had limited ability to speak English or could not teach.[14]

Over many years, a generous endowment by the Rockefellers has created excellent working conditions for scientific research. Several other institutes founded at about the same time were also very well endowed: the Phipps Institute in Philadelphia, established by the steel magnate Henry Phipps; the Memorial Institute for Infectious Diseases in Chicago, funded by Harold McCormick, a son-in-law of John D. Rockefeller Sr.; and the Carnegie Institution in Washington, endowed by Andrew Carnegie. However, the history of the Rockefeller Institute, viewed in a comparative perspective, suggests that although financial resources are necessary for outstanding research, they are less important than having the right strategy, structure, personnel, and leadership. An organization must be able to do excellent work on a day-to-day basis, but at the same time must be willing to reorient itself on a continual basis in anticipation of scientific change.

The Rockefeller Institute, with its laboratory structure, was sufficiently ambidextrous so that it was able to adapt quickly to its environment; i.e., to move in new directions at the same time that it was carrying on more established lines of research. One of the most important resources for a research organization if it is to continue making major discoveries is the quality of its leadership—a variable that many organizational sociologists give scant attention. Over the years, Rockefeller has had several directors (later presidents) who were capable of interacting in a meaningful way with its scientists and who personally knew the leading biomedical scientists of the world. Of the eight directors or presidents since the founding of the Rockefeller Institute, six made major discoveries in biomedical science, and the two who made no major biomedical discoveries (Detlev Bronk and Fred Seitz) were distinguished scientists who had been presidents of the National Academy of Sciences. Four of the eight were Nobel laureates in physiology or medicine.[15]

Originally, a single Board of Directors designed and implemented plans for the development of the new institute; but in 1910, Welch, who had been president of the Board of Directors, became president of the Board of Scientific Directors, and due in part to the prestige he lent the Institute, some of America's leading biomedical scientists subsequently agreed to serve on the Board of Scientific Directors. Over time, board members included future Nobel laureates Vincent du Vigneaud, Herbert Gasser, and George Whipple; and three other scientists who made major breakthroughs in biomedical science Walter B. Cannon of Harvard, Ross Harrison of Yale, and Theobald Smith of Harvard (discussed earlier). In addition, Bronk, then president of the Johns Hopkins University, and James B. Conant, president of Harvard, served on the Board.

Governance of the Institute

The board was responsible for the appointment of the scientific staff and for the establishment of general policies concerning the scientific investigations, and it did much to keep the research organization performing optimally. The director of the Institute (Flexner) was appointed by the Scientific Directors and was in intimate contact with the scientific staff. Beginning in 1910, there was also a Board of Trustees that had oversight over the financial affairs of the Institute. The distinctive role of the Board of Scientific Directors, combined with the skills of Flexner and his successor Herbert Gasser, facilitated the recruitment of some of the most innovative scientists assembled to that time. Permanent appointments had to be approved by both boards, although the director appointed nonpermanent members of the staff, determined their rank, and fixed their salaries. Flexner personally interviewed every scientist, even those who were at the Institute for only a single year, before any appointment was made.

The original Board of Trustees consisted of John D. Rockefeller Jr., Gates, and their lawyer Starr J. Murphy. Welch and Flexner served on both the Board of Trustees and the Board of Scientific Directors, providing communication between the two boards. The existence of two boards lasted until 1953, when the two were merged into a single Board of Trustees. Since then, the Rockefeller organization has not had a separate board of world-class scientists making the final decisions about personnel. The quality of recruitment, while continuing to be high, has not had the same degree of extraordinary consistency as during the time when the Institute had a Board of Scientific Directors with distinguished scientists intimately involved in making staff appointments and overseeing the scientific research of the Institute. The Board of Scientific Directors met three or four times a year and focused in great detail on the quality of Rockefeller appointments. Since 1953, there have been scientists on the Board of Trustees, but they have never exercised the same degree of oversight on the organization's appointments as when there was a separate board for scientific affairs.

At the Institute, permanent scientists were called members and had indefinite appointments corresponding to professorial appointments in American universities. The next highest title was associate member, a three-year appointment renewable for three more years. In general, after a second term, associate members either were appointed as members or were expected to resign. Associates were appointed for two years, and assistants and fellows for one. Eligible for reappointment, scientists in the lower ranks left the Institute or rose to higher rank after three to five years. Like the Kaiser-Wilhelm or Max-Planck Institutes, which later had similar promotion policies, the Rockefeller Institute provided advanced training for what became the elite of biomedical scientists in America. The process of appointment as a member was extremely rigorous. Not all senior scientists received their initial appointments at that level. For example, in 1934, 46 percent of senior scientists had initially been appointed to the rank of member, whereas 54 percent had been promoted from a lower rank. Members rarely left: only one resigned by the mid-1930s, and even he returned.

Although the Board of Scientific Directors was responsible for the scientific policies of the Institute, the research problems under investigation were chosen by individual scientists. Members and their associates and assistants made up laboratory groups that were organized into divisions. Funds for scientific investigations were allocated to laboratories and administered by the head of the laboratory, though budgets were of course modified from time to time by special action of the Board of Scientific Directors.

The meetings of the Board of Scientific Directors were held quarterly, and for these meetings, the head of each laboratory or division submitted a technical scientific report. Discussion of the reports became the most important item of business at the meetings. The reports played an important role in communicating to the board what was going on in the Institute.

Members of the Board of Scientific Directors generally attended all meetings, and they read the reports carefully. Some members of the board made a habit of consistently visiting various laboratories, not in the spirit of monitoring but because of their genuine interest in the Institute's research. An important incentive to be a board member was the opportunity to be informed about the Institute's research activities.[16]

Reflections of Flexner

During the first three decades of the Institute, its overall governance and operating procedures were reflections of Flexner's philosophy, ideals, personal mannerisms, and scientific style. The insistence after 1910 that every laboratory prepare periodic scientific reports for the Board of Scientific Directors was due in part to Flexner's insatiable appetite for learning. As the Institute developed, these reports reflected some of the latest trends in science, and provided opportunities for Flexner and the directors to consider what the Institute might do next. Although Flexner had been primarily interested in infectious diseases during the 1890s when he was at Johns Hopkins, by the time of Jacques Loeb's appointment to the Institute (1909), Flexner's cognitive framework had significantly expanded to encompass a very broad view of biomedical science. He increasingly believed that biomedical sciences must rely primarily on chemistry, physics, and biology, and that investigations had to be based on the methods of those fields. This change was due in part to the fact that the Institute provided a rich learning environment. Flexner held the view that most scientific knowledge is interrelated. For him, all forms of life were "related organically and . . . united physiologically and pathologically." In the pursuit of knowledge, there should be no disciplinary boundaries separating the study of different forms of life, though there had to be separate laboratories for purposes of "economy of action."[17]

Flexner also was very much aware that knowledge changes very rapidly in the global world of science, and he believed that if a biomedical institute was continuously to absorb and integrate new knowledge, there had to be an intimate commingling of investigators in various fields of science, even if in the short term some fields of biomedical science appeared unrelated to others.[18] He believed that the range and scope of the Institute should provide considerable scientific diversity. Moreover, the internal organization should be highly flexible so that it could quickly adapt to new knowledge. For Flexner, the culture within the Rockefeller Institute should be such that scientists would be willing to communicate and cooperate with each other. Such a strategy meant that each scientist should internalize extensive scientific diversity, and should be able to communicate with every other scientist. Indeed, scientific diversity and ability to communicate with others on the scientific staff were prerequisites for recruitment. Because so many of the scientists were fluent in multiple languages, foreign scientific publications were frequently discussed by the staff, and scientists from abroad were eager to visit the Institute and to discuss research of mutual interest.

Flexner was aware that scientists who had the kind of scientific diversity that he wanted to recruit were in short supply. His strategy was that the Institute over time should train a number of its own staff, and during his directorship, the Rockefeller Institute became one of the world's leading centers of training for young postdoctoral biomedical scientists. This meant carefully recruiting able young people and providing them with excellent opportunities to grow scientifically. Although the overwhelming majority departed after a few years of training, Flexner retained the most exceptional. This obviously meant that members were constantly attentive to the strengths and weaknesses of younger staff. Although only one in twenty was retained, by 1950 almost one-half of those with permanent Institute appointments had risen through the ranks.

Flexner's correspondence demonstrates that he was enormously attentive to the well-being of young investigators. Even if they failed in particular investigations, he would encourage and console them and give them new opportunities. When a depressed young investigator told him that he had accomplished nothing worthy of publication, Flexner warmly consoled him by remarking, "Nothing? . . . you don't seem to realize that to have nothing is to have something."[19] Flexner was wise enough to know that for the young people coming to the Institute, it was one of the great experiences of their lives, and he encouraged his senior colleagues to make certain that this was the case. Even if Flexner did not retain a young scientist, he frequently paid the investigator a salary for a year after his departure as an incentive for another academic institution to recruit the person. This kind of practice let young people know that if they went to the Rockefeller Institute, they would have an excellent opportunity to have a position upon exiting, and this did much to keep a steady stream of able young scientists.

Over time, hundreds of young people passed through the Institute and went on to be prominent biomedical scientists. Flexner was highly committed to upgrading the quality of America's universities and medical schools, and believed that one of the major contributions of the Institute was its development of young investigators and teachers for universities and medical schools. He was very proud that by the early 1920s, the leading American universities in the country eagerly sought the Institute's young investigators.[20]

With so many scientists passing through the Institute, some errors in judgment were made. Not everyone retained was of world-class distinction, but probably no other research organization in the world had such a high proportion of the scientific staff eminent in biomedical science. Still, the Institute encouraged a few scientists to depart whom it should have kept. One such scientist was Michael Heidelberger, whose exceptional qualities kept him at the Institute for a very long period (1912–1927, except for a short period during World War I). Eventually, Heidelberger was encouraged by Flexner to leave for fear that he was not getting sufficient recognition for his many achievements that were invariably co-authored with a senior scientist. In the words of Elvin Kabat, Heidelberger was a "Leonardo da Vinci–type Renaissance man . . . who became the father of quantitative immunochemistry."[21]

As director, Flexner also worked to maintain close research communication with members of the original Board of Directors and the subsequent Board of Scientific Directors and the Board of Trustees, and this was important in promoting cohesion and trust among those governing the Institute. Flexner and Christian Herter became intimate friends, and their families visited one another's homes. The Flexners and the Herters had summer houses at Seal Harbor, Maine, and one of Flexner's sons married one of Herter's daughters. With Hermann Biggs, Theobald Smith, and Emmett Holt, Flexner's relations were somewhat formal, though they became closer over time. He was especially respectful of Smith's scientific knowledge, and he wrote a book with Holt on dysentery among infants.[22] Among the trustees, Flexner developed a very warm relationship with Gates, and the Flexners frequently visited the Gates' home in New Jersey and their summer house on Lake George, New York. Over time, he also developed a close relationship with Rockefeller Jr. As Mrs. Flexner and Mrs. Rockefeller liked each other, the Flexners frequently joined the Rockefellers at their New York City residence and were invited from time to time to the family estate at Pocantico Hills.

More than anyone else, Flexner institutionalized a culture of excellence within the Institute. Throughout his directorship, he did not become a full-time administrator, but continued to work in the laboratory.[23] Within the Institute, he was usually too busy to engage in small talk. He set very high standards not only for himself but also for everyone around him. In some respects, he was a bundle of contradictions. He could be extraordinarily charming, but if he believed the situation called for it, he could be coldly blunt. He tended to be extremely instrumental in his dealings with the scientific staff. He was willing to be very harsh with individuals if he believed this was the most effective way of getting "the most out of a man and was best for his development."[24] On the other hand, he worked tirelessly to establish a nurturing environment in the Institute. Overall, he was a very considerate and affectionate individual. He kept in touch with the lives of most everyone in the Institute, and all staff—scientific or otherwise—usually received birthday or wedding anniversary cards. He was solicitous of the needs of the nurses, secretaries, porters, laboratory helpers, keepers of animals—all of the unheralded people essential for a high-quality research organization. When they encountered family emergencies, he would help them cope with the problem—financially if necessary.[25]

Salaries and Assessments

On the other hand, there is evidence that during the Flexner years, the Institute was often conservative—if not outright stingy—with regard to salaries. In part, this practice stemmed from Flexner's fear that universities would accuse the Rockefeller Institute of stealing faculty by paying inflated salaries, and this did not happen. Rather, it was the universities that from time to time attempted to lure Rockefeller members away with extremely high salaries. Because he was solicitous about the welfare of American universities, Flexner was determined to keep Institute salaries within the range of American salaries at high-quality universities.[26] However, for research expenses within the Institute, the situation was different: Institute scientists received generous research funding from the director in comparison with the leading universities in America.

Funding for research was administered by Flexner in a somewhat personal style. Even so, the decision-making process about funding research within the Institute was in some respects more effective than what currently exists in most contemporary American funding agencies. Flexner had a great deal of information about the research potential of almost everyone in the Institute, and he and his colleagues were in an excellent position to make well-informed decisions about what was high risk and low risk research, and who had the abilities to conduct high risk, long-term projects and who did not. They were well positioned to monitor investments in scientific research, as a result of periodic scientific reports and their ability to discuss and advise about the progress of specific research projects. Moreover, having the *Journal of Experimental Medicine*, and other high-quality journals, edited at the Rockefeller Institute provided the director with a great deal of information about papers produced at the Institute. In sum, the Institute strategy for funding science was highly flexible because of the large amount of information possessed by those making scientific investment decisions.[27]

A New Department at Princeton

From the very beginning, the culture of the Institute was entrepreneurial and high risk oriented. Flexner regarded trivial and unimportant research with contempt. He had no objection if labs were unproductive for lengthy periods of time, as long as they were addressing important problems. He would wait a long time before concluding that a young scientist was not suitable for the Institute. Mindful of the weakness of his own early education, he took the view that one of the missions of the Institute was to provide research training for young postdoctoral researchers.[28] And because of the Institute's rich scientific diversity and the excellent internal communication among the scientific staff, he frequently encouraged scientists to move into totally new fields of research. On one such occasion, he informed a young scientist who was moving to a new problem that it would take at least two years to begin to understand the parameters of his new problem. "I will not expect anything of you until after that," he said. Flexner's ability to identify, and to fund new areas of research—as with the work of Peyton Rous—was emblematic of the Institute's capability to anticipate new directions, even radically different directions, and move towards them rapidly.

On almost all occasions, Flexner was available as both an intellectual and scientific resource. Often, he went out of his way to inform young investigators that they needed an assistant and that he would provide the funding.[29] At the height of the Depression, when Tom Rivers told Flexner that he needed extra funding for his research (though he did not specify the amount), "without batting an eye" Flexner provided $10,000, a great deal of money at the time.[30] On the other hand, Flexner did not hesitate to be stern—even with a senior member—if he believed the person was not being prudent with the resources provided by the Institute.[31]

Gates and the two Rockefellers did much to set the tone for the research strategy of the Institute. From the beginning, they told the original Board of Directors that they expected no short-term utilitarianism or results. Indeed, Gates and the Rockefellers had early concluded that no important discoveries were likely to result from the Institute. Their major hope was that the Institute would conduct high-quality research, be a training ground for young investigators, and serve as an example for other philanthropists. Research on important problems, even if long periods of incubation were necessary, was encouraged at the outset.[32] Thus, without pressure to produce results in the short term, Flexner could encourage his staff to think "big," to take risks, but to be aware that rigorous standards of excellence would be the criteria by which all results would be assessed.

From the beginning, Welch, Flexner, and others on the Board of Scientific Directors had advocated a research program on animal pathology, in part because certain diseases are transmitted from animals to humans. An unanticipated event in 1913, the widespread outbreak of hog cholera, brought the matter to the fore. After studying the epidemic, Flexner and Theobald Smith proposed that the Institute create a full-scale department of animal pathology, to which the board agreed. Smith was asked to head the new department and the decision was made to locate the department in the Princeton, New Jersey area. In 1917, the Institute's Department of Animal Pathology opened with a state-of-the-art facility, with a faculty that grew to be an integrated scientific community, with research and social life tightly intertwined.[33]

The new department at Princeton was almost the equivalent of establishing a new institute. Although organizationally under the direction of Flexner, the department's day-to-day operations, most staff appointments, and local policies were under the direction of Smith. The Princeton department had scientific leadership with a vision of how to address "do-able," major problems, with the capacity to identify scientific talent from diverse fields, and to integrate this scientific diversity in a rigorous, but nurturing environment. As well, the Princeton site had scientific diversity, depth, and integration, and a high-quality staff. Significantly, several major discoveries did occur in the Princeton branch of the Rockefeller Institute, breakthroughs that resulted in Theobald Smith's being awarded a Copley Medal and John Northrop and Wendell Stanley receiving Nobel Prizes in Chemistry for separate research conducted in the Princeton laboratories between 1917 and 1937. However, these recognitions are only a part of the story of the Princeton department.

Smith was a very cautious director of a research, and unlike Flexner, adverse to risk. Thus, he added relatively few staff who were unrelated to his immediate research interests. Because Flexner exercised scientific oversight over the Princeton department, he was able to counterbalance Smith's conservative tendencies, with fortuitous consequences for the Princeton program. This was seen most dramatically in the career of John Northrop, one of the most innovative scientists during the first forty years of the Institute. Flexner arranged for Northrop to move to the Princeton site in 1926, even though Northrop clearly did not focus on animal diseases.

Flexner's moving Northrop to Princeton contributed to a creative research program culminating with Northrop's being awarded a Nobel Prize for Chemistry in 1946. At the Rockefeller Institute, Northrop had worked closely with Jacques Loeb, who taught him how to design complex experiments in order to answer important well-focused questions. Loeb also influenced Northrop to be interested in the colloidal properties of proteins and to work on pepsin and trypsin. Northrop was a creative and highly productive scientist with a magnetic personality, and over the years he attracted several first-rate scientists to his lab.[34] Using solubility measurement, ultracentrifuge analysis, and electrophoresis, Northrop and his colleagues demonstrated that pepsin is a pure enzyme, thus challenging the then-dominant views of Richard Willstätter that enzymes were carriers of other molecules that give them specificity. As a result of the work of Northrop's lab as well as that in the Institute's New York labs, Rockefeller investigators "led the world" in enzymology by the early 1930s.[35]

By the time of Smith's retirement (1930), Flexner had decided that the Institute should have a program in plant pathology, also located at Princeton. He believed that a program on plant disease, especially plant viral diseases, would be of enormous benefit to the Institute.[36] One of the nation's leading plant pathologists, Louis O. Kunkel was appointed to head a program in plant pathology, with a mandate to study plant diseases caused by bacteria, fungi, and viruses. Kunkel decided to concentrate on tobacco mosaic virus (TMV), and he recruited a diverse group of talented young scientists (including Wendell Stanley) who could work on most aspects of the biology of TMV.

Stanley's training had made him a promising investigator in physiological chemistry, but he was devoid of training about viruses. At the time Stanley began his work, no one had previously isolated a virus. Stanley assumed that viruses were proteins, and in the small Princeton environment, he quickly became very familiar with the work of Northrop's lab, which had demonstrated that enzymes were crystallizable and were, in fact, proteins. Stanley then set out to discover if viruses could be purified by methods similar to those used by the Northrop group.[37] After several years of hard work and more than 100 chemical reagents later, Stanley reported that he had isolated a "protein" virus, and after further purification had obtained highly infectious needle-like crystals. In a 1935 paper, he reported that he had "strong evidence that the crystalline protein herein described is either pure or is a solid solution of proteins."[38] According to George Corner, "No discovery made at the Rockefeller Institute, before or since, created such astonishment throughout the scientific world as this."[39] Immediately, Stanley became a national celebrity. For many, he was raising fundamental problems about life, just as Jacques Loeb had earlier done at the Institute. Because Stanley's 1935 paper attracted so much attention in the popular media, it naturally stimulated great interest in the scientific community, and criticism was not long in coming. From Britain, researchers reported that TMV was not a pure protein as reported by Stanley but contained approximately six percent nucleic acid (RNA) and that it was a nucleoprotein. Why had Stanley missed the RNA?

Over the years, Stanley received severe criticism both for missing the RNA in his paper and for not recognizing that the "crystals" were paracrystalline in nature.[40] But when Stanley began his research in 1932, the true nature of viruses was still a mystery. It had not been established whether they were inorganic, hydrocarbon, carbohydrate, lipid, or protein. No one had isolated them as such. Though Stanley's 1935 paper had shortcomings, it was a major step forward in the field of virology. Later, with input from Thé Svedberg, Stanley was able to extend his work and publish a portrait of the rod-shaped TMV. By 1946, largely due to Stanley's initiatives, work on the concentration and purification of different viruses was proceeding in several laboratories, and over a dozen viruses had been obtained in a highly purified form—primarily by the techniques of high speed centrifugation.

Having a distinguished program established at Princeton—a program initially focused on animals and then incorporating research on plants—not only brought new kudos to Rockefeller scientists, but brought to the fore whole new lines of inquiry. To some extent, the local circumstances at Princeton mimicked the New York example of intense and frequent communication among scientists of very diverse interests, although internal disagreements were also a part of the Princeton locale. In establishing an off-site program, the Rockefeller Institute took a gamble, acting somewhat precipitously in choosing the Princeton location.

Journals at the Institute

The Institute also took the lead in enhancing scientific excellence in America by editing and publishing journals. By developing journals of the highest quality and encouraging the staff to publish in them, the leadership of the Institute further emphasized its independence from the existing institutional environment. The *Journal of Experimental Medicine* (founded by Welch) was the first journal to be edited at the Institute. Flexner became the editor in 1904, and in addition to all his other responsibilities, he served as the chief editor for fifteen years, though assisted at the outset (1904–1910) by Eugene Opie. Eventually, he asked Peyton Rous in 1921 to be co-editor, and Rous essentially functioned as the editor for the next thirty-six years, though Flexner continued to be listed as co-editor. Flexner's successor Herbert Gasser served as co-editor from 1935 to 1953, the entire period for which he was director.[41]

In 1918, Jacques Loeb, with John Osterhout of Harvard, launched the *Journal of General Physiology*, which was subsidized by the Rockefeller. With Institute support, Loeb also launched a monograph series designed to advance the development of experimental biology from a quantitative and physiochemical point of view. Through these publications, Loeb helped to unite various fields of field of biology by breaking down barriers among various specialties.[42] The Institute also published numerous other monographs, sometimes at irregular intervals. There was a series entitled *Studies from the Rockefeller Institute for Medical Research*, which by 1930 had seventy volumes of 600 pages each. The *Journal of Biological Chemistry* also was published by the Institute for many years, and Phoebus Levene, Donald Van Slyke, and others at the Institute published a high proportion of their papers there.[43]

During his long directorship (over thirty years), Flexner played a major role in improving the quality of the Institute's publications. These aided the productivity and creativity at the Institute and were important in drawing attention to the Institute's accomplishments. Overall, probably no journal published at the Institute has had greater impact in establishing new trends in biology than the *Journal of Biophysical and Biochemical Cytology*, later renamed the *Journal of Cell Biology*. Its founding was inspired by Keith Porter and had the strong support of Herbert Gasser.[44]

Frequent and Intense Interactions

The experience of the Rockefeller Institute demonstrates that diversity and depth of knowledge in a well-integrated research organization have the potential to change the way people view problems and to minimize their tendency to make mistakes and/or to work on trivial problems. Frequent and intense interaction among people with low levels of diversity tends not to lead to major breakthroughs; however, if scientists work in environments where there is moderate to high scientific diversity and depth, and have frequent and intense interaction with those having complementary interests, they increase the probability that the quality of their work will improve. It is the diversity of disciplines and paradigms to which individuals are exposed in frequent and intense interactions that increases the tendency to develop new ways of thinking about fundamental problems. To permit such a process to continue long term requires that the organization provide not only the stimulating, resources, and environment for today, but that it, in a sense, anticipate the future by undertaking whole new lines of research.

Intellectual and social integration were maintained at Rockefeller Institute by a variety of devices. Eating meals together while conversing about serious scientific matters was an important part of the Rockefeller culture and an important means of integrating the scientific diversity and depth of the Institute. There was invariably high-quality food at lunch, served at tables for eight. The idea was that a single conversation could take place at such a table, but not at a larger one.

The degree of intellectual and scientific diversity was much less at the Rockefeller Institute than that at the colleges of Oxford and Cambridge, where eating at "high table" was also an important part of the culture. At the English colleges, diversity ranged all across the board (e.g., from archaeology and as well as ancient and modern languages to chemistry, physics, biology, and mathematics). With so much diversity, it was considered poor etiquette to talk about one's work at the tables, as many of those present would be unable to comprehend the line of discussion. But at Rockefeller, diversity was only within the biomedical and related sciences, and the norm was to carry on lively lunch time discussions about these fields. Indeed, these luncheon experiences not only led to new factual information and changes in philosophical viewpoints, but also to collaborative research projects across fields.[45]

For many, the lunch table at the Institute was the high point of the day. Paul de Kruif, a scientist at the Institute who later was a strong critic, nevertheless thought the dining room was one of its most stimulating characteristics.

> . . . at the lunch break there was balm for my discouragement. Here I could listen to the scintillating talk of my betters . . . I never tired of listening to the philosophy of Alexis Carrel, who had won the Nobel Prize in medicine . . . Carrel, who had been in America a long time, had carefully preserved his French accent, which made him sound to me even more learned than he was . . . . Then at the luncheon table there might be Dr.

> Peyton Rous, refined, gentle, exquisitely cultured . . . In this refectory there was an air of solemnity to be expected and appropriate to the unveiling of mysteries.[46]

And in the words of Dubos:

> There never was a symposium—in the etymological sense of the word . . . that was more scientifically productive and intellectually pleasurable than those held daily in the lunch-room of the Rockefeller Institute, though coffee and ideas were the only intoxicants.[47]

Apart from lunch, scientific integration was also facilitated by the weekly conference everyone was expected to attend, at which Institute investigators or distinguished scientists from all over the world reported about their work. In the Hospital department, there were afternoon tea times that most scientific staff attended.

One of the most important integrating devices was the journal club, especially the Hospital Journal Club which generally met twice a month. Everyone was expected to attend, and to be prepared to report on a paper outside one's own research field, but of general interest to everyone. No one knew in advance who would be called upon to present materials to the journal club. Why would world-class scientists agree to participate in such activity? Scientists did this because they knew they were members of an extraordinarily distinguished organization, and they believed that one reason it was so outstanding was that they were continuously learning from each other. This kind of regular reading outside one's own specialization and in areas of interest to others in the organization was one way of integrating scientific diversity. In short, the Institute had developed a culture of continuous learning for its scientists.

Its learning environment was compounded by being located in New York City. Before World War II, most distinguished foreign scientists traveling to America arrived in New York and invariably visited the Rockefeller Institute. Certainly, no other biomedical research organization in America was so favored with foreign scientists. If this small institute could not have all the diverse ways of approaching biomedical science represented on its permanent staff, it had the opportunity to have many of the world's leading scientists passing through with reports about their work. Moreover, Rockefeller Foundation grants often brought to New York the cream of the world's crop of young scientists, who typically visited the Institute for days or weeks.

A Temple of Science

Institute scientists took great pride in being associated with what many viewed as a temple of science.[48] As soon as one crossed from York Avenue onto the grounds of the Institute, one was in a sanctuary, separated from the hustle and bustle, the grime and dirt, the shouting and cursing of the city. The original idea of the Institute had been conceived in part by a Protestant minister, Frederick Gates, and throughout the century, some observers have referred to the Institute in religious terms. Not only for Gates but also for the Rockefellers, Flexner, and Welch, biomedical science certainly acquired religious proportions.

How did this happen? Gates spoke for the two John D. Rockefellers when he wrote that "disease is the supreme ill of human life and is the main source of almost all other human ills: poverty, crime, ignorance, vice, inefficiency." He went on to explain that these ills could not be cured by the economic and social restructuring of society, as many socialists believed.

Rather, society's problems were technical in nature and required technological solutions, which medical science could provide.[49] For Gates, these views did have a religious quality to them, because scientific medicine was the means for building a new and better world, and for uplifting and civilizing one's fellow men. Thus, the Rockefeller Institute was envisioned to become the functional equivalent of a temple for the new religion, and the medical investigators who would reduce suffering and poverty were to be its priests. Gates referred to the Institute as a theological seminary, and Flexner as the scientific "Doctor of Divinity." Indeed, De Kruif thought "Flexner looked as if he might be high in the College of Cardinals."[50] And in writing about the Institute, de Kruif reported that for Flexner, the greatest achievement of the Institute was not "the scientific output, its undoubted saving of lives, its contributions to basic knowledge," but rather "it was the harmony, the serenity, [and] the brotherhood with which the staff had always worked together."[51]

Welch had early on advised Flexner to recruit scientists "who agree well together."[52] Both believed that new ways of thinking about scientific problems were most likely to emerge in a scientific environment in which scientists had intense and frequent interaction with one another, so that a fundamental new way of thinking about a problem could occur. For this, an environment of harmony, trust, and dignity is essential because whether one is in a religious or scientific monastery, the priesthood must be passionate in their quest for the truth. Thus, in recruiting staff for this sanctuary of science, it was important to select individuals who were imbued with a spirit of cooperation and to avoid the prima donnas.

To recruit staff who would pursue problems on a large scale, Flexner thought it was important to find scientists concerned with deep philosophical problems. During the first half century of its existence, the Institute had numerous scientists who not only internalized vast scientific diversity, but whose scientific thinking was well integrated with a rich philosophical framework. This kind of scientific staff generated enormous excitement at the Institute lunch tables, which became famous over much of the world. As in most monasteries, there was some conflict. Some members cared little for others. But relative to most research organizations, there was a high degree of communication and cooperation among the scientific staff, and this contributed to its rich learning environment.

Flexner's Achievements

In 1935, Flexner at age seventy-two retired as director of the Institute after more than thirty years of service. Though he had been able to recruit only a "motley" group of scientists at the outset, by the time he stepped down as director, the Institute had emerged as one of the world's leading centers of biomedical science. Whereas in the first decade of the century, most scientists with established reputations would not consider accepting an appointment there, the Institute had long before eclipsed the Pasteur Institute, the Lister Institute of London, and others. During the years that Flexner served as director, ten of the Institute's research scientists were cited for major discoveries in biomedical science. Five—Alexis Carrel, Karl Landsteiner, John Northrop, Peyton Rous, and Wendell Stanley—received Nobel Prizes either during or after Flexner's tenure. Theobald Smith received the Copley Medal for research he conducted at both the Institute and at the Harvard Medical School. Oswald Avery, Simon Flexner, Jacques Loeb, Theobald Smith, and Hideyo Noguchi made breakthroughs that yielded numerous nominations in multiple years for Nobel Prizes in Physiology or Medicine (enough to meet the criteria established in Appendix I as major discoveries). During the Flexner years, no other research organization in the world had more major breakthroughs in biomedical science than the Rockefeller Institute, and for a comparable period (thirty-four years), no research organization in the world since then has had so many major breakthroughs!

During the Flexner years, the Institute had distinctive advantages in identifying both junior and senior talents throughout the world. Although the Rockefeller Foundation was not a major funding agency for the Rockefeller Institute, the Rockefeller Foundation had become a major funding source for biomedical science throughout Europe and North America. To access the quality of scientists and their labs, the Foundation obtained reports about research in every major biomedical research organization in Europe and North America. Because Simon Flexner was a trustee of the Foundation and because his brother Abraham had a long affiliation with the Foundation, Simon had extensive knowledge about who was "up coming" and he was in a strategic position to invite outstanding young scientists to the Institute. Similarly, his prominence in the National Research Council provided him with inside information about many promising young scientists.[53]

During the 1920s, aspiring biomedical scientists in America took the view that they needed to spend at least two to three years at the Institute for postdoctoral training. By 1935, more than 150 Rockefeller-trained scientists had become professors in America's leading universities and were beginning to establish their own training programs, a process which in the long run would narrow the gap in quality between the Rockefeller Institute and other organizations in biomedical science. But until the National Institutes of Health (NIH) became the leading training center for young biomedical scientists during the 1950s and 1960s, the Rockefeller Institute was clearly the major center for postdoctoral training in America, with younger people from Europe increasingly going to the Institute for advanced training. When future Nobel laureate Alan Hodgkin went there in 1938 from the University of Cambridge, he was struck by the high quality of its scientists, its instrumentation, as well as its greater formality and seriousness in contrast to Cambridge.[54]

Among the reasons for the continued excellence of the Rockefeller Institute were its flexibility, derived in large part from its autonomy, and its independence from the institutional environment in which it was embedded. Unlike many research organizations at the time in both Europe and America, it was not dependent on external funding; therefore, it was immune to the kinds of constraints that funding sources place on organizations.[55] Until the mid-1950s, the Rockefeller Institute seldom accepted grants or any funding from sources other than the Rockefeller family. Moreover, it was relatively autonomous from the norms and rules imposed by most scientific disciplines. Most universities, organized around academic disciplines and their academic departments, are constrained in their behavior by the norms and rules of existing academic disciplines. Because the Rockefeller Institute was organized around laboratories rather than scientific disciplines and fields, it had a greater capacity to be flexible and to adapt quickly to new research strategies. And in contrast to the institutional environment in Germany and France, the Rockefeller Institute had high autonomy to appoint anyone to its staff. For example, in Germany, most scientists who became professors first had to qualify for habilitation, which is access to an academic field by preparing an original book-length scholarly work after receiving the PhD. The Rockefeller Institute imposed no such requirement and appointed as members well-trained scientists with credentials from many parts of the world.

Transition to a New Director

The Institute was still performing well when Flexner retired, but it was in need of a new director with different scientific perspectives. Even high-performing research organizations undergo demographic changes and need new leadership from time to time in order to become better adapted to the fast pace of scientific change. In the case of the Rockefeller Institute, many of the original members of the Scientific Board of Directors had died (Biggs [1923], Holt [1924], and Prudden [1924]), as had some of its most distinguished scientific investigators (Meltzer [1920], Loeb [1924], Noguchi [1928], and Smith [1934]).

During the 1930s, the Institute was one of the world's leading centers in enzymology, virology, bacteriology, and pathology. Indeed, there have been suggestions that Herbert Gasser, the next director, was appointed to succeed Flexner in an effort to prevent the Institute from becoming too narrowly concerned with virology and bacteriology.[56] Even though the Institute had attained a high level of excellence in several areas of biomedical science, it had clearly made no effort to cover all fields of biomedical science. Flexner believed that an effort to work in too many fields would lead to uneven quality, and that research programs of low quality would bring down standards of excellence in the entire organization.[57] Hence, during the Flexner years, the Institute had made few or modest efforts to conduct research in several areas in which other research organizations in either Europe or America had already become quite prominent (e.g., research in vitamins and other areas of nutrition, endocrinology, genetics, and neurophysiology). Flexner's strategy had been to have areas of core competence that were complementary and to avoid having too much scientific scope and diversity, lest the organization become less integrated and have less communication among its various component parts.

The decision to bring in an outsider (Gasser) as the new director was a wise one. Many organizations, because they have a distinctive culture, tend to choose their new leaders from within, but such choices may well enhance organizational inertia and hamper the organization's capacity to adopt to the fast changing environment. Among its eight directors or presidents since the founding of the Institute, seven were recruited from the outside, and the sole exception, Torsten Wiesel, spent most of his career elsewhere, moved to Rockefeller University at the age of sixty, and had been at Rockefeller for less than ten years when he was appointed as president. The Rockefeller organization has been much more flexible in adapting to new strategies and different styles of science than would have been the case had they recruited their directors and presidents from among people who had spent most of their careers there.

Gasser, like Flexner, had grown up in America's heartland. He was born in 1888 in the small town of Platteville, Wisconsin; attended the University of Wisconsin–Madison and studied physiology there with Joseph Erlanger, and later was a student at the Johns Hopkins Medical School. He became a colleague of Erlanger at Washington University; and by 1921, he had been appointed professor of pharmacology. Gasser went to London in 1923 to work with A.V. Hill, the neurophysiologist who was awarded the Nobel Prize in Physiology or Medicine in 1922. Gasser also developed a close collegial relationship with Henry Dale and Edgar Adrian, both of whom were awarded Nobel Prizes in the 1930s. In the long run, these relationships were important in establishing a network between English neurophysiologists and the Rockefeller Institute. Gasser later moved to New York to serve as professor of physiology at the Cornell Medical College, which allowed him to become quite familiar with the neighboring Rockefeller Institute.

Like all subsequent directors or presidents, Gasser worked to preserve the culture that Flexner and his colleagues had developed. However, Gasser had his own distinctive style of doing science, and this was enormously beneficial in facilitating the Institute's adaptation to changes in the world of science. Like Flexner, Gasser made continuous efforts to extend the scope and depth of his knowledge. The more he observed increasing specialization in science, especially in American universities, the more he was motivated to contain the centrifugal forces of differentiation within research organizations by promoting the unity of the biomedical sciences. His ideal of an outstanding scientist was someone who internalized considerable intellectual diversity, was a theorist, an experimenter, a mechanic, and an artist. Indeed, he believed that at the Institute there should be serious efforts to blend humanistic and scientific knowledge.[58]

A major difference between Gasser and Flexner was Gasser's greater concern with methods of measurement. By building on his awareness of the new initiatives in measurement, Gasser extended the kinds of problems pursued in existing kinds of research and steadily pushed the organization into new lines of work. This was an example of a major change at the Institute, but folded into ongoing programs. Reaching his scientific maturity during the early days of electronics, Gasser attempted to master areas of physics with implications for biomedical sciences. As director, he demonstrated that he was attuned to the latest methods and ideas in the biological sciences. In his own work, he was at the frontier of using electronic amplifiers and recording for observing the most minute signs of nerve action.

When Gasser became director in 1935, the United States was experiencing the worst economic depression in its history, and this adversely affected the Institute. Even before Gasser arrived, Flexner had written to Rockefeller Jr. assuring him that over the next several years the Institute would be especially frugal and would not ask for additional funds. As a result of the fiscal problems brought about by the Depression, Gasser was severely limited in terms of the new fields of science that he attempted to introduce at the Institute. Salaries were tight and when young scientists left the Institute, most were not replaced. Between 1935 and 1941, the total scientific staff of the Institute declined from 134 to 105. During the Depression, the income from the Institute's endowment declined dramatically, with the result that in 1939 the Institute's expenses exceeded its income by 23 percent. The Institute was able to cover its deficit only because it had accumulated a surplus during the Flexner years.[59]

Partly due to the economic problems of the Depression followed by the disruption of war, Gasser modified the Institute's strategy with regard to younger scientists. During the Flexner years, when a member left the Institute, the lab was closed; but, on numerous occasions, Gasser permitted a remaining associate member to head a lab and to develop a research program. Both Flexner and Gasser were willing to take risks with younger scientists, but Gasser was more inclined to grant some young scientists a high degree of autonomy in developing their own research programs, a strategy which paid off handsomely with several younger scientists who later made major discoveries (e.g., Henry Kunkel, Stanford A. Moore, George Palade, Keith Porter, and William H. Stein). Among these scientists, three were subsequently awarded Nobel Prizes, two Lasker Prizes for Basic Biomedical Science, and two Horwitz Prizes for research conducted at Rockefeller.

A Shift toward Neuroscience

Despite the budget constraints, Gasser provided leadership for altering the research strategies of the Institute. As retirements occurred, the research emphasis on bacteriology and infectious diseases—paramount during the Flexner years—decreased. Gradually, Gasser facilitated the development of different research programs. One of the most significant, with long-term consequences, was neuroscience. Rather quickly, Gasser developed a program in neurophysiology that focused on the fundamental properties of nerve cells, dendrites, and the primary synaptic endings of nerve fibers. He surrounded himself with several competently trained foreign investigators—Harry Grundfest and Rafael Lorente de Nó from Spain, David Lloyd from Oxford, and Jan Friedrich Toennies from the Berlin Technische Hochschule. By the late 1940s, three from the neurophysiology group held the rank of Member: Gasser, Lloyd, and de Nó.[60]

Although the work for which Gasser was to win the Nobel Prize had been done at Washington University before he arrived at the Rockefeller Institute, he did lay the foundation for a rich neuroscience program at the Institute. His successor as director of the Institute, Detlev Bronk, was also a neurophysiologist who expanded on the foundation begun by Gasser's work. This tradition led to H.K. Hartline's work in the neurophysiology of vision that was awarded a Nobel Prize for Physiology or Medicine in 1967. By the mid-1970s, Rockefeller had a major program in three areas of neuroscience: (1) molecular and cellular mechanisms; (2) neurophysiology and behavioral physiology; and (3) information processing, communication behavior, cognition, memory, and brain function. And, the scientists in them composed one of the largest groups in the organization. Eventually, Nobel laureate Gerald Edelman developed one of the most prominent theories in the broad field of neurobiology,[61] and he was instrumental in arranging for the Neurosciences Institute to be at Rockefeller University (where it was located until 1991). Edelman was also instrumental in recruiting Torsten Wiesel, who had received the Nobel Prize for his work in the area of neurophysiology of vision, and who became a professor at the Rockefeller University in 1983. At the same time, Paul Greengard, who was awarded in the year 2000 a Nobel Prize for his neuroscience research, joined the faculty. From the time of Gasser to the present, these and numerous other distinguished scientists have placed Rockefeller in the vanguard of neuroscience.[62]

Proteins to the Fore

Research organizations may stay at the forefront of science by hiring senior scientists who have already been the trail blazers in their field as well as by having their current investigators develop new frontiers. The capacity to do both is a result of past and present strategy choices and good leadership. This is most evident with regard to the role of biological chemistry at Rockefeller. In this case, Emil Fischer's school of organic chemistry was partially transplanted to the Institute in the early part of the twentieth century; this transplantation subsequently branched in numerous directions, one of which was protein chemistry, giving rise to several major discoveries in the process. Indeed, the prophecy of Fisher in his 1902 Nobel lecture was very much realized at Rockefeller: "Since the proteins participate in one way or another in all chemical processes in the living organism, one may expect highly significant information for biological chemistry from the elucidation of their structures and their transformations."[63]

At the Institute, there were several scientists who had studied with Fischer and who in turn inspired many luminaries of protein chemistry (e.g., John Northrop, Moses Kunitz, Wendell Stanley, Stanford Moore, William H. Stein, Lyman Craig, and Alfred Mirsky). Loeb, although not trained as a chemist, also had a major influence in developing the tradition of protein chemistry at Rockefeller.[64] This lineage was responsible for Rockefeller becoming a world-class center for major discoveries within the broad outlines of protein chemistry. In many respects, the critical period for the development of protein chemistry was between 1925 and 1960 when there was increasing evidence in both Europe and America that many important biological activities were due to specific proteins. Although there was vast information that earlier supported this view, it was only during this period that protein chemistry was put on a firm experimental basis, largely as the result of the development of new methods and instruments that substantially increased the knowledge of the function and structure of proteins.

One of the great protein chemists of the twentieth century, Max Bergmann, was appointed to Rockefeller in 1934, leaving Germany after the Nazi ascent to power. A former student of Emil Fischer, Bergmann attracted to the Institute a group of able young scientists who would later develop into some of the leading protein chemists in the postwar world: William Stein, Stanford Moore, Joseph Fruton, Klaus Hoffman, Emil L. Smith, Paul Zamecnik, among others. Work on proteins at the Institute was largely suspended during World War II, and after Bergmann died of cancer at the height of his career in 1944, the lab was without a chief. Gasser, demonstrating that he had an excellent ability not only to discern the direction in which science was moving but also to identify talent, asked Moore and Stein to stay at the Institute and gave them the freedom to do most anything they pleased in the biochemical field. In 1949, they were appointed as associate members and they received permanent appointments at the Institute in 1952. They won the Nobel Prize in Chemistry in 1972 for their collaboration leading to the development of quantitative chromatographic methods for amino acid analysis, especially their automation techniques, which led to the entire sequence for ribonuclease A, the first complete description of the chemical structure of an enzyme.

Gasser also demonstrated imaginative leadership with his support of other young scientists who were engaged in fundamentally new kinds of research. One example was his support of Lyman Craig—long associated with Walter Jacobs—who also worked independently in developing other techniques for purifying some proteins. For this work, Craig was later awarded the Lasker Prize for Basic Biomedical Science.

Rise of Cell Biology

But nowhere did Gasser demonstrate better insight in judging the direction in which science might move than in his support of a group of young cell biologists. Albert Claude had arrived at the Rockefeller Institute in 1929 and worked in the laboratory of James B. Murphy in an effort to purify and characterize the agent (known as the Rous sarcoma virus) that caused a transmissible form of cancer in chickens. Working in the area of virology, Claude used a high-speed centrifuge to spin fractionated cells infected with viruses in an effort to isolate and purify their agents. His investigations led to the determination that cells contained tiny bodies he termed "microsomes." The critical problem was to understand their structure and function. To address this problem, Claude used an electron microscope, a new laboratory tool in the 1940s. Under the pioneering role of Claude's younger colleague, Keith Porter, the Institute then led the way in the development of electron microscopy for the study of cell biology. Aside from Porter, Claude also had the assistance of several other young scientists including George Palade, Roland Hotchkiss, George Hogeboom, and Walter Schneider.[65]

It was the interdisciplinary environment of the Rockefeller Institute that facilitated Claude's imaginative investigations. He brought to the study of cells deep insights from the fields of oncology, virology, biochemistry, histology, and cytology, and his ability to internalize so much scientific diversity enhanced his ability to see things in fundamentally new ways, and to lay the foundation for the development of cell biology at Rockefeller.

Claude left the Institute in 1949 to return to his native Belgium, and Murphy (the head of the lab) retired in 1950. But Gasser's keen ability to recognize promising research and willingness (as in the case of Stein and Moore) to keep a lab open when its head disappeared from the scene, set the stage for major new advances. Technically, Gasser became the head of the Porter–Palade group so that it might continue to function; nevertheless, for several years Porter actually provided the day-to-day leadership of the newly developed electron microscopy laboratory. It is no exaggeration to suggest that modern cell biology was born at the Rockefeller Institute under the leadership of a diverse group of junior scientists.[66]

Without the nurturing role of Gasser in deviating from the precedent of disbanding laboratories, these developments would not have occurred. Significantly, it was Gasser's support for the development of new technologies needed for new fields of research that facilitated the Institute's becoming one of the world's leading centers for protein chemistry and cell biology.

Avery, MacLeod, and McCarty

Perhaps the single most notable achievement in the entire history of the Rockefeller Institute was the paper published by Oswald Avery and his younger colleagues Colin MacLeod and Maclyn McCarty in 1944, offering evidence that genetic specificity is embedded in the chemical structure of DNA.[67] The story of this work, which had little to do with Gasser's leadership, has been recounted many times, and there is no need to go into great detail here. However, it is worthwhile to note certain aspects of the process of this discovery in order to illustrate how the structure and culture of Rockefeller facilitated scientific creativity.

Today, there is universal recognition that the paper from Avery's group represents one of the most important discoveries in the history of the biomedical science. Nobel laureate Joshua Lederberg has observed that between twenty and twenty-five Nobel Prizes were subsequently awarded for research dependent on it. Similarly, Peter Medawar, the Nobel laureate immunologist, called the discovery "the most interesting and portentous biological experiment of the twentieth century."[68]

Notwithstanding general agreement on the significance of the results, there are several intriguing problems about the Avery paper. Since the Rockefeller Institute was the dominant center of the protein central dogma, how was it that the challenge to this paradigm came from within the Institute and was made by a bacteriologist and physician who lacked formal training in chemistry and genetics? Could this discovery have been made anywhere else at approximately the same time?

As a trained physician, Avery spent much of his career concerned with understanding pneumonia and attempting to devise strategies for either treating or preventing the disease. It is no exaggeration to report that by 1940 he was one of the world's foremost, if not the most prominent, authority on various types of pneumococcus. Over the years, his research shifted from an interest in the development of an effective serum for the treatment of pneumonia to an immunochemical understanding of the chemical basis of the biological specificity of different types of pneumonia. For more than two decades, a dialectic was operating in Avery's mind: the applied scientist's concern with treating and preventing pneumonia, on the one hand, and a basic scientist's concern with the underlying chemical and biological processes on the other hand. It was the tension between these two forms of inquiry and the effort to integrate them that was the key to Avery's scientific creativity. In our own day, as those trained as either basic scientists or physicians tend to drift further and further apart, the story of how Avery integrated the concerns of both the clinician and the basic scientist needs to be carefully considered.

Avery spent his entire Rockefeller career in the pneumonia section of the Hospital Department. Although the leading investigators in the Hospital (e.g., Rufus Cole, Alfred Cohn, A.R. Dochez, Frank Horsfall, Thomas Rivers, and Donald Van Slyke) were clearly distinguished investigators by national standards, there was a tendency after World War I among many in the Laboratory Department to perceive the Hospital investigators as applied investigators and therefore somewhat inferior. Avery was very much aware that although he was highly specialized and knowledgeable about pneumonia, he was an outsider as far as fundamental knowledge of physics, chemistry, and biology was concerned. Like all his colleagues in the Hospital Department, he was obsessed with learning, and he constantly tried to absorb basic knowledge from his Laboratory colleagues in an effort to expand the scope of his specialty, pneumonia.

During the 1930s, Avery had lunch at the Institute's famous tables with such distinguished organic and biological chemists as Phoebus Levene, Karl Landsteiner, Van Slyke, Alfred Mirsky, and Max Bergmann and his brilliant young associates William Stein, Stanford Moore, Joseph Fruton, Emil L. Smith, and Paul Zamecnik. Never has one organization had such a stellar collection of biological chemists all at one place and all clearly working at the frontiers of science. No wonder that on two separate occasions, Linus Pauling, one of the century's greatest chemists and at the other end of the continent, collaborated with members of this group, such as Landsteiner and Mirsky. For Avery, the ability to lunch on a daily basis with such a collection of scientists was exhilarating, but also somewhat intimidating.

Once he set out to identify the substance responsible for transforming one type of pneumococcus to another, Avery was determined to seek information from any available source. He frequently sought the counsel of the Institute's great scientists. Revealing his ignorance about the latest methods in chemical analysis that had been developed at Rockefeller and elsewhere, he was not shy in approaching his scientific colleagues in the privacy of their labs. Had he been a microbiologist in a large university in America, he would never have had the opportunity to learn so much about the recent advances in protein chemistry during the previous twenty years.

Although Avery recognized the need to borrow from other fields in order to address his particular research problems, he generally preferred to work with young scientists who had been trained as physicians rather than as basic scientists. However, on several occasions he did work with young basic scientists, including Michael Heidelberg and René Dubos, with notable success, and those collaborations helped to prepare the way for his 1944 paper. It is doubtful that Avery could have acquired the degree of scientific diversity required to do the experiments underlying his 1944 paper in any other organizational environment.[69]

In his years at the Institute, Gasser had the assistance of many of the country's leading scientists who were on the Institute's Board of Scientific Directors: Detlev Bronk, who during his tenure became president of the Johns Hopkins University, president of the National Academy of Sciences, and chairman of the Board of the National Science Foundation; James B. Conant, president of Harvard University; Vincent du Vigneaud of Cornell University (future Nobel laureate); Warfield Longcope of the Johns Hopkins University and one of the nation's leading professors of medicine; and Nobel laureate George H. Whipple of Rochester University. With their guidance, and the participation of the scientific staff, new pathways were opened not only in such broad areas as protein chemistry and cell biology but also in the mechanisms of heredity and virology.

A Change in Direction

During the Depression and the Second World War, the Board of Trustees as well as the Board of Scientific Advisors were troubled by the decline of the Institute's investment income and by rising expenditures. Partly for this reason, the trustees decided in 1947 to close the Institute's research site in Princeton, New Jersey. In addition to financial considerations, the two governance boards were very much concerned by the physical separation of the two facilities. This was a very controversial decision because two members of the Princeton staff, Northrop and Stanley, had recently been awarded the Nobel Prize in Chemistry. With the closure of the Princeton department, some Princeton staff returned to New York City, and others departed from the Rockefeller Institute.

The Institute had never been content to rest on its laurels and had continuously been willing to make serious reassessments of its performance. Accordingly, in anticipation of Gasser's retirement, the trustees appointed a committee in the early 1950s to make recommendations about the Institute's future. Given the fact that by that time no research organization in the world had made so many major discoveries in biomedical science during the twentieth century, it is remarkable that the committee took into account a series of radical options for the future. The committee seriously considered whether the Institute should be closed down and its assets distributed to other research organizations, whether it should move from New York to a less costly environment, or whether the Institute should merge with an existing university.

By the early 1950s, it was clear to the Board of Trustees that the Rockefeller Institute had more than achieved its original purpose of providing a model of a high-quality research organization in biomedical science, one which would set the standard of excellence in biomedical science. Partly because of the existence of the Rockefeller Institute, there were now numerous research organizations making important discoveries and training very good scientists. By 1953, more than 200 former members of the scientific staff held rank of full professor (or the equivalent) in research centers throughout the country. Thus, if the Institute had attained its goal of helping to develop centers of biomedical research excellence in the country, why should it be continued? Perhaps Rockefeller wealth should be used for some other societal purpose not yet being addressed.

The committee consulted with several leading scientists throughout the country. Detlev Bronk, the most influential member of the committee, was adamantly opposed to closing the Institute. Recognizing that the Institute had achieved its initial goals, Bronk took the view that the Institute should revise its goals and purposes. In the future, it should not only be a center of research excellence, but it should also provide graduate education for future scientific leaders of the country. Because it would be a new kind of training center, the Rockefeller organization would continue to do something distinctively different from all other educational centers in America.

A New Vision

Impressed with Bronk's vision, the trustees prevailed upon him to become Gasser's successor. Thus, in 1953, the trustees voted to change the Institute into a graduate university with the authority to grant the degrees of doctor of philosophy and doctor of medical science. As a result, the Board of Scientific Directors was abolished and the Board of Trustees became the sole governing authority of the organization. Rockefeller Institute became a small university, the only solely graduate university in the United States. However, it was not until 1965 that the name was changed to the Rockefeller University.

Bronk, who served as president from 1953 until 1968, was very troubled that the nation's leading centers of training were producing highly specialized people whom he pejoratively characterized as technicians. In contrast, he wanted Rockefeller to produce scientists who had broad knowledge in a variety of fields. He recognized that scientific excellence required a mastery of subject, but thought it was important that scientists understand how their own research was intricately related to other fields of science. A recurring theme in his public speeches was the desire for the unity of knowledge, and for him the ideal university was one in which there would be intense and frequent interaction among scientists from diverse fields. Ideally, each scientist would have a broad competence in many areas of science. Moreover, Bronk was very humanistically oriented, and frequently spoke of the importance of scientists' understanding how they were intricately connected to the past, present, and future of their society. For Bronk, the importance of scientific research was to be measured by its larger humanitarian contributions to society. The transformation that he proposed for the Rockefeller organization was that it would be a training ground for the future leaders of science; these scientists would aspire to break down artificially segregated areas of knowledge and to struggle for the realization of the unity of knowledge for the benefit of society.[70] From time to time, Bronk preached to the Board of Trustees about the kind of university he had in mind, as he did at the Trustees meeting of May 22, 1961:

> It is unwholesome, and indeed dangerous for the future welfare of mankind, for scientists to live and work, to study and teach, in an environment in which they are not in close contact with creative, critical scholars in the humanities and arts. Such associations are a valuable quality of a university. Lack of such contact with those who help determine the future of civilization makes specialized research institutes barren intellectual environments. Q1]

But how might a small university attain such goals? Paradoxically, a small university such as Rockefeller had more potential to produce broadly trained scientists than larger research universities that teach most everything. Bronk believed that it was inappropriate to include all fields of science in their research program. In the largest research universities with their increasing fragmentation and specialization, such a goal had become increasingly difficult. When universities attempt to encompass all fields of science, some areas are invariably mediocre, and when mediocrity develops in some fields, it leads to mediocrity elsewhere. Because of the small size of the Rockefeller University, Bronk recognized that it could not offer programs in the humanities. As a result, the university in his presidency offered each student a fund of $1,000 to take advantage of the rich cultural offerings in New York (e.g., concerts, opera, theater, ballet, museums, and galleries). Moreover, he arranged for humanists and social scientists to present frequent public lectures at the University and for concerts to be held in its facilities.

Because it was not feasible to encompass all specialized fields of science, in Bronk's view the University should focus on the "most significant, most fundamental and most broadly relevant areas of mathematics, physics, chemistry, and biology." Moreover, because the University was organized around individuals rather than departments, its structure also should encourage cooperation in teaching and research. Accordingly, in recruiting faculty to the university, emphasis was placed on the choice of people who had broad interests and who by inclination enjoyed collaboration with others in diverse fields of science. However, the emphasis on breadth of scholarly interests and interdisciplinary cooperation did not mean that certain individuals or groups would be recruited simply to provide service for more fundamental areas of science. Indeed, the philosophy at Rockefeller was that every scientist and group was encouraged to be autonomous, with their own identity and dignity.

Growth and Community

The program that Bronk espoused had implications about the growth of the university, however. When Bronk became president in 1953, there were 21 members; in contrast, at the end of his tenure as president, there were 51 professors. In the same period, there was a tripling in the size of the scientific staff from 99 to 303.[71] Although in 1953, there were biological scientists, medical doctors, biophysicists, and physical chemists, the faculty was quickly expanded to include scientists in psychology and animal behavior, physics, mathematics, and philosophy. Moreover, the fields of biology, chemistry, and biophysics were extended. Within three years, Rockefeller appointed as professor several scientists who had either already been awarded or would later be awarded Nobel Prizes: Keffer Hartline from Johns Hopkins, Fritz Lippman from the Harvard Medical School, and Edward Tatum from Stanford University. Other distinguished, senior faculty appointed during the Bronk years were as follows: the philosopher Ludwig Edelstein; the biologist Paul Weiss; the mathematician Marc Kac; physicists George Uhlenbeck and Abraham Pais; behavioral scientists Carl Pfaffmann, Neal Miller, and Floyd Ratliff; the geneticist Theodosius Dobzhansky; the cell biologist Christian de Duve; and the chemist Theodore Shedlovsky. Bronk arranged for many of the world's leading scientists to spend a week or two, over a period of several years, with students, including Lord Adrian, Isidor Rabi of Columbia University, David Goddard of the University of Pennsylvania, Ragnar Granit of Stockholm, John Kirkwood of Yale University, Kaj Ulrik Linderstrom-Lang of Copenhagen, Louis Marie Monnier of Paris, Alex von Muralt of Bern. By the end of Bronk's term as president, Rockefeller University had one of the most distinguished collections of biomedical scientists in the world.

For Bronk, the University was ideally a genuine community of scholars with graduate students, post-docs, and faculty having intense and frequent interactions, all engaged in learning from one another. An important key to such a university was in the selection of students, and he frequently argued that it was important that students be selected with the same care as the faculty. Hence, during his presidency, Bronk personally interviewed most of the students before they were admitted. The only students selected for admission were those whose commitment to advanced study and research was believed to be equal to that of the faculty. All students were considered to be intellectually mature, highly motivated, and capable of self study. As a result, there was to be no core curriculum. Each student was to engage in a program of study based primarily on learning from advanced textbooks, professional journals, tutorials and seminars on special subjects, and work in the labs of some of the world's most distinguished and experienced scientists. In a sense, there was a separate curriculum for each student. Even though Rockefeller technically had been transformed into a university, it remained more of an institute than a research university of the type normally known in American society. Rarely would more than 25 graduate students be admitted a year, and by 1966 there were only 128 students—the level maintained throughout the rest of the century.[72] Because there were so few students relative to the number of faculty, close associations developed among students and faculty.[73]

Normally, admitted students had completed an undergraduate baccalaureate or held a doctor of medicine degree. Students were usually candidates for the degree of doctor of philosophy, but those who were doctors of medicine could pursue a degree of doctors of medical science. Thus, one of the major goals in moving from an institute to a university was to prepare young people to be scientific leaders of the nation, or as David Rockefeller expressed it, "a reaffirmation and an expansion of prior objectives, a reaching out to new opportunities for the pursuit of excellence."[74]

Small and Diverse

During the years of Bronk's presidency and ever since, the Rockefeller organization has been confronted with somewhat conflicting goals. It aspires to have considerable breadth in its scientific interests, but it is determined to remain small and to permit each lab to be autonomous. It has been difficult to maintain strength in chemistry, physics, mathematics, and in different fields of biology, and at the same time to promote interdisciplinary cooperation. The University has attempted to address this paradox by promoting the unity of science through the interpretation of biological phenomena in physical and chemical terms. Perhaps unsurprisingly, several scientists who were recruited to Rockefeller as organic or physical chemists over time became biochemists. Some physicists became biophysicists, and some mathematicians emigrated to other fields as a result of their interests in computer science and various technologies. Thus, at the Rockefeller University, there has long been a strategy of recruiting scientists who have broad interests and who by temperament have been eager to collaborate with and learn from those in other fields. Because of its small size, the University has generally been reluctant to recruit those who by temperament prefer to work in isolation, although over time there have been exceptions.

Another aspect of the continuity between the Bronk years and the culture of excellence institutionalized during the Flexner years was the historical emphasis on providing services for the scientific staff, such as the design and construction of instruments, illustration services, glass blowing, and a spectroscope laboratory. To keep these and other services at a high level of excellence, the organization over the years has recruited an extraordinary staff trained in the techniques of mechanical, electrical, and chemical engineering.[75] Having state-of-the-art support services has been important in keeping the Rockefeller University at the cutting edges of multiple fields of science.

The Limits of Expansion

Accompanying the expansion of faculty during the Bronk years was a building program that reshaped the physical setting of the Rockefeller University. This included a residence for graduate students and a building with two wings: the Abby Aldrich Rockefeller Hall (containing a dining room, lounges, library, and accommodations for visiting scholars) and the Alfred H. Caspary Hall (with administration offices). Connected to Caspary Hall was a new auditorium. A modern nine-story laboratory and several smaller buildings were constructed.[76] Bronk's aesthetic aspirations for the University were revealed by his arranging for one of the world's leading landscape architects, Daniel Urban Kiley, to design the university's grounds in the late 1950s. The result was the development of one of the most beautiful grounds in the city.

Bronk was a dreamer, a person whose ambitions for The University were virtually without limit. Hence, it is not surprising that it soon became obvious that the University could not survive primarily on its endowment, as in the past. Once substantial extramural funding from NIH became available in the 1950s, the Rockefeller organization began to turn to the federal government for research support. This marked a critical turning point in the history of the organization: labs began to grow in size, turned somewhat inward, and became somewhat more independent. No longer did everyone have lunch together. There were too many senior scientists and students for the early twentieth century type of communication and integration to exist. Many labs began to have their own journal clubs, and attendance at the weekly Friday afternoon scientific presentations for the entire organization dropped off dramatically. There was no longer the same degree of horizontal communication across labs as during the first half of the century. Of course, the Rockefeller University was still quite small relative to most American research universities, but as size increased, the degree of integration and communication among the scientific staff diminished.

It is not unusual that an organization undergoing rapid expansion and reorganization under one leader later finds that the rate of change is not sustainable; therefore, the next leader faces a period of major readjustment and stabilization. This is precisely what happened under the University's next president, Fred Seitz (1968–1978), a physicist. Like Bronk, he had been president of the National Academy of Sciences.

With hindsight, it is obvious that the University was extravagant in its expenditures during the Bronk years. Shortly after Seitz became president, the economic environment of the University quickly changed. By 1970 the University, like many others throughout the country, found itself confronting serious financial problems, exacerbated by inflation, including rising salaries as well as construction and energy issues. There were cuts in some federal grant programs, causing the University to draw money from its endowment to support programs to which it was committed. Moreover, the recession that began in 1968 led to a drop in income from the endowment. Because nonacademic pay scales had fallen below city standards during the Bronk years, Seitz and his staff now had to address this problem. For the first time in its history, the organization was not only confronted with a deficit, but a mounting one. This was the shape of things as Seitz completed his first year as president. As during the Depression of the 1930s, the University was forced to undertake a serious assessment of its operations, the result of which was the recognition that the institution could not sustain the rate of growth of the Bronk years.

Overall, the 1970s and 1980s were difficult. For financial reasons, if for no other, Seitz had no alternative but to undo some of the decisions of his predecessor. In contrast to the years of fanfare and ceremony under the presidency of Bronk, the tone during the presidency of Seitz was more restrained, due to the financial difficulties. Recruiting continued, but less aggressively. On-site staff were carefully reviewed, and laboratories were warned that long-term prospects for funding their researcher were very limited.

And yet, the decades of the 1970s and the 1980s also were ones of outstanding achievement and recognition. In 1969, Bruce Merrifield was awarded the Lasker Prize for Basic Biomedical Research for his work in developing a method for the synthesis of polypeptides and proteins. In 1972, Gerald Edelman was awarded the Nobel Prize in Physiology or Medicine (shared with Rodney Porter of Oxford University) while William Stein and Stanford Moore (with Christian Anfinsen of the National Institutes of Health) received the Nobel Prize in Chemistry. Two years later, Albert Claude, George Palade, and Christian de Duve shared the Nobel Prize in Physiology or Medicine for work they had conducted at Rockefeller.

The University trustees became increasingly concerned about their dependence on federal funding for research. Cuts at the federal level could imperil ongoing research, just as, to the contrary, the possible "war on cancer" could cause coffers to open. Fearful that in the distant future, federal funding would prove unstable and would decrease the University's autonomy and flexibility, the trustees instituted campaigns to raise funding from the private sector (individuals, foundations, and business firms). The trustees intended that federal grant money would provide about half of the University's budget, and the other half of the budget would be covered by private fund raising and income from the endowment. Private sector funding was absolutely necessary if the University was to remain at the frontiers of biomedical science, especially to expand its research program in cell biology and molecular biology.

Governance and Administration

By the end of the Bronk years, the trustees approved the creation of a university senate and an academic council, which was the executive committee of the senate. As a result, several senior faculty increasingly insisted on being involved in decision-making in university affairs, very much in contrast to the years when the organization was a relatively small institute. During the Flexner and Gasser years, even senior members rarely knew what major decisions were being made by the director and the two boards. Indeed, during the Gasser years, the Institute offered senior positions to Linus Pauling, Carl Cori, Vincent du Vigneaud, and Francis Schmitt[77] (all of whom declined) but the author of this paper has been unable to find any evidence that any Member of the Institute's staff was informed about these efforts.

During the Bronk years, the scientific staff had continued to be relatively uninvolved in the governance of the Rockefeller University. But difficult choices the University had to make because of the financial deficits of the 1970s and 1980s, drew the faculty into the governance of the University. Although there had been virtually no discussion among the scientific staff in the early 1950s as to whether there should be a graduate program at the University, during the Seitz years the faculty began to discuss what proportion of funds should be devoted to teaching as distinct from research, the degree to which heads of laboratories would have complete autonomy in appointing scientists in their own labs, how many Rockefeller-funded scientists might be in a single lab, and how decisions would be made about the appointment and promotion of laboratory staff. Although the process of institutionalizing new modes of decision making in an era of fiscal constraints created stress within the organization, Seitz was a very able and unflappable administrator. He facilitated the faculty's larger role, long-term financial planning. As research became much more expensive and the structure of research organizations more complex, many more factors entered into the management of the organization. In short, the complex demands of administering the organization between 1970 and 1990 made necessary a marked departure from the more personal style of management that existed before Seitz's presidency.

Nevertheless, Seitz and his successor, Joshua Lederberg (1978–1990) were very attentive as well to the infrastructure of the University, keeping it as a world-class center in instrumentation, design, and construction, and in attempting to add new laboratory space.[78] During the Seitz presidency, Hidesaburo Hanafusa, James Darnell, and several other senior faculty were recruited, but most efforts to add other senior staff were futile. The University continued its efforts to make distinguished appointments during the early years of Lederberg's presidency, and added, most notably, Jan Breslow, Paul Greengard, and Torsten Wiesel to the faculty.

Through the presidency of Lederberg, the financial condition of the University continued to be constrained by the poor performance of the American economy. Believing in the desirability of the continued smallness of the Rockefeller University, Lederberg reduced some layers of administration and attempted to make himself directly available to faculty. Many of his plans—whether very general or more programmatic (e.g., parasitology or toxicology)—were hard to realize without more discretionary funds. Meanwhile, a great deal of administrative, trustee, and faculty energy was invested in addressing fundamental issues such as fund-raising and problems attendant upon life in the city (e.g., lack of affordable housing for both junior and senior faculty).

Throughout the twentieth century, the two John D. Rockefellers and David Rockefeller were always available to lend support to the Rockefeller organization during times of stress. In fact, David Rockefeller joined the Rockefeller Institute Board of Trustees in 1940 and served for more than fifty-five years. In 1950, he succeeded his father as president of the board. It is difficult to imagine how Rockefeller could have remained a center of scientific excellence without his counsel, his financial assistance, and his ability to be a bridge between the University and other sectors of American society.

Years of Turmoil

Several perspectives about the behavior of organizations need to be kept in mind in order to understand some of the internal turmoil that occurred at the Rockefeller University between 1989 and 1991. By the late 1980s, there was an increased perception both within and outside of Rockefeller University that it was not performing as well as it had some decades earlier. Changes in the environment, apart from the availability of NIH funding, had a major effect on the University. The center of gravity of basic science research had shifted westward, as increasing numbers of scientists were willing to have careers in Berkeley, Seattle, Los Angeles, San Diego, and elsewhere on the West Coast. Furthermore, as the cost of living in the New York area escalated, it had become increasingly difficult for the University to recruit scientists of their first choice, a constraint that had been quite rare in earlier years.

In the early part of the twentieth century, ambitious young biomedical scientists were eager to spend a few years at the Rockefeller Institute. By the latter part of the century, there were many centers of biomedical excellence in the United States, and the best of the nation's young scientists were increasingly unwilling to go to the University, largely because most young scientists were not able to be heads of their own labs until they attained the rank of full professor. By the late 1980s, it was well known that for many years it had been common for the nation's best biomedical scientists to head their own labs when they were quite young (including Joshua Lederberg and Howard Temin at Wisconsin, Paul Berg and Dale Kaiser at Stanford, Jim Watson and Walter Gilbert at Harvard, Mike Bishop and Harold Varmus at the University of California, San Francisco). With numerous research centers throughout the country, good young scientists increasingly expected to have more autonomy and their own laboratories before becoming senior professors. This was a widely discussed problem within the Rockefeller University; but by the late 1980s, more often than not, young scientists were not heads of labs. As senior scientists retired, it became increasingly difficult to recruit distinguished replacements. At the same time that these problems arose, the Rockefeller University, like most of the nation's leading research universities, was required to institute salary and wage freezes in response to the poor performance of the American economy.

Apart from the fiscal problems and the junior staff problems, the University faced the persisting tasks of developing new labs and renovating old ones—a constant at all serious research organizations. With changes occurring at an ever-increasing rate in the larger world of science, there were unrelenting pressures to recruit new faculty in molecular biology, neurobiology, and cancer research, as well as in other areas. However, by 1990, the University had recruited only one senior scientist in the previous five years. The average age of the tenured faculty was fifty-eight in 1990, meaning that within another decade, many distinguished faculty would retire.

In the midst of these changes in the larger environment, David Baltimore, a Nobel laureate, became president of the Rockefeller University in July of 1990. A former graduate student at the University, Baltimore was one of the nation's most productive scientists and was widely perceived to have been a very successful administrator of the Whitehead Institute for Biomedical Research, an affiliate of the Massachusetts Institute of Technology (MIT). His appointment was strongly opposed by a sizable minority of the University's faculty, primarily because of the complex and unresolved investigations of a scientific paper that he and several of his MIT collaborators had published in *Cell* in 1986.[79] There were allegations that some of the experiments in the paper were misreported by the senior author, Thereza Imanishi-Kari. Although there were no suggestions that Baltimore personally misrepresented the data in the paper, he was widely criticized for failure to conduct a proper investigation into the allegations about the paper and for defending the "flaws" in the paper too long and vigorously. Because of this cloud over Baltimore, his tenure as president of Rockefeller became very controversial.[80] His most vocal critics, both inside and outside the University, charged that he had been extraordinarily arrogant in his handling of many of the issues related to the disputed paper.

By the time Baltimore arrived in the summer of 1990, the Rockefeller University had undertaken efforts to address some of its outstanding problems. A new laboratory building was under construction, and in 1989 several junior faculty had been appointed as heads of laboratories. Still, numerous procedures for dealing with the retention, dismissal, and promotion of junior faculty had not been resolved and the University's budget was seriously unbalanced, with a deficit of $12.3 million during Baltimore's first year.

Authority and Legitimacy

Baltimore immediately initiated a $250 million fund-raising drive and instituted a wage freeze. At the same time, he established several search committees to recruit junior and senior faculty, and proposed major changes with regard to the status of junior faculty. In short, although Baltimore addressed problems already on the University's agenda, he was clearly a catalyst, dramatizing the University's problems and acting decisively with regard to some of them.

This was not an auspicious time. With so many major issues crowding his agenda, it was especially difficult for Baltimore, as a new president, to establish his authority and legitimacy. He was attempting not only to manage the University; but simultaneously to operate his laboratory. Relocating and setting up his own lab was quite time consuming. The tensions created over the 1986 *Cell* paper continued, casting a pall over his presidency. Within Rockefeller, turmoil over the paper was compounded by the fact that a few of the senior faculty had known Baltimore since his graduate student days at the University, and several disliked him intensely. Moreover, some senior faculty resented Baltimore's demeanor as president: they felt that he viewed himself as the man on horseback who was coming to save the University from a group of entrenched oligarchs. Some faculty were embittered by rumors heard around the country that he had long bad-mouthed the University. The sentiment of one senior faculty member captured the views of many others: "To portray this faculty as a bunch of old dying swans who have lost touch with modern biology is complete and utter nonsense."[81]

Almost everything Baltimore proposed quickly became controversial in one way or another. Although the senior faculty was essentially in agreement about the desirability of changing the role of the junior faculty with regard to heading labs (as indicated by the virtually unanimous approval of the Academic Senate in the fall of 1990 of Baltimore's proposals for junior faculty), controversy continued about even this issue. Despite the agreement on the principle that some scientists who were not professors might head labs, issues about which junior faculty would head labs were unresolved. In May 1991, five assistant and associate professors were selected as heads of labs, bringing the number of nontenured heads of laboratories to sixteen.[82] As Baltimore rewarded some junior faculty with their own labs, cleavages emerged within the junior ranks. It appeared as though a two-tiered system of junior faculty was emerging. Some junior faculty received internal promotions, whereas others realized that their long-term chances of heading labs were no better than before Baltimore's arrival.

The issue of the *Cell* paper would simply not disappear. In early 1991, there were leaks in the press to the effect that the U.S. Secret Service had uncovered evidence of fraud by Imanishi-Kari. In the spring, Baltimore's public comments about the *Cell* paper led to an intensification of criticism of him and the University both in the press and among some of the nation's most respected scientists about the paper. As these criticisms reverberated within the University, Baltimore turned to junior faculty for support, leading to criticism that he "was using the junior faculty at some risk to their own careers."[83]

Finally, in the fall of 1991, in the midst of all of this turmoil, the overwhelming sentiment of the senior faculty was conveyed to the trustees that Baltimore was incapable of being an effective president, and shortly thereafter he resigned.[84] With hindsight it is obvious that the Baltimore presidency was unfortunate for the University as well as for Baltimore. In July 1996, a three-person board appointed by the Department of Health and Human Services concluded that the "preponderance of evidence" indicated that the allegations about misconduct in producing the data in the *Cell* paper could not be proven.[85]

There was a great deal of ill-chosen rhetoric on the part of both supporters and critics of Baltimore during the affair. Some of the rhetoric of Baltimore and his supporters early on suggested that the University's faculty was depleted and that the quality of science was no longer distinguished. The validity of these claims requires some perspective. It is true that there was a time when it was believed at Rockefeller that anyone receiving a permanent appointment at the organization should do work of a caliber to make the person a serious contender for a Nobel Prize. But with increases in size and the emergence of several dozen major centers of biomedical scientific research throughout the nation, it was clear that such goals were unrealistic and that Rockefeller no longer exercised the hegemonic influence over biomedical science as it had in the past. However, by 1990, the organization was still a distinguished and major center for biomedical research: within a decade, many of its most innovative scientists were singled out for major recognition with Nobel Prizes, the Lasker Prize for Basic Biomedical Science, and the Louisa Gross Horwitz Prize. Just a few years earlier, Hidesaburo Hanafusa received the Lasker Prize for Basic Biomedical Science. Also, Gerald Edelman was one of the world's most creative theoreticians in neuroscience, though his work, like most other theoretical work, was controversial. Although Bruce Merrifield had done the research for which he was awarded a Nobel Prize some years earlier, his lab was still very active in work involving ever more difficult synthetic challenges and much higher molecular numbers. Moreover, there were numerous other scientists doing excellent science at the University.

Wiesel Appointed

Upon Baltimore's resignation, the trustees appointed as president Torsten Wiesel, a world-renowned neurobiologist who had shared a Nobel Prize in Physiology or Medicine with David Hubel in 1981, and who had moved to the University from Harvard Medical School in 1983. The trustees could not have found a more suitable person for the task. Wiesel, who served until 1998, was an excellent president, one of the very best in the history of the organization.

Wiesel, born and educated in Sweden, had moved to the United States in 1955. When he became president of the Rockefeller University, he was sixty-seven years old, and he immediately became completely focused on serving the University. Wiesel had many of the traits of an outstanding president: a good sense of the direction in which science was moving, a keen ability to identify talent and to raise money to support good science, and a capacity to create a nurturing environment for both senior and junior scientists. After the intense cleavages of the Baltimore presidency, the University's faculty was eager to have stability and harmony and to rebuild their damaged reputation. Wiesel, an eminent scientist with considerable modesty and humility, was highly successful in bringing people together. Almost intuitively, he was able to integrate the traditions of the Rockefeller University with the directions in which science was changing as it moved toward the twenty-first century. Early in his presidency, he encouraged open faculty participation in discussions of both the weaknesses and strengths of the University. He then coordinated the development of an Academic Plan, an effort involving unprecedented collaboration of faculty, administration, and trustees. His strategy of bringing all parties to the table was typical of a rather low key management style, very different from the bombastic style of Bronk. Very quickly, a consensus emerged that the University would build on its current 70 laboratories, and slowly expand to between 80 and 100 labs as resources became available and appropriate talent was identified.[86]

Because the University was structured around laboratories rather than departments, a critical problem was how to keep the centrifugal forces created by so many different labs from becoming unmanageable. Wiesel seemed to have an innate ability to solve the problem, especially by emphasizing the tradition and culture of excellence that had been institutionalized at Rockefeller. Through the use of a broad array of rituals, the organization throughout the 1990s highlighted its strong, widely shared culture, a process that helped to promote harmony and communication among the different laboratories. Without a strongly shared culture, it would have been much more difficult to generate the trust and predictability necessary for a well-functioning organization.

New Centers, New Funding

In addition to the emphasis on the common culture, the Rockefeller University also promoted the coordination of labs by grouping them around seven research centers, in recognition of the natural affinities among the interests of scientists. The seven centers financed in part by successful University fund-raising in the private sector during the 1990s were (1) the Center for Biochemistry and Structural Biology; (2) the Center for Sensory Neuroscience; (3) the Center for Human Genetics; (4) the Center for Research on Alzheimer's Disease; (5) the Center for Studies in Physics and Biology; (6) the Center for Immunology and Immune Diseases; and (7) the Center for Mind, Brain, and Behavior.[87] These centers were intended to enhance communication and strengthen collaboration across labs, and to provide coherence for fund-raising from both federal and private sector sources. Depending on the interests of scientists, they could be affiliated with more than one center. In the process of developing the centers, some faculty gained a much better understanding of the complementary interests of different labs. Although the centers have varied in their performance, as well as in size and resources, they have provided a meaningful strategy for promoting communication across laboratories. The functioning of the centers has been complemented by the fact that in recent years, labs at the University have become somewhat smaller, reducing the tendency for labs to be so internally focused.

Although governance of the University is shared by the labs, the research centers, the academic council, and the university senate, the office of the president played an extremely important role in governing by making financial and personnel decisions, and in determining the allocation of laboratory space and laboratory budgets (if non–grant funds are being used). During Wiesel's first four and a half years as president, the Rockefeller University raised approximately $135 million in private gifts and pledges, much of which was used to support the recruitment of new faculty and to create state-of-the art laboratories. The University increased the number of laboratories and recruited many junior and senior scientists. During these same years, 20 new laboratories were headed by nontenured scientists.

When Wiesel left the presidency in 1998, there was a widespread perception both within and beyond the University that Rockefeller was once more in very sound condition, both scientifically and financially. The University had restored stability to its budgets and operations, and had increased its endowment by over 50 percent in a five-year period. Part of this increase resulted from the performance of the American economy, but much of the improvement was also due to the management team Wiesel and the trustees had put in place.[88]

Into a Second Century

Very mindful of the turmoil and embarrassments of the early 1990s, the University by the turn of the new century was anything but complacent. There was a tone of rebuilding, but with modesty as the University attempted to learn from its competitors. In retrospect, perhaps the turmoil of the early nineties had been healthy for the University, as one of its effects had been to create more of a community among its faculty than had existed for decades.

To lead the Rockefeller University into its second century, the trustees in 1998 appointed Arnold Levine as president, a renowned cancer researcher and former chair of the Department of Molecular Biology at Princeton University. Levine epitomized the Rockefeller scientist, as he internalized a great deal of scientific diversity (with broad knowledge of molecular biology, cell biology, and genetics) and had a good sense of the history of various fields of science. As was the case with the first director Simon Flexner, Levine thought strategically. He had a good sense of where science was moving, was conscious from the beginning of where he wanted to direct the University, and was keen to promote the training of young scientists.

Levine took leadership of an organization that had undergone profound changes over the past century. Even in its recent past, there had been exponential growth in its infrastructure, with hundreds of new research associates, post-docs, technicians, and other support staff. However, it was still very small relative to other American universities, with approximately fifty full professors, twenty-seven associate professors, and fifty-three assistant professors.[89] Because of its small faculty, there was far more frequent and intense communication among a larger proportion of its scientific staff across diverse fields of science than at any other American research university. True, Rockefeller was more fragmented than it was forty years ago because it had so many labs, but it was much less differentiated internally than every other American university. The fact that there still were no departments and that a lab was likely to close down when the head of the lab departed meant that the organization had an extraordinary flexibility to adapt to the fast pace of change in the global environment of science.

This flexibility and adaptiveness explain why in its centennial year of 2001 Rockefeller University, despite its small size, still towered over most research organizations in America. It had a higher proportion of its faculty who were either members of the National Academy of Sciences or Howard Hughes investigators than any other research organization in the United States; and, its scientists received more funding for biomedical research per scientist from the NIH than in any other research organization in the United States. In 1999 and 2000, the Rockefeller University demonstrated that its extraordinary excellence as a center for major discoveries is still very much alive when members of its faculty received four of the most coveted prizes in biomedical science: Robert Roeder received the Louisa Gross Horwitz Prize in basic biomedical science, Roderick MacKinnon received the Lasker Prize for Basic Biomedical Science, and Günter Blobel in 1999 and Paul Greengard in 2000 received Nobel Prizes in Physiology or Medicine. These four prizes in a two-year period represent more recognition for major discoveries than four-fifths of the leading American research organizations received in the whole of the twentieth century.[90] In short, at the turn of the millennium there was excellent evidence that the Rockefeller University was still one of the world's premier biomedical research organizations.

Appendix I: Defining Major Breakthroughs in Biomedical Research

For purposes of this essay, and my related research, a major breakthrough in biomedical science is defined as a finding or process, often preceded by numerous "small advances," which leads to a new way of thinking about a problem.[91] This new way of thinking is highly useful for numerous scientists in diverse fields of science in addressing problems. This is very different from the rare paradigm shifts Thomas Kuhn analyzed in his classic *The Structure of Scientific Revolutions* (1962).[92] Major breakthroughs about particular problems in biomedical science occur within the paradigms about which Kuhn was writing. Historically, a major breakthrough in biomedical science was a radical or new idea, the development of a new methodology, or a new instrument or invention. It has usually not occurred all at once, but has involved a process of investigation taking place over a substantial period of time and a great deal of tacit and/or local knowledge.

The indicators of major discoveries are as follows: (1) discoveries resulting in Copley Medals (awarded since 1901 by the Royal Society of London), insofar as the award was for basic biomedical research; (2) discoveries resulting in a Nobel Prize in Physiology or Medicine since the first award in 1901; (3) discoveries resulting in a Nobel Prize in Chemistry, also since the first award in 1901, if the research had high relevance to biomedical science (this includes discoveries in biochemistry as well as an occasional breakthrough in several other areas of chemistry); (4) discoveries resulting in ten nominations in any three years before 1940 for a Nobel Prize in Physiology or Medicine, or in Chemistry if the research had high relevance to biomedical science. (The rationale is that this number of nominations suggests that broad support existed in the scientific community to the effect that the research represented a major scientific breakthrough even if it did not result in a Nobel Prize. Because the number of people who could make nominations for Nobel Prizes in the first half of the twentieth century was quite restricted by present day standards, this criterion of "10 and 3" represents broad recognition among nominators during those years.) (5) Every year, the Royal Swedish Academy of Sciences and the Karolinska Institute each appointed a committee to study major discoveries and to propose Nobel Prize winners (in Chemistry, and in Physiology or Medicine, respectively). These two committees have made short lists of discoveries considered to be "prize worthy," and some of the discoveries were recognized for Nobel Prizes. I include in my population the discoveries on the short lists through 1940 that were not recognized for Nobel prizes. I have access to the Nobel Archives for the Physiology or Medicine Prize at the Karolinska Institute and to the Archives at the Royal Swedish Academy of Sciences in Stockholm for this period, but for reasons of confidentiality, access to these archives is not permitted for the past fifty years.

To capture the variety of major scientific discoveries during this period, I also use several other criteria. I included (6) discoveries resulting in the Arthur and Mary Lasker Prize for basic biomedical science; (7) discoveries resulting in the Louisa Gross Horwitz Prize in basic biomedical science; and (8) discoveries in biomedical science resulting in the Crafoord Prize (awarded by the Royal Swedish Academy of Sciences). For purposes of this essay, I have included the aforementioned forms of recognition through the fall of 2000.

The emphasis on diverse fields of science is critical for my definition of a major breakthrough. Most biomedical research is highly specialized and is therefore reported to highly specialized audiences. And while I do not suggest that this kind of research is trivial or unimportant, its impact is more confined to specialized researchers, whereas the research that is perceived as a major breakthrough is accorded the kind of recognition described above because it is knowledge absorbed by scientists in many different specialties.

Appendix II

Scientists Whose Major Discoveries, All or Part, Were Made at Rockefeller Institute/University and the Forms of Recognition for Them

Name of scientist	Forms of recognition
Oswald Avery[a,b]	Nominated ten times in three different years for Nobel Prize in Physiology or Medicine 1931. For the discovery that the immunological specificity of type II pneumococcus is due to a polysaccharide. Copley Medal 1945. For recognizing the transforming principle of DNA.
Günter Blobel	Horwitz Prize 1987; Lasker Prize 1993; Nobel Prize in Physiology or Medicine 1999. For his discovery that proteins have intrinsic signals that govern their transport and localization in the cell.
Alexis Carrell	Nobel Prize in Physiology or Medicine 1912. For his work in suturing blood vessels and in the transplantation of organs.
Albert Claude	Horwitz Prize 1970; Nobel Prize in Physiology or Medicine 1974. For applying the techniques of centrifugation and electron microscopy to the isolation and identification of subcellular structures.
Lyman Craig	Lasker Prize 1963. For his countercurrent distribution technique as a method for the separation of biologically significant compounds, and for the isolation and structure studies of important antibiotics.
Christian de Duve	Nobel Prize in Physiology or Medicine 1974. For combining subcellular fractionation with biochemical analysis in order to discover the cell organelles of lysosome and peroxisome and for identifying their functions.
Gerald Edelman	Nobel Prize in Physiology or Medicine 1972. For determining for the first time the complete chemical structure of immunoglobulins (antibodies), the key molecules of immunity.
Simon Flexner[a]	Nominated ten times in three different years for Nobel Prize in Physiology or Medicine 1911. For developing serum treatment of cerebrospinal meningitis.
Paul Greengard	Nobel Prize in Physiology or Medicine 2000. For his discoveries concerning signal transduction in the nervous system.
Hidesaburo Hanafusa	Lasker Prize 1982. For demonstrating how RNA tumor viruses cause cancer, and elucidating their role in combining, rescuing and maintaining oncogenes in the viral genome.
H.K. Hartline	Nobel Prize in Physiology or Medicine 1967. For work on the physiology and chemistry of vision.
Bertil Hille[c]	Horwitz Prize 1976; Lasker Prize 1999. For elucidating the functional and structural architecture of ion channel proteins, which govern the electrical potential of membranes throughout nature, thereby generating nerve impulses and controlling muscle contraction, cardiac rhythm, and hormone secretion.
Henry Kunkel	Lasker Prize 1975; Horwitz Prize 1977. For his discoveries in immuno-pathology.
Karl Landsteiner	Nobel Prize in Physiology or Medicine 1930. For his classification of blood groups and for his further discoveries over the years of subgroups within the original groups which he identified.
Jacques Loeb[a]	Nominated ten times in three different years for Nobel Prize in Physiology or Medicine 1911. For his research on the colloidal behavior of proteins.
Roderick MacKinnon	Lasker Prize 1999. For elucidating the functional and structural architecture of ion channel proteins, which govern the electrical potential of membranes throughout nature, thereby generating nerve impulses and controlling muscle contraction, cardiac rhythm, and hormone secretion.
Bruce Merrifield	Lasker Prize 1969; Nobel Prize in Chemistry 1984. For his development of a simple and ingenious method for synthesizing peptides and proteins.
Stanford Moore	Nobel Prize in Chemistry 1972. For research on enzymes, body proteins central to life; particularly for working out for the first time the chemical structure of pancreatic ribonuclease, an enzyme that breaks down ribonucleic acid (RNA).
Hideyo Noguchi[a]	Nominated ten times in three different years for Nobel Prize in Physiology or Medicine 1921. For his research in demonstrating the relationship between Oroya Fever and verruca peruviana and cultivation of the causative agent.
John Northrop	Nobel Prize in Chemistry 1946. For the preparation of enzyme and virus proteins in pure form.

Scientists Whose Major Discoveries, All or Part, Were Made at Rockefeller Institute/University and the Forms of Recognition for Them (continued)

Name of scientist	Forms of recognition
George Palade	Lasker Prize 1966; Horwitz Prize 1970; Nobel Prize in Physiology or Medicine 1974. For contributing important techniques of centrifugation and electron microscopy and using them to define how cells synthesize proteins and how they package proteins for secretion.
Keith Porter	Horwitz Prize 1970. For his fundamental contributions to the electron microscopy of biological materials.
Robert Roeder	Horwitz Prize 1999. For his research on the processes of gene activation.
Peyton Rous	Nobel Prize in Physiology or Medicine 1966. For establishing a virus as the cause of chicken sarcoma.
Theobald Smith[a]	Nominated ten times in three different years for Nobel Prize in Physiology or Medicine 1921; Copley Medal 1933. For his research on host-parasite interrelationships.
Wendell Stanley	Nobel Prize in Chemistry 1946. For the preparation of enzyme and virus proteins in pure form.
William Stein	Nobel Prize in Chemistry 1972. For research on enzymes, body proteins central to life; particularly for working out for the first time the chemical structure of pancreatic ribonuclease, an enzyme that breaks down ribonucleic acid (RNA).

[a]Scientists who are included in this study as a result of having 10 nominations in three different years are identified as “10 in 3” and the date listed for them is the first odd-numbered year in the decade in which they received the largest number of nominations. Thus, a scientist receiving two nominations in 1911, three in 1913, and five in 1921 would be listed with the year 1921.

[b]Oswald Avery received recognition for two major discoveries. One was his work on polysaccharides in the 1920s, and the other was his work on DNA in the 1940s (Dale, 1946; Dubos, 1976; McCarty 1985; Amsterdamska, 1993; Bearn, 1996).

[c]The body of work for which Hille was recognized began while he was a student at the Rockefeller University.

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Endnotes

1. The theoretical literature for confronting this problem consists of the following: J. Rogers Hollingsworth, Ellen Jane Hollingsworth, and Jerald Hage, eds., *The Search for Excellence: Organizations, Institutions, and Major Discoveries in Biomedical Science* (New York, forthcoming); Michael L. Tushman and Elaine Romanelli, “Organizational Evolution: A Metamorphosis Model of Convergence and Reorientation,” *Research in Organizational Behavior* 7 (1985): 171–222; Michael L. Tushman and Charles A. O’Reilly III, “Ambidextrous Organizations: Managing Evolutionary and Revolutionary Change,” in *California Management Review* 38 (1996): 8–30; Elaine Romanelli and Michael L. Tushman, “Organizational Transformation as Punctuated Equilibrium: An Empirical Test,” *Academy of Management Journal* 37 (1994): 1141–66; Michael E. Porter, “Toward a Dynamic Theory of Strategy,” *Strategic Management Journal* 12 (1991): 95–117; Jerald Hage and J. Rogers Hollingsworth, “Idea Innovation Networks: A Strategy for Integrating Organizational and Institutional Analysis,” *Organization Studies* 21 (2000): 971–1004; J. Rogers Hollingsworth, “Doing Institutional Analysis: Implications for the Study of Innovation,” *Review of International Political Economy* 7 (2000): 1–50.
2. J. R. Hollingsworth, E. J. Hollingsworth, and J. Hage, eds., *The Search for Excellence*.
3. Abraham Flexner, *Medical Education in the United States and Canada* (Boston, 1910).
4. Simon Flexner and James Thomas Flexner, *William Henry Welch and the Heroic Age of American Medicine* (New York, 1941); Charles Eliot, *Harvard Memories* (Cambridge, 1923), 28, 35; Kenneth M. Ludmerer, *Learning to Heal: The Development of American Medical Education* (New York, 1986); J. Rogers Hollingsworth, *The Political Economy of Medicine: Great Britain and the United States* (Baltimore, 1986), 82–125.
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6. Frederick T. Gates, *Chapters in My Life* (New York, 1977), 165; Richard E. Brown, *Rockefeller Medical Men* (Berkeley, CA, 1979), 179–88.
7. Peyton Rous, “Simon Flexner,” *Obituary Notices of Fellows of the Royal Society* 6 (1949): 417; George W. Corner, *A History of the Rockefeller Institute, 1901–1953: Origins and Growth* (New York, 1965), 35; Paul F. Clark, “Theobald Smith: Student of Disease,” *Journal of the History of Medicine* 14 (1959): 490–514; Hans Zinsser, “Theobald Smith,” *Biographical Memoirs of the National Academy of Sciences* 17 (1937): 261–303.
8. Donald Fleming, *William H. Welch and the Rise of Modern Medicine* (Baltimore, 1954), 131–7; S. Flexner and J. T. Flexner, *William Henry Welch*.
9. Simon Flexner, “The Rockefeller Institute for Medical Research, New York,” in *Forschungsinstitute Ihre Geschichte, Organisation und Ziele*, eds. Ludolph Brauer, Albrecht

Mendelsohn Bartholdy, and Adolf Meyer. (Hamburg, 1930), 458; S. Flexner and J. T. Flexner, *William Henry Welch*, 462–464; Gates, *Chapters in My Life*, 1979–88.

10. Adrea K. Blumenthal, "Leadership in a Medical Philanthropy: Simon Flexner and the Rockefeller Institute for Medical Research," (PhD diss., Drew University, 1991). 326 pp.
11. Rous, "Simon Flexner" (n. 7 above), 417.
12. Philip J. Pauly, *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology* (New York, 1987), 134–136; Rous, "Simon Flexner" (n. 7 above), 418.
13. Rous, "Simon Flexner" (n. 7 above), 418.
14. Flexner, "Rockefeller Institute" (n. 9 above), 2: 461-2.
15. Simon Flexner served as director until 1935 and Herbert Gasser from 1935 to 1953. After 1935, the title director was dropped in favor of president. Detlev Bronk served as president from 1953 to 1968; Fred Seitz, 1968–1978; Joshua Lederberg, 1978–1990; David Baltimore, 1990–1991; Torsten Wiesel, 1991–1998; and Arnold Levine 1998–2001.
16. Tom Rivers, *Reflections on a Life in Medicine and Science* (Cambridge, 1967), 198; unpublished and untitled lecture by Simon Flexner, folder Simon Flexner, box 6, RG 303.1 Bronk Papers, Rockefeller University Archives, Rockefeller Archive Center, Sleepy Hollow, New York (hereafter RAC).
17. Paul F. Clark, *Pioneer Microbiologists of America* (Madison, WI, 1961), 172; see also Simon Flexner to Abraham Flexner, July 4, 1924, Flexner Letters, Flexner Papers, American Philosophical Society, Philadelphia, Pennsylvania.
18. Flexner, "Rockefeller Institute" (n. 9 above), 461.
19. Rous, "Simon Flexner" (n. 7 above), 427.
20. Ibid, 425.
21. Elvin A. Kabat, "Michael Heidelberger," *Journal of Immunology* 148 (1992): 301–307.
22. Rous, "Simon Flexner" (n. 7 above), 421.
23. Peyton Rous, "Simon Flexner and Medical Discovery," *Science* 107 (11 June 1948): 613.
24. Clark, *Pioneer Microbiologists* (n. 17 above), 172.
25. Rous, "Simon Flexner" (n. 7 above), 427; Alfred E. Cohn, "On Simon Flexner," *No Retreat From Reason* (New York, 1948), 228; Rivers, *Reflections on a Life* (n. 16 above), 123–27.
26. Rivers, *Reflections on a Life* (n. 16 above), 124–125; Rous, "Simon Flexner" (n. 7 above), 425.
27. The process of funding science at the Rockefeller was very different from the process of funding science by the National Science Foundation (NSF) and the National Institutes of Health (NIH) in contemporary America. With numerous proposals arriving before study groups and program officers, these two organizations are less well positioned to assess the degree of risk involving a researcher and a research project. The NSF and NIH grant proposal submission process and the decision-making process about research funding have become more standardized and bureaucratized, with the consequence that high risk research tends to be discouraged.
28. Rous, "Simon Flexner and Medical Discovery," 612; Bayne Jones, "Simon Flexner," *American Philosophical Society Yearbook* (Philadelphia, 1946), 295; Rous, "Simon Flexner" (n. 7 above), 424.
29. Rous, "Simon Flexner" (n. 7 above), 424.
30. Rivers, *Reflections on a Life* (n. 16 above), 121.
31. Simon Flexner to Phoebus A. Levine, November 30, 1931, Simon Flexner Papers, APS.
32. Gates, *Chapters in My Life* (n. 6 above), 182–183; Fleming, *William H. Welch* (n. 9 above), 157.

33. Lily E. Kay, "W.M. Stanley's Crystallization of the Tobacco Mosaic Virus, 1930–1940," *Isis* 77 (1986): 454; Corner, *History of Rockefeller* (n. 7 above), 134.
34. Paul de Kruif, *The Sweeping Wind: A Memoir* (London, 1962), 3–35.
35. Robert Olby, *The Path to the Double Helix*, 2d ed. (New York, 1974); Roger M. Herriot, "A Biographical Sketch of John Howard Northrop," *Journal of General Physiology, Supplement* 45 (1962): 4–5.
36. S. Flexner and J.T. Flexner, *William Henry Welch*, 295–96; Corner, *History of Rockefeller* (n. 7 above), 313.
37. Norman W. Pirie, "The Viruses," in *Scientific Thought, 1900–1960*, ed. R. Harré. (Oxford, 1969), 232–33; John T. Edsall, "Wendell M. Stanley," *American Philosophical Yearbook* (Philadelphia, 1971), 184–90; Wendell M. Stanley, "The Isolation and Properties of Crystalline Tobacco Mosaic Virus: Nobel Lecture, December 12, 1946," *Nobel Lectures: Chemistry, 1942–1962* (Amsterdam, 1964), 137–59.
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