Fred Hutchinson Cancer Research Center History Project

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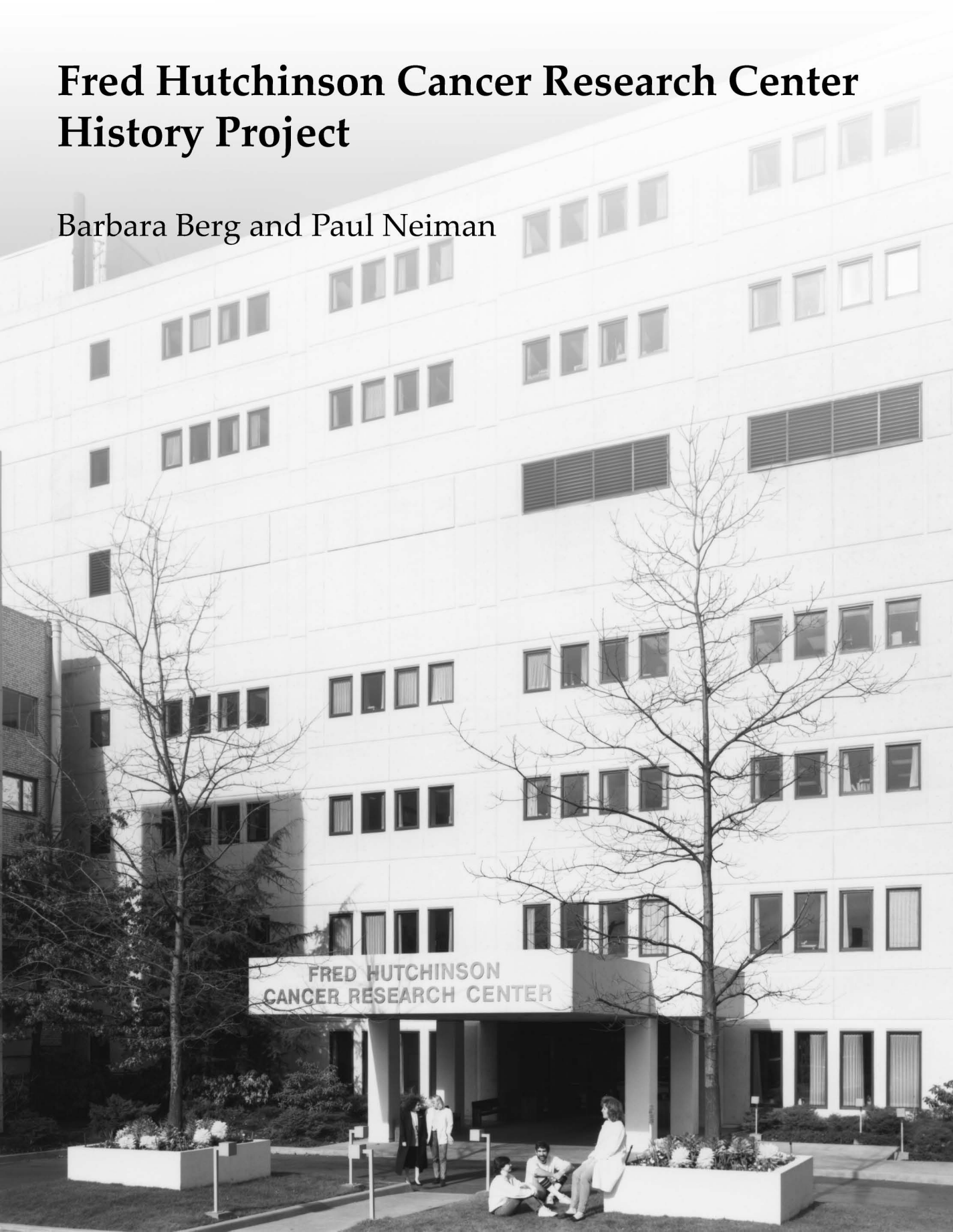

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Fred Hutchinson Cancer Research Center History Project

Foreword and acknowledgements: In less than three decades the Fred Hutchinson Cancer Research Center developed from one surgeon's commitment and drive to help cancer patients in the Pacific Northwest into a renowned biomedical research institute, a major asset in the war against cancer and holder of a highly respected place among leading academic research institutions world-wide. This uniquely rapid record of development was not underwritten by a major philanthropic endowment, nor driven primarily by singular leadership (though effective leadership there was), but rather achieved through the combined efforts of a remarkable group of men and women: scientists, physicians, administrators, staff professionals and volunteer members of the community. The challenges faced and decisions taken by individuals and groups within the Center make a remarkable story of institution-building, a story that should be recorded for the benefit of those who follow and seek to sustain and enhance the work of the Center.

Beyond the formal literature recording the scientific achievements of its faculty, the FHCRC does not have, to this point, a systematic document archive on which to base an institutional history. We undertook this exercise in an attempt to illustrate the need, and perhaps set the stage, for the development of such a resource. We set out to produce a series of necessarily concise monographs intended to introduce the history of the principal elements which make up the Center. This volume is composed of the first two of these: the early history of the Center from its formation in 1972 to the end of the tenure of its founding President and Director William B. Hutchinson, MD in 1981; and the history of basic research and the Division of Basic Science at the Center through 1996. We hope to see this series extended with monographs on: clinical research, public health sciences, interdisciplinary research and the Division of Human Biology and the story of the administration and volunteer boards of the Center to include the

development of our magnificent research campus at southeast Lake Union.

Absent a comprehensive archive we relied a great deal on personal memory as recorded in interviews. We thank Don and Dottie Thomas, Charles Evans, Maxine Linial , Ron Reeder, Gerry Smith and Steve Henikoff for subjecting themselves to this process and to Jim Pendleton for help in transcribing them. We obtained additional information and insight through the following written materials: Warren G Magnuson Archive at the University of Washington, minutes of the first meeting of the Fred Hutchinson Cancer Center Board of Trustees Jan. 6, 1972. William B Hutchinson, "The Establishment of a Cancer Center," Journal of Surgical Oncology (1977), transcripts of additional interviews of Don and Dottie Thomas by Peter Donaldson for his play "Heart of the Hutch" 2000, "Allogeneic Marrow grafting -A story of Man and Dog" by E.D. Thomas, in History of Marrow Transplantation: Thirty-five Recollections . ed. P. Terasaki. 1991, the Fred Hutchinson Cancer Center Scientific Reports 1974-1976 and 1976-1978, news clips from the External Relations Media Archive. We also thank Bob Eisenman, Steve Henikoff, Maxine Linial, Ron Reeder, Larry Rohrschnieder, Dottie Thomas and Meng-Chao-Yao for reviewing the draft narratives. Many of their helpful corrections and suggestions have been incorporated. Contemporary photographs (or as close as possible) were obtained from various archival and personal sources. We especially thank Ron Reeder and Theresa Naujack for help in identifying, processing and assembling the photos we used.

Paul Neiman and Barbara Berg, November 2003

Early History of FHCRC

FORMATION of FHCRC

Initial vision for a cancer center/overview

The Fred Hutchinson Cancer Research Center owes its formation to the vision of Dr. William Hutchinson, a Seattle surgeon. Hutchinson in 1956 established the Pacific Northwest Research Foundation, the first private, nonprofit, biomedical research institute in the Pacific Northwest, from which the Hutchinson Center eventually developed.

Hutchinson's foundation, which was eligible to receive research grants from the United States Department of Public Health, was established to provide practicing physicians and surgeons with a facility in which to conduct research investigations related to their areas of practice. Initial areas of research included open-heart surgery methods, endocrinology and development of instrumentation for blood chemistry analysis. The foundation's first home was the historic Captain William Ballard mansion in Seattle's First Hill neighborhood, which was owned by Swedish Hospital and Medical Center. The mansion was no longer in use by the hospital and had been destined for destruction until Hutchinson convinced the hospitals trustees to donate it for an independent research institute. In 1961, cancer research was named as a primary objective of the foundation. In the same year, PNRF relocated to the fifth and sixth floors of Eklind Hall, a former nurse's dormitory of Swedish Hospital.

In 1963, Hutchinson's brother Fred, then a 44-year-old manager of the Cincinnati Reds major league baseball team, was diagnosed with lung cancer. Fred Hutchinson began his baseball career as a pitcher for the Pacific Coast League's Seattle Rainiers. Before his move to the Cincinnati ball club, he had been a pitcher and manager for the Detroit Tigers. In November 1964, despite surgery and radiation treatment, Fred Hutchinson died of his disease.

Motivated by his brother's death, Bill Hutchinson, with the support of the institute's board of trustees, began planning for a cancer institute. Mrs. Donald Drew, a member of the board, suggested that new facility be named Fred Hutchinson Cancer Center and approached the board of Swedish Hospital about providing the land on which the institute would be located. The hospital donated a site on the corner of Minor and Marion streets in the First Hill neighborhood.

The plan for the new cancer center was that it would interface with the Tumor Institute and Swedish Hospital and would be physically linked with the hospital in order to minimize costly duplication of basic facilities. The institute, which was planned to house 150 staff, would support basic research programs in microbiology and immunology as well as a clinical oncology program with a 20-bed patient unit. In addition, the center would maintain the Automated Tumor Registry, a program formerly overseen by the Regional Medical Program that tracked cancer cases in Washington and Alaska. In 1972, following commitment of federal funds to establish it as a comprehensive cancer center, the new institute was renamed Fred Hutchinson Cancer Research Center.

Seattleites named as members of the cancer center memorial committee included Fred Blanchett, Royal Brougham, Marvin Burke, Maxwell Carlson, Victor Denny, Ed Donohoe, Donald Drew, Claire Egtvedt, Alan Ferguson, Charles Frankland, Jodep Gandy, Thomas Gleed, Maurice Vining, Moritz Milburn, Michaael Dederer, Lawrence Calvert, Jim Owens, William Allen, John Lor Locke, Horace McCurdy, Lowell Mickelwait, Robert Morris, Victor Rael, Dietrich Schmitz, David Skinner, Paul Smith, Roscoe Torrance, Edo Vanni, Emmet Watson, Bert West, Walter Williams, Frank Wold, William Wods, Howard Wright and Hy Zimmerman.

The architect for the proposed five-story building, estimated to cost $7.5 million, was Naramore, Bain, Brady & Johanson. Skilling, Helle, Christiansen, Robertson were the structural engineers; Bouillon, Christofferson & Schairer were the

mechanical and electrical engineers; and Century Construction Company was the general contractor.

Groundbreaking ceremonies for the Hutchinson Center were held on August 23, 1973. Speakers included: Wesley Uhlman, mayor of Seattle; Mr. T. Evans Wykoff, president of the Seattle Chamber of Commerce; John Spellman, King County Executive; John Cherburg, Lieutenant Governor; Dr. Donal Sparkman, director of the Regional Medical Program; William Hutchinson; and Senator Warren Magnuson.

Funding for FHCRC

In 1967, the National Cancer Institute awarded a planning and development grant to Hutchinson for the purpose of conducting a feasibility study for the new cancer center. In 1968, a $2 million construction grant was submitted to and approved by the National Institutes of Health, which was to be supplemented by an additional $1 million raised locally. But because in 1969 President Richard Nixon halted all cancer center construction grants, the money was not awarded.

In 1970, U.S. Senator Warren Magnuson of Washington, a member of the Committee on Appropriations, prepared a Congressional report concerning a Departments of Labor and Health, Education and Welfare, and related agencies appropriations bill (PL91-667) for fiscal year 1971, which included the following passage:

"the Committee understands that the cancer treatment programs and resources sponsored by the Regional Medical Program and located in the Northwestern part of the country are approaching a critical stage in their development. Lacking is such a facility that would serve as a focal point for organizing a system of health care that is acceptable and responsive, but linked to regional resources not available locally. The committee has added funds to the bill to expedite the construction of such regional cancer centers--$5,000,000."

This bill was signed by President Nixon on January 11, 1971, with the money for the new Northwest cancer center to be administered through the Washington-Alaska Regional Medical Program, directed by Dr. Donald Sparkman. Regional Medical Programs were established in 1965 by the Heart Disease, Cancer and Stroke Amendment (Public Law 89-239) for the purpose of aiding the establishment of regional cooperative arrangements among medical schools, research institutions, and hospitals for research and training as well as patient care.

According to those involved in the planning efforts for the Hutchinson Center, the need for funding had been made clear to Magnuson by Hutchinson. Hutchinson had performed surgery on Magnuson's wife, Jermaine, during her treatment for cancer. Sparkman had not requested the funding.

There is no record of formal application for the funding by local institutions or individuals that were considered qualified recipients, such as the University of Washington Medical School, Bill Hutchinson's Pacific Northwest Research Foundation, and Children's Hospital. However, recollections of Dr. E. Donnall Thomas and Dr. Charles Evans, Fred Hutchinson's first scientific director, indicate that Dr. Robert Van Citters, then dean of UW Medical School, was informed by Sen. Magnuson that the medical school should not compete with Bill Hutchinson for the funding. According to a congratulatory telegram to Hutchinson from Magnuson dated June 8, 1972, the $5 million was formally awarded in June of 1972, with 10 percent local matching funds required.

The passage of President Nixon's National Cancer Act in December of 1971 made possible an additional grant of $1,217,667 from the National Cancer Institute in June of 1973. On that date, the NCI named the Hutchinson Center as one of eight new national comprehensive cancer centers to be established. According to a telegram dated June 27, 1973, the $1.2 million was to support construction and fixed equipment in portions of the first and second floors and the entire fourth floor of the

new six-story building. Correspondence from Sen. Magnuson's archives suggest that the Office of Management and Budget had proposed releasing only $913,250 of this grant, but that threat was not carried out. Private donations, including $10,000 from a Teamsters Unions fund drive, contributed more than $1 million to the construction effort, more than double the amount in local matching funds required. Ground broke for the new center on First Hill on August 23, 1973. Total construction costs for what became a seven-story building were $11.8 million.

Through fiscal years 1974 to 1976, the federal government appropriated an additional $11,581,000 to the Hutchinson Center, which included $1,977,000 in construction funds. A dedication ceremony for the center was held September 5, 1975. Magnuson delivered the keynote address, and Governor Dan Evans, Sen. Edward Kennedy and baseball Hall-of-Famer Joe DiMaggio were among the notable figures present.

Development of a regional cancer center/collaboration with other regional hospitals

According to Hutchinson, in a 1977 article published in the *Journal of Surgical Oncology*, the development of a regional cancer center in the Northwest was first entertained in 1970, coincident with Magnuson's efforts to appropriate federal funding. Such a center would serve five states: Washington, Alaska, Montana, Idaho and, to some extent, Oregon. In June of 1973, as described earlier, the Hutchinson Center was named as one of eight new comprehensive cancer centers to be established in the country under the National Cancer Program that was authorized by the National Cancer Act of 1971.

Unlike the three long-established cancer centers at that time, Memorial Sloan Kettering Cancer Center, M.D. Anderson Cancer Center and Roswell Park Cancer Institute, the Hutchinson Center was founded with minimal patient-care facilities that were focused exclusively on bone-marrow transplantation. In his article,

Hutchinson maintained that there had been no desire to "alter established patterns of cancer referrals in the Northwest" or to duplicate cancer-care facilities already in existence. Presumably, local health-care institutions were concerned about the potential diversion of patients and funding from their institutions to the new center. Dr. E. Donnall Thomas recalls a great deal of anxiety in the greater Seattle area that the new institute would take over the practice of oncology.

Hutchinson and others engaged in negotiations with area hospitals, including the University of Washington, Children's Orthopedic Hospital, Swedish, Evergreen Hospital, and Virginia Mason. According to Thomas, these discussions spawned the formation of the Northwest Oncology Consortium, a group of regional health-care institutions that would effectively serve as partners in the patient-care aspects of the new regional cancer center. The group was later renamed the Puget Sound Oncology Consortium following oncologist Dr. Saul Rivkin's arrival in Seattle, when he took on a leadership role in this effort. Thomas recalls regular meetings with these local institutions to establish relationships and to alleviate concerns, which in reality were largely unfounded given the size and staff constraints of the Hutchinson Center. He also recalls that Hutchinson had initially envisioned the new center housing programs in "drug genetics, clinical pathology and surgical oncology," but again, given space and funding constraints, establishment of such services was unrealistic.

According to Hutchinson's article, a total of about 200 beds in designated cancer wards of seven local institutions would be affiliated with the regional cancer center. He expected that about half of patients in such cancer units would be treated on research protocols. The center would provide education to help insure that community hospitals and physicians could keep abreast of the latest developments and treatments. In addition, the center would provide salary for a nurse trained in care of cancer patients, a data technician and part of the salary for an oncologist at the participating institution to oversee the cancer unit. The Hutchinson Center was

established without major surgical facilities, with the expectation being that the peripheral cancer units in local institutions would keep surgeons abreast of new developments in cancer therapy.

Hutchinson described a statewide organization of cancer physicians known as the Extramural Council (chaired by Dr. David Smith of Mount Vernon), whose role was to coordinate the work of the doctors, help to make their needs known to the regional cancer center and to assist them in bringing these concepts in to practice. Dr. John Hartmann, the center's associate director of extramural activities, served as liaison to this council. Hutchinson states that through this collaboration, the center would provide cancer education for area physicians. Dr. Donald Sparkman, the former director of the Washington-Alaska Regional Medical Program, was hired by the center to help coordinate all cancer-related resources in the area.

Hutchinson's goal was to have the center's programs in biostatistics and epidemiology, as well as its basic research programs, serve as resources for local physicians and researchers designing studies or needing research expertise.

Original Board of Trustees and their role

The first meeting of the center's Board of Trustees was held January 6, 1972. The members of the first board included Dr. Harvey W. Baker, Dr. Thomas Carlile, William Christoffersen, C. Spencer Clark, Edmund Donohoe, Dr. Charles Evans, Dr. William Fletcher, Elmer Gagnon, Dr. J. Thomas Grayston, Dr. John Hartmann, Dr. William Hutchinson, Kay Jones, John Larson, Dr. Allan Lobb, David Lycette, Patrick Lynch, Volney Richmond, Jr., Dr. Walter Ricker, James Ryan, Chester Stocks, Dr. Jess Speilholz, Dr. S. C. Taylor, Dr. Donovan Thompson, Dr. Roberrt Van Citters and T. Evans Wyckoff.

At that meeting, Hutchinson was appointed president and director, Evans was named vice president, and Lycette was appointed secretary/treasurer. Individuals

named as members of the scientific board included Dr. Robert Kola, Dr. Robert Petersdorf, Dr. Robert Parker, Dr. Orliss Wildermuth, Dr. Willis Taylor, Milton Evans, Dr. Edward Parrin, Dr. Samuel McIvanie, Dr. Winthrop Fish, Dr. J. Bruce Beckwith and Dr. Douglas Morningstar. In addition, three committees were established to deal with finance, publicity and building issues. The minutes also refer to a site visit to the center (then at Eklind Hall) on Jan. 24-25 by representatives of the Regional Medical Center.

Early FHCRC-UW relationship (from interview with Charles Evans)

With the National Cancer Institute's decision to award $5 million to Hutchinson to establish a new cancer center, the University of Washington Medical School began discussions with Hutchinson regarding details of the relationship between the two institutions. Dr. Robert Van Citters, dean of the medical school, asked Dr. Charles Evans, chairman of the microbiology department, to be the University's representative in these efforts. Dr. Evans had done pioneering work on the Shope Papillomavirus, a precursor field to modern tumor virology. Evans recalls several points of friction that needed to be resolved, including center faculty appointments in university departments and the ability of center faculty to train graduate students. He also recalls that there had been an understanding between Hutchinson and UW that the university would be responsible for appointing a representative for these negotiations.

Evans served as the center's first Scientific Director, from 1971 until 1975. Initially, his role was focused on interactions between the center and the university. Over time, he led some of the initial faculty recruitments for program heads in the laboratory sciences. Throughout his time in this position, Evans' salary was paid entirely by the university. Although the medical school dean proposed that Evans'

salary be augmented by the center, he chose to remain independent of center funds so as to avoid pressure on his decision-making activities.

Early recruitments/division formation

The first faculty, or scientific program heads, at the center were not selected by a formal national search with a search committee; rather, they were recruited from other local institutions. Dr. E. Donnall Thomas (see next section), head of the university's program in medical oncology, was chosen by Hutchinson to lead the program in medical oncology, responsible for the patient-care arm of the center. Dr. Donovan Thompson was selected to head the Program in Epidemiology and Biostatistics.

The basic sciences were represented initially by programs in immunology, membrane biochemistry and chemical carcinogenesis. Faculty, who were recruited from either the university or PNRF, included Drs. Karl Erik and Ingegerd Hellstrom (University of Washington, Depts. of Pathology and Microiology, respectively), and Dr. Sen-Itiroh Hakomori (UW School of Public Health).

Evans recalls that no salary support was available for faculty through the center. All were given university appointments, which paid for 100 percent of their salary. Program heads recruited junior faculty to their laboratory programs.

Evans had a strong interest in formalizing the appointments process and established the Committee on Personnel and Programs, charged with overseeing faculty hiring and promotion. Thomas and Thompson were members of the committee, as were the Hellstroms, Dr. Paul Neiman, who later became the director of the Basic Sciences Division, and Drs. Russell Ross and Edwin Krebs from the university. Evans, with his background as a microbiologist, felt that his expertise was best applied to the further development of the laboratory-based programs and recommended that the clinical and epidemiology programs function as independent

entities with respect to hiring and promotion decisions. Evans consulted with prominent scientists around the country, including Dr. Michael Bishop of the University of California at San Francisco, who served as informal advisors to the center's efforts to develop programs in basic research. Candidates for new program areas were recruited both for their innovative science as well as to strengthen areas that were absent or underrepresented at the university. The first basic scientist to be hired through a formal search committee was Dr. Robert Nowinski in 1975.

Evans recalls a strained relationship between the university departments and the center. With their university appointments, center faculty who took on some university teaching responsibilities were able to train graduate students in their laboratories. This arrangement was resented by university faculty, who felt that center investigators, with their superior resources and limited teaching responsibilities, would have an unfair advantage in attracting graduate students. The resolution of this arrangement is discussed in the history of the Basic Science Division section.

In 1975, Evans retired, and Dr. Hans Neurath, chairman of the biochemistry department at UW, became the next scientific director. Dr. Neurath arrived just as the Hutchinson Center was undergoing review of its first NCI Cancer Center Support (Core) Grant since the opening of the new center building. Neurath's appearance at the site visit was judged by the NCI reviewers and the center staff to be an important element in the success of that critical grant renewal.

From 1975 through 1978, there was an active period of recruitment in the basic sciences lead by Dr. Neurath. Although several new faculty members were successfully recruited, a clash occurred between the scientific director and the faculty search committee over the appropriateness for the center of some fields of basic research. This argument presaged a governance controversy that dominated basic sciences several years later.

During this time, faculty salaries were paid by the first core grant awarded to the center from the National Cancer Institute. In about 1979, as the center was awarded its next core grant renewal, Neiman recalls the center entering a period of transition and upheaval with respect to finances and scientific organization. As comprehensive cancer centers began to grow around the country, NCI could no longer offer full faculty support through its core grants. With no endowment to fall back on, center faculty were faced with the problem of how their salaries would be covered. Most believed at the time they were recruited that the Hutchinson Center had a firm financial base. In fact, Neiman recalls, there were no financial statements made available to the faculty (nor does Evans recall ever seeing one). With this change in NCI funding policy, faculty members were required rather abruptly to cover part of their salary with their research grants. A phase-out of faculty salary support (the Staff Investigator budget component) on the core grant was negotiated with NCI staff, with smaller and smaller contributions from that source with each year and each core grant renewal. The NCI core grant became, principally, a major source of support for the shared resources of the scientific program, reducing costs to research grants for these important services. Faculty salaries became shared between faculty research grants and other center financial resources such as money raised through annual fundraising.

A second challenge of that time, at least for the basic sciences faculty, was the scientific organization and governance of the center. The Hutchinson Center was established based on a program structure suggested by guidelines set forth by the NCI Cancer Center Support Grant. As more junior faculty were recruited to the center, the program structure became increasingly controversial in some quarters. The younger faculty, especially in the basic science laboratories, desired a more egalitarian faculty organization, with each member leading an independent laboratory. Several of the original program heads were comfortable with the status

quo, which enabled them to build large programs with many junior faculty working for them, but the majority of the laboratory heads agreed with the junior faculty. A center faculty retreat was held at the Battelle Institute in Seattle, organized and chaired by Dr. Neurath, at which the program structure concerns of the junior faculty and other issues were discussed. Shortly thereafter, those program heads opposed to the program structure and related issues prepared a statement of concerns to Neurath, who was to present it to Bill Hutchinson. At a subsequent meeting of the Programs Heads Committee, then the governing body of the scientific staff, Neurath informed the program heads that Hutchinson did not plan to act on their complaints. In response, at the meeting, most of the program heads resigned from Program Head Committee. Very shortly following this traumatic meeting, Hutchinson announced Neurath's resignation, and that he would take over Dr. Neurath's duties temporarily.

In addition, a third governance-related issue was causing unrest among the scientific staff. During this period, Hutchinson had announced his plan to retire when a new director could be recruited. Controversy swelled over the qualifications of the new center director, which many faculty believed should include a reputation as a respected leader in the national scientific community. Candidates were selected by a committee of the Board of Trustees with minimal consultation with the scientific staff. Almost all of the candidates who were invited to visit the center received faculty responses ranging from indifference to (in one case thought to be favored by Dr. Hutchinson as his replacement) overt hostility. As a result, the identification of a new director was stalled.

In this superheated environment, a few months after Neurath's departure, Bill Hutchinson asked Paul Neiman to serve as acting Scientific Director and to work with him as a liaison to the faculty to resolve these controversies and to enable the center to move on with the selection of a director and then a new permanent scientific director. Neiman spent a year as interim scientific director, and in 1981, the

Board of Trustees appointed Dr. Robert Day as president and director of Fred Hutchinson. Day, a cancer-prevention researcher, was at that time the dean of the School of Public Health at UW. He served as director of the center until June of 1997.

After Day's appointment, the center began a formal search process for a scientific director. After a faculty search committee was organized and a list of candidates generated, Neiman removed himself from the committee and became a candidate for the position. He made clear that if selected, he would work for reorganization of the faculty structure. Neiman was appointed scientific director in 1981, and a series of discussions with Dr. Day were initiated to reorganize the center faculty into scientific divisions. Following these discussions, Neiman was named Associate Director, Basic Sciences; Thomas was named Associate Director, Clinical Research; and Thompson, Associate Director, Public Health Sciences.

HISTORY OF THE TRANSPLANT PROGRAM

The formation of the Hutchinson Center is intimately tied to Dr. E. Donnall Thomas' development of bone-marrow transplantation as a treatment for leukemia and other blood disorders. Thomas, the first director of the Clinical Research Division, shared the 1990 Nobel prize in physiology or medicine with Dr. Joseph Murray for their accomplishments in transplantation. Thomas' marrow transplant program, already well established at the time the doors of the Hutchinson Center officially opened in 1975, formed the basis for center's Medical Oncology program (later the Clinical Research Division).

Thomas had begun his studies on marrow transplantation while chief of medicine at the Mary Imogene Bassett Hospital in Cooperstown, N.Y., in 1955, where he worked with Dr. Joseph Ferrebee. Although Thomas and his colleagues performed a small number of transplants on human patients, primarily between identical twins, most of their research at that time was devoted to studying marrow

grafts in canines. His research team demonstrated that dogs could survive lethal irradiation if subsequently transfused with their own marrow. Recipients of marrow from littermates, however, died due to either graft rejection or from a complication known as graft-vs.-host disease, a condition in which donor immune cells react against host tissue. With immunosuppressive drugs, a small number of dogs survived the transplant procedure, suggesting that bone-marrow transplantation might be feasible with additional research to identify the factors contributing to the procedure's success or failure.

In 1963, Thomas joined the faculty of the Hematology Division at the University of Washington School of Medicine. Dr. Robert Williams, chairman of the department of medicine and a former colleague, recruited Thomas to the medical school to establish a marrow transplantation unit at the aging, 12-story U.S. Public Health Service Hospital (USPHS) in Seattle. Funding for the marrow transplant program was provided by the Adult Leukemia Center Grant from the National Institutes of Health, which Thomas had transferred from Cooperstown to be administered through the University of Washington.

Thomas and colleagues worked almost exclusively with dogs well into 1967, postponing work on patients until treatment complications could be resolved. During that time, members of the research team included Thomas' wife, Dottie, a medical technologist; Ted Graham, an animal technician who moved with Thomas from Cooperstown, Dr. Dean Buckner, a medical fellow from NIH; Reg Clift, a member of the British Colonial Army who left a medical post in Africa to join Thomas; and Dr. Rainer Storb, a Fulbright fellow who had left a position in Paris to move to Seattle.

In 1967, Dr. Robert Petersdorf, chairman of the department of medicine, decided to create a program in medical oncology. With scarce resources to offer to potential outside recruits for the program head position, Petersdorf asked Thomas to

take on the role. When Thomas agreed, oncology formally became a separate program from the hematology division in 1968.

Thomas secured NIH funding to establish an eight-bed inpatient unit at the public health hospital as well as a training grant to support six fellows. Among the fellows to join at the time were Dr. Paul Neiman, who later became the first director of the Basic Sciences Division, and Dr. Alex Fefer, an immunologist. Thomas hired Mary Stevens to head the nursing program and Saundra Aker, a nutritionist, to head the nutrition program. The first transplant was performed in March of 1969. Total-body irradiation of patients being readied for transplants was performed at an unused former military bunker in West Seattle, which also housed the canine laboratory and the ^{60}Cobalt unit.

In 1970, Thomas was invited by Bill Hutchinson to engage in discussions regarding organization of a new Pacific Northwest cancer center to be funded in part with $5 million awarded to the Regional Medical Program. Hutchinson had been introduced to Thomas through a mutual friend, a Seattle hematologist named Quinn DeMarsh. In 1971, Hutchinson asked Thomas to head the Medical Oncology program at what was to be the Fred Hutchinson Cancer Research Center.

In 1973, the Nixon Administration ordered the closing of many USPHS hospitals, including the Seattle facility where Thomas' transplant program was housed. At a site visit for the renewal of Thomas' NIH grant, the dean of the UW medical school, Dr. Robert van Citters, made clear that the university had no intention of providing space for the transplant unit when the public health hospital closed. With the help of his friend DeMarsh, Thomas was able to negotiate successfully with Providence Hospital for the use of two empty floors, where he established a 14-bed unit and laboratories to support the transplant program until the new Hutchinson Center building's scheduled completion in 1975. The National Cancer Institute provided $250,000 for the remodeling effort.

Establishment of the Medical Oncology program at the Hutchinson Center

The continued growth of the transplant program enabled the Hutchinson Center to open in 1975 with an established program in medical oncology and a 20-bed transplant unit. Initially, the program grew based on needs that arose from patient care, rather than by strategic planning, because of a lack of funds for salary for recruiting new faculty.

Among the first new faculty members to be hired was Dr. John Hansen, a human immunogeneticist. Hansen joined the center in 1977 to oversee the HLA-typing laboratory responsible for matching patients and marrow donors according to tissue type. Until that time, Thomas had performed the typing himself with the aid of two laboratory technicians. Thomas was able to arrange for Hansen's salary to be paid by the Puget Sound Blood Center, which hoped to develop a tissue-typing facility for the growing number of a kidney transplants performed locally. Hansen's work on tissue typing led to the first successful transplant with unrelated donor marrow in 1979, performed on 10-year-old Laura Graves. Graves' father, Robert, was instrumental in obtaining federal funding to help establish in 1986 the National Marrow Donor Program, a national registry of six million donors worldwide.

The numerous infections that plagued the immunocompromised transplant patients prompted the development of a program in infectious diseases, headed by Dr. Joel Meyers. Meyers, a physician with the Centers for Disease Control in Atlanta, had visited Thomas' transplant program in 1972 to investigate an outbreak of hepatitis on the ward. Meyers, whose investigation revealed the source of the hepatitis to be a blood donor, became intrigued by the infectious complications of the transplant patients and returned to Seattle permanently in 1975. Thomas and Meyers wrote a grant application to support Meyers and the development of an in-house infectious diseases program. Meyers died in 1991 of colon cancer at the age of 46.

Other programs established around that time were pediatric transplantation, headed by Dr. Jean Sanders, and a program in gastroenterology, headed by Dr. George MacDonald. MacDonald, a physician at the Seattle Veterans Affairs Medical Center, had provided consults for Hutchinson Center transplant patients suffering from graft-vs.-host-disease, which frequently causes severe damage to the gastrointestinal tract. MacDonald was paid as a consultant until Thomas was able to establish a gastroenterology program through the Adult Leukemia Center Grant.

By 1978, Thomas' group had performed a total of 500 bone-marrow transplants. To accommodate the increasing number of patients, an additional 14-bed unit unit opened in 1980 at Swedish Hospital.

Thomas' transplant program attracted highly talented fellows, many of whom stayed on to become faculty members at the Hutchinson Center, where they developed research programs of their own.

Origins of Public Health research at the FHCRC.

The beginning of what eventually became the Division of Public Health Sciences was called the Program in Epidemiology and Biostatistics, headed by Donovan J. Thompson. The initial members of this program, like Thompson, were all regular faculty of the Departments of Epidemiology and Biostatistics of the School of Public Health at the University of Washington.

An initial database for cancer statistics and derivative epidemiologic studies was the Cancer Surveillance System (CSS), part of a collaborative effort of nine participants in an NCI sponsored effort called the SEER (Surveillance, Epidemiology, and End Results) program. The CSS began before the Center opened in 1973 and was charged with developing a registry for recording cancer incidence and survival in the Puget Sound region. The principal investigator on the Hutchinson Center contract was Dr. Thompson; Dr. David Thomas served as CSS Director.

A second important initial element of the center's public health focus, beginning in 1974, was the Statistical Center for the National Wilm's Tumor Study. The Wilm's study was an 80-institution consortium to conduct randomized clinical trials in this pediatric neoplasm, which is the most common solid tumor in children. The consortium's statistical center was headed, and continues be headed, by Dr. Norman Breslow.

Another early recruit to public health sciences shortly after the center opened was Dr. Ross Prentice, who nucleated research at the center in biostatistical methodology. In addition to developing and applying new statistical tools, this group provided consultation on study design and data analysis to the marrow transplant team at the center, to a local clinical-trials consortium of local clinicians and center investigators known as the Northwest Oncology Group (now the Puget Sound Oncology Consortium), and for several studies by Hutchinson Center epidemiologists.

All of the investigators in the program were regular faculty members of the UW School of Public Health faculty and activities at the center were well integrated with activities on campus, such as graduate training. Most of the organizational challenges derived from relations between the center and the university, which affected faculty in clinical and basic research programs, were not as problematic for the biostatisticians and epidemiologists. Issues parochial to the center itself, however, as described above and in subsequent sections, were of concern to program faculty. In addition, the fact that at that point in history there was little or no postdoctoral training tradition in academic biostatistics (as was true in other branches of mathematics) raised controversy with respect to junior faculty appointment criteria among the scientific programs. (By contrast, basic biological scientists considered for faculty appointments had completed lengthy post-doctoral training experiences). Establishment of agreed distinctions in required experience for

new Assistant Members in Biostatistics, Basic Sciences or Clinical Research did not become established until the transition to the divisional faculty structure in the early 1980s.

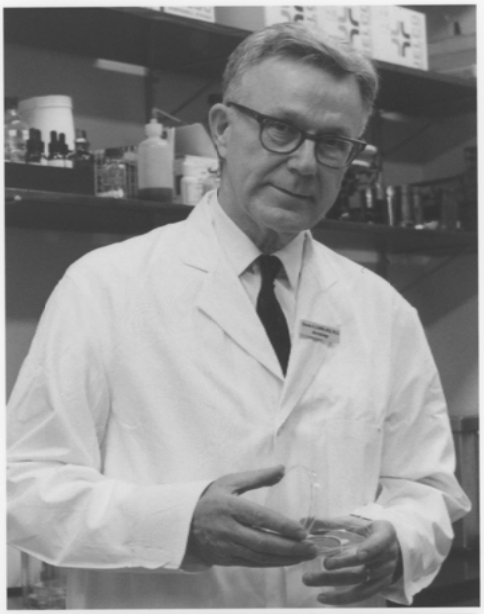
A transition in institutional vision and scope

The early center leadership, spearheaded by Bill Hutchinson, did a remarkable job in assembling the initial elements of the Hutchinson Center, including attracting the support of the National Cancer Institute and other public agencies and community resources and constructing a new research and treatment facility. However, one of the most striking changes recorded in this early history of the center is the rapid evolution of the focus and breadth of the scientific program. Written documents from Warren Magnuson and Bill Hutchinson both testify to a core rationale for the new regional cancer center based on enhancement of service to and education of regional health care professionals and cancer patients. By the end of this early formative period, however, it is clear that the center was developing a scientific program of innovative basic, clinical and population-based research with broad national and international impact and recognition. The story of how the transition occurred from a primarily regional institution to a biomedical research institute of international prominence is recorded in the histories of the center's Divisions: Basic Sciences, Clinical Research, Public Health Sciences, as well as the of the Administrative Division and the Board of Trustees, which evolved at the end of this early formative period. These histories are described in the chapters to follow.

First President and Director William B. Hutchinson (left) Senator and Mrs. Warren Magnuson. Ground breaking August 23, 1973

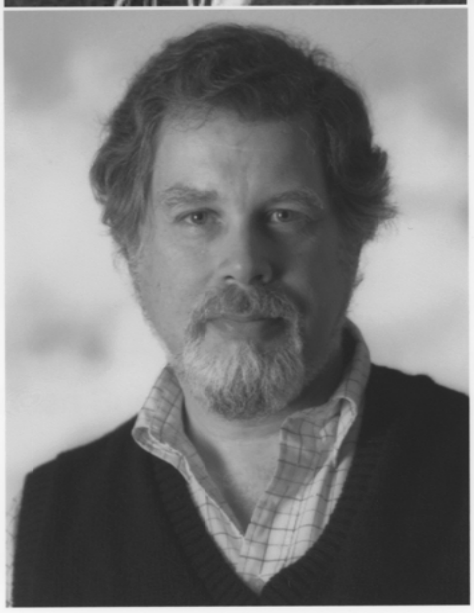
Original Center building, 1124 Columbia St

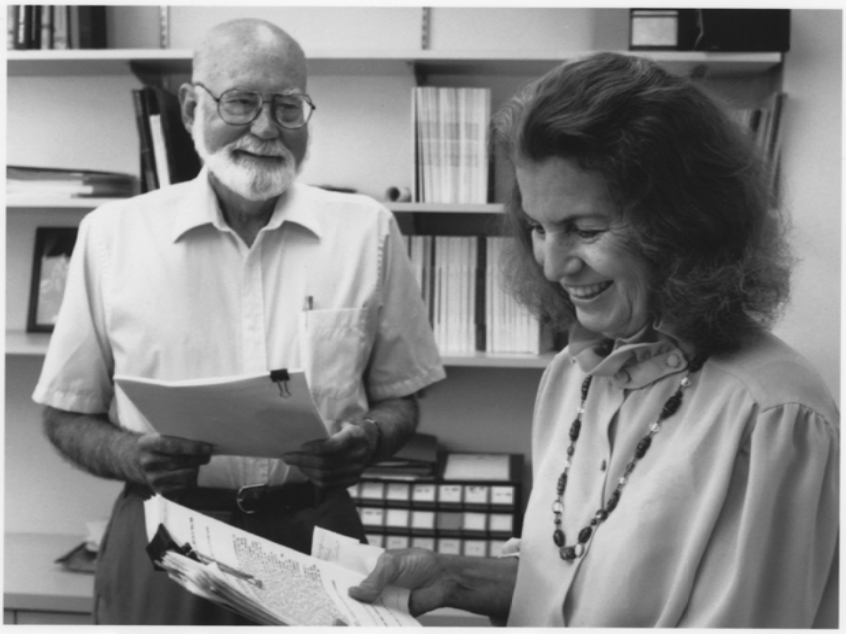
Charles Evans, M.D.,Ph.D., first Associate Director, Intramural Research (Scientific Director) 1972-1975



Hans Neurath, Ph.D. Scientific Director 1975 -1980

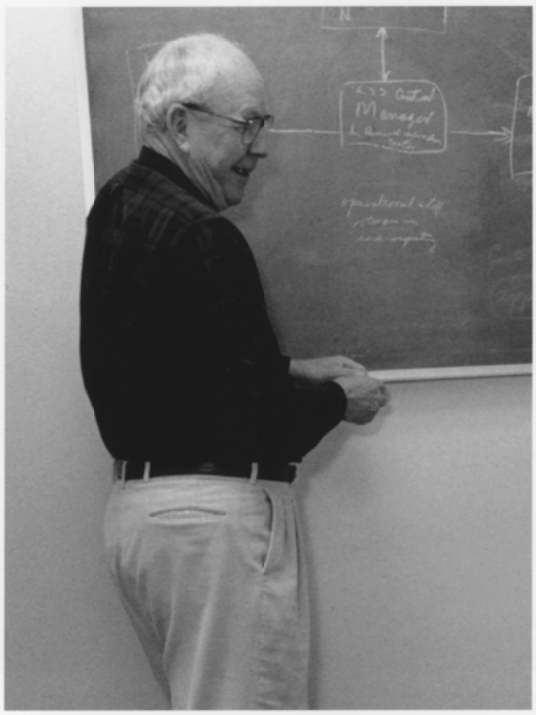
Paul Neiman, MD Acting Scientific Director 1980-1981, first Director, Division of Basic Sciences 1981-1996





E. Donnall Thomas MD and Dottie Thomas. Dr. Thomas was Head of the Medical Oncology Program 1975 - 1981 and first Director, Division of Clinical Research 1981 - 1990

Don Thomas and some early members of the marrow transplant team:
L to R, Paul Neiman, Alex Fefer, EDT, C. Dean Buckner, and Rainier Storb



Donovan Thompson, Ph.D
Head Program in Epidemiology
and Biostatistics 1972-1981

David Thomas M.D, Epidemiology
Ross Prentice, Ph.D, Biostatistics
Dr. Prentice became the first Director,
Division of Public Health Sciences
1981-2003.

Norman Breslow, Ph.D
Pat Norkool. National Wilms
Tumor Study

Robert W. Day MD, Ph.D Dean,
UW School of Public Health,
Member, FHCRC Board of
Trustees replaced Bill Hutchinson
as President and Director,1981

Bob Day and Sen Hakomori at the first FHCRC
all Center Scientific Retreat, October 1981

History of the Division of Basic Sciences

The technical history of basic research at the center is formally recorded in the scientific literature and summarized in the scientific reports and brochures published by the center. In contrast, this monograph attempts to provide a concise, essentially introductory, view of the major organizational events and issues that played a formative role in establishing the Division of Basic Science and molding its development. The year of arrival and departure for basic science faculty up to 1996 are shown in figure 1, and listed in table 1, which serve to provide a framework in time for the topics discussed below. All of these talented men and women made invaluable contributions to the success of the Division. Individuals whose work and role is briefly amplified in the text below were those who arrived during the period covered by this history and were or became members of the senior faculty. The individual descriptions were selected to illustrate the points under discussion, and in no way are meant to diminish accomplishments not described or the value of individuals not named in the text.

Assembly of basic science at the new center

The formation of what became the Division of Basic Sciences at the Fred Hutchinson Center Cancer Research Center began in 1975 with the opening of the center on First Hill. Research at the center, including its laboratory-based science, was organized into programs based on specific areas of investigation. Program areas included a number of fields that would at that time have been considered conventional basic cancer research as well as some more novel programmatic initiatives. Fields such as cellular and tumor immunology, chemical carcinogenesis, some aspects of membrane biochemistry and tumor virology were among the topics that most cancer centers would have considered appropriate for their laboratory programs. In the area of cellular immunology/tumor immunology, Drs. Karl Erik and Ingegerd Hellstrom and

Dr. Chris Henney played senior leadership roles and brought several junior faculty members in their large programs to the newly formed center. However, as will be described, the effort in basic immunology at the Hutchinson Center did not persist very far into the history of the Basic Sciences program. In fact the major programs in basic immunology left the center shortly after the divisional structure replaced the program structure, and went on to constitute a significant part of the regional biotechnology industry that persists today.

Dr. Sen-Itiroh Hakomori, a prominent cell membrane biochemist working on abnormal proteins on the surface of cancer cells, was one of the founders of the laboratory base at the new center but did not stay long after the formation of the Basic Sciences Division. He left to start his own privately funded research institute, the Biomembrane Institute. Dr William Carter, one of his postdoctoral trainees, remained at the center to become long-term member of the faculty. Carter anchored the development of research at Hutchinson Center concerned with the extracellular matrix, a complex mixture of molecules that surrounds and supports cells, and adhesive interactions between cells and the extracellular matrix, which control such processes as cell movement and wound healing.

Research in chemical carcinogenesis, the process by which chemical agents induce tumor formation, was represented in the early days of the center by the activities of two laboratories headed by Drs. John Scribner and Tom Slaga in the Pacific Northwest Research Foundation. Slaga left and Scribner stayed as an Associate Member. Tragically, Scribner died in an avalanche in the mountains. Since then, traditional chemical carcinogenesis has not been a focus of basic research at the center.

Tumor Virology. Two highly emphasized areas of research in the early development of basic research at the Hutchinson Center were tumor virology, the study of the role in viruses in tumor formation, and molecular biology. These major fields

were seriously underrepresented at that time in the Seattle scientific community outside of the center. Dr. Paul Neiman, a medical oncologist with clinical training at the Medicine Branch of the National Cancer Institute, came to the center as a member of the original Program in Marrow Transplantation to work with Dr. E. Donnall Thomas. Neiman's laboratory made early contributions to the detection of a tumor-causing virus in birds, known as Rous sarcoma virus, in the genome of host cells. His laboratory was, and remains, focused on the role played by a class of viruses known as retroviruses on cancer development. Retroviruses, which contain RNA rather than DNA as their genetic material, insert their genetic information into a host cell's genome as part of its life cycle. Neiman, as head of the Viral Oncology program, recruited a new junior faculty member, Dr. Maxine Linial, initially a postdoctoral fellow with Dr. Peter Vogt at the University of Southern California and then in Neiman's laboratory, who joined the viral oncology group and remains a senior virologist at the center. She continues her work on critical elements in the multiplication of retroviruses, and related viruses, including her more recent pioneering work on one class known as foamy viruses. Robert Eisenman next joined the Viral Oncology Program after a postdoctoral fellowship with Dr. Heidi Diggelman's group at the Swiss Cancer Research Institute in Lausanne. Eisenman had done pioneering work on aspects of retrovirus replication. During his long career at the center, Eisenman has become internationally recognized for his work on a cancer-causing gene called the Myc oncogene. He also has led key studies of a network of proteins (the Myc/Max/Mad network) that control the activity of numerous genes regulating cell behavior which, when defective, contribute to the development of cancer. Eisenman's achievements have been recognized by his election to the National Academy of Sciences. A second program in retrovirology established at that time was led by Dr. Robert Nowinski, who was recruited from the University of Wisconsin. Nowinski was a national leader in the study of the genetic aspects of lymphomas in mice that were caused by Murine Leukemia Viruses. He recruited Dr.

Fayth Yoshimura from Dr. Robert Weinberg's laboratory at the Massachusetts Institute of Technology, who also worked on the molecular biology of Murine Leukemia Viruses, and also Dr. Larry Rohrschneider, as new Assistant Members. Rohrschneider went on to lead key studies of cell-signaling proteins, including one known as Fms, which play important roles in the regulation of normal and abnormal differentiation of blood-forming cells.

The other prominent branch of tumor virology during that period was based on DNA-containing viruses that were associated with cancer development. At the center, this field was represented by a senior scientist, Dr. James McDougall, who was recruited from the Cold Spring Harbor Laboratory, and his wife, Dr. Denise Galloway, recruited as an Assistant Member. Their initial work on the possible role of herpes simplex viruses in human malignancies evolved into an interest in the role of HPV (human papillomaviruses) in cervical cancer and in other cancers, and in the cellular genes corrupted by these viruses during cancer development. Galloway and McDougall migrated from Basic Sciences to the Division of Public Health Sciences, where they founded the laboratory-based Cancer Biology program within that division. These events formed the early basis of interdisciplinary interaction between the community of epidemiologists and the laboratory-based molecular biology community at the center.

Molecular and Cellular Biology. A major stimulus for the interest in virology during the late 1970s and early 1980s was that viruses represented the most convenient tools available for analyzing molecular changes in cells of higher animals. A virus could be viewed as a small package of genes, capable of introducing its genes into target cells to convert them from normal to malignant behavior. This property provided both useful technical handles for the analysis of cancer development as well as an entree into the emerging field of cellular and molecular biology, which, at that time, was not a central part of the cancer research community.

The revolution in cellular and molecular biology derived from the discovery, several decades earlier, of the structure of DNA and the genetic code. The leading scientists in that field drove a large part of historically important progress in biological science. Yet most of these individuals were not deeply involved in the problem of cancer. Additionally, this growing field of cellular and molecular biology, which was central to biological research in major institutions worldwide, was not particularly well represented in the Seattle scientific community. Arguably, one of the centers' major contributions was its establishment of a very strong program in cellular and molecular biology in the Seattle area, which involved some very talented and productive scientists in that field who led the effort toward an enhanced understanding of cancer.

Central to this effort in molecular biology was the recruitment of Dr. Harold (Hal) Weintraub from Princeton University. At the time he joined the center, in 1979, Weintraub had already attained an international reputation for his work in defining the structure of active chromatin, regions of the genome that house expressed (active) genes. He was able to show that active genes were organized into structures known as nucleosomes and were arranged in a more "open" configuration than that of unexpressed (inactive) genes. Weintraub therefore brought to the center a strong program in the regulation of gene expression in higher animal cells. He also seeded, by virtue of his interest in the center, the notion within the leaders of field of cell and molecular biology that the effort at the Hutchinson Center should be taken seriously. Weintraub's interest in, and then commitment to the center, made possible the recruitment of a number of other outstanding scientists.

Weintraub's first recruitment was his partner in chromatin research and close friend, Dr. Mark Groudine. Groudine and Weintraub met in the MD/PhD program at the University of Pennsylvania and Groudine spent the last year of his thesis work in Weintraub's lab at Princeton. Groudine then joined the center in 1976, initially as a postdoctoral fellow in the Viral Oncology Program with Neiman while he completed

his clinical training in radiation oncology at the University of Washington. During this time, Weintraub spent two summers working with Groudine in the Neiman lab, and this was an important component in Weintraub's decision to join the center. Groudine then became an Assistant Member in the Program, called Genetics, headed by Weintraub. Over subsequent years, Groudine has played a leading role in research on gene expression, and the role of chromatin in the regulation of gene expression, which has been recognized broadly by the scientific community as well as by his recent election to the National Academy of Sciences.

Weintraub next recruited Dr. Virginia Zakian, who was exploiting the experimental model system of the baker's yeast *Saccharomyces cerevisiae* to study the regulation of chromosome mechanics, particularly the role played by telomeres, the tips of chromosomes, and their effects on the stability of chromosomes in yeast cells. Zakian's hiring signaled an appreciation by the center's basic scientists of powerful and tractable model systems in which both biochemistry and genetics could be brought to bear to study central problems in cell biology applicable to understanding regulation in higher animal cells, including human cells. Neiman recalls that Weintraub, upon recruiting Zakian, indicated that one of her challenges was to convince the faculty that yeast was an important experimental system for the development of our research program. Zakian was instrumental in seeding that concept at the center; the Basic Sciences Division now houses more than half a dozen laboratories using this model organism in their studies.

In addition to Weintraub's personal scientific achievements, which were recognized by election to the National Academy of Science and the National Academy of Arts and Sciences, he played an exceptional role as a mentor, colleague and scientific personality within the culture of the laboratory-based community at the center. Neiman, who became the first director of the Division of Basic Sciences, said "he [Weintraub] was the source of a great deal of our sense of quality and commitment to

excellence, and he kept our feet to the fire with respect to maintaining the highest possible standards for the recruitment and development of other scientists at the Hutchinson Center. He was an enormous help to me as the acting scientific director and director of the Basic Science Division. I always felt Hal's point of view was something to be very carefully considered. Although we did not always agree on everything, there was a very strong sense of partnership between us in the development and progress of the Division. Hal's premature death at the age of 49 was a tremendous blow to all of us, and me in particular. There was always a strong bond of both friendship and mutual respect, and I miss him to this day."

Weintraub's contributions to the scientific excellence of the center as well as to the development of the Basic Sciences Division philosophy are reflected in quotes from many of his colleagues hired in the early years:

"I don't think we would have managed to do what we did without Hal." [Ron Reeder].

"I think he had a tremendous influence in keeping the department egalitarian and directed towards doing good science." [Gerry Smith]

"I'd say Hal was a major shaper of the center." [Maxine Linial]

Weintraub's enormous legacy is reflected in the naming of the Basic Sciences Building as the Harold M. Weintraub Basic Sciences Laboratories. In addition, as an expression of his wishes, an endowment called the Weintraub-Groudine Fund was established in honor of Weintraub's scientific legacy and his long-standing scientific partnership and close personal friendship with Groudine. This fund, established through the generosity of Weintraub's family, Groudine and many of Weintraub's friends and colleagues, supports, among other initiatives, the Harold M. Weintraub Prize and Symposium, an annual symposium recognizing outstanding research by graduate students from across the nation. Groudine succeeded Neiman as Director of the Division of Basic Sciences in 1996.

Other scientists who were recruited at about the same time as Weintraub included Dr. Ron Reeder from the Carnegie Institution in Baltimore. Reeder was studying the biochemistry of gene expression and the cell's control of this processes' start (initiation) and stop (termination) mechanisms. These studies were carried out on a subset of genes, known as ribosomal genes, which serve as blueprints for the construction of the ribosome, the cellular machine that synthesizes proteins. At that stage in history, ribosomal genes were perhaps the most accessible system for the study of gene activation, and had occupied the attention of researchers at the very top of the field. Reeder was one of the leaders in that field and played an important role in establishing the division's interest in gene expression and its control. He also served as Associate Director of the division with Neiman beginning in 1993.

Reeder, shortly after arriving, led the recruitment effort to hire Dr. Steve McKnight, a postdoctoral fellow at the Carnegie Institution. Although this was his first faculty position, McKnight was already a nationally recognized pioneer in the field of regulation of gene expression. He could not stay at the Carnegie because of their policy to not promote their own postdoctoral fellows into faculty positions. McKnight was one the division's bright young stars for several years and resisted recruitment attempts by other institutions, including the Howard Hughes Medical Institute (HHMI), which hoped to recruit him to a major opportunity in his home state of Texas. Eventually, McKnight succumbed to Dr. Don Brown's blandishments to return to the Carnegie Institution after a suitable number of years had passed, and so he left the center in its early years.

Reeder also played a leadership role in recruiting Dr. Steve Henikoff, who came from a distinguished graduate career with Dr. Matt Messelson at Harvard University, and a postdoctoral fellowship with Dr. Charles Laird in the Department of Zoology at the University of Washington. Henikoff represented expertise with the fruit fly *Drosophila*, which was at the time and continues to be today one of the most powerful

experimental systems for defining principles that can be applied generally to complex organisms. As was the case with Zakian and the yeast system, Henikoff introduced *Drosophila* as a valid and important experimental system in a basic science enterprise at a cancer research institute. Henikoff has gone on to establish a leadership role in research on the role of chromosome structure in regulating gene expression. He also was a pioneer in genomics research at the center and developed tools for analyzing protein sequences that enable researchers to understand the evolutionary relationships among genes from different organisms. Henikoff's creativity was recognized, as was Weintraub's, by the Howard Hughes Medical Institute (HHMI), which selected both as investigators. The appointment of Weintaub and Henikoff to HHMI investigator positions represented the institute's initial effort to establish a group of investigators at the Hutchinson Center, rather than trying, unsuccessfully, to recruit scientists away from center to units established elsewhere. Weintraub and Henikoff were the first center scientists to be so recognized. The relationship between the center and HHMI has since enlarged and remains a productive element of the scientific program.

Molecular and cellular biology has continued to be a central theme of the Basic Sciences Division since these formative years. The impact of this facet of center research was documented in an article in *Science* [1992, 256:460] that ranked American and European research institutions on the basis of the frequency of citations of research publications between 1981 and 1991 in cellular and molecular biology. Internationally, according to the ISI Citation Database, the Hutchinson Center was ranked as one of the leading five institutions in terms of citation frequency in this field. Whatever the limitations of this type of comparison, it is clear that basic science at the center had, by that early date, climbed into the front ranks of comparable institutions. What follows is an attempt to summarize what lead to and sustained that achievement.

Organizing principles of the Division of Basic Sciences

Principles and procedures. As the center transitioned in 1981 from the original program structure to a faculty-based divisional structure, the individuals who made up the nascent Division of Basic Science came to a consensus regarding the principles used to establish a division faculty, a consensus that has lasted to the present. First, going forward from that time, each new faculty member was selected by the division as a whole, as opposed to filling particular slots in a pre-existing small program. This was accomplished through advertised national searches. Recruitment of in-house trainees was discouraged, although, as described, some early recruits during the program period were center trainees. The reasoning for this general policy (but not immutable rule) was that faculty recognized that there was a very large national pool of talent from which to recruit new members, and, hence, no particular reason to select new faculty from the pool of center trainees. A second reason, one that is recognized in many other institutions, is that limiting recruitment of junior faculty from an institution's own laboratories avoided the development of empires, which was a liability, many felt, of the original program structure.

A second principle was to maintain relatively modest laboratory sizes for each investigator. Division policy limited the amount of laboratory space available to senior faculty to a total of five modules, which would be sufficient to comfortably accommodate 10 to 12 workers at the bench (although in some cases popular laboratories managed to pack in larger numbers into this relatively modest space allocation). There were several motivations for limiting the maximum laboratory space for established scientists. The center was a relatively small free-standing research institute. To have made indefinite commitments to large research enterprises within that small institution would have limited the number of independent programs to a number too small, it was believed, to form the basis of a viable, front rank, research

enterprise. Not being on a large university campus dictated a need to cover biological science fairly broadly and to recruit as many independent creative units as possible. Smaller laboratories also meant that many center investigators would remain active bench scientists and not simply administrators over a large number of postdoctoral fellows and students, as sometimes is the case with successful scientists. Moreover, the small laboratory model encouraged collaboration between laboratories to create needed critical mass, not only for intellectual exchange and sharing of techniques and approaches, but also for the purchase of heavy equipment and other space-occupying requirements and research resources that could be shared among laboratories, thereby helping to cement the community together.

During the early period, recruitment of established faculty seemed to be essential to nucleate the program. However, most of the initial "senior" faculty were in fact rather early in their careers and had only just begun to make the major impacts that they were to have over the lifetime of their scientific careers. Weintraub, as a prime example, went on from his early work in chromatin structure to at least two other high-impact accomplishments: (1) the use of anti-sense RNA technology, a strategy to regulate the expression of specific genes in higher animal cells as an experimental approach and ultimately, as an approach for the development of important agents in both therapy of patients and in agricultural research; and (2), his identification of a master regulatory gene called Myo-D that directs the development of a whole program of muscle differentiation and opened the field of understanding of the molecular biology of cellular differentiation in vertebrate cells. Building on these examples, the focus of development of the program from that time forward was to recruit and develop talented young faculty whose career body of work would be done at the center. It was believed that this approach would have greater impact, and be of greater social value, than simply moving established celebrity scientists from one institution to another.

The primary approach was to recruit entry-level faculty of apparently exceptional ability and then to do everything possible to help them succeed. A cardinal tenet was to have as many faculty as possible have a stake in these recruitments. Broad-based enthusiasm for individual recruitments in the division led over the years to broad-based help for each of the young faculty members who were recruited, providing the young recruits with the sense that they were respected and supported by their colleagues. Career development policy for these new faculty involved two peer-reviewed "up-or-out" promotions to achieve Full Member status. Allocations of space, increases in salary, and distribution of other resources were based on these reviews, which were carried out in conjunction with the promotional processes. Therefore, all faculty members understood that increases in space and salary and other resources would come about based solely on rigorous peer review. This approach served to cut down considerably on internal politics within the divisional scientific community and to allowed energy to focus mostly on the conduct of research.

Applications. Recruitment of established investigators to the faculty was not precluded. However, such recruitments were largely opportunistic, occurring primarily when exceptionally productive individuals indicated to a faculty search committee (originally called the New Staff Committee) that they were leaving their institution and were interested in moving to the Hutchinson Center, rather than as an overt recruitment attempt by the division. To achieve the broad faculty support necessary to generate an offer, senior recruitments were seen as a strategy for bringing an important new dimension to the research program of the division. An example of an early recruitment of an established scientist included Dr. Gerry Smith from the Molecular Biology Institute at the University of Oregon in Eugene. Smith brought to the center the study of DNA recombination in the model bacterium *E. coli* , and later on, in yeast. A bit later, Dr. Harvey Eisen from the Pasteur Institute in Paris, who had done pioneering

work with bacteriophage lambda, a virus that infects *E. coli* that has served as a seminal experimental system for molecular biology, joined the division. Another senior recruit, Dr. Meng-Chao Yao from Washington University in St. Louis, brought a new model system to the center, a single-celled organism called *Tetrahymena*, useful for analysis of complex changes in DNA structure, rearrangement and a process known as amplification. Dr. Keith Fournier, from the University of Southern California, was recruited jointly with the Program in Molecular Medicine, which later evolved into a separate Division of Human Biology. Fournier brought technology for the analysis of regulation of gene expression higher vertebrate cells. Finally, and most recently, Dr. Dan Gottschling from University of Chicago joined the division. Gottschling originally trained at the center as a postdoctoral fellow with Zakian, and left in part because of the policy against recruiting in-house trainees. He then returned to Seattle after Zakian left for Princeton University to continue research in understanding the regulation of chromosomes by telomeres (the ends of chromosomes) and related aspects of cell and molecular biology in the yeast model system.

Aside from recruitment of these relatively young, but established scientists, the policy of recruiting entry-level faculty included a long list of individuals who began their faculty career and developed their independent research programs and their international reputations while at the center. These include Dr. Jon Cooper, who trained at the Salk Institute and who joined Rohrschneider and Carter in establishing a critical mass of scientists focused on investigation of cell signaling from the cell surface. Dr. Barry Stoddard was recruited to nucleate efforts in structural biology (described more fully below). Dr. James Roberts, an exception to the policy of not recruiting individuals from the center, had developed his interest in cell cycle molecular biology while working as a postdoctoral fellow with Weintraub. In Robert's case, there was unanimous enthusiasm among the faculty for making this exception. This decision has been amply rewarded by Roberts' exceptional and widely acknowledged productivity.

To continue this list, Dr. Steve Hahn, trained at MIT, has become a leading scientist in the field of the biochemistry of gene expression using yeast as a model system. Dr. James Priess, recruited from the University of Colorado because of his interest in the roundworm *C.elegans* experimental system, has led cutting-edge studies of the early stages of metazoan embryonic development. Roberts, Hahn, and Priess joined Weintraub and Henikoff as Howard Hughes Medical Institute investigators.

Other individuals who have developed their faculty careers at the Hutchinson Center and who become Full Members of the faculty include Dr. Linda Breeden, who extended the division's efforts in cell cycle research. Dr. Susan Parkhurst broadened the program based on studies in *Drosophila* and discovery and analysis of genes important in development of higher organisms. Dr. Mark Roth established a national reputation as a junior faculty member at the center through his discovery and characterization of what are known as SR proteins, which are required for a process known as RNA splicing, an essential step in gene expression. Roth has since gone on to a number of other quite distinct accomplishments. Dr. Bruce Edgar has exploited *Drosophila* in penetrating studies of the role of specific genes in cell growth (size) control in intact tissues, and how that control is integrated with control of cell division and with nutritional status. There were additional junior faculty recruitments carried out jointly with the Program in Molecular Medicine, which included Dr. Arthur (Dusty) Miller from the Salk Institute, who nucleated the center's program in human gene therapy; and Dr. Michael Emerman from the Pasteur Institute, who established a research program in study of the Human Immunodeficiency Virus, which causes AIDS.

All of these individuals came to the center for their first faculty positions, have gone on to achieve international recognition and are now Full Members of the Basic Sciences Division faculty. These brief descriptions have emphasized their areas of research. It is important to point out, however, that in most cases it was not specific programmatic interest alone, or even primarily, that drove the recruitment of most of

these individuals but rather their manifest talent and potential for high-impact pioneering work over a career. A result of this approach was the development of a basic science faculty that exploited or led development of most of the tractable experimental models extant, addressing their work to a large number of the major problems in biology. Outside of the center, these scientists interacted with many different groups in the national and international scientific community. Within the culture of the center, despite this broad diversity of interests, which might have had an isolating effect, the faculty established strong bonds of community, interacting and learning from each other and sharing in the tasks of collegial governance. The elements supporting this cohesion are elaborated below.

Targeted versus untargeted program development

The iconic Hutchinson Center basic scientist, typically recruited early in his or her career for their creative talent as an investigator, might undergo several shifts in research focus during a professional lifetime, making seminal contributions in each case. This point was illustrated by Weintraub and Eisenman, as well as by some of the later recruits. For example Roth moved from studies on splicing factors early in his career, to work on autoantibodies—immune system components that react against self-tissue—and their potential use in the diagnosis of autoimmune disease, and later, to a novel contribution to defining reversible states of "suspended animation" triggered in developing organisms by oxygen deprivation. The rationale for a relatively untargeted approach to recruiting was that focused recruitment to fill program needs, in a narrow sense, would limit the size of the talent pool from which selections were made. With targeted recruitment, the argument held, the division might be left with faculty scientists who were unable to make changes in direction necessary to move forward as science evolved over time. Thus, short-term benefits to the current program from

focused recruiting might lead, in the longer term, to mediocrity. It must be admitted, however, that defining the basic science program of the Hutchinson Center was sometimes frustrating to the lay leadership of the center, who were charged with explaining and promoting the research program to the community and the public at large. Also, despite the attempt at division-wide consensus and avoidance of competitive overlap in selecting new faculty scientists, there was a tendency to hire investigators with similar research expertise, leaving obvious deficiencies in the program relative to that of peer research institutions. Thus, on specific occasions, more targeted recruiting was employed in order to provide breadth to the program.

A clear and successful example of targeted recruitment was in the area of structural biology. The strategy by which this was accomplished provides a good illustration of the scientific culture of the Division of Basic Sciences. In the process of deciding whether to proceed with focused recruitment in structural biology, the division began with a period of self-education in which a series of field leaders were invited to the center to give seminars. In the beginning, there were varying levels of enthusiasm among the faculty for this targeted recruitment, and the process of learning together what the field had to offer was intended to explore whether broad-based support for such recruitment could be generated. The seminar series in structural biology turned out to be very popular and highly appreciated within the division and the recruitment began for a structural biologist. The next question was whether to select a senior investigator with broad recognition in the field to nucleate this effort, or whether the division could develop a top-flight program with a group of junior faculty. Interestingly, both outside advice and internal inclination was to what other junior recruits in the division had done: development of their own programs and conducting their seminal work at the center. The search resulted in recruit, at the junior level, a small group of structural biologists who would achieve the recruitment of Stoddard as an entry-level faculty scientist, who has gone on to become a Full Member of the

faculty, provided leadership for the further development of structural biology at the center, and, in the process, taught division faculty how to incorporate structural approaches into other aspects of biology. Following Stoddard, recruitment of additional junior faculty who have gone on successfully to establish research programs, including Dr. Roland Strong, has created a critical mass adequate to sustain the structural biology enterprise within the broad based biological sciences.

The recruitment of Emerman in research on AIDS, mentioned previously as an early collaboration with Molecular Medicine, was another example of a successful, programmatically-targeted search. In a few cases, rather than a targeted search process, opportunistic recruitment of an exceptional young investigator solved a problem of deficiency in breadth. The recruitment, with Molecular Medicine, of Miller, who pioneered development of delivery vehicles for human gene therapy, was an early example. A later example involved developing technology for introducing genes into mice at the center. During earlier searches for new Basic Sciences Division faculty, problems were encountered in identifying candidates who were both skilled in this transgenic technology and were sufficiently attractive in terms of their scientific abilities to compete successfully in the recruiting process. A broad sense was already present among many faculty members that transgenic mouse models were essential for advanced work in higher animal systems and translational work in human diseases. Dr. Phillipe Soriano, who trained with Dr. Rudolph Jaenisch at MIT, had established a reputation for innovation and productive exploitation of transgenic technology for the study of cancer-causing genes and signaling proteins during mammalian development. Soriano was actively looking for a new position, was recruited in the context of the Molecular Medicine Program with a joint appointment in the Basic Sciences Division and has ultimately remained in the Basic Sciences Division, providing leadership, both in terms of his own research, in collaborations with numerous members of the division

and supervising a shared resource that allows scientists within the Hutchinson Center to exploit transgenic technology as appropriate.

These examples of success can be contrasted with other attempts at targeted programmatic recruitments that did not produce longstanding results in the development of the division. For example, very early in the development of the center, there was strong interest in cancer pharmacology, an area concerned with identification and testing of new chemotherapeutic agents. The search committees devoted to that effort were unable to identify an available candidate, either senior or junior, who met the standards for scientific talent. As has occurred in other similar situations, that effort was terminated so as not to recruit to a lower standard. A similar outcome resulted from targeted searches in basic immunology. In contrast to those who believed in a broad basic science faculty, the majority of the early immunologists at the center wanted a separate faculty unit specifically committed to immunology. At one point, early after the establishment of the division, two junior faculty immunologists were recruited who were not content with the orientation of the Basic Sciences Division and left after several years for leadership positions in a new local biotechnology company. Eventually the development of a Department of Immunology at the University of Washington, a broadening and deepening of applied immunology in the Division of Clinical Research at the center and research programs in the regional biotechnology industry served to fill in this important area of research in the regional scientific community

Finally, the emphasis on tractable experimental model systems in which major and convincing progress on central problems in biology could be made rapidly was clearly the experimental approach favored by the majority of the Basic Sciences Division faculty at the center. This preference left applicants for faculty positions from some important areas of science, particularly those related to human biology and disease where experimental models and approaches were less tractable and where progress was

generally slower, in an unfavorable competitive position. As a result, human biology, translational research and various topics of importance between the area of basic research and applied research in populations or patients were for a time underrepresented in the center's scientific program. Although specific recruitments mentioned above with potential in these areas were successful, the Basic Sciences Division did not, and realistically was not large enough, to address this issue in any systematic way. Instead, this broad research need was ultimately addressed by the Program in Molecular Medicine and the Cancer Biology Program of the Division of Public Health Sciences, which recently were grouped with a new initiative in Genomics to form a second laboratory-based division called Human Biology.

The Basic Sciences culture and its impact on development of the institution as a whole

The basic science enterprise at the Hutchinson Center is relatively small for a freestanding research institute and has not increased dramatically the number of faculty positions from the early days of the center. In 1976, during the period of development of the center's laboratory base, there were some 22 faculty members directing laboratories which would later become the Basic Sciences Division. By 1986, about five years after the establishment of the division, the overall numbers of divisional laboratories had only risen to 27. When the division moved to the new Southeast Lake Union site, the Robert W. Day Campus, the building that was established for the faculty of the Division of Basic Sciences was sized to accommodate some thirty laboratories. At the same time, the overall laboratory base of the center had increased to a total of 90 laboratories, including the laboratory components of the Clinical Research Division, the Public Health Sciences Division laboratories, and the new Human Biology Division. It can be argued that the recruiting power of the Hutchinson Center for laboratory scientists is

based on the combination of the scientific culture and quality of research that developed in the Basic Sciences Division and made possible the success of the expanded laboratory base of the center's scientific program.

What were the elements of the culture and scientific cohesion that were important in creating an environment that fostered successful competition in the national marketplace for top-flight faculty talent? Some of these elements have already been mentioned, including the use of small laboratories to foster high levels of collaboration and the use of shared resources among the laboratories to leverage available space and resources and to avoid overlapping or redundant commitments between labs. Clearly, the system of collegial governance, such as the recruitment and the development of junior faculty, and also shared responsibilities for scientific training, gave each faculty member a sense of a stake in the overall success of the enterprise. There were, in addition, a number of intellectual functions that have been important. In the original building at First Hill, there was a small 6th floor conference room where faculty assembled for all administrative meetings and intellectual functions. Out of these collegial interactions that took place in this famous 6th floor conference room evolved the tradition of faculty lunch, a weekly meeting of the division faculty in which each faculty member takes a turn describing to his or her colleagues a current focus of research in their laboratory. In addition to the faculty lunch, there were weekly meetings for the whole division in which one or more postdocs or students from each laboratory would describe their work for the benefit of the whole community and receive feedback. Finally, there was an annual scientific retreat for the entire division during which each of the faculty members would present a short summary of their year's progress.

Although participation in these functions was not considered optional, such activities are not sustainable by compulsion. These functions were broadly supported among the faculty because they were seen as valuable by virtually all, and have

remained at the core of the divisional scientific culture. They demonstrate clear evidence of an intense interest and involvement among the faculty of the division, despite the substantial diversity of the scientific program. Divisional laboratories were led by individuals who attended different meetings and who were involved in different scientific constituencies than their neighbors. Still, the broad-based program of the division demonstrated the profound commonality of basic biological research. The faculty discovered many things to learn from each other, both about the details of their own fields, and about the common intellectual and technical approaches and concepts which can be translated from one field to another. This atmosphere of shared goals and interests sustained the early cohesion of the scientific program of the Division and has continued. Interestingly, the standard hallmarks of collaboration that institutional review groups often use, such as co-publishing and joint grants, occurred spontaneously, but were not particularly emphasized. To summarize, faculty, postdoctoral fellows and students can and did benefit from scientific expertise of different labs in immensely useful ways without necessarily requiring formal collaborations or administrative structures.

Postdoctoral and graduate training in the Basic Sciences Division, and relationships with basic sciences at the University of Washington

From the beginning, Hutchinson Center laboratory science attracted large numbers of postdoctoral trainees who have made up the most numerous component of laboratory personnel. For example, by 1982 there were over 80 postdoctoral fellows, and that number has grown to more than 200 in recent years. Many of the intellectual functions of the division, including specific interest groups and journal clubs, the weekly division-wide research meeting and the annual scientific retreat were, to a large extent, established to enrich the training environment. To support this large training

activity, most postdocs competed successfully for external fellowships for a significant period of their tenure here. Additionally, this strong postdoctoral training record was reflected in several consistently renewed training grants: Virology, directed by Linial; Chromosomes, directed by Reeder and then Yao; and Carcinogenesis, a shared training grant directed by Dr. Larry Loeb at UW and Neiman (more recently by Groudine) at the center. To fill out the needed support, investigators' research grants and, more recently, a limited number of one-year-at-a-time center-funded postdoctoral slots, have been used. Division postdocs have participated in most of the scientific achievements of the division, and, as a group, have a sterling track record in going on to productive research careers at other academic institutions and biotechnology companies. Despite the division's emphasis on recruiting from outside the center, several in-house trainees are now senior faculty members (Groudine, Linial, Roberts, Gottschling, Tapscott). One former postdoc in Weintraub's lab, Dr. Nancy Hutchison, has modeled the alternative career pathway by establishing the Science Education Partnership (SEP) at the Hutchinson Center. Under Hutchison's leadership, SEP provides direct exchange between center professional scientists and regional secondary school science teachers, including tools and kits that are loaned to enrich the practices in participating teachers' classrooms. This program has continued to broaden its science education activities, attracted major financial support from HHMI and other agencies and continues today as among the most effective of outreach programs at the center for the regional community.

In contrast to postdoctoral training, graduate training in cell and molecular biology at the center took many years to develop. In the first instance this was because the license to conduct such training was held by the University of Washington and was only available to center faculty through affiliation with the university. The first basic science program heads, during the early development of the center, all had full University of Washington appointments in relevant departments, and basic scientists

participated in the University of Washington graduate programs through the departmental programs. With the subsequent extensive recruitment at the Center, the University basic science departments began to balk at making appointments for all of the new center faculty. The Basic Sciences Division was left with the situation where a few of the original senior founders had graduate appointments, while the bulk of the developing faculty in the division were not able to participate in graduate training. The feeling among the faculty was that graduate training was a very important element of the intellectual life and productivity of a research institute, and that participation in training for science and doing science well are so intimately connected that a full range of training activities, graduate as well as postdoctoral, was important to the future of the center. This idea was particularly important to newly arrived young faculty who felt more capable of attracting and supervising graduate students than postdocs. Although some were sympathetic, many colleagues at the university in the basic science departments were not enthusiastic about sharing graduate training with center-based faculty. They felt that graduate training activities in their departments were a kind of reward for carrying out all of their responsibilities within the university, such as heavy loads of service teaching of undergraduates and professional school students. This point of view held that Hutchinson Center faculty were advantaged by their lack of such responsibilities. It was, for those reasons, felt by some at the university to be unfair that students should be shared with center faculty, a concern which extended to worry about a disproportionate movement of students from university departments to the Hutchinson Center.

All of the center's scientific directors, beginning with Charles Evans, then Hans Neurath, and then Paul Neiman, made serious efforts to ameliorate these concerns at the university and to create a working partnership in graduate training between the basic science communities at both institutions. A position was established within the new Basic Sciences Division of a director of graduate training, whose responsibility was

to help the division develop appropriate programs for graduate students. The first to hold that responsibility was Gerry Smith, whose prior experience in graduate training, it was hoped, would serve to encourage university colleagues to find a pathway for accepting Hutchinson Center faculty into the university graduate training community. However, several attempts to organize a joint program were rejected by either individual university chairs or by the dean of the School of Medicine. Shortly after the Basic Sciences Division was formed, a meeting was held between the university basic science department chairs and Hutchinson Center senior faculty to discuss establishing a working relationship in graduate training. It was clear at that meeting that the university chairs themselves did not have a consistent opinion as to what ought to be done. Some chairs, for example, Drs. Herschel Roman and then Ben Hall, the successive chairmen of the Department of Genetics, felt that the center should be responsible for its own graduate training because Genetics Department graduate program was highly specific to the environment of the department on campus. On the other hand, other department chairs, such as Dr. Earl Benditt in the Department of Pathology, felt that an independent Hutchinson Center graduate training program would not be a good idea and should be integrated in some fashion into the university's graduate activity.

What emerged from these discussions was a plan to incorporate the entire Basic Sciences Division faculty into the Department of Pathology at the university for purposes of running a graduate training program through the department's program. This idea was proposed by Benditt and some of his senior faculty. This plan proceeded as far as development of graduate affiliate appointments in the Department of Pathology for a relatively large number, but not all, of the Hutchinson Center's Basic Sciences Division faculty. At that point Benditt retired and was replaced by Dr. Russell Ross as the new chairman. Ross's vision for the department did not include a joint program. He was concerned that the center faculty individually were not sufficiently committed to the priorities and programs of the Department of Pathology to participate

at a level commensurate with the department's goals; a joint graduate program was, by itself, not enough. However, as a residual outcome of the attempt to develop a program with the Department of Pathology, many of center faculty obtained graduate appointments in the Department of Pathology, and a number of Pathology graduate students earned PhD degrees with center advisors.

Gerry Smith asked to be replaced, and Meng-Chao Yao took over as head of the graduate training efforts. About this time, the university recognized a need for a broad-based interdisciplinary molecular and cell biology program that was supra-departmental. The university departmental programs were not filling with students of the caliber that faculty of both institutions thought could be attracted to the Seattle biomedical scientific community. Interdisciplinary programs in cellular and molecular biology had become a popular approach in many competitive academic centers around the country. The first step to develop such a program at the university was the creation of the Interdisciplinary Molecular and Cell Biology Program (IMCBP), a non-degree-granting initiative headed by Dr. David Morris from the Department of Biochemistry. This program functioned as a joint recruiting mechanism as well as to coordinate molecular and cell biology training activities in the multiple departments at the university. Hutchinson Center faculty members who had university appointments could participate, for example through the residual appointments in the Department of Pathology and the original appointments that some of the senior faculty had in other departments. This situation, however, excluded large numbers of center faculty, particularly young recent recruits, a condition that was felt by all at the center to be unacceptable.

What ensued was connected to the general affiliation agreement between the University of Washington and the Hutchinson Center, which was undergoing renegotiation. The principal issues between the institutions at that point involved the nature of the practice arrangements for Clinical Research Division faculty who had

university clinical department appointments, coupled, on the basic science side, with the concern over graduate training. There were a number meetings and negotiations, culminating in a meeting of University of Washington Board of Regents members, university senior leaders, and senior leaders from the center faculty, administration and Board of Trustees at Snoqualmie Falls Lodge. At that meeting, Dr. William Catterall, chairman of the Department of Pharmacology representing the university, and Neiman, representing the center's Basic Sciences Division, worked out language that was built into a provisional agreement. This marked the first mutually agreed upon approach between the center and the university basic science communities about how to conduct joint graduate training in cellular and molecular biology.

However, this arrangement did not proceed because of the continuing dispute between the University of Washington School of Medicine and the center regarding clinical practice arrangements, and the whole affiliation agreement was put on the shelf until that dispute could be settled. There were several attempts made by leaders from both institutions, including Drs. Lee Hartwell and Ed Krebs (future and current Nobel laureates respectively) from the university along with IMCBP director Morris, to argue that the issues between the institutions no longer involved graduate training, and that therefore a joint graduate training activity should go forward. This was not acceptable to the leadership of the School of Medicine, which took the position that no joint activities could take place until the overall affiliation agreement was consummated, and no progress toward that goal appeared to be forthcoming.

In frustration, the center applied to the State of Washington to be recognized as an independent degree-granting graduate training entity. The State of Washington regulates graduate training through the Higher Education Coordinating (HEC) Board, which grants authorization to conduct training at all levels, including Ph.D. training. The State of Washington had approved Ph.D. programs in biological sciences only at the University of Washington and Washington State University, and, at that point in

history, no other institutions. The HEC Board, however, recognized the Hutchinson Center as a locus for high-quality graduate training, and did grant recognition for the development of a program at the center. At about the same time, the University of Washington submitted its own plan to the HEC Board for a degree-granting interdisciplinary molecular and cell biology program separate from that of Fred Hutchinson. The HEC Board members, in approving both programs, expressed a preference that the two institutions work together to carry out these programs.

Shortly thereafter, the issues dividing the Clinical Research Division and the School of Medicine were resolved. The university then took the position that they could not enter into a new affiliation agreement if the center took on an independent graduate training program. At this point, rather than resisting Hutchinson Center-based graduate training within their own programs, the School of Medicine leadership insisted that the two institutions conduct a joint program. This is exactly what was then achieved, again with Catterall representing the university and Neiman representing the center in negotiations regarding details of the plan and obtaining agreement from their respective faculties and administrations. The present Molecular and Cellular Biology graduate training program, jointly administered between the two institutions, was thereby established and was built into the renewed affiliation agreement at the end of 1993. The center remains an independently recognized graduate training entity by the State of Washington, a circumstance which serves to insure continuation of graduate training at the Hutchinson Center in the event that any problem should arise in the future with regard to institutional affiliation. However, short of that unlikely event, the center remains committed to a joint training activity with the university.

The joint program was formalized in January of 1994 with two co-directors, Yao for the FHCRC and Morris for UW. After two successful recruiting seasons, and setting the joint program off administratively on the right track, in 1995 Yao was succeeded by Jon Cooper as the next director of graduate training at the center-and Dr. Randall Moon

as the co-director at the University. Under this joint leadership and that of their successors, Dr. Barry Stoddard at the center and Dr. Henk Roelink at the university, the joint program has flourished in the fashion predicted by its early advocates. The center and the university together comprise a very attractive training opportunity for the best and brightest students nationally. The program competes with increasing effectiveness with the strongest training programs around the country to generate outstanding classes of molecular and cell biology students. The annual class size varies in number from 13 to 25 students, reflecting the recruiting success of any given year, and comprises a total of about 110 students distributed equally between the two institutions. There are now (2003) approximately 55 graduate students at the Hutchinson Center.

Regional biotechnology industry and the Basic Sciences Division

The history of immunology at the Hutchinson Center, already described, is especially important with regard to the origins of the Seattle biotechnology industry. Robert Nowinski, an immunologically oriented tumor virologist who was recruited in the early years of the center, became excited about the potential of monoclonal antibody-based technology as it first emerged in the late 1970s. Nowinski felt that this potential was best developed in the context of the new biotechnology industry that was beginning to burgeon elsewhere in the country. He was among the first scientists in the region to become interested in developing a biotechnology company and ultimately, he did found a pioneering company in Seattle, Genetic Systems, based on monoclonal antibody technology. Shortly thereafter, a sister company called Oncogen was formed by the Hellstroms and Nowinski, and yet another company, called Immunex, was formed with scientific leadership from Chris Henney and Steve Gillis, who was briefly a junior faculty member in the Basic Science Division before leaving with Henney. The internal debate at the center about the program structure versus a broad based

divisional faculty structure (which preceded the formation of the Basic Sciences Division) was thus resolved, largely because Henney and the Hellstroms and their junior colleagues, the principal advocates for maintaining the original program structure, left to form these new companies. The foundation of these companies together with another company, Zymogenetics, founded by faculty from the University of Washington, comprised the core of the early development of the regional biotechnology industry.

As a result of that experience, a number of policies developed with regard to Basic Sciences Division faculty relationships with biotechnology companies and conflicts of interest. The principle on which those policies were based was the notion that membership in the Basic Science Division was a full-time commitment, both in terms of scientific productivity and the expected level of interaction with other members of the center faculty, postdoctoral fellows and students. Developing a company was another full-time commitment; the two commitments could not be met by one person. Therefore, the decision to become involved seriously in biotechnology companies, particularly becoming a line officer or responsible member of the company, was not compatible with membership at the center. Individuals like Nowinski, the Hellstroms or Henney, who wished to develop companies, needed to resign their position at the center. In fact, those individuals did not appear to disagree or contest that approach.

There was recognition, however, that expertise within an institution like the Hutchinson Center could often be very important and helpful in establishing new biotechnology enterprises that could lead directly to products and devices useful for addressing human needs. Therefore, there was a perceived responsibility on the center's part to help the development of these new biotechnology companies in a fashion that did not damage the center's scientific effort. For this reason, service on a scientific advisory board, within significant time constraints, was, and continues to be, permitted.

The compensation for participation in biotechnology companies on this limited basis remained an issue. Initial attempts to encourage compensation on a fee-for-service basis, so that individuals did not have a capital position in the companies that could constitute some kind of conflict of interest, turned out to be impractical. New biotechnology companies rarely had funds available to compensate individuals on a fee-for-service basis and preferred to do so by assigning them founders' stock. Many companies also felt that this arrangement served to reassure investors about the seriousness of a scientific advisory board member's commitment to the company. In order to monitor the level of faculty involvement on a company's advisory board, and the level of compensation involved, these arrangements were subject to review on at least an annual basis. If any of these involvements appeared to cause problems at the center, that is, if individuals involved were compromised in meeting their responsibilities as members of the faculty, the center was in a position to insist that changes be made or involvement be ended.

In general, that approach worked out well for laboratory-based faculty. In fact a number of FHCRC basic science faculty have made significant contributions as advisors to new biotechnology companies. A good example is illustrated by the experience of Weintraub, who was the original inventor of antisense technology, a strategy exploited to control the activity of specific genes in higher animal and plant cells. When a company was formed in the San Francisco area to develop this technology for various applications, both clinical and agricultural, Weintraub and other leaders in the field were asked to serve on the advisory board. Although a very valuable advisor, Weintraub was never a company line officer and never spent enough time on this task to constitute any perceived problem with regard to his participation at the center. On the other hand, the company was for a time quite successful, and the appreciated stock that he received as compensation for that participation was important for the financial security of his family at the time of his premature death. A creative inventor of a useful

and novel technology was thus compensated for his contributions in such a way that his family was secured in the face of disaster, well beyond the center's standard benefit package. Although conflict of interest policy continues to evolve, both nationally and at the center, it seems difficult to envision serious objections to such an outcome.

The role of Scientific Advisory Boards in the development of the Basic Sciences Division

Institutions sometimes use outside advice in a fairly superficial way, often to meet funding agency requirements. NCI core grants, for example, have required such outside advice. These exercises can be viewed as having little more than nuisance value by both the faculties of the institutions and the reviewers who are asked to serve on such committees. In the case of the emerging Basic Sciences Division, though, it seemed important to learn how leaders in the relevant national research community viewed the division's progress, particularly as a new, possibly unique institution. A Scientific Advisory Board (SAB) was formed with reviewers who were greatly respected by the faculty. The approach taken was to treat their time as very valuable and to focus questions and issues in a way so as to obtain maximum use of their responses. The division learned to recognize that the useful responses obtained were both formal and informal. Formal written reports, usually a diplomatic consensus of committee opinion, were useful on general issues. Verbal and informal responses both by the SAB as a whole, and by individual members of the review boards, were also important and powerful sources of useful help.

The first outside scientific review board was chaired by Donald Brown from the Carnegie Institution and included James Darnell from Rockefeller University, Arnold Levine from the State University of New York at Stony Brook, Lee Hood and Mel Simon from the California Institute of Technology, and Irv Weissman from Stanford

University. Subsequent SABs were chaired by Levine and then by Harvey Lodish from MIT. Such meetings were focused on two to three questions of current importance to the division, as defined by the faculty as a whole, as well as by division and center leadership. Focused discussions on these particular issues were supplemented by a review of division decision-making processes, for example promotions and recruitments, and also by meetings between individual faculty members and members of the board to allow for discovery of issues of general importance that might come up in private one-on-one discussions. The SAB reported at several levels: verbally to the division director, to the director of the center and to selected members of the executive committee of the Board of Trustees. They then submitted a written report that was circulated to the faculty.

An example of an issue that arose at the first SAB meeting, and had a lasting effect on the development of the division, was the rigor with which the promotion processes, particularly "up-or-out" decisions concerning junior faculty, were conducted. The SAB pointed out that in larger institutions, there was a body of expert faculty opinion from which to draw reviews outside of individual departments so that departmental faculty could be kind to their colleagues and leave the difficult decisions to the actions of deans or *ad hoc* committees formed by non-departmental faculty. In contrast, the Basic Sciences Division, with its small size, had only one voting peer review group, its own faculty. This concern on the part of the SAB led to considerable discussion, initially with the SAB members, and then among the division faculty, about whether an outside review body above the level of the divisional faculty should be formed. In the end, it was decided that division faculty would take responsibility for the necessary level of rigor in making these decisions, but that to transmit a positive recommendation to the director, promotion of junior faculty would have to be supported by at least a 75 percent majority of the voting faculty. Divisional promotional recommendations were accompanied by serious analysis by both the division faculty

and written letters of evaluation by a number (at least ten) outside experts. The track record of the division in terms of scientific productivity documents that, after a serious and careful discussion stimulated by the SAB, a successful formula was found for making these sometimes difficult, but always important decisions. There were many other similarly important issues that were reviewed with help from outside scientific advisers, and that have had positive impact on the development of the Division.

New facilities for Basic Sciences at Southeast Lake Union, the Robert W. Day campus

By the end of the 1980s, the laboratory component of the center, principally the Basic Sciences Division, had overrun the laboratory space available in the original First Hill facility. Without new laboratory space, the planned growth of junior faculty laboratories would be blocked and some of the most productive members of the junior faculty would have had to move on to other institutions for their full development. Even with the five-module limit for senior faculty, it was estimated that the center, restricted to its original facilities, might comprise as few as twenty fully developed laboratories with no room for additional junior faculty, and without any significant growth in laboratory components of the other divisions, or development of a new division like Human Biology. The decision was made by senior center leadership and the Board of Trustees that development of new laboratory space was essential for the long-range development of the center. Basic Sciences Division faculty supported the idea of development of new laboratory space, and a move to another site to achieve that goal was acceptable, so long as it could be done in such a way that it did not have deleterious effects on the rest of the institution, for example, the Clinical Research Division. A letter to that effect was drafted, after a faculty meeting to discuss these

options, and sent to the center director as the Hutchinson Center continued its plans for the development of new facilities.

One reason for concern about moving to a new site was that there were, in fact, some advantages resulting from the tight physical packing of the original building. For example, the interspersion of the Basic Sciences and Clinical Research divisions' laboratory space led to useful interactions between the groups, including the sharing of equipment, ideas and personal relationships as well as learning techniques from one another. These interactions were valuable on a day-to-day level, even without formal collaboration or creation of the translational science programs. The positive effects of those interactions would obviously be lost by moving the Basic Sciences enterprise to another site, and this was a topic of serious conversation as plans moved forward.

In the end, the decision to leave First Hill and move the whole institution in stages over an extended period of time to the Southeast Lake Union site was a decision, and an achievement, of the senior leadership of the center. The result was obviously magnificent in terms of the resulting beautiful, highly functional facilities, which are a very beneficial aspect of center life, yet this was achieved at some cost. The divisions remain physically separated in different buildings, and interactions among them will require continued planning and building of programmatic structures for that purpose over the coming years. The senior leadership of the center devised a careful and conservative financial plan in the development of the facilities, but, despite the best of planning, forces beyond their control led to a period of time when resources for the scientific program were significantly compromised because of the financial obligations accompanying the financing of the new facilities. Factors that aggravated the situation were a period of general economic downturn and a significant decrease nationally in funding from the National Institutes of Health, coupled with an unavoidable decrease in income from the patient-care operations of the center. Inevitably, these constraints

led to serious internal competition for remaining funds that were available to sustain a scientific program.

Shortly after moving into the new basic science building (now the Harold M. Weintraub Basic Science Laboratories) in 1993, the division found that, for lack of funds, new recruiting, even to replace faculty who left because of promotional decisions and other reasons, would be delayed. This circumstance led to empty laboratory space, and, if extended long enough, could have undermined the rationale for the promotional decision-making process in the Basic Sciences Division. An additional strain brought on by these financial constraints was the desire on the part of the center leadership to develop new initiatives in interdisciplinary research, genomics and collaboration between laboratory-based and applied sciences, both with respect to the Public Health Sciences and Clinical Research divisions. This effort entailed the development of additional laboratory programs for those divisions, and for the development of a separate faculty unit, which ultimately became the Division of Human Biology, which could fill this programmatic gap. While there was support in principle for this concept within the Basic Sciences Division, there was also concern whether the center would (or even could) build an effort in human biology and translational research as an addition to the basic research enterprise, or only do so by replacing the basic research in part or in whole.

Fortunately, this period of constraint and frustration was relatively short, lasting only for two or three years. As the general economy boomed in the later 1990s, increased annual fundraising by the center made resources available to sustain the basic sciences enterprise and pursue the development of laboratories in the other aspects of the scientific program. The climate with respect to NIH funding also improved, and the center moved on to an era from the last half of the 1990s to close to the present in which all of the elements of the scientific program have enjoyed healthy levels of support from both the center and federal grants. The lessons from this fortunately brief period of

institutional stress lie in recognition of the priorities for the long-term financial maintenance of the center and ordering those priorities in a way that allows adaptation to periods of constraint.

The end of the period covered by this history

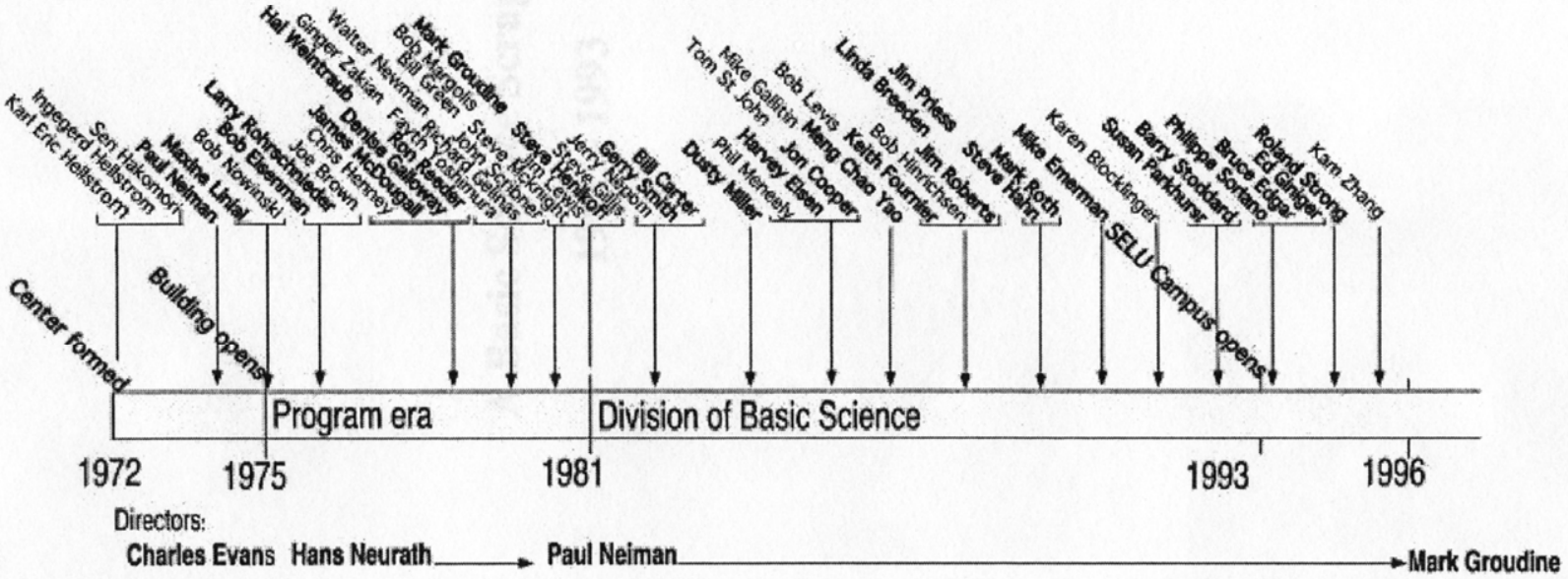
In 1996 Paul Neiman stepped down as director of the Division of Basic Sciences to return to full-time research in his laboratory. Mark Groudine was selected to assume this position by the center director as a result of an election by the faculty. Groudine has added his own special stamp to the development of the institution, and continues to lead the Basic Sciences Division, building positively and effectively on the lessons and experiences of the past.

Table 1, FHCRC Basic science faculty

Name	Year Appointed	From	Year left	to
Karl-Eric Hellstrom	1972	University of Washington	1983	*Oncogen
Ingegerd Hellstrom	1972	University of Washington	1983	*Oncogen
Sen -Itiroh Hakomori	1972	University of Washington	1987	Biomembrane Inst.
Paul Neiman	1973	University of Washington		
Robert Nowinski	1975	University of Wisconsin	1980	*Genetic Systems
Maxine Linial	1975	FHCRC, U.W		
Joe Brown	1976	University of Washington	1983	*Oncogen
Robert Eisenman	1976	ISREC, Switzerland		
Larry Rohrschnieder	1976	Justus Liebig Univ. Germany		
Chris Henney	1978	Johns Hopkins	1983	*Immunex
Denise Galloway	1978	Cold Spring Harbor	1987	FHCRC, PHS
James MacDougall	1978	Cold Spring Harbor	2001	FHCRC, PHS
Ron Reeder	1978	Carnegie Institution	2002	retired
Hal Weintraub	1978	Princeton	1995	died
Virginia Zakian	1978	University of Washington	1996	Princeton
Walter Newman	1978	Albert Eisnstein Coll. Med.	1983	Ortho Pharmaceuticals
Fayth Yoshimura	1979	MIT	1986	Uniiversity of Washington
Richard Gelinas	1979	Cold Spring Harbor	1990	*ICOS
John Scribner	1979	Pac. Northwest Res. Found.	1981	died
William Green	1979	FHCRC	1983	Dartmouth
Robert Margolis	1979	U. Cal. Santa Barbara	1991	CNRS, France
Mark Groudine	1979	FHCRC, U.W		
Steve Mcknight	1980	Carnegie Institution	1985	Carnegie Institution
James B. Lewis	1980	Cold Spring Harbor	1988	*Oncogen/Bristol Meyers-Squibb
Steve Henikoff	1981	University of Washington		
Steve Gillis	1981	Dartmouth	1983	*Immunex
Jerry Nepom	1982	Harvard	1983	Virinia Mason
Gerry Smith	1982	University of Oregon		
Bill Carter	1982	FHCRC		
Dusty Miller	1984	Salk Institute		
Phil Meneely	1985	University of Colorado	1995	Hanover College
Harvey Eisen	1985	Pasteur Institute	2001	retired
Jon Cooper	1985	Salk Institute		
Tom St. John	1985	Stanford	1990	*ICOS
Michael Gallitin	1985	Stanford	1990	*ICOS
Robert Levis	1986	U. Cal. Berkeley	1996	Syracuse University
Meng Chao Yao	1986	Washington University		
Keith Fournier	1987	Univ. Southern California		
Robert Hinrichsen	1987	Univiversity of Wisconsin	1997	University of Indiana
James Roberts	1987	FHCRC		
Linda Breeden	1987	Cambridge University		
James Priess	1987	University of Colorado		
Steve Hahn	1988	MIT		
Mark Roth	1988	Carnegie Institution		
Michael Emerman	1989	Pasteur Institute		
Karen Blocklinger	1991	ISREC, Switzerland	1997	Law School
Susan Parkhurst	1992	Cal Tech		
Barry Stoddard	1992	MIT		
Philipe Soriano	1993	Baylor College of Medicine		
Bruce Edgar	1993	U. Cal. San Franciso		
Ed Giniger	1993	U. Cal. San Franciso		
Roland Strong	1994	Cal Tech		
Kam Zhang	1995	UCLA	2001	Structural Genomics

*Regional Biotechnology start-ups

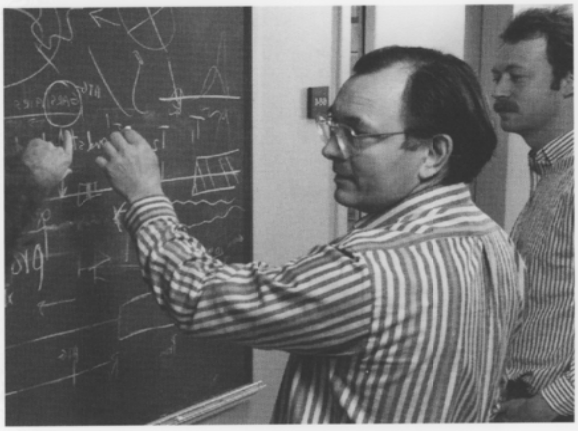
Fig. 1
FHCRC Basic Science Faculty
1972-1996



*remainder of career at FHCRC (2003)

A Basic Science Scrapbook

1981 – 1993



Ron Reeder

Bob Eisenman, Steve Henikoff, Jim Lewis

Mark Groudine, Ginger Zakian, Hal Weintraub

Karl Eric Hellstrom, Chris Henney

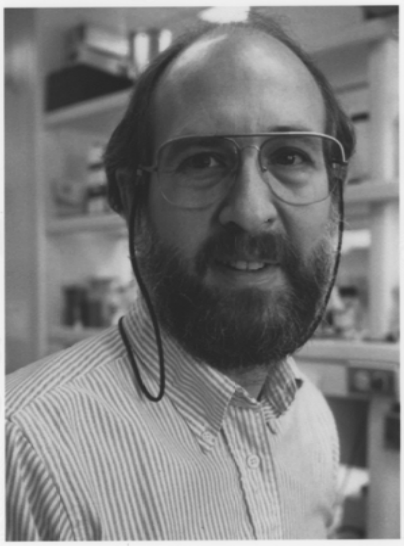
Sen Hakomori

Paul Neiman, Joel Myers (Clinical Res.)

Jim McDougall

Fayth Yoshimura

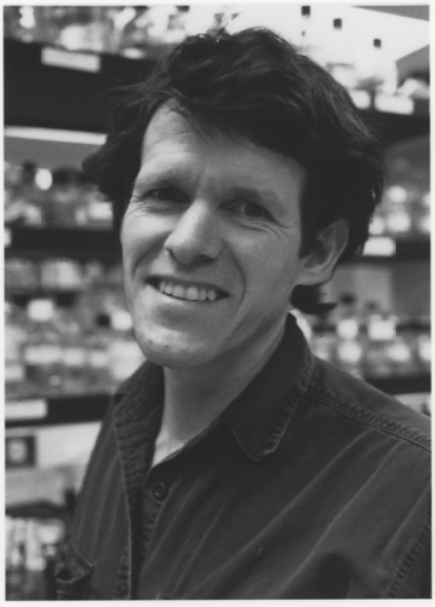
Hal Weinraub, Denise Galloway, Maxine Linial



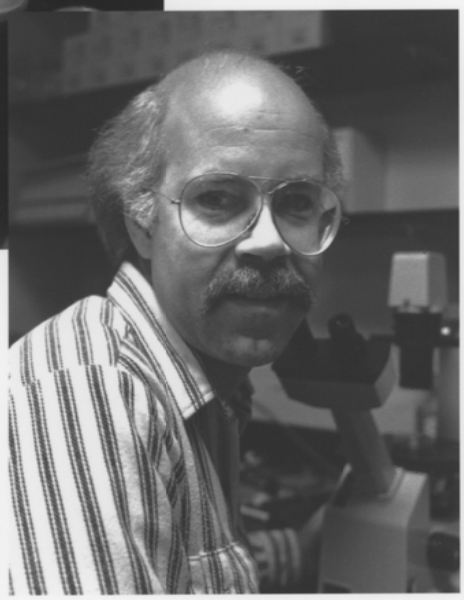
Larry Rohrschnieder

Larry, Bob Margolis, Rich Gelinas

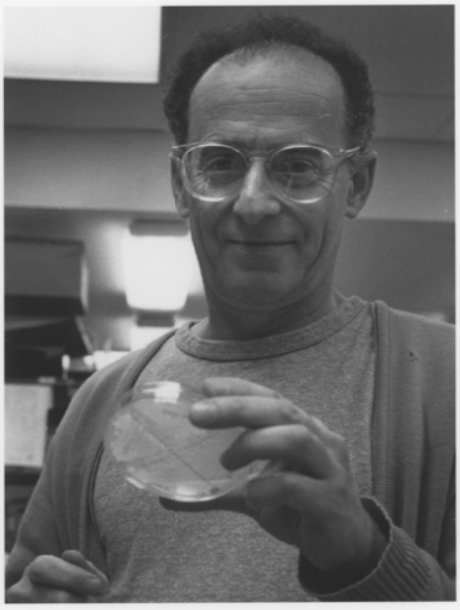
Gerry Smith



Bill Carter

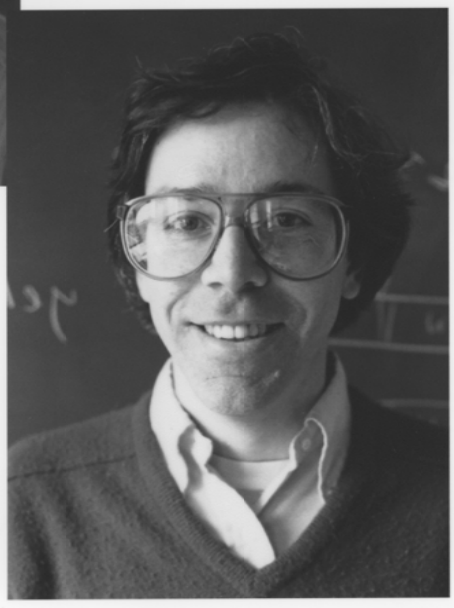


Dusty Miller

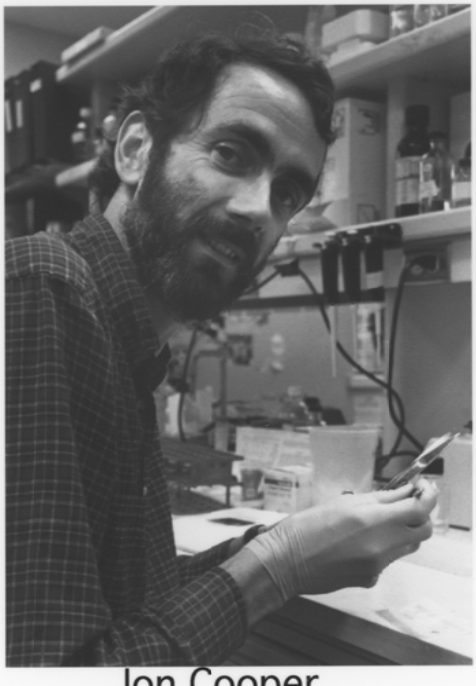


Harvey Eisen

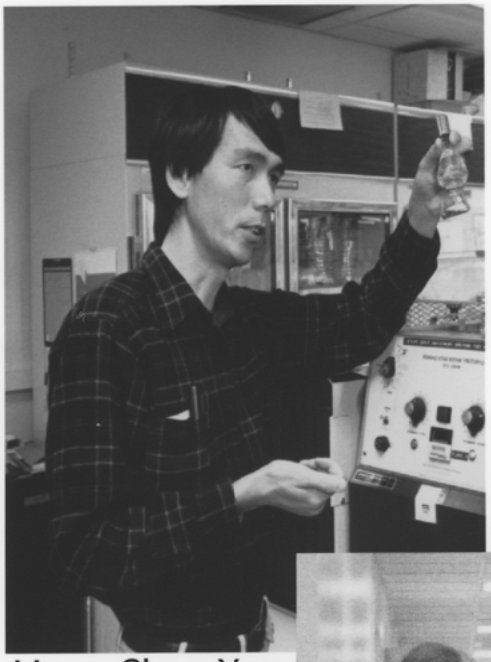
Phil Meneely



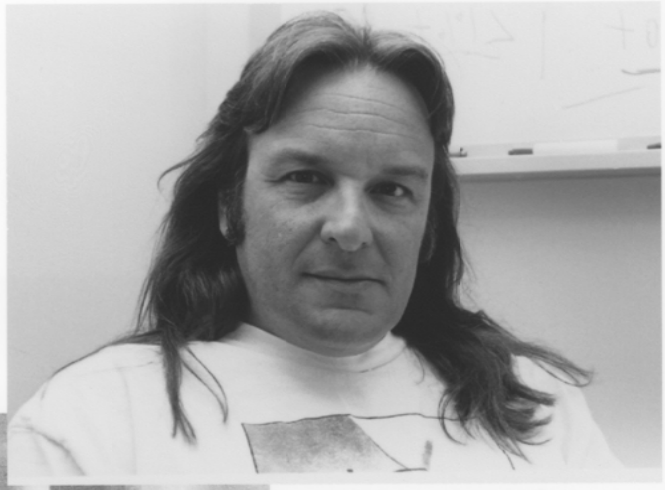
Bob Levis



Jon Cooper

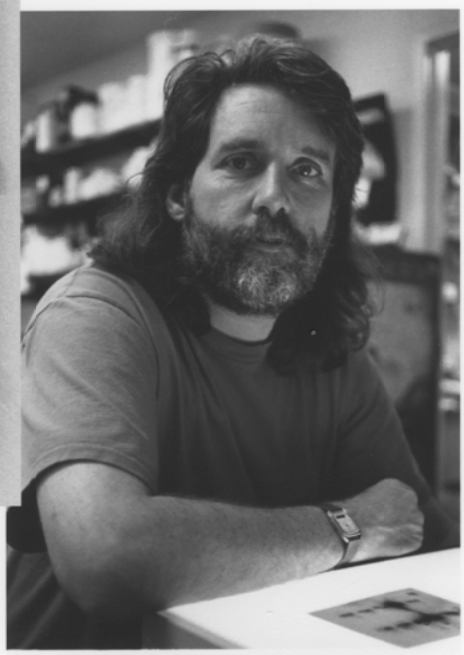


Meng Chao Yao



Keith Fournier

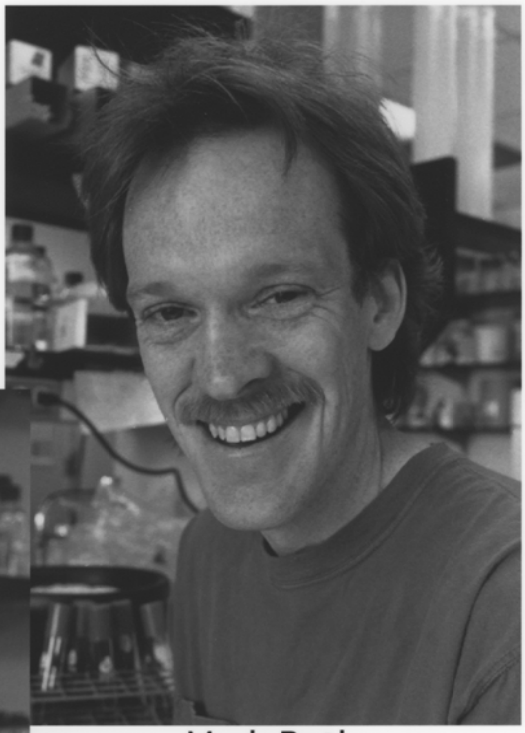
Hal Jim Roberts



Bob Hinrichsen

Linda Breeden

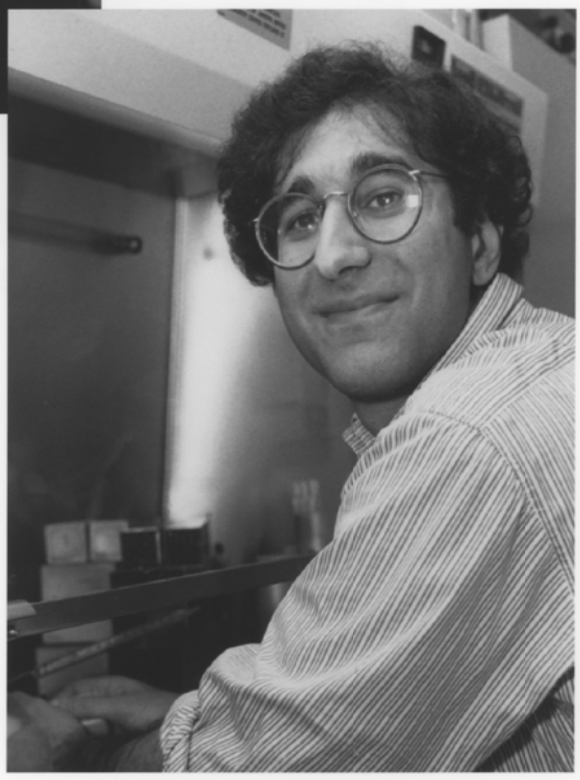
Jim Priess



Mark Roth

Steve Hahn

Karen Blocklinger



Michael Emerman

Susan Parkhurst

Phil Soriano

Barry Stoddard

SELU campus buildings A, B and C, 1993

Bruce Edgar

Roland Strong

Ed Giniger