

Regional Oral History Office
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UCSF Oral History Program
Department of the History of Health Sciences
University of California, San Francisco

The UCSF Oral History Program
and
The Program in the History of the Biological Sciences and Biotechnology

William J. Rutter, Ph.D.

THE DEPARTMENT OF BIOCHEMISTRY AND THE MOLECULAR APPROACH
TO BIOMEDICINE AT THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

VOLUME I

With an Introduction by
Lloyd H. Smith, Jr., M.D.

Interviews by
Sally Smith Hughes, Ph.D.
in 1992

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William J. Rutter

PREFACE

In 1990, the Department of the History of Health Sciences at UCSF, working closely with the UCSF Library's Archives, developed a formal Campus Oral History Program as an essential tool to document the oldest health sciences campus in the UC system. We were charged with the task of recording postwar development of this unique institution, which rose from a good regional medical school in the mid-1960s to arguably one of the best medical schools in the nation. Oral History Program personnel quickly found that local stories represented important, hitherto undocumented landmarks in the development of postwar American biomedical science.

To provide fuller documentation of this institution's exemplary basic sciences program, in 1991 Dr. Sally Smith Hughes was commissioned to begin a series of archives-based interviews covering the story of molecular biology and the university-industry relationships at UCSF. This volume represents the first of this series of interviews conducted with the pioneers of molecular biology and mediators of its commercial applications. The choice of Dr. William Rutter for the pilot interview is an obvious one, as readers of this interview will soon discover. His recruitment to UCSF in 1969 did much to create the entrepreneurial institutional environment for some of the most exciting developments in molecular biology and provided the catalyst for the nascent biotechnology industry. Other forthcoming interviews originally sponsored through UCSF's Campus Oral History Program include conversations with Dr. Herbert Boyer and Dr. Keith Yamamoto, scientists in UCSF's basic science programs. We gratefully acknowledge Dr. Rutter's generous participation in the arduous interview and editing process, and his role in the inauguration of an important series in the history of molecular biology and biotechnology in America.

Efforts are now underway to expand the initial charge of the UCSF Campus Oral History Program and conduct an exploration of the beginnings of molecular biology and biotechnology on several northern California campuses, using oral history interviews and collection of associated papers and records as essential tools. The future will bring expert collaboration among scholars, scientists, and archivists at UC Berkeley, UCSF, and Stanford, united in this important goal.

Nancy Rockafellar, Ph.D.
Director, UCSF Campus Oral History Program

San Francisco
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INTRODUCTION by Lloyd H. Smith, Jr., M.D.

It is a privilege to offer these few comments about William J. Rutter as the Introduction to this unique documentary of an extraordinary career. I do so in part from the perspective of a friendship of thirty years duration, but Bill Rutter has innumerable friends, personal and professional, from his many-faceted activities. The leitmotif of this brief essay will therefore focus more specifically upon his impact on UCSF as an institution in transition.

Among the more interesting philosophical speculations that recur in literature is the question of whether men create history by the sum of their acts of free will or whether the innate momentum of the historic events creates men. No history of UCSF in the past generation would be complete without an analysis of Bill Rutter's seminal catalysis. Most of his academic colleagues, of whom I was privileged to be one, would concur that no other single individual played a more pivotal role in guiding the future of the institution during the past generation--in part, because of the importance of the position that he occupied as chair of the Department of Biochemistry and Biophysics, but more particularly because of his vision, vigor, and leadership of the whole of UCSF's basic science community. The details of those attributes emerge in the specific chapters that constitute this important history. It remains to place these compelling achievement in a larger context.

Henry Ford said, "History is bunk." Most of us, however, prefer the sonorous prose of Samuel Johnson, who, in Rasselas, wrote, "To judge rightly on the present we must oppose it to the past, for all judgment is comparative, and of the future nothing can be known. The present state of things is the consequence of the former, and it is natural to inquire what were the sources of the good that we enjoy, or the evil that we suffer. If we act only for ourselves, to neglect the study of history is not prudent; if we are entrusted with the care of others, it is not just." We are therefore justified to offer a truncated foray into history, to be both prudent and just, to understand the lineaments of "the good that we enjoy."

Founded in 1864 as the Toland Medical College, the UCSF School of Medicine is the oldest branch of the University of California as a continuing entity. Few in Berkeley are aware of that distinction. Like much of California, the School had a turbulent history, but unfortunately the perturbations were largely around a mean of mediocrity as judged by national standards. In his recent book concerning his tenure as president of the University of California, The Gold and the

Blue: A Personal Memoir of the University of California (1952-1967),¹
Clark Kerr has vividly described his analysis of UCSF after its first 100 years and his overall disappointment in its performance. This modest academic record stood out in sharp contrast against the continuing dominance of Berkeley in virtually all areas of scholarly pursuit, perhaps particularly in the physical and chemical sciences. In the late 1950s and early 1960s UCSF began slowly to emerge from a century of comparative somnolence. Among the many complex events in this emergence, the following can be identified:

-The return of the basic science departments from Berkeley to San Francisco to create, for the first time since 1907, a unified academic community;

-The rapid rise of funding for biomedical research from the National Institutes of Health;

-The construction of new clinical and basic science buildings-- e.g., the Herbert C. Moffitt Hospital and the research towers;

-The move of the clinical activities of Stanford from San Francisco to Palo Alto. For the clinical departments this move opened up new opportunities at our affiliated hospitals;

-The development of an epicenter of excellence in the Cardiovascular Research Institute under the astute leadership of Professor Julius Comroe. It can be said that Julius Comroe was the Rutter of the 1950s, particularly in the physiological sciences.

-The gradual emergence of new leadership, beginning in the clinical departments, with national rather than regional ambitions.

These events occurred not without controversy, especially in the transitions in leadership at the levels of chancellor, dean, and departmental chairs. Some of this turbulence is described in Clark Kerr's memoirs, as noted above, and will not be revisited here.

In this oral history, Bill Rutter describes the events surrounding his recruitment as chair of the Department of Biochemistry and Biophysics (1968-69). He cannot be fully aware, however, of the long gestation period and the dystocia that culminated in the birth of this new era. Our Department of Biochemistry and Biophysics at that time was rightly perceived at the national level as lacking in both prestige and resources. As chair of the search committee, I presided over a prolonged and wearisome search during which many of the then recognized national leaders in the biochemistry of that day were approached as candidates for this position. Always we were rebuffed, but were often able to use this failure to advocate the assignment of more resources from the administration to this key department. I do not now recall how we learned more than thirty years ago that hidden in the rain forests of Seattle, along with Hans Neurath and the spotted owl, there was a

¹ The University of California, forthcoming

promising young investigator who was doing imaginative work on the development and function of the pancreas. His credentials on review seemed impeccable, although marked by a remarkable propensity for peregrinations--Idaho, Harvard, Utah, Illinois, Wisconsin, Stockholm, Illinois again, Stanford, University of Washington. The details of these fruitful wanderings are once again documented in this history. We decided to take a chance on someone who was considerably younger and, at the time, less eminent than our previous candidates had been--and, fortunately, he decided to take a chance on us. With him as a "package" came the late Gordon Tomkins, who himself had been a candidate for the chairmanship but with his usual penetrating intelligence saw in Bill Rutter the ideal leader for the future of the Department of Biochemistry and Biophysics.

Leadership is difficult to define but easy to recognize in action. There is no single style that makes effective academic leadership, which has been defined as the singular ability of an individual to stand up and pull the rest of us over the horizon. Suffice it to say that the arrival of the Rutter-Tomkins team almost immediately began to transform the climate of the whole basic science community at UCSF. New standards of performance were both exhibited and demanded. Bill had then, and still retains, an innate and uncanny ability to judge people. It has been said that horse sense is the good sense horses have not to bet on people. But academic leadership depends, in considerable measure, in betting on people, especially during the ascending curves of their respective careers. The appointments in Bill's department were astutely made and many of these individuals remain today as leaders of our campus.

Fortunately, Bill Rutter fostered lateral dendrites as well, such that UCSF's whole basic science community synaptically improved in parallel with the transformations that were so evident in the Department of Biochemistry and Biophysics. Many of these campus improvements came through simple suffusion of the newly established standards of performance. Others came through more formal arrangements, such as the Program in Biological Sciences. PIBS has served as a permease among departments and organized research units not only in graduate education but in research collaborations as well. Based on the striking success of PIBS, an analogous program was established at UCSF in the more integrative sciences. As a result of these initiatives, and the uniquely talented group of investigators who were attracted in those early heady days of change, the model for UCSF science was established--small laboratories, elite participants, highly interactive research; a philosophy strongly supportive of the individual scientist as opposed to large research teams. I shall not attempt to list here the remarkable group of scientists who were attracted to San Francisco as participants in this nationally recognized transformation. Many of these names are woven into the recitation of this oral history. Notably, Bill Rutter's interests transcended the boundaries of his own department and even the

community of the basic science faculty. His balanced judgment was called upon to help guide the growth in size and quality of the whole UCSF academic health science center.

It has been said that a central tragedy of life is that generally by the time you've made it, you've had it! Not so with Bill Rutter who has developed a second distinguished career as a pioneer in biotechnology. But with his departure from our institution on Parnassus Avenue, Bill Rutter's interest in and influence on UCSF's future have not been attenuated. He has been the major impetus behind the organization of the Bay Area Life Science Alliance (BALSA). Through this entity, of which he serves as chairman, Bill Rutter is at the forefront in shaping the future of UCSF at its new Mission Bay site. Few would deny that this is the single most important development for UCSF in the last half century.

Thomas Hobbes defined curiosity in this quaint manner: "Desire to know why, and how, curiosity, which is a lust of the mind, that by a perseverance of delight in the continued and indefatigable generation of knowledge, exceedeth the short vehemence of any carnal pleasure." Throughout his career, Bill Rutter has exhibited an unabated lust of the mind. UCSF has been and remains the grateful beneficiary of that lust. The Greek concept of happiness was: the exercise of vital powers along lines of excellence in a life affording them scope. Anyone who reads this account will quickly encounter vital powers, excellence, and scope constantly displayed.

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November 1998
San Francisco

INTERVIEW HISTORY--William J. Rutter, Ph.D.

William Rutter's oral history inaugurates a series begun in 1991 under the auspices of the Department of the History of Health Sciences, UCSF, and continued at the Bancroft Library, UCB, as the Program in the History of the Biological Sciences and Biotechnology.

Dr. Rutter was a logical choice to initiate the first three oral histories, all with members of the Department of Biochemistry and Biophysics at UCSF.¹ As chairman from 1969 to 1982, he is credited with starting the department on the path to its current first-rank position in biochemistry and for spearheading UCSF's rise to prominence in biomolecular science.

The situation was far different when Rutter assumed the chairmanship in the late 1960s. He was confronted with a moribund department that had been without a chairman for six years and a faculty engaged in research in classical biochemistry. "Probably every good scientist in the United States," as he put it in the oral history, "had been asked to take that job. Sooner or later all those asked turned it down." In fact, Rutter himself rejected offers three or four times. A deciding factor in his change of mind was the twenty open faculty positions, which he saw as a bonanza for recruiting top-flight scientists who espoused his molecular view of science. It was a view buttressed by a few farsighted individuals on campus--Holly Smith in Medicine, Bert Dunphy in Surgery, Stuart Cullen Dean of the School of Medicine--who recruited Rutter as the prime architect of a coordinated, molecularly oriented basic science program. They wished Rutter, and those to be recruited after him, to transform a mediocre, clinically oriented school of medicine into an institution in which the "New Biology" suffused the clinical sciences. "New" of course meant molecular.

Rutter, a biochemist, was an attractive figure because of his research on RNA polymerase and other enzymes, and his interest in building a multidisciplinary research approach to the biology of eukaryotes, that is, "higher" organisms with nucleated cells. Molecular biologists to that point had largely focused on "lower" organisms, particularly the bacterial viruses and bacteria. Rutter was also seen as possessing the energy and vision to accomplish the multilevel task of building a cooperative research enterprise for the school as a whole. Departmental walls were to be figuratively torn down and fruitful interdepartmental collaborations to be encouraged, particularly between basic and clinical scientists. Despite pervasive sentiment to the contrary, Rutter and his supporters were set to prove that top basic science could be conducted in a medical school setting.

¹ The others are Herbert W. Boyer and Keith R. Yamamoto.

The going was not easy, as Rutter recounts in the oral history. Dead wood had to be tactfully cleared, contiguous physical space garnered and maintained against predation, promising scientists attracted to a budding but uncertain endeavor, and internecine jealousies and squabbles settled or squelched.

Rutter is quick to emphasize, in the oral history and elsewhere, that he did none of this alone. He considers himself a team player--a team player, one might observe, as long as he is the leader of the team. In the early 1970s, his closest ally was Gordon Tomkins, who was department vice chairman and a scientist seemingly known to everyone in contemporary biology for his idea-a-minute mind and engaging personality. He was also an accomplished classical and jazz musician, and, like Rutter, the leader of a large and ambitious laboratory group. The two formed a daunting team--Rutter, the strategic thinker and indefatigable leader, and Tomkins, the charismatic link to the leading lights in the basic and clinical sciences.

Rutter describes in the oral history how the two criss-crossed the country, canvassing the scientific scene for promising young scientists who could be convinced to adopt their multidisciplinary molecular attack on eukaryotic cell biology. It came to a tragic end in the summer of 1975 when Tomkins died after a brain tumor operation. The stunning impact of this personal and professional loss is detailed in the Rutter oral history as well as that with Keith Yamamoto, at the time a member of Tomkins' group.

It was in this period that Rutter and his colleague Howard Goodman launched a program to clone the genes for insulin--first the rat gene and later the human--using expertise and techniques largely available in the department. Perhaps most notable was the recombinant DNA technology developed in 1973 by Herbert Boyer at UCSF and Stanley Cohen at Stanford. Subsequent events brought triumph and turmoil: the Rutter-Goodman team's successful cloning of the rat insulin gene in 1977; the tensions generated by high-profile, cutting-edge research; an alleged violation of the NIH guidelines for recombinant DNA research; and the bitter controversy engendered by the rise of the biotechnology company Genentech within the department.

All this occurred against the backdrop of the international controversy over the possible hazards of recombinant DNA technology, the confusion engendered while federal guidelines for such research were being formulated, and the threat of federal and state legislation to regulate the new technology. The reader doubtless will be interested in Dr. Rutter's interpretation of these and other key events in the early history of genetic engineering.

The Oral History Process

These seven interviews were recorded between March and August 1992, either in Dr. Rutter's office in the Hormone Research Institute at UCSF,

or in the Office of the Chairman at Chiron Corporation, the biotechnology company that he co-founded in Emeryville, California in 1981.

With the exception of the first, the interviews were conducted on weekends when Dr. Rutter had slightly more flexibility in his frenetic seven-day-a-week, fourteen-or-more hour work days. His retirement from the university in March 1994 merely meant that he had more time to devote to Chiron and myriad other activities, including chairmanship of a fundraising campaign for a second UCSF campus, and membership on the Board of Overseers of Harvard University, his undergraduate alma mater. He has received several honorary doctorates and in 1995 the Heinz Award in Technology and the Economy.

Despite his pressing schedule, Dr. Rutter appeared relaxed and focused on the interviews. Because of limited funding for the oral history, the interviewer was unable to conduct extensive preparatory research and hence had to rely largely on Dr. Rutter for the historical account. Thus, more than usual in this series, this is a history told from the narrator's viewpoint. Its emphasis is not on the details of scientific research, but rather on administration and strategies, institution-building, and entrepreneurialism.

The researcher interested in this history will want to consult Dr. Rutter's correspondence which, as a result of this project, is archived at the UCSF Library. Also relevant are the oral histories in this series with Herbert Boyer and Keith Yamamoto,¹ and others being conducted at the Bancroft Library on the history of molecular biology and biotechnology in California.² The various manuscript collections in the UCSF Library related to the School of Medicine, including some referenced in this oral history, provide additional information. Stephen Hall's book on the race to clone the gene for insulin includes extensive information on the Rutter laboratory and its competitors.³

As one might suspect, Dr. Rutter had difficulty in finding time to edit the interview transcripts. This volume represents a compromise; it contains the final version of seven of the twenty-five mostly short

¹ Yamamoto's correspondence, and that of several colleagues mentioned in the Rutter oral history, Bruce Alberts, Gordon Tomkins, and Harold Varmus, are also on deposit at UCSF Library.

² As of February 1998, interviews under the auspices of the Bancroft Library's Program in the History of the Biological Sciences and Biotechnology have been conducted with Paul Berg, Arthur Kornberg, Niels Reimers, and Robert Swanson.

³ Stephen S. Hall. Invisible Froniters: The Race to Synthesize a Human Gene. Redmond, WA: Tempus Books, 1988.

recorded sessions.¹ Interview 10 was included in this volume because it addresses the subject of interview 6, the cloning of the rat insulin gene and the controversies related to it. Interview 6 was recorded before and interview 10 after Dr. Rutter provided testimony for the UCSF, Eli Lilly, Genentech insulin gene patent case. The remaining interviews, including seven through nine, will be available eventually as Volume II of the oral history.

Dr. Rutter edited heavily, in a few instances adding several paragraphs of new material. In most cases, although the syntax is improved, the content remains largely unchanged from the original transcription. As usually happens with extensive editing, much of the spontaneity of the original discussions has been lost, although they have without doubt gained in clarity.

The oral history program to document the history of molecular biology and biotechnology in the San Francisco Bay Area began at UCSF in 1991, when I was asked, as a science historian at the Regional Oral History Office of The Bancroft Library, to conduct three oral histories. Dr. Rutter's oral history was completed by the Bancroft Library's Program in the History of the Biological Sciences and Biotechnology. The Program's mission is to establish an integrated collection of research materials--primarily oral history transcripts, personal papers, and archival collections--relating to the history of the biological sciences and biotechnology in university and industry settings. The Program is presently focused on the Bay Area and northern California, but its ultimate aim is to document molecular biology and biotechnology on the entire West Coast.

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Research Historian/Interviewer-Editor

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¹ The remaining interviews on a wide range of topics, including Hepatitis B research leading to the first recombinant vaccine and the foundation of Chiron Corporation, will be available after Dr. Rutter has reviewed the transcripts.