CHAPTER VI

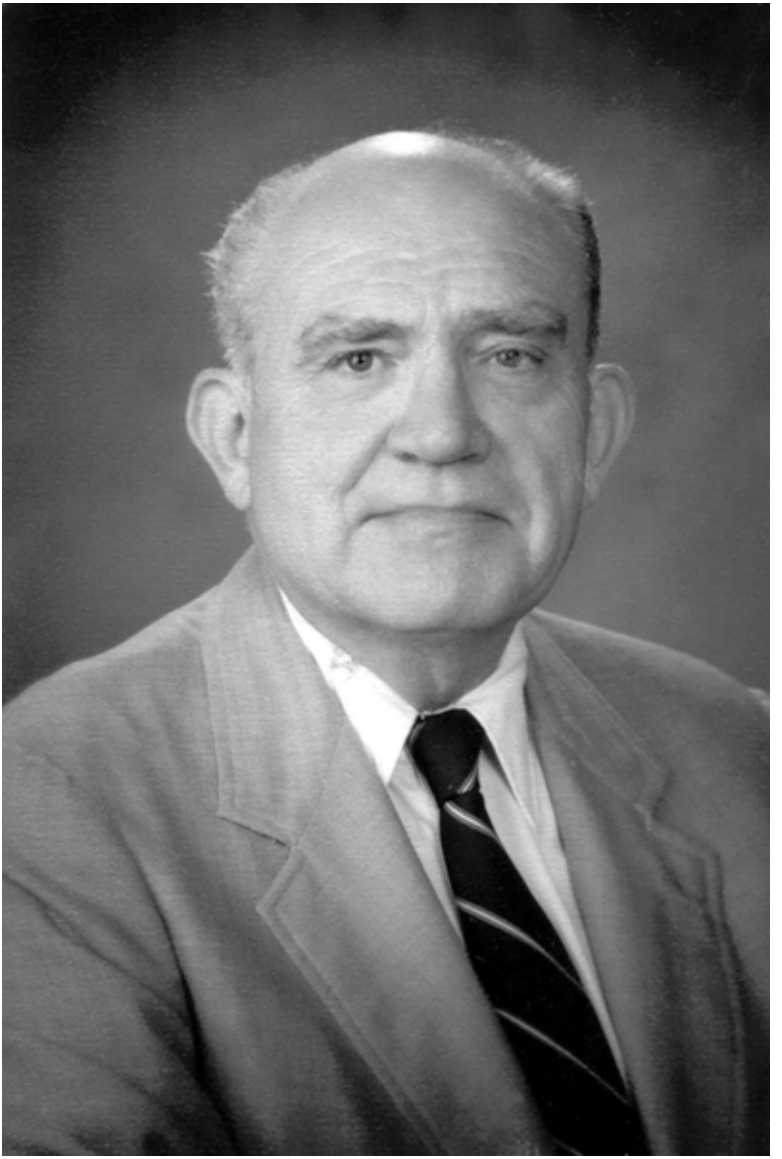
On Toward Our Goal (1973-1988)

1973-1980

A New Chairman

On January 1,1972 Darby resigned as Chair of the Department in order to become President of the Nutrition Foundation, headquartered in New York City. This post offered him even greater opportunities to influence the development of human nutrition worldwide. John Coniglio was appointed Acting Chairman of the Department during the search for Darby's replacement as Chair, and Harry Broquist succeeded Darby as Director of the Division of Nutrition.

All of this occurred during a period of considerable change in the upper administrative echelons of the Medical Center as well. Randolph Batson, who had just won designation as the first Vice Chancellor for Medical Affairs along with his title of Dean, opted in September of 1972 to drop the title of Dean. John Chapman, Associate Dean for Medical Education was appointed Acting Dean. A few months later in March 1973, Batson resigned as Vice Chancellor for Medical Affairs, and Chapman became Acting Vice Chancellor! Allan Bass, former chair of Pharmacology who had just been appointed my successor as Associate Dean for Biomedical Sciences, became also Acting Dean of the School of Medicine. This shuffle settled down when Vernon Wilson became Vice Chancellor in 1975. Chapman was named Dean.



Leon W. Cunningham, Chair of the Department of Biochemistry, 1973-1988

In the midst of this, on January 1, 1973, on the recommendation of the search committee and the Executive Faculty, I was appointed by Acting Dean Chapman to be Chairman of the Department of Biochemistry. I was very glad to be released from the role of Associate Dean for Biomedical Sciences, especially as the HSAA and its useful budget phased out. Also, I was really delighted to be back among my colleagues in Biochemistry. As Associate Dean, it had been my assignment to organize several searches for departmental chairs, and I was very aware of a view held by several key faculty that, to insure against parochialism, new chairs should be sought from outside Vanderbilt. However, this had certainly not been scrupulously adhered to in the past. Indeed, experience with search committees in those years suggested that Vanderbilt's arcane finances were often a distinct surprise and, occasionally, deterrent to external candidates. In any event, this was an opportunity to see if we could build the Department toward higher national and international recognition. Based on the HSAA experience, there was a very strong feeling that Vanderbilt was on the way to top rank national stature in biomedical research, and that Biochemistry had a key role to play.

Between the time that the Search Committee made its recommendation in July of 1972 and my formal acceptance in November, negotiations about finances and space proceeded under rather unusual conditions. First, there was the fluctuation in those holding the titles of Vice Chancellor and Dean which led to some confusion as to who was in a position to make commitments. And secondly, there was the problem that, from my position as Associate Dean, I was well aware of some rather serious limitations in available space and financial resources. Discussions proceeded slowly.

The final arrangement was "thin," my word at the time, but realistic. I give it here as a factual illustration of just how limited resources were in 1973. The continuing annual level of Dean's office support was increased by $16,000 to $196,333 but included all support previously allocated separately for Nutrition and Toxicology. An additional sum of $50,000 was to be made available, and continued, as actually needed for the addition of new faculty.

A further $50,000 would be available for renovation of Biochemistry's original 1925 space. The most painful problem was additional departmental space. Without space there is great difficulty in raising extramural cash. Very little additional space had been made available for Biochemistry for some years. This situation was made pressingly difficult by the success of the HSAA program that had brought six new faculty into the Department. A hard-won University commitment to create additional space specifically for the overall HSAA program had morphed into a theoretical budgetary allocation of approximately one million dollars for that purpose. There was, however, no actual cash, or plan or site for construction. In addition, these theoretical million dollars were proving a tempting and accessible target for a variety of unrelated projects. Yet another pressure on space involved the very specific acute need for sufficient space to recruit a permanent Director of the Toxicology Center. In a letter to the NIEHS, which was obviously concerned about our plans for recruiting permanent leadership for Vanderbilt's major toxicology program during this time of change at so many administrative levels, I tried to outline our situation.

"I have been offered the position of Chairman of Biochemistry but have not yet accepted because of our inability so far to agree on space and because of delays caused by the appointment of an Acting Dean of the School of Medicine.

The space matter relates directly to the Toxicology Center since I have been insistent that adequate space for the effective recruitment of the Center Director be available.

I am determined to give full support to the Toxicology Center. I obviously have additional goals for the Department but I am intellectually committed to the importance of "environmental biochemistry" in a medical school department."

Eventually, Biochemistry had to accept a commitment of an additional 3000-5000 nsf "at the point in time when the University has provided us the space they have confirmed in commitment but not in location" plus "the highest priority consideration for additional space when it should become available." Knowing this

truly represented the best the Dean could do, it was very reluctantly accepted.

The continuing, program-limiting shortage of space in the Medical Center during these years was addressed again when Allan Bass became Interim Dean in 1974. I fired away at my old friend though I knew it was not really within his power to help; but the space shortage was hindering all efforts to expand and improve research, and I wanted our space needs to stay on the record, near the top.

"I believe that (in comparison with other Medical Center programs) the acute needs of Biochemistry, and Microbiology, Physiology, and Pharmacology for that matter, have been bypassed or given temporary solutions which depend on the generous but uncertain future attitude of other Departments (such as Medicine and Anatomy).

I believe that the modest easing of the existing space problems of the basic science departments is important for the financial health of these departments. I believe the development of limited new space for our needs can not be deferred beyond the development of the next new construction of any kind or the reassignment of any existing space without being in direct violation of existing commitments."

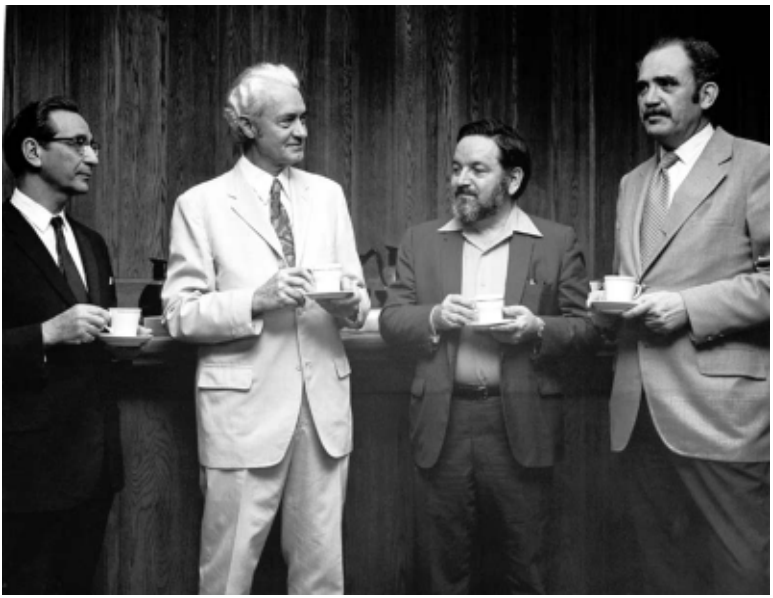
The national financial constraints in health research of the Viet Nam era continued on in relation to research grants and training as well as to research space construction throughout my early years in the chair. With the encouragement of Bob Grant, then Director of Public Affairs of the Federation of American Societies for Experimental Biology, I sought and received the serious and helpful interest of Senator Howard Baker in the problem. He contacted the Secretary of Health, Education and Welfare, Caspar Weinberger, and obtained some clarification of administration policy and, perhaps, some easing.

Although the Department of Biochemistry was quite strong in 1973, there was a very clear need to strengthen some specific areas vital for national prominence. Equally important was the need to create a stable and supportive environment of space and

other resources that would permit us to hold on to the excellent faculty we had and the new ones we might recruit. I believed that our best practical strategy in competition with other universities and within our then existing fiscal and space constraints was to retain our best faculty while recruiting primarily at the assistant professor level, hoping to develop another generation of outstanding scholars.

Some specific aspirations for the future development of Biochemistry were described in some notes I made for discussions with the Dean during "negotiations." They included (1) the strengthening of the field of biophysical chemistry and macromolecular structure; (2) a determined effort to sustain and build upon the existing very strong "growth factor" research; (3) the maintenance of the strong programs in nutrition and in toxicology with an increasing emphasis upon their biochemical foundations and (4) a contribution to the remediation of the University-wide deficit in molecular biology/genetics. Much of this had been indicated and even begun as a result of the Health Sciences Advancement Award. As Principal Investigator of that program and as Associate Dean, I had shared in significant faculty development throughout the School of Medicine, not least in Biochemistry. The main thrust of the HSAA program had been faculty development in three areas: Molecular Structure, Cell Structure and Function and Genetics and Cell Differentiation. Faculty development was meant to include both recruitment of new faculty and assistance to existing faculty through acquisition of new technology and exposure of our faculty to visiting faculty of international renown for relatively extended periods. With the wholehearted cooperation of Darby and Coniglio, the Department was, as we have seen, strongly influenced in terms of future direction and quality. Both the spectacular international development of molecular biology and the recent reinvigorated interest in "structural biology," (*i.e.* physical biochemistry or macromolecular structure) were presaged in the goals of the HSAA program. Among those most responsible for the success of the HSAA program was Sidney Colowick, an internationally known biochemist. Sidney's

faculty appointment was in Victor Najjar's eclectic Department of Microbiology. But his reputation as a biochemist, his wide contacts and his calm wisdom were crucial in the growth of biochemistry, big and small "B," at Vanderbilt. In addition to the faculty additions facilitated by the HSAA program previously noted, the investigations of Stanley Cohen, Tadashi Inagami and Jan van Eys were substantially aided. Key instrumentation including x-ray crystallography, automated amino acid analysis, central cell culture facilities, spectropolarimetry, and molecular electron microscopy were introduced into Vanderbilt for the first time. Impetus was given in several modest ways to the development of computing expertise and hardware at what can be seen in retrospect to have been a crucial point in the development of that new field.



Reception on the occasion of the election of Sidney Colowick, Department of Microbiology, and William Darby, Department of Biochemistry, to the National Academy of Sciences, 1972; left to right, John Coniglio, Darby, Colowick, Leon Cunningham

Departmental Organization

At the request of the Dean, the Department of Biochemistry generated a brief mission statement in 1973.

"The mission of the Department of Biochemistry, through its faculty, is to serve the needs of the School of Medicine, the Graduate School and other units of the University for specialized training in the field of biochemistry, including the maintenance of a vigorous and diversified research program of nationally competitive quality."

The general administration of the Department continued largely as before. The faculty advised the Chair through a Graduate Education Committee, a Medical Education Committee and a Departmental (faculty) Appointments and Promotion Committee. The Center in Environmental Toxicology and the Division of Nutrition were organizationally under the Chair but functioned semi-autonomously. A number of new multi-investigator grants, centers and program projects were also being developed and incorporated into the departmental structure.

The Division of Nutrition

The Division of Nutrition as originally created by Dean Youmans and Darby in 1948 was seen as a true interdepartmental unit based primarily in Medicine, Pediatrics, Biochemistry and Biostatistics (Preventative Medicine). Darby held a faculty appointment in both Medicine and Biochemistry, and the Division was the vehicle for his national and international ventures into nutrition research and education and brought international recognition to Vanderbilt in those fields. The faculty of the Division thus included those trained in all of these fields: biochemistry, medicine, pediatrics, statistics, and history of medicine. Following Youmans' retirement and leadership changes in the Departments of Medicine and Pediatrics, the major burden for new faculty appointments in the Division fell to the Department of Biochemistry. In time this nutrition program came to be viewed by medical administration as simply a Division of the Department

of Biochemistry. This put substantial pressure on the tenure process for the less-biochemical members of that faculty. Following Darby's resignation as Chair of Biochemistry, the organizational position of nutrition as a division of Biochemistry was accepted. As such it continued strong under the leadership of Harry Broquist and Connie Wagner, featuring biochemical aspects of nutrition. It has also nurtured a renewal of interest in clinical nutrition in other departments and kept Vanderbilt's reputation as a national center for nutrition research alive and well. By the 1990s, the central "hub" of nutrition had moved to Medicine under Ray Burk, who in the course of his studies for the M.D., spent four years in the mid 1960s in the Department of Biochemistry working in research with Bill Pearson and Bill Darby. The current (2002) Biochemistry component of Vanderbilt's nutrition program includes Conrad Wagner and David Ong and remains strongly involved in the overall Vanderbilt effort.

The NIH, "Big Science" and "Centers"

In the late 1960s, the NIH began to place increased emphasis upon its "Centers" programs and the related "program projects." These were essentially substantial grants for research that were made to interdepartmental groups of faculty whose research focused in an integrated way upon especially important health related topics. In the early 1970s, President Nixon's "Cancer Crusade" was launched. This, the nation's first experience with "big science" in biology, projected the funding of large groups of investigators and targeted programs. Some thought it might threaten the roles of individual investigators and of private granting agencies such as the American Cancer Society. In 1972, then Chancellor Alexander Heard asked me to react to an editorial in *Science* by Irvine Page in which Page worried about these potential negative effects of "targeted" "group" science. Since the 1970s, different forms and "sizes" of "big science" including centers, program project grants, consortia with industry, focused institutes and similar activities have grown steadily. Some excerpts of my mid-1972 response to

Heard describes how, in my view at least, Vanderbilt managed and usually mastered this trend.

"Our direct experience with the new "Cancer Crusade" has so far been very limited as we are still in the planning stages of Center development. In our few pending applications, we have taken our usual position—we have asked for funds to do things we want to do and which are compatible with our overall goals as an educational institution. We have had considerable success, at least so far, in adapting other new forms of directed research to our goals and needs. I refer to the Hypertension (Dr. Foster), Newborn Lung (Dr. Stahlman) and Population (Dr. O'Malley) Centers. Still, I know of no one who would argue that such large, goal-oriented programs should be the only, or even the major, research activities funded by federal health agencies."

"I suppose that I believe we are in a transition period and that the present "mix" is not really so bad. The problem, of course, is the trend. I strongly share Page's concerns about the ultimate result of following the Cancer Crusade line to the exclusion of independent, individual, minimally targeted research projects. Our faculty involved in Cancer Center activities are very aware of and sensitive to these dangers. So long as our programs are originated by the faculty, I am hopeful we will achieve reasonable balance. We certainly must be continually alert to insulate our academic "core" from the gyrations that can occur in federal agencies."

"Nothing justifies the placing of control for the expenditure of a *major portion* of the federal health research dollars in the hands of a few individuals acting on the premise that the search for key basic knowledge can be systematized and scheduled. Anyone with any experience in research knows that this is unrealistic. This is, of course, not necessarily true of the *development* of existing basic knowledge, no matter how expensive and difficult, from the laboratory to actual medical use."

"Although I do believe that medical schools should participate in target-oriented health research and development, I think a medical school with Vanderbilt's tradition of basic research and scholarship should avoid as explicit policy an undue commitment

to such programs or dependence on such funds and give highest priority to locally directed, basic research. This all depends, of course, upon both kinds of programs being supported by the federal government, and I would hope we all would exert our strongest efforts to that end. It also depends upon skillful local management of available funds and other resources in a way that provides maximum local support for individual basic research.

"We must expect to seek most support for research on the basis of its relevance to specific human problems, and we must depend upon the intelligence and training of federal health administrators and our own wits to use portions of such support for the very fundamental basic studies which provide the data base for all the more applied research and development. We cannot maintain the illusion that our participation in such major (directed) federal health research programs is entirely optional. Not only have we become dependent upon the federal government for support of schools of medicine through this device, but the public has become dependent upon the research output of schools of medicine for those deeper understandings of human biology and biochemistry which will influence the quality of health care in the next generation."

At Vanderbilt, from the earliest days of NIH, "centers" in nutrition and toxicology had been active in Biochemistry. A Clinical Pharmacology Center was established very early in Pharmacology. This concept was expanded to areas such as hypertension, population control, reproductive biology, newborn lung physiology, diabetes, psychopharmacology, neuromuscular disease and pulmonary disease. Unfortunately, the development of a comprehensive Cancer Center never really took off until the late 1990s when the generosity of the Ingram family made it possible.

Although welcome as a much-needed source of additional research funding, the center concept initially caused concern also because of its potential for muddying the departmental organizational lines that underlie academic considerations of educational program and faculty tenure. The high dependence of the School of Medicine upon grant funds for the salaries of tenure

faculty meant a very real and heavy responsibility of the department chairman to keep an overall sharp eye on the ultimate resources for "his or her" faculty. Fortunately, Vanderbilt's long-standing and strong tradition of interdepartmental cooperation made possible the successful assimilation of a large number of NIH-supported centers into the School of Medicine, including into the Department of Biochemistry. They provided crucial strengthening with no loss of that departmental structure which has been the fundamental organizational focus for the development of Vanderbilt School of Medicine since its inception. Based in Biochemistry, the interdepartmental "center" style programs in Nutrition and in Toxicology moved strongly forward under the guidance of Harry Broquist and Connie Wagner in Nutrition and Robert Neal and Fred Guengerich in Toxicology. Participation of Biochemistry faculty in Centers in many of the other areas mentioned grew rapidly so that Centers and the related "program project" grants swiftly became mainstays of faculty research support. The early roles of Inagami in the Hypertension Center, Puett and Chytil in the Population Center (reproductive biology) and Chytil in the Newborn Lung and Pulmonary Centers were particularly important.

Maintaining balance between major Center programs and the Department required understanding of their respective roles and constant attention. Faculty salary considerations were sometimes stressful, as it is the chairman's assignment to set reasonably comparable and appropriate salaries and to be responsible for seeing that they were "backed up" with definite financial resources. For tenure faculty, the chairman must stand ready with the Dean to fund salaries regardless of the fate of various grants. A letter to a Center Director describes part of the problem. "My philosophy, which is probably the only philosophy a chairman can live with at Vanderbilt, is that I deal individually with all tenure and tenure track faculty on level and source of support; I make no assumptions about Center support beyond those communicated to me by individual faculty and cleared with the Center Director by the Departmental Administrator. Negotiations on percent support from

any grant are basically between the faculty member and the principal investigator, and I only get directly involved in case of a problem, usually a short fall in resources." This fairly conservative approach worked reasonably well, though mistakes were certainly occasionally made. Disagreements were typically more frequent when grant funds were abundant than in dry spells since it is quite normal to argue for an increase in salary when grant funds are plentiful, but few suggest a decrease when grant funds dry up. Since the early 1990s, administrative attitudes toward tenure and salary level described above appear to be changing, at least at the discussion level, as the School of Medicine moves into an even more "entrepreneurial" phase. "Bonuses" for achieving higher external sources of salary from grants or commercial contacts have been discussed since the very first grants were made in the early 1950s but now seem to be seriously being reconsidered. Entrepreneurial skill has certainly played a key role in the development of Vanderbilt School of Medicine in the past 50 years but its extension into the very core of the academic process can easily lead to dissension and further loss of respect for the teaching function that is the manifest reason for our identity and existence. Tenure remains a critical factor in the recruitment and long-term stabilization of a creative and dedicated faculty, at least for the non-M.D.

"Family," the Departmental Staff

Few things are more useful to an academic department than a stable, attentive and smoothly functioning administrative base. Soon after becoming Chairman, I made one of my most important appointments. Marlene Jayne was "stolen" from a good friend in the Department of Economics and Business Administration to be my secretary. It is hard to acknowledge sufficiently how important she has been for my own work and for the development of the Department. She became a universally admired and integral member of the Department as she quickly mastered the administrative routine and moved on to full and helpful participation in all aspects of Department life. She is able to make

old and new staff and students feel comfortable in coming to her with problems of any type and will go to any lengths to solve them. She remained, as indispensable as ever, as the chief Departmental Administrator when I stepped down from the Chair in 1988.

Marlene Jayne, Administrative Officer, Department of Biochemistry 1973-

Juanita Frazor served as departmental Financial Administrator during my entire tenure as Chairman. She began her career at Vanderbilt in 1954 as Darby's secretary and had been moved to the Administrator post while Coniglio was Acting Chairman. That move had been necessitated when I plucked Tom Barnes from the Financial Administrator post in Biochemistry to serve in a

comparable but broader capacity in the Grants Management Office of the School of Medicine. In the shuffle of 1953, I ended up in Biochemistry and Barnes went on to a very successful role in Medical Center administration. The Department has clearly been blessed with remarkably low turnover and very high quality and commitment of key non-academic staff over the years. All who have had any contact with the Department over these years will especially appreciate the multiple helpful contributions of Melvin Fitzgerald who has been an indispensable colleague since joining the Department in 1961. He was honored with the Commodore Award for outstanding service to the University in 1998, joining Juanita Frazor as the second Biochemistry staff member to receive this high recognition. Most will remember, too, the long years of dedicated service to the Department of Lorena Douglas and Susan Heaver, valued members of the staff for over 20 years. A few of us remember Harriet Trabue who served as the Department's secretary/administrator in the 1950s with Southern dignity, and sometimes shocking frankness. In recent years the Department's Financial Administrative Office, and the faculty, have benefited from the presence of Peggy Fisher and Brenda Bilbrey. Robert Dortch took over as Financial Administrator in 2001, only the third person to serve in that crucial role since 1965.

In the earliest days of the Department when there were very few faculty and staff, informal social contacts prevailed as described by Robinson in *Shavings* (Appendix). Sunday afternoon gatherings at the Robinson's home for faculty and medical and graduate students were common. As the Department grew, these interactions and gatherings necessarily became fewer and somewhat more formal, but Thanksgiving lunches, provided potluck, and occasional departmental picnics continued. More recently, an annual departmental research retreat off campus and a full-scale departmental Christmas party, also off campus, have prevailed. However, the steady increase in size of the Department means inevitably that individual faculty social interactions become at least quantitatively more important than group functions.

Faculty and Budget

The 1972-73 Annual Report to the Dean, the first I prepared, listed for the Department of Biochemistry, $1.66 million in research grants, primarily from NIH, and approximately $180,000 of School of Medicine funds, so called "hard money." Although these numbers grew more than five fold over the next 15 years, the ratio between the two was fated to remain about the same, 90% dependence upon federal funds. This continued strong reliance upon competition by the faculty for external research funds as the basis for growth and development of the School of Medicine has been at once a difficult challenge and an effective stimulus toward keeping the Department of Biochemistry on a path toward excellence. This dependence on external financial support was certainly not limited to this Department or to Vanderbilt. However, the degree and persistence of the reliance on faculty to develop resources for salary and research appears to have been rather higher at Vanderbilt than at other comparable institutions, as judged in our competitive efforts to recruit at senior levels.

The space available to the Department in 1974 as described in a letter to newly arrived Vice Chancellor Vernon Wilson in January of 1975 was 16,752 nsf, primarily in the original B1300 area of the old building (MCN) plus 1895 nsf on loan from other departments. In the same letter, I requested space to (a) enlarge the Center in Toxicology; (b) ease the crowding of new faculty (Lembach and Puett); (c) relocate Chytil and Brady (who were working in space loaned by Medicine and Anatomy, respectively); (d) create a departmental conference room and (e) provide for my own research (which I was trying to resuscitate).

Dixie Frederiksen

In 1974, Dixie Frederiksen joined the Department as the first new faculty member after I became Chairman. Her background in physical chemistry with a Ph.D. from Washington University was in line with the goal of strengthening molecular structure expertise.

She initiated a research study of contractile proteins utilizing the slime mold, dictostylium. An excellent teacher, she was a great favorite of the medical students. I especially enjoyed working with her on a series of *Methods in Enzymology* volumes entitled *Structural and Contractile Proteins.*

Frederiksen's background in physical chemistry, her interest in contractile proteins and her expertise in a variety of physical methods for study of macromolecules widened the horizons of many on-going research activities in the Department.

"On the side" she gave informal lectures to some of the medical students on "personal finance" aimed at their special problems. She was a staunch and eminently satisfactory role model for the long overdue increase in the participation of women on the tenure faculty.

It was a great disappointment and a real loss when she elected to leave the Department to go into private business.

Carl Hellerqvist

The second appointment I was able to make in 1974 was aimed at shoring up our obvious weakness in the field of structure of complex carbohydrates, especially those associated with glycoproteins. This had particularly concerned me because of my own interest, but lack of expertise, in that area. Hellerqvist came from a Swedish background that included participation in some of the very earliest studies of the structure of complex carbohydrates. He had then spent a couple of years at Johns Hopkins with Saul Roseman, another expert in carbohydrate biochemistry. The structure and function of the heterosaccharide "prosthetic groups" of glycoproteins were areas of research where general appreciation was slow to develop but which, by 1990, were in the front rank in terms of interest and potential application to medicine.

At Vanderbilt, Carl became interested in a series of complex bacterial heteropolysaccharides that led him in later years into clinically related studies and ultimate participation in the new

fashion of university-industry cooperation with a view toward patents. The potential of some of these heteropolysaccharides to inhibit tumor growth, apparently by blocking vascularization, has been Carl's major research concern in recent years.

David Ong

David Ong first came to the Department in 1970 as a Research Associate with Robert Brady and later Frank Chytil. He joined the faculty as a Research Assistant Professor in 1975 and has continually enlarged his studies of structure and function of retinoid binding proteins into novel and important areas. In 1983 he was a co-recipient of the Osborne and Mendel Award of the Nutrition Foundation. An excellent teacher, Ong has been a key member of the graduate faculty. He joined the tenure track in 1984, a strongly independent and invaluable colleague.

Lubomir Hnilica

In 1976, Lubomir Hnilica was attracted to the Department from his post as Professor of Biochemistry at M.D. Anderson Cancer Center (University of Texas). His appointment was as Mary Geddes Stahlman Professor of Cancer Research. In this role he could have chosen any department as his "home," and we were very pleased that he chose Biochemistry. Hnilica had received his initial training in then Czechoslovakia followed by a postdoctoral fellowship year with J.A.V. Butler at the Chester Beatty Cancer Research Institute in London. Hnilica's prescient interest in the proteins of the nucleus and their active role in cell division and differentiation provided stimulation to the nascent activity in molecular genetics throughout the School. His early studies of the crucial structural and regulatory roles of histones reflected his unique and pioneering insights. His untimely accidental death in 1986 left a great void in the faculty. His unique contribution to the Department continues to be recognized by the annual Hnilica Lecture.

F. Peter Guengerich

Also in 1975, a former graduate student, Frederick Peter Guengerich, returned to the Department as Assistant Professor, beginning a very productive career in the area of biochemical toxicology. After receiving his Ph.D. in 1973 under Harry Broquist, Guengerich undertook postdoctoral study with Minor Coon at the University of Michigan. Upon his return to Vanderbilt in 1975, Guengerich's primary focus on enzyme structure and mechanism fit well into the strong departmental theme of molecular structure. Following the departure of Robert Neal to the Research Triangle, North Carolina, to be Director of the Chemical Industry Institute for Toxicology in 1980, Guengerich was appointed as successor Director of the Vanderbilt Center in Environmental Toxicology. He led the further development of this internationally recognized pioneering program in biochemical toxicology. The renewed thrust was evident in the name change to the Center in Molecular Toxicology. His main areas of research are the mechanisms of activation and detoxification of chemical carcinogens and toxicants and the characterization of enzymes involved in these processes. He has been widely honored for his research, including Vanderbilt's Earl Sutherland Prize for Achievement in Research (2001) and the Bernard Brodie Award in Drug Metabolism of the American Society for Pharmacology and Experimental Therapeutics (1992).

Graham Carpenter

During this same period, another investigator who had first joined the Department in association with the research program of Stanley Cohen, won appointment in 1977 to the faculty on the merit of his personal contributions. Graham Carpenter established a strong independent program in the field of growth regulation, emphasizing the role of the epidermal growth factor (EGF) receptor. He was also instrumental in building a multidisciplinary program project grant and a research training grant based on Cohen's fundamental observations of EGF and its receptor. In this way,

this new field of biochemical endocrinology, hormones, growth factors, their membrane receptors and the mechanisms through which they influence cellular metabolism, was developed vigorously at Vanderbilt by Graham and his colleagues. These developments played an important early role in the development of cancer research at Vanderbilt and in recent years to the success of the Vanderbilt Ingram Cancer Center.

James Staros

Another recruit onto the faculty in 1978 was James V. Staros, who was trained at Yale and Harvard in physical chemistry of proteins and in organic synthesis. His research dealt largely with a broad variety of approaches to the determination of structure-function relationships in proteins, especially the epidermal growth factor (EGF) receptor. The biophysics of the interaction of EGF and related compounds with the receptor in cell membranes was a continuing interest. He served exceptionally effectively as Director of Graduate Studies for the Department for several years, working closely with the Graduate School to strengthen an already vigorous program. He had an active interest in the ethics of biomedical research and was a leader in the development of programs for the recruitment of minority students. His administrative talents were recognized in 1988 when he became Interim Chairman of the Department. During this time there were several important accomplishments including the creation of the Stanford Moore Professorship, the John Coniglio Prize, an interdepartmental Molecular Biophysics Training Grant Program and the NIH-sponsored Vanderbilt Minority Summer Research Program.

In 1991, he became Chairman of Vanderbilt's Department of Molecular Biology and in 2002 he was named Dean of the College of Arts and Science at the Stony Brook campus of the State University of New York. He received the Thomas Jefferson Award of Vanderbilt University in 1999 for "distinguished service to Vanderbilt through extraordinary contributions as a member of the faculty in the councils and government of the University."

Toxicology

Toxicology had first gained definitive recognition within the Department in 1967 by the creation, under Frank Blood's leadership, of a Division of Toxicology. Shortly afterward, in 1969, with the encouragement and support of the NIH, the interdepartmental Center in Toxicology, based in Biochemistry, was established with Blood as its first Director. The National Institute for Environmental Health Sciences provided basic support for this Center. This interdepartmental, cooperative program owed its initial success at Vanderbilt to the skillful entrepreneurship and programmatic integrity of Blood and Darby. When Frank Blood died suddenly in January 1971, Bob Neal succeeded Frank as Director. In 1981, Fred Guengerich succeeded Bob in that role. Thus, the strong continuation of this Center was assured. In the succeeding years, it gave international leadership to the increasing biochemical foundation of this field. Leaders in toxicology have indicated that Vanderbilt's pioneering role in creating a new and closer interaction of toxicology, chemistry and biochemistry together with the strong succession of leadership provided by Blood, Neal and Guengerich have been crucial in the national and international development of modern toxicology.

Facilities

In the late 1960s and early 1970s, the Health Science Advancement Award and the needs of new and strengthened Center programs had brought about the availability of only very limited additional research space, typically areas renovated piecemeal within the 1925 structure. Some space was made available in 1968 to the HSAA program components in the Departments of Biochemistry and of Anatomy by the completion of shell space in the A-North wing just below the then new Medical Library. This wing (1964) and the "Werthan" structure (1970), the latter entirely for clinical departments, both fronting on 21st Avenue, were only the second and third significant "departmental" or "research" areas

(after Learned Lab) added to the original 1925 School of Medicine (now Medical Center North) building. Although not convenient in relation to the rest of the Department, this area in the basement of the A-North wing was entirely new in its furnishings and utilities. It served those housed there, David Puett and Kenneth Lembach, very well.

However, the continued growth in strength and size of faculty research programs kept an increasing strain on research laboratory space until the eventual move of the bulk of the Department into the newly completed top floors of Light Hall in 1979. This move would quite possibly not have occurred, at least in any reasonable time frame, had not an opportunity presented itself to focus the attention of the School of Medicine administration on the greatly increased national recognition of Biochemistry's programs and on the depth of our need.

The Graduate Program Evaluation (1976)

In 1976 the Graduate School decreed a series of evaluations of all the graduate programs in the University, and in April, the Department of Biochemistry undertook an internal self-study in preparation. We then underwent an external review. The external review committee was composed of three faculty members from other Vanderbilt graduate departments, Daniel L. Friedman from Molecular Biology, Thomas Martin from Chemistry and Joe Hamilton from Physics. In addition, there were two influential outside members, Robert Hill, Chairman of Biochemistry at Duke, the then President of the American Society of Biological Chemists, and Carl Vestling, Chair of Biochemistry at Iowa and a nationally recognized authority on graduate education in Biochemistry. (Vestling also happened to have been my Ph.D. thesis advisor.) As you will see, the Department of Biochemistry owes these men a great debt.

Our self-study pointed out that "Biochemistry is the largest graduate program in the biomedical sciences. More importantly, the formal course offerings of the Department of Biochemistry are

the most comprehensive and form the 'core' of graduate course work for students in the other biomedical departments." Also, "Faculty of the Department of Biochemistry are presently camped in Medicine and in Anatomy. No member of the faculty has adequate space, by any standard, for his scholarly activities." At that time Biochemistry occupied the following scattered areas: on the first floor of the main medical school building (now Medical Center North, MCN) the B1300 corridor (its original space from 1925); half the B1200 area (the original 1925 Medical Library) as well as the first floor of Learned Lab; half the B2300 corridor (formerly Pharmacology) and half the A0300 area in the basement under the then new Medical Library. This amounted to a fragmented total of 16,752 nsf (net square feet) plus loaned space of 2814 nsf. Research grants had grown to "over $2 million." There were at that time 20 faculty, 25 graduate students (down from as high as 42 in 1970 as a result of decreased federal funding, space limitations and departmental concern over national overproduction), 17 postdoctoral fellows and 50 other personnel. Concerning graduate students, the departmental self-study had stated, "Our present projection is that the number should be maintained between 20-25. Growth beyond 25 should be permitted only on the basis of clear data which indicate changes in several parameters such as significantly increased faculty size, improved recruitment potential, increased demand nationally for Ph.D. graduates and improved funding." In terms of general philosophy, the report went on "The Department of Biochemistry feels that it should serve as the "basic" chemically-oriented anchor of the wide spectrum of research in the Medical Center. While it should obviously participate fully in clinically related targeted research (and service), it must also maintain a diversified faculty of independent investigators whose special knowledge and skills contribute in a number of other fundamental ways to the present and future health of the School of Medicine."

After reviewing the self-study and making its own on-site evaluation, the external Evaluation Committee gave a report to the Dean that is excerpted here. "The space need (of the Department

of Biochemistry) is critical and has both short and long range implications. This has evidently been a long-standing problem of the Department and, in the Committee's view, has not received the attention of the University that the Department deserves and must have. Even the halls of Biochemistry have been used as actual research laboratory and storage space. There are too few specialized facilities. The lack of cold rooms limits research. There is no space for a computer terminal. Sometimes five graduate students must work in one small lab designed for two workers." This was followed by an unflattering comparison with both the area and modern character of Biochemistry laboratories at Iowa and at Duke. The report further stated, "A problem which Biochemistry faces is the need to recruit new faculty in new rapidly developing fields. Dr. Cunningham points out a need for development in Molecular Genetics. His efforts to recruit a faculty member with this expertise have been delayed because of a lack of funds. There was a pervading concern that the intellectual vigor of the preclinical departments might decline during the next decade due to weakening internal and external financial support. Funding of all Medical School departments, including preclinical departments, from University resources appears marginal or low in comparison with such funding in other private universities." Other emphasis was on "increased university support for faculty and staff salaries."

Finally, "This committee finds the present Biochemistry Department to be academically sound and healthy. Biochemistry is now qualifying as a nationally front-rank department, and we commend its faculty and graduate programs. It will take a period of strong achievement, however, to gain greater national recognition." They recommended more space, more University support for graduate student stipends and fellowships and an improved number and quality of postdoctoral fellows. In his own subsequent review of this report, Dean Earnest Campbell of the Graduate School added in August of 1976, "I go around thinking of the Ph.D. program in Biochemistry as one of the crown jewels in graduate education at Vanderbilt." With this mixture of praise, encouragement and criticism, Biochemistry gained considerable

momentum toward new space when it eventually became available in the Rudolph Light Hall.

Selection of Biochemistry for a move to Light Hall was certainly not automatic, however. Vice Chancellor Vernon Wilson requested a full-scale audition of the competing department's goals, objectives, research, services and education as points of emphasis in Departmental program and School Program, and governance and organization." So we organized the requested two-hour program to cover these modest topics, adding a whirlwind tour of the Department, since our own priority was to show how crowded we were. It happened that in the run up to this event, I was out of the country. I have, however, a more or less verbatim transcript of a telephone conversation with Marlene Jayne in which I described how I thought we should try to manage this compressed but valuable opportunity to "show and tell" before senior Medical School administration. This document is embarrassingly candid in describing the emphases we should seek to make, but the event went off on schedule and must have been reasonably effective since Biochemistry was indeed selected to move to Light Hall.

Moving to Light Hall

The construction of Rudolph Light Hall as a major new teaching facility in 1977 was based largely on a plan for medical education developed for the School of Medicine by John Coniglio as Chair of a faculty committee which had worked during a number of preceding years. The basement housed animal care facilities and building services. The main floor housed offices for functions of the office of Associate Dean for Medical Education and three excellent lecture rooms. The second floor housed a bookstore, lounge and lockers for the medical students. The next two floors were designed as small conference rooms for small group discussions between medical students and faculty plus a series of group laboratories where medical students could undertake "hands on" experiments utilizing modern biochemical techniques and illustrating fundamental

concepts of biochemistry in medicine. The top three floors were left as undeveloped or "shell" space.

In an illustration of another fundamental law of academia, the completion of this elegant laboratory suite in 1977 signaled the beginning of a steady decline in the role of laboratory for the education of medical students. Within 15 years, medical student laboratory had disappeared completely. Light Hall has, however, continued to serve well as the only real teaching space for all educational functions in the School of Medicine, including Medical School courses, Graduate School courses, post graduate medical education, and Hospital support service trainees.

The top three floors of the eight floors of Rudolph Light Hall had been finished in 1977 as "shells" for use in future expansions, and the future arrived in 1979. Biochemistry had a strong claim on new space in Light Hall because of its obvious overcrowding in its current space, happily documented by the recent Graduate School review. Our case was also greatly aided by a generous gift from the Samuel R. Noble Foundation of Ardmore, Oklahoma, for the purpose of renovating such "shell" space for specific research programs active in the Department. Our request for assistance to the S.R. Noble Board had been strongly supported by a Ph.D. graduate of the Department, Manford "Bud" Patterson, who was then Vice President of the Foundation and very active as Director of their in-house research program in biomedical science. When the research floors of Light Hall were completed in 1979, all of the Department of Biochemistry, except for the faculty directly associated with the Center in Environmental Toxicology and a few in the Division of Nutrition, was consolidated on the fifth and part of the sixth floor of Light Hall. (The "old" floor numbers are used here. They were renumbered up by one some years later.) Physiology and Biochemistry shared use of space on the sixth floor designated for the Diabetes Center and for a joint departmental library. There was also some limited research space assigned to Biochemistry on the sixth floor as well. Later Biochemistry's faculty in sixth floor space was moved "temporarily" to the fourth floor.

The Toxicology faculty had already been located together in an area of the B1200 corridor of the original old medical school building (now Medical Center North) and remained there as a unit. Still, it was a bitter disappointment to me and to Bob Neal that Toxicology did not move then with the rest of the Department to newer quarters in Light Hall.

The division of the space on the top three floors of Light Hall by the administration involved intense negotiations and lobbying. Although Biochemistry, Physiology and the Howard Hughes Medical Institute (HHMI) had been tentatively selected to move into this space, no one was satisfied since there was manifestly not enough space in Light Hall to realistically satisfy the needs of these three strong units. Furthermore, the funding budgeted for the completion of the two floors to be occupied by Biochemistry and Physiology was very limited. The level of completion of the 5th and 6th floors was based initially on the estimates made earlier by HHMI for their 7th floor where financial constraint was not a problem. When this proved unrealistic for the School of Medicine budget, a serious effort was undertaken to reduce, where possible, the requirements for the 5th and 6th, "departmental," floors. A letter to Vice Chancellor Wilson from the Project Manager presented a long list of possible changes that would result in savings. Rollo Park, Chairman of Physiology, and I were faced with accepting many of these painful changes or delaying, even possibly losing, our toehold in Light Hall. Reaction and tactics are apparent in this same letter. "Most of the items on this list have been reviewed favorably by Doctors Cunningham and Park. A few items are on this list to give us an estimate of their savings, so that in upcoming discussions with Doctors Park and Cunningham, should they need to dig deeper for savings, they will have this information. At the meeting Monday, we shared all of the detailed estimating with both doctors. They were very supportive of our need to cut back and were helpful in our dialog. I must say that in our discussions with Paul Gazzerro since the last Management Committee meeting, and in looking at the documents and other communications about planning the 5th and 6th floors, I think it would be wise to reconsider

the budget for this project. It is probable that, in my opinion, we set an objective based on a standard slightly lower than which we want to adopt for a reasonable yet modern research laboratory." We were trying by sweet reasonableness to prevent too severe a change and to get a more realistic assessment of the actual needs of a modern research faculty. The initial reassessment had been done by persons unknown on the premise that asking a researcher what he or she needed was an invitation to a raid on the treasury. Not an unreasonable proposition! On the other hand, only those directly involved with specific research projects were in a position to characterize their actual needs. One specific example of the basic problem was a struggle over fume hoods. The initial design of these areas envisioned only a very few fume hoods, and it was obvious to the faculty that this would be a serious problem. A survey of the number of fume hoods actually in use in existing areas of Physiology and Biochemistry was carried out, and to the amazement of the Project Manager, the number of fume hoods requested was almost identical to the number presently in use. By similar mechanisms the laboratory areas on the 5th and 6th floors of Light Hall were developed in workable, if not deluxe, form and have served with minimal renovation for over 20 years. Admittedly, some of the areas designed by faculty were rather "personalized," but the facilitation of the superb research (*e.g.* Stan Cohen) in those areas by such design was, in my view, well worth it.

To the chagrin of Vice Chancellor Wilson, immediately upon our occupation of these new laboratories, agitation began for additional space to bring Biochemistry together again. Although surely seen by the administration as a ploy to gain additional space, it was far more based on the conviction that neighborliness is crucial to the faculty cooperation characteristic of the Department. Our pleas were unsuccessful, however, and Biochemistry remained divided physically until the construction of the Ann and Roscoe R. Robinson Research Building (originally called Medical Research Building I or MRB I) in 1987.

1980-1986

State of the Department, 1981

By 1981, according to the Liaison Committee on Medical Education (LCME) Self Study of that year, the Department of Biochemistry occupied 27,613 nsf in Light Hall and MCN and had a total budget of over $3.3 million of which $360,000 was from School of Medicine funds.

Non-School of Medicine funding was preponderantly from NIH and was almost entirely research and research-training grants obtained in national competition by individual faculty and small groups of faculty with related research interests. Maintaining a fair and equitable salary structure within the Department when the bulk of funds come from without, was, and is, a considerable challenge. This situation is exacerbated when another large external source of salary support comes on the scene. This came to a head in Biochemistry in 1981 when, in its earlier, less formal incarnation, the Howard Hughes Medical Research Institute (HHMRI) wanted to support a specific new young faculty member in the Department of Biochemistry. We handled the appointment itself through normal departmental committee channels but ran into trouble on salary. HHMRI wanted to pay a salary that was very considerably higher than any we were then paying. I felt I could not agree to that without some major increases in other faculty salaries. Neither HHMRI nor Vanderbilt was interested in that; so, negotiations collapsed, and the new colleague was accommodated in another department. On other occasions when the salary discrepancy was not so large, it was quietly accepted and then used, by appropriate comparison, to gently "jawbone" increases in other faculty salaries. Some flexibility in individual faculty salaries is a welcome feature of non-state supported universities, but there are obvious limits. From time to time mistakes are made, but it is very disturbing to a cooperative academic environment if it appears that salaries are being set by other than internally consistent professional evaluations.

Faculty

Michael Meredith

Mike Meredith joined our faculty in 1982 after a postdoctoral stint in the Department of Physiological Chemistry at Johns Hopkins and a year as a Research Associate at the Environmental Health Sciences Center, Department of Biochemistry and Biophysics at Oregon State University. He was an important addition to our Center in Environmental Toxicology. His research interest centered on the function of glutathione in detoxification reactions in cultured cells. He was also interested broadly in the metabolism of sulfur-containing amino acids in normal and tumor tissue. He left us in 1990 to return to the University of Oregon Health Science Center, an environment where he indicated fishing and hiking were much better.

Molecular Genetics and NMR

An appreciation of the crucial need to strengthen molecular biology or molecular genetics in Biochemistry was strong among the faculty in the early 1980s, but it took considerable persuasion of Dean Chapman to obtain financial support for recruitment in that area. The main resistance surely arose from the chronic shortage of funds plus the general expectation, at that time, that this was an area that would be covered by the Department of Molecular Biology in the College of Arts and Science.

An effort to include additional funds for a new position in this field was included in our budget proposal for 1982 but was deferred by the Dean. I countered in a letter; "Vanderbilt is, as you know, desperately weak in the area of molecular genetics. Our teaching and research programs cry out for expertise in this area. Molecular Genetics is not only one of the most active areas of biomedical science in the sense of progress in knowledge, but it has also furnished an entirely new array of technological and methodological advances. We in Biochemistry acutely need this expertise in the immediate future. Certainly given the overall budgetary situation, we can not object to

the deferment of this position; but I earnestly hope that deferment will be for only a very few months, or that we can hasten recruitment for this position by other budgetary changes."

Chapman did indeed work with us later in the year to move forward on this increasingly critical need, and we began to investigate likely candidates. The rapidly growing worldwide interest in this area made the recruitment of strong, independent young "molecular biologists" a time consuming and highly competitive endeavor. Our efforts happily culminated in the appointments of Neil Osheroff and Stephen Lloyd in 1983.

Neil Osheroff

Neil Osheroff came to Vanderbilt from a postdoctoral position with Douglas Brutlag in that hot bed of molecular genetics, Stanford. He had, however, received his Ph.D. at Northwestern in protein chemistry under Margoliash, so he was an excellent "fit" to existing departmental strengths and offered much to the development of molecular genetics in the Department. Osheroff is also a very successful teacher. His rapport with students of all kinds is unusual. When John Coniglio retired, Neil took over Coniglio's long time role as the key leader of the medical biochemistry course, with appreciation from all sides. In addition, Osheroff's strong background and commitment have made it possible for him to develop and continue a research program in topoisomerases that enjoys international recognition. These enzymes, which permit the solution of the topological problem of "unwinding" of DNA necessary for transcription and cell division, are at the center of many biologically and clinically important processes.

Stephen Lloyd

Steve Lloyd arrived in the Department as a member of the Toxicology Center in 1983. He came after a highly useful exposure to the newly flourishing industrial effort in molecular biology with the Genex Corporation. He had received his Ph.D. in molecular

biology at the University of Texas Graduate School of Biomedical Sciences. A postdoctoral fellowship at Stanford with Philip Hanawalt had followed. With this background, he developed a research program at Vanderbilt in several aspects of molecular genetics emphasizing site-directed mutagenesis and DNA repair. His research went very well, but equally important, he was a potent source of assistance throughout the School, through advice and collaboration, in the introduction and application of the powerful tools of molecular biology to many systems previously under study by more conventional methods. Another excellent teacher, he was important in introducing the concepts and techniques of molecular genetics to graduate students. Steve was also the instigator of a land grab attempt reminiscent of Jan van Eys' successful effort in earlier times to take over and renovate the men's restroom for badly needed research space. Steve noted that the post office, which was quite near his crowded laboratory, was evacuating an area, and we tried to capture it for him. Unfortunately, our entirely reasonable and vigorous approach to the Dean failed in this case. Steve eventually returned to the University of Texas, Galveston in 1994 to accept a senior position in Molecular Biology but continued an adjunct appointment at Vanderbilt.

Peter Gettins

The continuing departmental commitment to the study of the molecular structure of biologically important molecules by newer technologies was addressed again by the addition to the Department of expertise in nuclear magnetic resonance (NMR). Peter Gettins joined the Department in 1984. He had received his doctoral training at Oxford University under R.A. Dwek and continued this early interest in the application of NMR to protein structure in a postdoctoral post at Yale with J.E. Coleman. His experience with the then novel application of NMR to protein structure and his broad understanding of physical biochemistry greatly influenced and strengthened the research of several other faculty members throughout the Medical Center. His own research featured novel applications of physical methods to the study of the structure and mechanism of action of

components of the human blood clotting system, including heparin and anti-thrombin. Yet another excellent teacher, he also served as Director of Graduate Studies for the Department. In 1994, he left Vanderbilt for a position at the University of Illinois, Chicago.

Research Faculty

An extremely valuable category of faculty appointments through the years has been those made at the levels of Research Instructor to Research Professor. These appointments made possible the association with the Department of talented individuals who, for a wide variety of reasons, did not fit or did not desire to be immediately on the tenure track and who wished to devote fulltime to research. Some eventually joined the tenure track and some stayed only very briefly at Vanderbilt with a specific program. All are listed in the appendix but several who remained at Vanderbilt for long periods and made significant contributions to the Department demand mention here. Carpenter and Ong, now tenure faculty, have been previously noted. Donald Horne, Research Professor of Biochemistry; Robert Cook, Research Associate Professor of Biochemistry; and Masaaki Tamura, Research Associate Professor of Biochemistry have been associated with the Department for several years and have established strong research programs. Horne came to Vanderbilt as a graduate student with Harry Broquist in 1969 and received his Ph.D. under his guidance. Cook received his Ph.D. from the University of Southhampton and came to Vanderbilt as a Research Associate in 1968. Both Horne and Cook have worked extensively in collaboration with Connie Wagner on aspects of folate and methyl group metabolism. Tamura joined the Department in 1982 as a Research Associate in Tad Inagami's laboratory. He has worked extensively with angiotensin receptors and other aspects of hypertension.

Facilities: Ann and Roscoe R. Robinson Medical Research Building (MRB-I)

The continued growth in the School of Medicine and the

Department of Biochemistry of ever stronger and more internationally recognized research programs led inevitably to steadily worsening overcrowding. This was finally and substantially relieved in 1987 by the construction of the Ann and Roscoe R. Robinson Medical Research Building directly south of and connecting on all floors with the Rudolph Light Hall. Biochemistry was assigned the 6th floor that connected to its existing space in Light Hall. The Biochemistry faculty associated with the Center in Molecular Toxicology then moved into this area, thus reestablishing the geographical unity of the Department.

Personal Research

Despite the encroachments of administrative duties, I continued some research in the late 1970s and 1980s in collaboration with graduate students and postdoctoral fellows and with the cooperation of faculty colleagues. We began to examine some aspects of the biosynthesis of glycoproteins and their role in cell adhesion (Edward Branson, Narinder Kumar, Paula Hewgley, and Charles Schwartz). We were now competing with what had become an international tidal wave of interest in glycoproteins. A study of the role of collagen in platelet activation (Sam Santoro, Nicolas Kotite, Gary Carnahan, and Krzystof Dolowy) opened a route to understanding this clinically important function. But this was really only satisfactorily pursued by Santoro, an M.D./Ph.D. graduate, when he later took a faculty post at Washington University, eventually becoming Director of the Division of Laboratory Medicine there. It is a pleasure to note with pride that as this is written in 2003, Sam has just accepted the Chair of the Department of Pathology at Vanderbilt. Finally, we (Larry Dangott and faculty colleague Peter Gettins) undertook a physical characterization of changes in alpha-2 macroglobulin upon enzymatic and chemical modification. Our NMR studies of alpha-2-macroglobulin were early demonstrations of the utility of NMR in specialized studies of even very large proteins. I continued this project well after I left the Chair in 1988, declining in

intensity through my official retirement in 1994. It provided me with the great pleasure of ending my career as it started, with work in the laboratory using the newer instruments for study of macromolecular structure.

It is impractical to chronicle in this brief volume the successful careers of all the graduate alumni of the Department, but perhaps it is illustrative to mention briefly the career choices of those students who worked in my laboratory. Jere Segrest is Professor of Medicine and Biochemistry at the University of Alabama School of Medicine, Birmingham. Bill Butler is Professor of Biochemistry and former Chair of the Department of Biochemistry at the University of Texas Health Sciences Center, Houston. Dick Nuenke is Associate Professor of Biochemistry at Ohio State. Gayle Jacobs has recently retired from her position as Director of Computer Operations in the Vanderbilt Pathology Clinical Laboratory. Paul Morgan is with the Mathematical Applications Group of Glaxo Wellcome Research Laboratories in North Carolina. Bill Porter is Professor of Biochemistry and Pathology in the School of Medicine of the University of Kentucky. Gary Carnahan is Director of Laboratories of the Children's and Women's Hospital, University of South Alabama in Mobile. Suwit Piankijagum is Professor in the Department of Biochemistry, Mahidol University, Bangkok. Carolyn Brown is Professor of Biochemistry at Clemson University. Soo Il Chung is a Senior Investigator in the Laboratory of Cell Development and Oncology, National Institute of Dental Research and Charles Schwarz is Staff Scientist with the Greenwood Genetics Center, Greenwood South Carolina. Sam Santoro is now Chairman of Pathology at Vanderbilt. When last heard from Jose Hector Aguilar was Professor in the School of Pharmacy in Guatemala City; Diana Trundle was Technical Director of a regional reference clinical laboratory in Clearwater, Florida; Cheng-Chung Huang was Research Professor of Otolaryngology at Columbia University and John Rainey was in clinical practice in Michigan. Any incorrect or out of date information in this summary is a joint responsibility since keeping up with all of our alumni colleagues is a pleasant but formidable task. It would

be greatly aided by occasional spontaneous communications with the Department.

Faculty Recognition

The brief recital of the general research interests of some of the faculty given so far in this narrative barely suggests the steady growth in national and international recognition of the Department of Biochemistry. The challenge of the Graduate School's external review committee of 1976 to mount a "period of strong achievement to gain greater national recognition" was taken quite seriously and effectively. Although it is difficult to select programs for particular mention, some are evident.

The Nobel Prize (1986)

Very early one October morning in 1986 while half listening to the news on the radio, I heard the words Nobel Prize and Stanley Cohen close together. It took a few seconds to be sure that I was not imagining this. I was not really surprised that the Nobel Committee had recognized Cohen's work because many of us had long known that it was certainly of Nobel stature. But we also knew that actual selection was a tortuous and unpredictable process. Our first brush with the Nobel Committee had been in 1969-70 when Dean Randolph Batson and others had been "invited" to submit the name of a candidate for the 1971 Nobel Prize in Physiology or Medicine. It was recognized that this was the result of earlier efforts within and without the University to bring our colleague in Physiology, Earl Sutherland, to the maximum attention of the Nobel Selection Committee. His discovery of "second messengers," cyclic AMP, was widely recognized as a turning point in understanding mechanisms of hormone action. As, at that time, Associate Dean for Biomedical Sciences, it fell to me to coordinate the preparation of the local recommendations that together with those of colleagues throughout the world contributed to Earl's receipt of the Nobel Prize in 1971.

Stanley Cohen, Distinguished Professor of Biochemistry, Nobel Prize in Physiology or Medicine 1986

In the mid-1980s we knew that colleagues in other universities had also been supporting the nomination of Stan Cohen. We were frequently called on to provide them with "ammunition" in the form of his *curriculum vita*, reprints and other information. We knew things were heating up in 1985 when we received a direct request from the Nobel Committee for a nomination. Not much discussion was required to "decide" that Stan was our candidate, and then the hopeful waiting began which was rewarded that October morning in 1986.

Knowing that a lot would be going on that day, I hurried to the Department of Biochemistry only to find Marlene Jayne already fielding telephone inquiries from everywhere. Excitement reigned, not only in Biochemistry but also throughout the University. With this second Nobel Prize, Vanderbilt School of Medicine's international stature was unarguable.

It had been apparent from the earliest days that Stan Cohen's insightful study of protein growth factors, carried on with a minimum number of co-workers, was of special quality. His receipt of numerous prestigious awards, culminating in the Nobel Prize jointly with his Italian colleague, Rita Levi-Montalcini, underscored international recognition and even brought a degree of local Nashville media appreciation! Among the awards Cohen had received prior to the Nobel Prize were appointment as an American Cancer Society Professor in 1976. This first serious national recognition of the quality and potential of Stan's research was largely originated and strongly supported by B.F. Byrd, Jr. our colleague Professor of Surgery. Subsequently, Cohen received Vanderbilt's Earl Sutherland Award in 1977, the Albert Lasker Award in 1986 and was elected to the National Academy of Sciences in 1980. He was appointed a University Distinguished Professor in 1986, the first in the School of Medicine.

The award of the Nobel Prizes is held annually in December in Stockholm. The number of individuals each awardee can invite to attend is quite limited. Along with his wife, Jan Jordan, and other members of his family, Cohen invited my wife, Jean, and me, Ike and Ann Robinson and John and Judy Chapman to attend.

We traveled to Stockholm with the Robinson's, enjoying not only their company but also the perks associated with their status, including a limousine and driver. Unfortunately, the driver deposited us incorrectly at the special door for the Nobel Laureates the night of the awards. We had an escorted grand tour of the building as they hurriedly took us to our correct destination, the Grand Dining Hall where in a group of several hundred we dined with the King and Queen of Sweden.

The ritual and mystique of the Nobel Prize must have some resonance with anyone in science. To be able to attend and see the full week of ceremony, the talks, the dinners, and the awards themselves was most memorable. Cohen's formal Nobel Lecture was given in the auditorium of the Karolinska Institute on December 8. The significance of the occasion was brought home for me most personally when Cohen began his talk with the very same slide showing the effect of nerve growth factor I had first seen in T2208 in 1959. On December 10, we watched with a mixture of emotions and memories as Cohen received the prize from the King of Sweden.

Upon his return to Nashville Cohen was deluged with requests for visits and talks and was honored by other awards. The interest generated by his work, the notoriety of the Nobel and the lucidity of his presentations made him a prime target for the lecture circuit internationally. He tried to fulfill as many requests as he could, especially from Vanderbilt and old colleagues elsewhere but he was determined to remain active in research. And, so he did. I tried to help by constantly reminding him that Marie Curie had won two Nobels!

It also seemed appropriate to suggest to the Dean that we should make a substantial increase in Cohen's salary in view of his accomplishments and stature. Dean Chapman replied in words that tell as much about the Vanderbilt ethos as any I ever heard. "That's a great idea, Leon! Can you afford it?" It must be added, however, that after some pressure from Marlene Jayne (by now as much Cohen's administrative aide as mine), Chapman provided Cohen the ultimate Vanderbilt "perk," a free and convenient reserved parking space!

Stanley Cohen receives the Nobel Prize from the King of Sweden, December 10, 1986

Looking back from the turn of the millenium, it is easy to see that the Nobel Committee's evaluation of the significance of Cohen's work was right on the mark. It has influenced to a major extent the subsequent worldwide approach to the understanding of cancer and development. A quote from an introduction written by Graham Carpenter to a Mini-Review issue of *Experimental Cell Research* on ErbB/EGF in March 2003 gives some perspective.

"In 1962 Stanley Cohen published an article entitled *Isolation of a Mouse Submaxillary Gland Protein Accelerating Incisor Eruption and Eyelid Opening in the Newborn Animal* (*J. Biol. Chem*. 237 (1962) 1555-1962). This report described the purification of a 'tooth-lid factor' which was subsequently renamed epidermal growth factor (EGF) by Cohen based on its capacity to stimulate the proliferation of epidermal cells.

In the following 40 years, research based on this tooth-lid factor has expanded at a prodigious rate to include the identification of other similar growth factors, a family of receptors (termed ErbB) that mediates the actions of these ligands; the relationship of the ligands and the receptors to human cancers; the development of clinical cancer therapies based on inhibition of these receptors and genetic analyses of this highly conserved signaling system in lower organisms. It is obvious that the biologic significance of EGF extends far beyond the tooth and eyelid."

Other Recognition and Awards

The Biochemistry faculty has been recognized in multiple ways for the excellence of contributions to Vanderbilt and to the field of biochemistry. Other internationally recognized long-term research programs of the Biochemistry faculty during the "middle" years would have to include those of Tadashi Inagami, Harry Broquist, Frank Chytil, Graham Carpenter, Conrad Wagner and Fred Guengerich.

A further elaboration here on the significance and quality of each of these research programs is greatly merited and would certainly be appropriate and informative in a history of these years.

I have, however, found it quite impossible to do them justice in any balanced way. Again, this is simply a difficulty that derives directly from having an active participant, especially a chairman, try to write a history of this period. So, despite the completely vital role these investigations played in the life and success of the Department of Biochemistry during these years, I must leave a more detailed evaluation of their individual impact to a later author.

It is the plain truth that the research of every member of the Biochemistry faculty was nationally visible during these years. This is evidenced by their membership in academic societies, their publications in key journals and membership on the editorial boards, and their participation on NIH, NSF, American Cancer Society, American Heart Association and other research granting agency boards and study sections. Perhaps most indicative of the status of the Department locally, and certainly the point dearest to the administration, was its constant position during the 1980s as number one in the University in total research funding, excluding research costs directed to patient care. Nationally it ranked in funding of Biochemistry departments between number 6 and number 1 for several years, depending upon the precise parameters of the ranking.

I have tried to mention some of the many other external awards in the brief discussion of each faculty member. But I am particularly proud of the local recognition of our faculty as an indication of the Department's role in bringing about the steadily rising national and international stature of Vanderbilt School of Medicine. Four of our faculty have won the Earl Sutherland Prize in Research: Tad Inagami, Stan Cohen, Lubomir Hnilica and Fred Guengerich. No other department in the University can top that record. Similarly, four have won the Harvie Branscomb Distinguished Professorship: Frank Chytil, Oscar Touster, Larry Marnett and I. Bill Darby, John Coniglio, James Staros and Oscar Touster were recognized with the Thomas Jefferson Award for outstanding service to the University. Stanley Cohen and Frank Chytil have been named Distinguished Professors by action of the Board of Trust. Tad Inagami occupies the Stanford Moore Chair, and Larry Marnett

the Mary Geddes Stahlman Chair in Cancer Research. More recently, Graham Carpenter has become Ingram Professor of Cancer Research, and Michael Waterman has taken the Natalie Overall Warren Chair in Biochemistry. William Darby and Stanley Cohen were elected members of the National Academy of Sciences.

1986-1992

Budget Matters

These years of growing national and international recognition and growing research support, primarily from NIH, were also times of increasing stress on the Department's sole source of unrestricted funding for faculty recruitment and support, the "hard" budget provided by the School of Medicine. Several years passed during which it was not possible to appoint new young investigators to the faculty in Biochemistry. In addition, faculty salary levels began to stagnate. During such times, only the excellent advice and even sharper eye of Financial Management kept us in the black. There was, in those days, no way to overspend a budget. This gave much credibility to plaintive letters such as my budget letter to the Dean in February 1988. I wrote, "Our salaries have dropped behind, largely as a result of the budgetary pressures to which we have been exposed over the past three years. No doubt there are reasons for these pressures, and I have tried to be responsible in reacting to them; but, it is apparent to me at this point that this cannot be allowed to bring salary levels of Biochemistry faculty to completely inappropriate levels." In writing this, I was fully aware of the Medical School administration's habit of placing the bulk of any new "hard" (Medical School) money into departments only at the time when a new Chair was appointed. I had, for that reason, already made the private decision to step down from the Chair after 15 years in that role. But I thought it "couldn't hurt" to try to get a little boost for Biochemistry before a new Chairman began his or her own negotiations. If successful, some very badly needed

and long-standing faculty development projects could be immediately implemented or, at the very least, resources would be available for the use of the new Chair.

Structural Biology

There had been a growing international appreciation for the need for studies of the structure and function of proteins in the exploitation of the many new discoveries in molecular genetics. Physical biochemistry or macromolecular structure, a continuing focus of the Department of Biochemistry from its very earliest days, and now known as "structural biology," was in the national spotlight. We had taken a major step in this direction with the appointment of Peter Gettins and his development with Chemistry of a strong program in NMR research. After an abortive multi-departmental approach to the Howard Hughes Medical Research Institute for support of structural biology, Biochemistry sought the interest of Vice Chancellor Ike Robinson in a special development of this area and found a sympathetic ear. With his help we had a series of evening meetings with key Chairs of other School of Medicine Departments, clinical and basic science, where I had the opportunity to present our belief that the School urgently needed to build up its expertise in "structural biology." In this unusual venue, even for Vanderbilt, we sought and won the support of these Chairs for the designation of special financial resources and research space to be used specifically by Biochemistry for the recruitment of an x-ray crystallography team. The formal report to Vice Chancellor Robinson of May 9, 1986, stated in part:

"In response to your charge of February 5 (1986), we have met to evaluate the potential of the School of Medicine in the strengthening of our resources in macromolecular structure or structural biology. In our meetings we have become convinced that such strengthening is a clear, high priority need for the future of many important research efforts at Vanderbilt. The existing faculty in this area is sufficiently strong and diverse to insure the high level of recruitment desired, but there are critical areas where

new expertise is essential if Vanderbilt is to retain and expand its role in medical research in the next decade. The area of x-ray crystallography as the unique source of detailed three dimensional macromolecular structure at the atomic level will play a truly central role in relationship to other areas of structural analysis such as nuclear magnetic resonance spectroscopy, molecular modeling/ graphics, electron paramagnetic resonance spectroscopy, protein engineering, amino acid and DNA sequence analysis, and molecular genetics."

The Chairs of Molecular Physiology and Biophysics (Daryl Granner); Pediatrics (David Karzon); Medicine (John Oates); Pharmacology (Joel Hardman); Cell Biology (Harold Moses) and Biochemistry signed it.

Robinson then provided financial support. I asked Jim Staros to chair an interdepartmental search committee. The search was a difficult one in that, again, we were playing catch up in competition with other universities in a newly "hot" field. In 1988 we selected two crystallographers, Wayne Anderson and Marcia Newcomer. A well-equipped x-ray diffraction laboratory was created on the 8th floor of the Robinson Building (MRB-I), and several studies of protein structure initiated, often in collaboration with other members of the faculty.

It is interesting in 2003 to recall this maximally stretched and marginally funded effort of the School of Medicine in the mid-1980s to get moving on "structural biology" in the light of Vanderbilt's major funding and expansion in this area in the 2000s.

Wayne Anderson

Anderson came to Vanderbilt in 1988 as the lead person in the development of the Biochemistry x-ray crystallography laboratory. He was then Associate Professor in the Department of Biochemistry, University of Alberta, Edmonton and a member of the MRC Group in Protein Structure and Function. He had received his Ph.D. at Yale in Tom Steitz group and continued postdoctoral studies in the Institute of Molecular Biology at the University of

Oregon, Eugene before moving to Edmonton. At Vanderbilt, he developed collaborative structural studies locally with Steve Lloyd and Jacek Hawiger as well as continuing previously ongoing studies with others outside Vanderbilt. He moved to Northwestern University Medical School in 1994.

Marcia Newcomer

Newcomer joined the Department in 1989 as Assistant Professor and rose rapidly to become Professor in 1999. She had received her Ph.D. at Rice in crystallography with Quiocho. She worked with Wayne Anderson to establish the Vanderbilt crystallography laboratory and undertook several structural studies including approaches to the structure and function of retinol binding proteins with Dave Ong and others. In 2002, she accepted a position at Louisiana State University at Baton Rouge.

Stahlman Chair in Cancer Research

Lawrence Marnett

The establishment of a number of chairs throughout the School of Medicine by the Stahlman family had first been especially beneficial to the Department of Biochemistry when Lubomir Hnilica had been recruited as Mary Geddes Stahlman Professor of Cancer Research in 1976. Following his death in 1986, a national search by an interdepartmental committee again resulted in an appointment in Biochemistry. In 1987, we were able to attract Lawrence Marnett to the Department of Biochemistry and the Center in Molecular Toxicology as Hnilica's successor. He came to us from Wayne State University in Detroit where he was Professor of Chemistry. His laboratory is located in the A.B. Hancock Cancer Research Laboratory on the 8th floor of the Robinson Research Building (MRB-I), convenient to his colleagues in the Toxicology Center. Marnett's work on the molecular basis of mutagenesis by naturally occurring carbonyl compounds and on the mechanism

of action of the arachidonic acid oxygenases had already gained him wide recognition. Within a very short period, he had reestablished and expanded these studies at Vanderbilt. Recently he was appointed as the Director of the Interschool Vanderbilt Institute for Chemical Biology.

Change of Leadership—Interim

In 1988, after 35 years at Vanderbilt, including 5 years as Associate Dean and 15 years as Chairman of the Department of Biochemistry, I formally asked Dean John Chapman to be relieved of the Chair in order to return to regular faculty status. It was apparent that yet another new scientific era in biochemistry was dawning which would demand new leadership. Also, new Chairs had just been appointed in Cell Biology and in Molecular Physiology and Biophysics. The search continued for a new Chair in Microbiology and one was about to be initiated in Pharmacology. The appointment of new Chairs in these departments meant that, in the Vanderbilt tradition, Biochemistry's increasingly acute budget needs would likely not be addressed except under the competitive pressure of the search for a new Chair. Thus, a major career decision for me was made relatively easy. The subsequent search was carried out during the interim Chairmanships of Jim Staros and Connie Wagner.

James Staros was appointed Interim Chair as the search for a permanent successor was initiated. Staros performed admirably in this typically trying role. Among his accomplishments was the development of the Stanford Moore Professorship, endowed in memory and honor of Vanderbilt's alumnus in chemistry who shared the Nobel Prize in 1972, and the establishment of the John Coniglio Prize for medical student research. Staros' strong interests in educational programs and his administrative skills led, in 1991, to his appointment as Chair of Vanderbilt's Department of Molecular Biology in the College of Arts and Science, succeeding Oscar Touster. Thus, he became only the second Chairman of that Department—both having come from the Biochemistry faculty!

Markey Grant

Another effort to press forward with faculty development during the final days of my chairmanship was assured when, in early 1986, the Department of Biochemistry successfully developed a proposal to the Lucille P. Markey Charitable Trust. This program, headed by Stan Cohen, focused strongly on the Department's need for young faculty interested in the application of molecular genetics to the study of growth regulatory mechanisms. This grant also included crucial funding for the Department of Cell Biology in support of new faculty and for the transgenic mouse core laboratory then getting underway. This facility was, and is, a crucial resource for all those interested in the application of the powerful modern techniques of molecular genetics. Support was also provided to the Department of Medicine for new faculty and for the establishment of a nucleic acid sequencing and synthesis laboratory. The Markey program was fully implemented, however, only during the period when Staros was Interim Chair of Biochemistry. It permitted the appointment of three new young faculty members in Biochemistry after a search directed by Stan Cohen.

Charles Albright

Albright came to Vanderbilt as Assistant Professor of Biochemistry in 1993 from a postdoctorate with Robert Weinberg at the Whitehead Institute at M.I.T. His major research interest is in *ras* signaling pathways and GTPase regulators of spindle assembly in yeast. He left the Department in 2000.

Ronald Wisdom

Wisdom received his M.D. from the University of California, Irvine in 1981. After residency training in Hematology and Oncology, he became a Research Associate in Inder Verma's laboratory at Salk Institute. He came to Vanderbilt in 1993 as Assistant Professor of Biochemistry and Medicine. He received the

Vice Chancellor's Award of Vanderbilt in 1995 and won an Established Investigator Award of the American Heart Association in 1998. He was active in the Graduate Education Program of the Department including service as the Director of Graduate Education and organizer of the departmental seminar series from 1993-1996. He has taught broadly in his field in Biochemistry courses and in the combined Interdepartmental Graduate Program (IGP). His research involves primarily mechanisms of transformation by AP-1 proteins and the role of *c-Jun* in endothelial cell function. He left the Department for a position at the University of California, Davis in 2001.

Wayne Wahls

Wayne Wahls joined the Department as Assistant Professor in 1995. He came to Biochemistry from a postdoctoral fellowship with Gerald Smith at the Fred Hutchinson Cancer Research Center in Seattle. His research interests included regulative biochemistry of meiotic recombination and meiotic origins of aneuploidy. He was a member of the Vanderbilt Cancer Center and a participant in the departmental teaching program, both medical and graduate. He left the Department in 2002.

The Markey program also brought important new instrumentation into the department, our first phosphoimager, a differential scanning calorimeter, an additional X-ray generator, a Silicon Graphics modeling system and a dynamic light scattering instrument. All of these contributed to the continued build up of research in molecular structure and molecular genetics.

Following the departure of Staros to the Chair of Molecular Biology in 1991, Conrad Wagner succeeded him as Interim Chair of Biochemistry as the search for a permanent chairman continued. Both as a member of the faculty and as Associate Chief of Staff for Research in the Nashville Veterans Administration Hospital, Connie Wagner had established himself as a scientist, teacher and strong scientific administrator. The Department was again in good hands, and awaiting the arrival in 1991 of its new permanent chair.

Some Sometimes Grants Management Bureaucrats; Left to Right John Hash (Professor of Microbiology and Associate Dean for Biomedical Sciences), Joel Hardman (Associate Vice Chancellor and Professor and former Chair of Pharmacology), Allan Bass (Professor and former Chair of Pharmacology, Associate Dean for Biomedical Sciences and Acting Dean of the School of Medicine), William Darby (Professor and former Chair of Biochemistry), Thomas Barnes (Director of Grants Management, Sponsored Research), Leon Cunningham

Dinner on the Occasion of Stan Cohen's Retirement; Left to Right Leon Cunningham, Stanley Cohen, Melvin Fitzgerald, Jan Jordan, Jean Cunningham

State of the Department, 1991

In 1991 the Department of Biochemistry had (Liason Committee on Medical Education, LCME, Self Study) 22 fulltime faculty, 36 graduate students (the largest program in the basic sciences), 34 postdoctoral fellows and over 8 million dollars in grants (direct and indirect costs, the largest sum of any of the basic science departments). This sum does not include direct costs awarded for the Hypertension SCOR directed by Biochemistry faculty but formally assigned to Medical Administration. The Department occupied 36,053 nsf in Light Hall and the Robinson Building (MRB-I). The contribution to the departmental budget from the School of Medicine was $630,000.

The Department ranked among the top five Biochemistry

Departments in the United States, both in terms of total NIH funding and in citation of publications of its faculty.

Despite a recurring note of financial and space limitations on departmental development, Biochemistry experienced throughout the years 1972-1988 the cooperation and as much financial support from the School of Medicine administration as was practically feasible. I believe that we, the faculty and staff of the Department, made good use of that support.