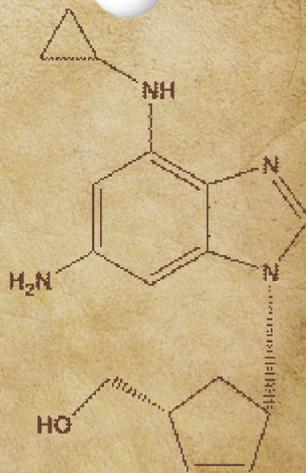
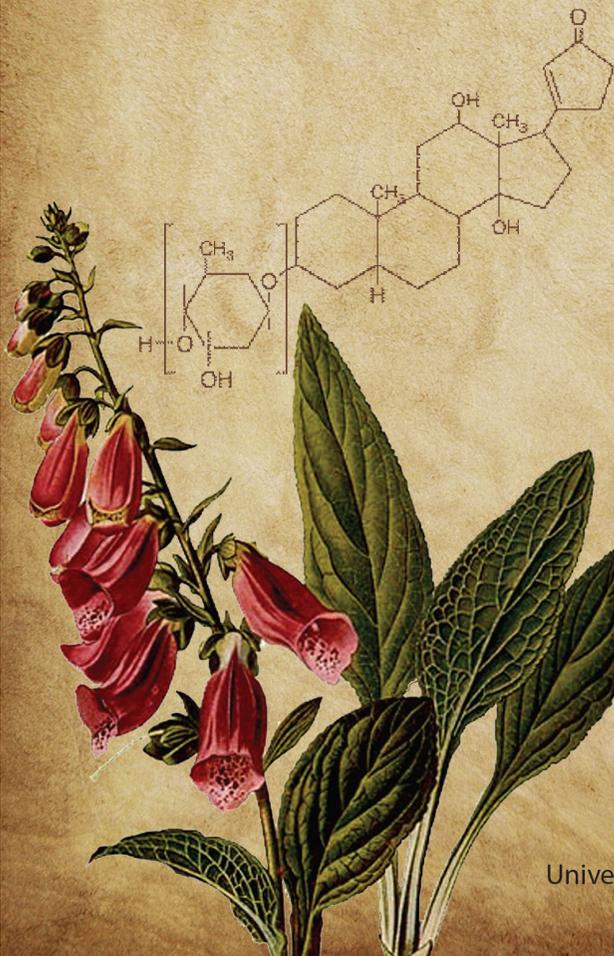
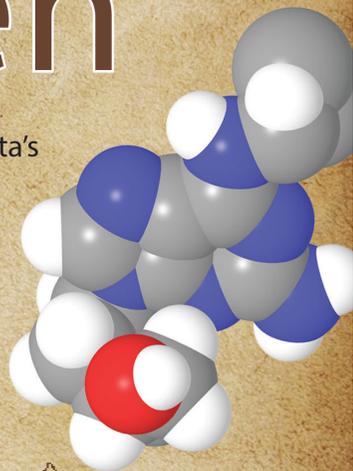


From Digitalis to Ziagen

The University of Minnesota's
Department of
Medicinal Chemistry



By

YUSUF J. ABUL-HAJJ
RICHARD BRODERICK

University of Minnesota • Minneapolis

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PREFACE

The genesis of this book goes back many years.

During the long period of time when I was head of the Department of Medicinal Chemistry, the department underwent dramatic changes in many different realms, from changing personnel to evolving research trends to sometimes wrenching shifts in administration and institutional structure.

In turn, my interest in the changes that have taken place just since 1968 led me to think that there was a need for a comprehensive history of Medicinal Chemistry beginning with the founding of the University of Minnesota's College of Pharmacy in 1892 until today. In turn that same period of time—1892 to 2012—also represents the most revolutionary era in the history of the entire discipline of medicinal chemistry, witnessing the transformation of the field from an artisanal, trial-and-error approach to isolating and testing therapeutic elements in natural elements to today's high-tech, computer-assisted discovery and design of new, targeted drugs.

Of course to tell this story in depth—the history of the University of Minnesota's Department of Medicinal Chemistry—requires telling the stories of the individuals who created and shaped, and, over the decades, worked in the department.

Perhaps even more than in other disciplines, this primacy of individual contribution holds true in the Department of Medicinal Chemistry for the simple reason that it has been an institution in which individual faculty members have had a major impact in its birth and ongoing development. Those contributions began when Frederick Wulling, one of the giants of the field, agreed to move to Minnesota from his very comfortable career on the East Coast and found the state's first college of pharmacy in improvised quarters on the campus of the University of Minnesota. For several years, Wulling was not only the school's first dean but also its first—and only—faculty member in pharmacognosy and pharmaceutical chemistry. His groundbreaking work not just in building the college and department but also in the research into products like digitalis was from the first built upon by other faculty members. These faculty played a key role both in shaping and reshaping the department and in making and remaking the field of medicinal chemistry, playing leading roles in changing the focus and methodology and, ultimately, even the objectives, of medicinal chemistry research.

The achievements of individual faculty members such as Earl Fischer, Ole Gisvold, Taito Soine, Philip Portoghese, John Staba, and Robert Vince lay the groundwork for today's widely expanded roster of younger faculty whose research involves cutting-edge collaborations with other departments and centers at the University of Minnesota. In undertaking the history of an organization with such a long and varied history—one that encompasses not only revolutionary changes in the goals, methodology, and technology of research but also changes to departmental and college structures necessitated by the explosive growth of the University, especially after World War II, and the school's emergence as one of the preeminent research institutions in the world—certain challenges had to be overcome.

Not the least of these was in deciding how best to organize that long history in a way that readers would find engaging. Rather than adopting a straightforward year-by-year chronological approach, we organized the department's rich history into four sections, each corresponding to turning points in the development of medicinal chemistry at the Uni-

versity of Minnesota. Within each of those sections we attempt to tell the story thematically, examining developments in research, personnel, administration, and departmental structure during the period covered by each section. In every case, we have kept the focus on the individual faculty members whose contributions in teaching, research, service, and administration have been critical to the department's success over the past 120 years.

One final consideration went into the making of this book. While we expect that its primary audience will be members, both past and present, of the department, as well as their families, friends, and students, we also hope readers will be others who have no direct relationship to the department. The Department of Medicinal Chemistry was born in the middle of the transition of medical remedies from a folk tradition to a modern, research-driven science. Since its founding in 1892, the department has mirrored the breathtaking changes that have taken place in the analysis, discovery, and—increasingly—the design of effective drugs for the treatment of some of humanity's most deadly and crippling disorders. And it has more than mirrored those changes, in many cases, playing a critical role effecting those changes.

We chose to title this book *From Digitalis to Ziagen* not simply because it's a catchy name but also because it captures the one overriding theme that has prevailed throughout the existence of the Department of Medicinal Chemistry and will continue to prevail into the future: the never-ending quest to help cure illness and thus make the world a happier and healthier place in which to live.

Yusuf J. Abul-Hajj
April 2012
Minneapolis

ACKNOWLEDGEMENTS

The authors would like to thank the many contributors for compiling the information for this book. Every effort was made to verify the facts such as names, dates, and events, but the flavor of the individual chapters is that of the authors. Some areas of work and periods of time probably are not covered as much as would have been optimal due to lack of records or people to provide an account from collective memory. In particular we also like to thank Erik Moore and other staff members from the University of Minnesota Archives for guiding and accessing the material for chapters 1 and 2. Thanks also to the Minnesota Pharmaceutical Association for using their archived materials.

Thanks go to several faculty members including Mahmoud Abdel-Monem, Elizabeth Amin, Gunda Georg, Patrick Hanna, Rodney Johnson, Philip Portoghese, Rory Rimmel, W. Thomas Shier, Marilyn Speedie, Natalia Tretyakova, Robert Vince, and Carston Wagner for historical accounts of their areas and other anecdotes. In particular we thank Drs. Portoghese, Hanna, and Georg for reading and critiquing sections of the manuscript.

We gratefully acknowledge several former faculty and alumni including Lee Schramm, Raymond Counsell, K. H. Lee, Lemont Kier, and William Soine for personal information on several aspects of departmental history during the 1950s and 1960s. Thanks to Dennis Worthen for providing input about the developments and changes to pharmacy education during the 1930s and 1940s and to Heather Wilson, Charles Wilson's daughter, for providing us with information from her father's records about pharmaceutical chemistry during the 1940s.

Gratitude is due to Genny Rosing from the Graduate School for the time she spent in double-checking the accuracy of the names, degrees, and dates for all graduate students. Thanks, too, to Drr. Elizabeth Amin for providing the molecular model of Ziagen for the cover

A special note of appreciation goes to the many staff members over the 70-plus years who have contributed in unique and substantial ways to the work that made this departmental history.

Funding for this project was supported in part by the Wulling Endowment Fund and the Department of Medicinal Chemistry at the University of Minnesota.

*Yusuf J. Abul-Hajj
Richard Broderick
April 2012
Minneapolis, Minn.*

Chapter 1

THE AGE OF WULLING

From the very beginning, medicinal chemistry has been an integral part of pharmacy education and research at the University of Minnesota. Although a formal department of medicinal chemistry did not exist at the University until the mid-1930s, today's department can track its origins back much earlier—to 1892 and the creation of the College of Pharmacy.



FREDERICK J. WULLING

The young pharmacist on tour. Portrait by Ostermeyer, 1889, Munich.

The year 1892 was also when the state Legislature, acting at last on the recommendations of the University of Minnesota Board of Regents and the nine-year-old Minnesota State Pharmaceutical Association (MSPhA), voted to appropriate money to establish a school of pharmacy at the University of Minnesota (Netz, 1971).

Following that vote, the University Regents began to look for someone to lead

the new school. Given his youth, the person they discovered might have seemed like an unlikely candidate to serve as dean and founder of the College of Pharmacy.

Frederick J. Wulling bore an impressive résumé, despite his young age. He was something of a prodigy in the New York City worlds of pharmacy, medicine, and teaching at some of the city's most important institutions of higher learning.

While still a teenager, Wulling had taken an apprenticeship with a Brooklyn pharmacist. After reading about medicine and studying botany with the family physician and a local pharmacist, he enrolled in the College of Pharmacy of New York—which would eventually become part of Columbia University—and immediately requested, and was granted, a transfer to that year's graduating class. Wulling then entered Columbia University's College of Physicians and Surgeons, where one of his professors, Dr. Peter Bedford, convinced him to pursue a degree in pharmacy prior to studying medicine. At the same time, Bedford appointed him as his classroom assistant—a lecture demonstrator—a title soon elevated to assistant lecturer. "The promotion followed an incident when Bedford, arriving back in New York from a lobbying trip to Albany later than he'd expected, walked into his classroom in time to hear the end of Wulling's impromptu lecture delivered in Bedford's absence. Impressed by his protégé's performance, Bedford declared that Wulling was "the only student in the world who is an unofficial faculty member, but who possesses the qualification of a full faculty member" (Wulling, 1944).

Although Wulling debated between a career in medicine and pharmacy, pharmacy education ultimately attracted him in the end. During his apprenticeship and education, he explained his choice in an undated talk, "Why I Entered Pharmacy." He said, "I became aware of two facts: First, that medical men were, except in comparatively few cases, quite insufficiently qualified in materia medica and therapeutics and hence in prescription writing...[and those who were mostly educated in Europe]. ... The second fact I discovered was an inadequacy on the part of pharmacists of a sufficient qualification in their own field, especially in the science divisions. There were no practical standards and requirements in those days in medicine or pharmacy comparable with those of today."

In 1886, Wulling further burnished his credentials when he was hired to head a prescription dispensing laboratory in a private New York hospital, where he was put in charge of expanding the facility to include laboratories for pharmaceutical manufacturing, clinical microscopy and chemistry, and research. Soon he took on the job of consulting pharmacist for the whole hospital as well. In his spare time, he traveled to Europe in 1887 and 1889 and played first violin in an amateur orchestra. In 1891, he joined the faculty of the Brooklyn College of Pharmacy as chair of a discipline called "pharmacodynamics." By this time, he had also developed a sideline performing clinical microscopy and writing and editing articles for journals such as *Pharmaceutical Record*. All together Wulling's teaching, writing, and laboratory

work was earning him a more than comfortable income of \$6,000 per year.

Having already remarked upon Wulling’s “exasperating efficiency mitigated by a winning friendliness,” Bedford would be among those who enthusiastically recommended Wulling to the University of Minnesota when the school began looking for a dean and principal faculty member at its proposed School of Pharmacy (Wulling, 1944).

In turn, what lured the accomplished and cultivated Wulling to the relative backwoods of Minnesota was this once-in-a-lifetime opportunity: the prospect of organizing the state’s first university-based school of pharmacy.

The opportunity was a challenge that the short, balding, but supremely self-confident Wulling could not pass up. It would turn out to be a challenge that, over the next 10 years, not only severely tested his formidable organizing skills and powers of persuasion—not to mention his equally formidable willpower—but also brought him on several occasions to consider resigning his new post as dean of the University of Minnesota’s School of Pharmacy and return to the more congenial (and certainly more lucrative) climes of the East Coast.

An Idea Germinates

The idea of organizing a school of pharmacy began to germinate about a decade before Wulling’s arrival in Minnesota. Until 1881, no pharmacy regulations existed in Minnesota. Nonetheless, since dispensing prescriptions and other medications was seen as a lucrative profession, the field drew a host of practitioners, including some qualified and many not.

That year, the Minnesota Legislature began to move toward licensing the field, passing an act forbidding the sale of “drugs, medicines, or poisons, except by registered pharmacists” (Anderson & Pennigton, 2005, 5).

Two years later, in 1883, a number of prominent St. Paul druggists, including William A. Frost, W. S. Getty, George Marti, and Fred Kult—no pharmacist from Minneapolis was present, a signal of the relative status of the two cities at that time—met at McMasters and Getty’s Drugstore, located on Third Street in St. Paul. The participants formed a committee to draw up a charter for the Minnesota State Pharmaceutical Association (MSPHA), in which articles of incorporation included a call for the creation of a statewide college of pharmacy. Those articles were adopted at a subsequent meeting a week later and the pharmacy association was officially launched (*ibid.*, 5).

In 1885, the Minnesota Legislature finally acted to fully regulate the licensing and oversight of pharmacy, passing laws mandating that in order to be registered as a pharmacist an applicant needed to be 21, have a degree in either pharmacy or medicine, pass an examination given by the state board of pharmacy, and have four

years' experience working in a drug store. The bill also specified how poisons such as belladonna, digitalis, potassium cyanide, and others were to be labeled, and, in recognition of pharmacy's status as a profession, exempted those covered by the act from jury duty. In 1886, the new MSPhA began actively lobbying for the creation of a college of pharmacy at the University of Minnesota.

The time was right for such an effort. "The Education of a Pharmacist," a pamphlet from the mid-1880s, noted that, "We live in an eminently practical age. ... The value of any education is in direct relationship to its utility in the struggle for



University of Minnesota presidents Cyrus Northrup (left) and William Watts Folwell (right), 1892.

existence. ... We now want true colleges of pharmacy and true pharmaceutical teaching." The pamphlet goes on to call for coursework that offered knowledge of how "to store, mix, and prepare drugs, follow the law and identify compounds in drugs, and use laboratory tools" (Eccles, 1885).

By then, a number of states, including Michigan and Wisconsin, had heeded the call for the professionalization of pharmacy and the need to locate such training within institutions of higher learning. The universities of Michigan and Wisconsin were two of the earliest schools to create pharmacy colleges. State pharmaceutical associations had also spread across the country.

For five years, Minnesota's pharmacy association pushed the Legislature to ap-

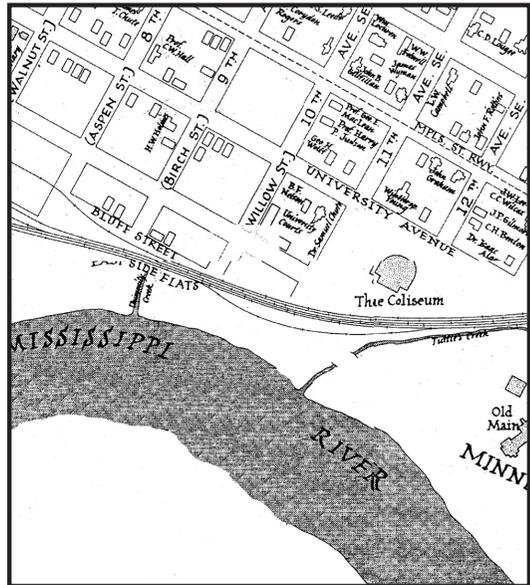
propriate \$100,000 for establishment of a pharmacy college at the University. Finally, its efforts paid off, although not as generously as association members had hoped. In 1891, the Legislature appropriated a mere \$5,000 for the creation of the new school, and even that money was mostly earmarked for laboratory equipment. No money was set aside to build a laboratory or for instruction in any course except in the basics of pharmacy, all of which were to be provided by whomever was hired to run the college. The remainder of courses were to be furnished by existing departments at the University and paid for out of those departmental budgets. Without the Legislature intending it, the parsimonious appropriation was a formula for years of conflict within the University's Department of Medicine—where pharmacy was to be housed—over scarce resources.

In addition to lack of funding, there were other reasons why the establishment of a college of pharmacy in Minnesota faced a rocky start (Wulling Collection, undated, 12).

The emergence of pharmacy as a separate discipline was still underway by the time Wulling arrived in Minnesota. Until the mid-19th Century, many American apothecaries were also physicians. In fact, soon after its founding in 1852, the American Pharmaceutical Association conducted a survey of apothecary shops in several states and discovered that only a small fraction of them were owned by individuals actually trained to "prepare and compound drugs." And an even smaller percentage was college graduates with any kind of degree whatsoever.

Meanwhile, during the late-19th Century the debate over the place of professional schools within university settings was far from settled. Originally conceived as centers of the liberal arts that included theology, American universities were undergoing wrenching changes. In response to industrialization, urbanization, and other forces, universities were transformed into centers of both basic and applied scientific research as well as home to professional schools; medicine was one of the first to make this inroad (Higby, 2005).

This was the backdrop against which Daniel Noyes, a University of Minnesota



Map of Southeast Minneapolis, 1889.

regent who was the head of a wholesale drug import company, sent Wulling a letter on March 17, 1892. Noyes informed the young scholar and scientist that a committee created by the Board of Regents to organize a pharmacy department had unanimously chosen him to be the first dean of the College of Pharmacy. The letter coincided with a visit to Wulling's home in Brooklyn by David Kiehle, another regent who also served as Minnesota's State Superintendent of Schools, to confirm the offer.



"Old Main" in 1885 was located on the present site of Shevlin Hall. It was destroyed by fire in 1904.

Wulling made it clear that he was interested, but would have to think it over. In the meantime, he received letters from Dr. Perry Millard, dean of the College of Medicine and Surgery, telling Wulling that, if he accepted the offer, he'd be starting the following fall with some 30 students. Dean Millard also offered details for a proposed new building that would contain a laboratory big enough to accommodate as many as 35 students and office space for the new pharmacy dean.

Thus reassured, Wulling made the trek to Minnesota to meet with President Cyrus Northrop, Dean Millard, and others to discuss his possible appointment. Arriving at the University early in May 1892, he found the physical surroundings spare to the point of spartan. At the time the campus consisted of only a handful of buildings and virtually no landscaping to mitigate the dreary impression made by the grounds.

It was not just the campus that struck Wulling as a little on the bleak side; it was also the buildings themselves and the facilities they contained.

President Cyrus Northrop's offices were in Old Main. The outer office as well



Perry Henry Millard, dean of the College of Medicine and Surgery, University of Minnesota.

as Northrop's own chamber were, Wulling recalled, "bare and unattractive," with an inner sanctum furnished with a small plain table and two chairs.

Fortunately for the history of medicinal chemistry at the University, the two men connected instantly. Wulling recalled that, after shaking Northrop's hand and being invited to sit, his first words to the young Wulling were, "You must be an angel." A little nonplussed, Wulling demurred, answering that if he were an angel, he must still be in training since he hadn't yet sprouted any wings. Wulling then asked a question that revealed much about his state of mind at that moment: Why did Northrop, who'd been a faculty member at Yale, leave the East Coast to take up his current position in Minnesota? To which Northrop gave just the right response to clinch the deal. "For the same reason you are thinking of coming: Because here are bigger opportunities for doing effective and much needed work for and in education" (Wulling, autobiography; Wulling Collection, 3).

After outlining some of the difficulties and disappointments he himself faced in his eight years on the job, such as a public indifference as reflected in a Legislature that (as with pharmacy) was reluctant to allocate sufficient resources to the University, Northrop sent Wulling to meet the man who would prove to be a challenge in the next few years: Dean Perry Millard. It was not an auspicious send off. Northrop confided to Wulling that the two "pressure groups" that gave him "the most headaches" at the University were the physicians and surgeons—a complaint that Wulling would soon share. This additional meeting ended with an ambiguous answer to Wulling's question of whether the dean of the College of Pharmacy would be answering to Millard or to the president. "He advised me to make every reasonable effort to work with Dean Millard, but in "case of trouble" to come to him—that his door would always be open," Wulling later wrote (Wulling, 1948, 36).

Shortly thereafter, he met with Millard where he found himself in yet another ambiguous discussion, this time about lines of authority; though Wulling at first found Millard "friendly and apparently not at all the dictatorial person he was said to be." Millard claimed to be largely responsible for the formation of all the departments and colleges in the Department of Medicine and expected their heads to take direction from him. He and Wulling had their first contretemps at the meeting when, after Wulling stated that it was his understanding that the College of Pharmacy would be located in Medical Hall (later named Millard Hall in 1906, pictured

on p. 24), Millard replied, "Don't you believe it. There's no room for you in that building. You'll have to find quarters in some other college building" (*ibid.*, 38).

Wulling then asked if pharmacy might be housed in the inadequate space of a temporary building known as the Bowling Alley because of its layout and that was also home to physiology, histology, and medical chemistry (predecessor of biochemistry) but again Millard said no (Kohler, 1982). He then told Wulling that as dean of the new school he would have to plead personally with the heads of several departments to see if pharmacy students would be allowed to attend classes in materia medica, bacteriology, medical chemistry, and other subjects required for graduation. Millard also made it clear that the degree course in pharmacy would be only two years and yet result in a D.Pharm., because doctorate was the only degree granted by the medical school. Wulling objected, but made no headway. It would be several years before he managed to expand the degree program to the four years he wanted in the first place.

Wulling spent the next few days making the rounds of department heads and faculty members in medicine and science, meeting, with few exceptions, with resistance and sometimes barely concealed hostility to the suggestion that pharmacy students be able to attend classes in other disciplines as originally envisioned. Only one faculty member, Conway McMillan, head of the department of botany, had even heard of Wulling because the latter was known for his lectures and articles on the evolution of botany. McMillan greeted Wulling as a colleague and immediately agreed to accept pharmacy students into his department's classes (Wulling, 1948, 44).

Returning to Brooklyn, Wulling sent a letter to Millard and Northrop detailing the conditions he gave to Regent David Kiehle for accepting the job as dean of the College of Pharmacy. The conditions—demands really—included:

1. There would be adequate laboratory space for instruction in "practically every subject of the curriculum" and cooperation from other departments and colleges at the University "to whom pharmacy students would have to be sent for the present for such instruction."
2. That the faculty and equipment would be increased as needed.
3. That the \$5,000 appropriated by the Legislature be used only for equipment and not for buildings or salaries.
4. That \$10,000 be appropriated at the next session of the Legislature for additional equipment.
5. That the degree program be expanded from a two- to a four-year program by the time the first class finished the two-year program.



The first home of the College of Pharmacy was called “Medical Chemistry Building” and was located where Johnston Hall now stands. In 1892 the College of Pharmacy was allocated 2,000 square feet in the center of the building, dubbed the Bowling Alley because of its shape. The College’s space is identified in Dean Wulling’s own handwriting. Later the building was occupied by the Chemistry Department, and then became the general storehouse before its demolition in 1924.

6. That the College not be subject to the medical college or any other college or department but answer directly to the Regents while given the latitude to administer its own affairs.
7. That the curriculum for the College be created exclusively by the pharmacy faculty.
8. That provisions be made for establishing a medicinal plant garden, a pharmacy library, and pharmacy museum to be housed in the College.
9. That two research fellowships be established in pharmacy.
10. That he have free hand to establish entrance exams and be supported in “the rapid development of the school.”
11. That pharmacy be a major leading to a doctorate.
12. That he be provided with an assistant right away and others as needed over time.

Other conditions included a provision that in short order he would receive a salary of about \$6,000 to offset the income he had been earning from his “business, editorial work, private students, clinical microscopy, and college position” (Wulling Collection, letter to Dean Perry Millard, 1892).

Wulling never received an overt acceptance of his conditions from either Millard or Northrop. Nonetheless, he made up his mind to make the leap, and thus showed up in Minneapolis in August 1892, determined to have everything in order for when the new College opened its doors to students just two months later.

He immediately ran into obstacles that might have defeated a more faint-hearted individual. To begin with, Dean Millard proposed postponing the start of the College until the Legislature appropriated money for a new pharmacy building—a delay that in all likelihood would have doomed the whole enterprise for another decade or more. Realizing that he would not, in fact, be given space in Medical Hall, Wulling renewed his efforts to get into the Bowling Alley, lobbying faculty in physiology, histology, and medical chemistry, all of whom had space in the building. At first he met with refusal but eventually was able to wrest a small space—about 40 square feet for a laboratory—in the Bowling Alley but no space for a lecture hall or office. He ended up sharing a lecture room and office in Medical Hall with a faculty member who taught *materia medica*. Meanwhile, Dean Millard turned down his request for two additional pharmacy faculty members, a laboratory assistant, and a part-time office assistant, informing Wulling that he was expected to teach all the pharmacy coursework beyond what already existing departments were willing to supply.

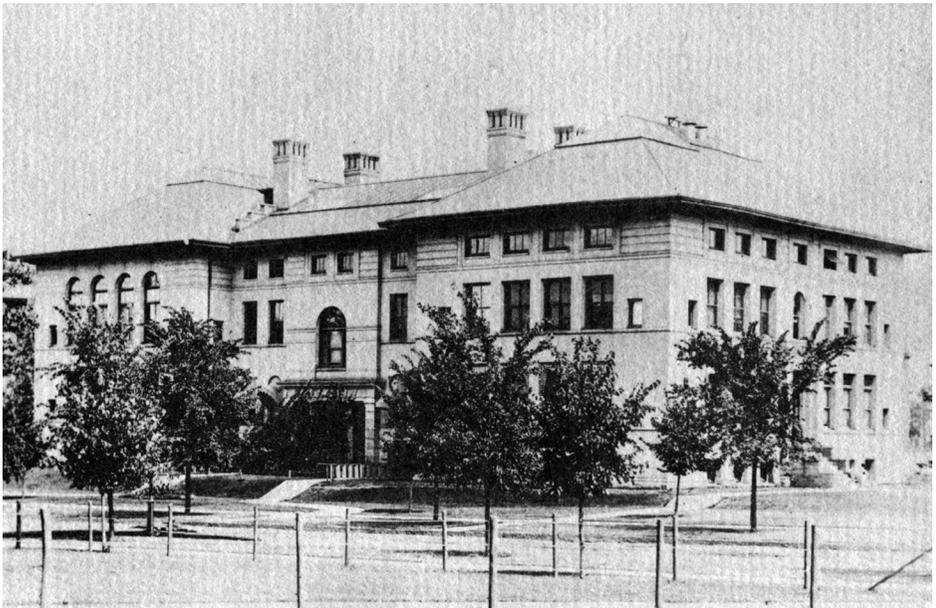
The College of Pharmacy began life, then, as a one-person college, although the faculty for the College listed in that fall's bulletin included Wulling, listed as “Professor of Theory of Pharmacy and Pharmacognosy,” H. M. Bracken, “Professor of *Materia Medica*, Toxicology, and Physiology,” C. J. Bell, “Professor of Chemistry,” and the aforementioned Conway McMillan, “Professor of Botany.” Among the courses Wulling taught those first years were classes in pharmaceutical chemistry.

Meanwhile, the course catalog, largely penned by Millard before Wulling had a chance to give his input, listed the new College of Pharmacy, as part of the “Department of Medicine.” Graduation requirements included four years of practical experience dispensing drugs, a provision sought by the state's practicing pharmacists, even though Wulling objected to this provision because of “the inconsistency of a University diploma covering a requirement over which the University exercised no supervision,” as he later wrote. Eventually, both the University and the state pharmacy association ended up accepting the two years spent in the College of Pharmacy as counting toward the four-year requirement. In 1895, the Regents dropped the stipulation altogether when it became clear that it was impractical for the University to act as preceptor for in-store work experience.

The 1892 school year began with less than half of the 14 students entering pharmacy meeting the entry requirements that Wulling already felt were too low; the requirements did not even include a high school degree. The first student admitted was Arthur Von Rohr of Winona. The second was Lucy Blanchard of St. Paul. Tuition for the two-year program was \$165. Classes commenced with a lecture by Wulling the morning of October 5, 1892. The average age of his students was 22. Wulling was 26. There were six students in all, each of them granted a Pharm.D. upon graduation in 1894.

It was a rigorous and, to Wulling's mind, underpaid job that he'd taken on. That first year, he spent 21 hours a week in the classroom or laboratory with students, while also attending to the administrative tasks of running the College. His official title was Dean and Professor of Theory and Practice of Pharmacy and Pharmacognosy, teaching courses in physiology, pharmacy Latin, pharmacy theory, and pharmaceutical chemistry (medicinal chemistry), in short, everything except chemistry, materia medica, and botany.

In November 1892, Wulling received an unpleasant surprise when he discovered that his salary amounted to \$1,800 a year, not the \$3,500 he thought he was to receive. That spring when the Regents rejected a proposal to raise his salary to \$2,500 per year, he turned in a letter of resignation—his first—which was rejected by President Northrop.



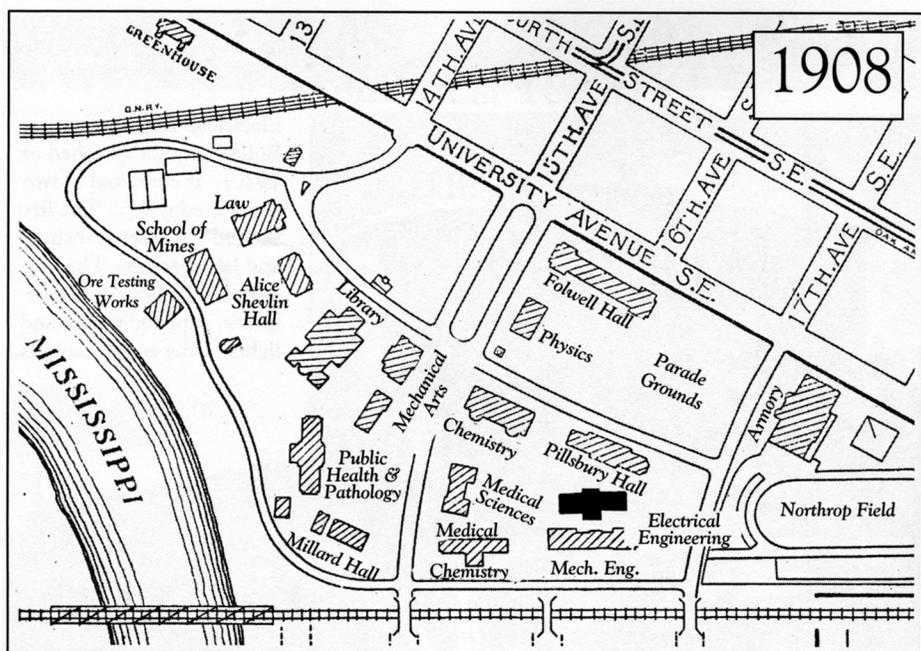
Laboratory of Medical Sciences Building, second home of the College of Pharmacy, 1894-1916. Pharmacy was accessed by the side entrance, the College of Dentistry via the main entrance. In 1912, the structure was renamed the Dentistry Building and in 1932 named Wesbrook Hall, which was demolished in 2011.

More unhappy news soon followed. Dean Millard tapped almost \$2,000 of the paltry \$5,000 legislative appropriation to help pay bills for the Department of Medicine. Confronted by Wulling, Millard refused to restore the money. Only two years later did President Northrop restore the lost funding.

The Board of Regents also “were cold to the idea,” as Wulling described it, of building a separate facility for pharmacy, even though this objective had been endorsed by the state pharmacy association. Eventually, the Legislature appropriated \$40,000 for what did not become the pharmacy building but rather the Medical Science Building.

Eventually, the College of Pharmacy would be allotted about a quarter of that building’s space.

In the spring of 1894, the mystery of his salary was finally resolved when he was called to a meeting with then-Governor Knute Nelson, an ex-officio member of the Regents, to discuss his compensation. There he got the bad news—the \$3,500 salary



A 1908 campus map shows the locations of the sites of the Medical Sciences, Medical Chemistry, and Millard Hall. These buildings housed the pharmacy program.

he'd been expecting had never been authorized, and the University representatives who initially contacted him had been under the misapprehension that the \$5,000 the Legislature had appropriated for the College included money for his salary. He did, however, come out of that meeting with the governor with a commitment to a

\$200 a year raise, bringing his salary to \$2,000 per year. It would not reach \$3,500 a year until 1907, 15 years after he started at the University.

By the end of the 1895 school year, the original appropriation of \$5,000 was exhausted and the Regents allocated about \$1,000 for the following year's operation. The next year, \$1,820 was appropriated by the Regents to furnish space for pharmacy in the laboratory of the Medical Science Building.

For 1896-97, the Regents were even stingier, granting only \$630 to pharmacy; Wulling had requested \$2,000 for supplies and equipment. "Our stock was thin, and living from hand-to-mouth was not conducive to the best kind of work nor to happiness. We never had enough microscopes. They were expensive," he complained. On the other hand, he wrote, "Medicine seemed able to get all they needed." Indeed, the College would remain underfunded until 1911, when efforts by Wulling and the state pharmacy association resulted in a legislative appropriation he finally considered adequate (*ibid.*, 116-29).

The laboratory of Medical Science Building opened early in 1896; the College of Pharmacy would remain there until it was moved to a reconstructed Millard Hall in 1913. Until that move, space would continue to be an issue. By 1898, pharmacy had 54 students enrolled and was bursting its seams when the Medical College threatened to boot the College of Pharmacy from the storage space it occupied in the basement of Medical Science. Wulling averted that crisis by agreeing to a humiliating compromise in which his College would physically vacate the disputed area for two months in the winter to make way for an animal surgery course; in return, pharmacy received portable storage cases that Wulling himself designed (*ibid.*, 168-70).

Cultivating the Pharmacy Profession

Despite all the problems, Wulling soldiered on, slowly building up the College and laying the groundwork for the Department of Medicinal Chemistry.

He continued to work like a navy, some days teaching five or six hours at a stretch, but in his second year on the job, he managed to acquire money to hire student assistants for \$100 a year plus free tuition. In 1893, tired of the constant power struggles within the Medical Department, the Regents relented to Wulling's repeated requests and turned pharmacy, along with homeopathy, dentistry, and medicine, into separate colleges reporting directly to the President. Late in 1895, the Regents approved the creation of a graduate program in pharmacy.

Two years later, the Regents acquiesced to his recommendation that the College no longer give out doctorates to students graduating with a two-year degree. A Masters of Pharmacy degree (Phm.M.) was created for students who completed an additional eight months of study beyond the basic two-year program, which now

granted a pharmaceutical chemist degree (Ph.C.). Students who completed yet another eight-month program beyond the masters' requirement were granted a Doctor of Pharmacy (Phm.D.), although neither of these advanced degrees were under the auspices of the University's Graduate School—that switch would not occur for another quarter century (Netz, 1971, 19). Meanwhile, in June 1898, entrance requirements for the College were finally raised to a point that met Wulling's approval (Wulling Collection, autobiography, undated).



The medicinal plant garden was located south of the University.

One of Wulling's most important steps in advancing medicinal chemistry at the College was his creation of small medicinal plant gardens that he established on the property of his own home in South Minneapolis and on a small plot of land on the south side of the Bowling Alley, and then, later, on the south side of the Medical Sciences Building (Netz, 1971, 190).

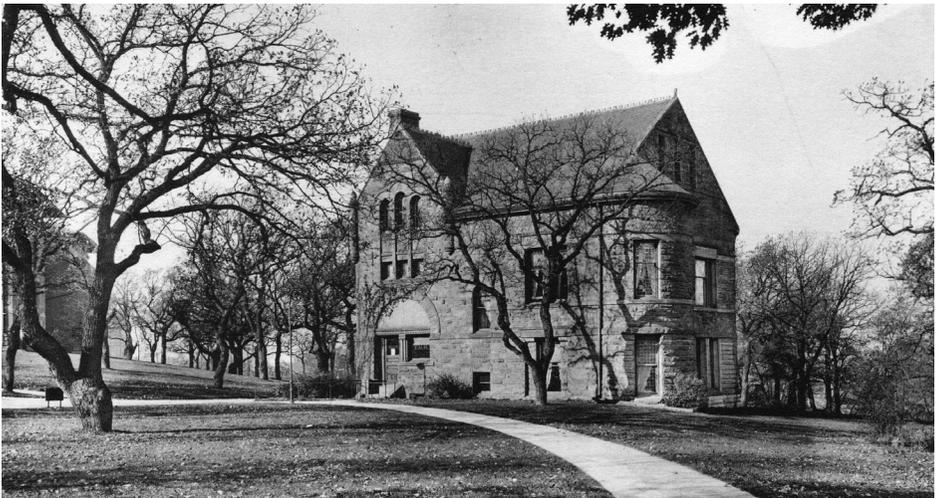
The two initial plots included only some 20 species of medicinal plants, including digitalis, belladonna, aconite, stramonium, larkspur, peppermint, and ricinis. Nonetheless these medicinal gardens were, in Wulling's mind, key to a deeper understanding of the substance and actions of pharmaceuticals. At the time the College of Pharmacy opened, most drugs were derived from plants. Sometimes, the actual plants—or the active parts (roots, stems, aerials, seeds, or berries)—were delivered in bundles to local dispensaries, sometimes ground up as dry powders or dissolved in tinctures. In any case, Wulling's insistence on creating a garden was

inseparable from his belief that pharmacy students should have a practical, hands-on understanding of the natural sources of the drugs they would be prescribing (Anderson & Pennigton, 2005, 13).

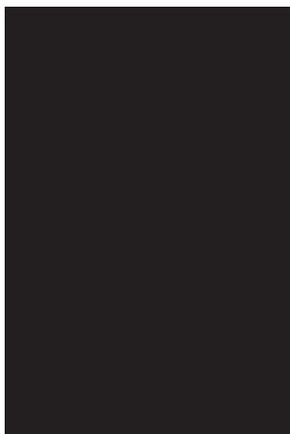
As usual, though, development of the College's medicinal gardens—and associated facilities needed to study the products of those gardens—did not follow an orderly process of development, but faced the kind of frustrating setbacks and delays Wulling encountered in almost every direction.

In 1900, he was granted a much larger space behind the Medical Sciences Building for growing medicinal plants—a 100 by 200 square-foot plot of land allotted for “a botanical garden provided no expense be incurred.” There was one big problem, however. That spring, when Wulling and several student volunteers began cultivating the site, they discovered that it had been used as a dumping ground for construction materials and needed to be restored with several feet of fresh topsoil before it could be planted. With no money appropriated for such an expenditure, development of the garden at that site was postponed a decade.

In 1909, the College's permanent faculty was expanded by the addition of Dr. Edward Newcomb, hired to take over for Wulling as professor of pharmacognosy. Newcomb had previously taught at the Philadelphia College of Pharmacy. Although the new faculty member was younger and less experienced than Wulling had initially wanted, Wulling was attracted by Newcomb's experience in horticulture and drug plant culture. It was, he wrote, just what was needed to develop “our drug garden nucleus into a representative garden.”



The Students Christian Association Building. This 1908 photograph shows the building with its new name, the YMCA Building. It is known in 2011 as the Music Education Building, but is not currently occupied.



EDWARD L. NEWCOMB

B.S. 1905, Philadelphia College of Pharmacy
M.S. 1914, University of Pennsylvania
Instructor 1909; Assistant Professor 1911-15;
Associate Professor 1915-19;
Professor 1919-27, University of
Minnesota.
Born, Pennsylvania, 1918.

Soon after joining the faculty, Newcomb took the lead role in transforming the medicinal plant gardens into a world-renowned facility widely considered one of the best in the country and internationally acclaimed for its great variety of medicinal plants under cultivation (*ibid.*, 316).

In January 1926 Newcomb took a leave of absence to become general representative of the National Wholesale Druggists Association in New York City. He resigned his university position in 1927 to become secretary and vice president of that organization and was one of the founders of the American Foundation for Pharmaceutical Education (Netz, 1971, 64).



Medicinal plant garden, circa 1922. Considered to be the first and most representative garden of its kind in America, it contained upward of 300 species representing about 70 percent of drugs commonly in use; however, the plants in the garden were cultivated for educational purposes only. Men's Union to the left, Pillsbury Hall to the right, and Folwell Hall in the distance.

The next year, Wulling took \$500 that the Regents finally granted for enlarging medicinal plantings—he originally had requested \$24,000 for this purpose—and, matching the Regents' money with \$500 of his own, he spent most of the summer of 1911 touring medicinal plant gardens in the United States and Western Europe. On the voyage home from Europe, he drew up specifications for a new garden at the



Students clearing and plotting the medicinal plant garden.



Half a century of leadership—the first four presidents of the University of Minnesota, from left: William Folwell, Cyrus Northrop, George Vincent, and Marion Burton; they met on June 18, 1918 to mark the 50th anniversary of the University of Minnesota. Note: “Peeping Toms” can be seen at right rear.

University that would achieve his goal of becoming “representative.”

For some years, Wulling had been taking pharmacy students on spring botanical tours of Minnesota and Wisconsin. With the arrival of Newcomb, these tours began to emphasize the riparian environment along the Mississippi River from the University campus to Fort Snelling, a region particularly rife with plant species possessing medicinal value. Over time, plants from this stretch of the river were transplanted to the grounds of the University's medicinal gardens.

Newcomb also took charge of planning and overseeing construction of a consolidated medicinal plant garden on a site where Northrop Auditorium now stands.



The medicinal plant laboratory adjoined the main pharmacy building by a tunnel, 1913. Its basement was used for drying, milling, and garbling. The upper floor was used to start plants from seeds in early February and March, which were then nursed for outdoor planting. Approximately 325 species and varieties of drug plants were developed from seeds in the greenhouse.

Students carried out the actual work of clearing and plotting the garden. Later a plant house with drying ovens, a drug mill, a facility for growing aquatic medical plants, and a heated tunnel connecting the facility to the building where the College was housed was built.

The new plot and plant house soon became the “representative garden” Wulling had dreamed of. By 1912, the College was offering assistance to a dozen other schools intent on setting up their own drug gardens, and, in addition to his other titles,



Greenhouse interior showing a variety of medicinal plants ready to be transplanted outdoors.

Wulling was named director of the University Medicinal Plant Gardens (Wulling, Collection, autobiography, undated).

Until then it had been widely assumed that growing conditions in the United States were not conducive to producing a wide enough array of medicinal plants and that the country had to rely on imports to fill its needs. Based upon his long study of botany and personal knowledge of the abundance of flora along the Mississippi, Wulling thought otherwise. Under his tutelage the University's medicinal garden was responsible for a number of advances, including the discovery that plantain,



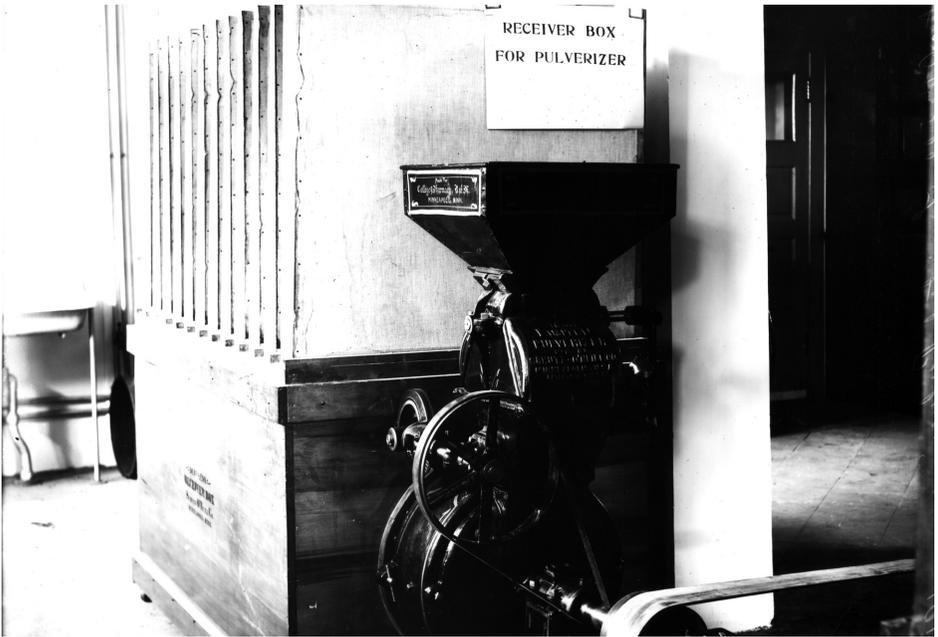
Members of the U.S. Navy collecting foxglove plants to make tincture of digitalis used by the American military during World War I, 1917-18.



Students did most of the work of indoor and outdoor planting, harvesting, garbling, drying, milling, assaying, and converting plant parts into medicinal preparations.



Students extracting active ingredients from digitalis.



Shutz O'Neil Limited Disintegrator, 1914.

abundant in Minnesota, was a source for psyllium seed, and that wild rice, quack grass, and wheat could be a source of ergot.

Within four years, the medicinal plant garden was nationally recognized for the groundbreaking research emanating from it, especially in the study and development of digitalis. By 1916 it had a greenhouse, drug plant, and milling laboratory, and was recognized for its advances in digitalis research (College of Pharmacy, 1992).

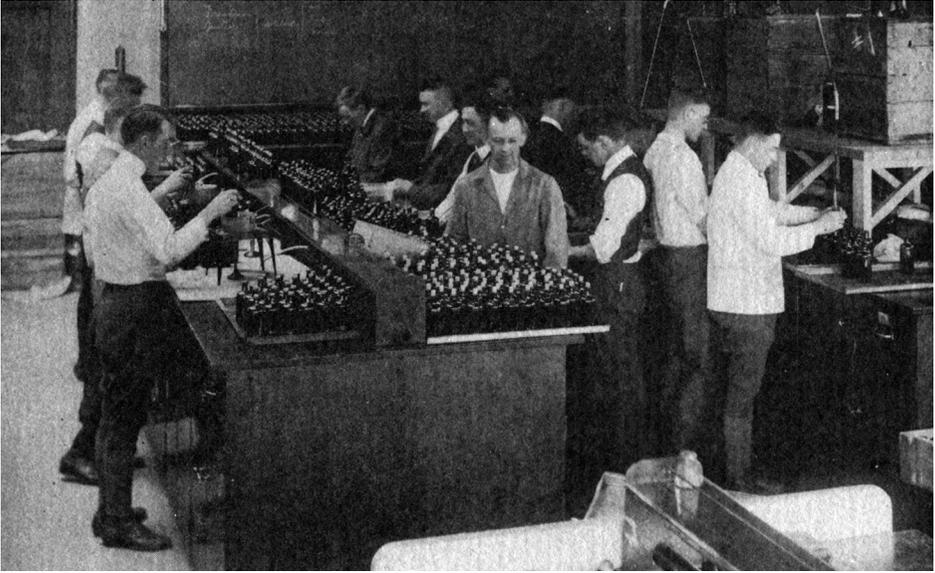
By then, the outbreak of World War I had caused a steep decline in drug importations, leading to a scarcity of medicinal plants and consequently a rise in prices for products made from them. The price of belladonna, for example, increased 700 percent by the time the United States entered the war in April 1917. In response, the Department of Agriculture called for a concerted effort to increase the domestic production of all drugs, including those derived from plants (Worthen, 2007).

Wulling reacted to the call of war with characteristic energy, contacting the Surgeon General of the Army and offering the services of the College to back the war effort. The Na-



Mucilage straining device, 1914.

tional Research Council responded asking Wulling that the College be prepared to supply all the digitalis the army might need—a request that the University went on to fulfill, setting aside two acres of the medicinal plant gardens to the exclusive cultivation of foxglove—the plant from which digitalis is derived—and shipping, by



View of freshman-junior laboratory, showing students bottling and labeling tincture of digitalis for the U.S. Army.



Various sized percolators in pharmacy laboratory, 1918.



Northrop Hall under construction.



The neoclassical-style Northrop Hall building was completed in 1929.

Wulling's reckoning, some 23,800 8-ounce bottles of tincture of digitalis and 2,000 capsules of digitalis powder to the American Expeditionary Forces before the war came to end (Wulling, 1948, 78).

By war's end, the gardens comprised more than 300 named species and varieties of plant life, from *Atropa belladonna* to *Thymus vulgaris* to larkspur, peppermint and *Datura stramonium*. The garden also included century plants and banana and rubber trees—the last two transplanted to the site from President Northrop's home. The College of Pharmacy's leadership in medicinal plants led to the University's first plant science seminar in 1921, and, eventually, the formation of the American Society of Pharmacognosy (Worthen, 2007, 656-7).

Despite the acclaim, the very next year, pharmacy was informed that the plant garden constructed only 10 years earlier was going to have to make way for the construction of Northrop Hall.

The garden was to be moved into an old garden and greenhouse space on University Avenue operated until then by the Department of Botany, which was building new greenhouse facilities elsewhere. Transfer of the pharmacy garden was completed in 1927 (Netz, 1971, 65-7).



Third home of the College of Pharmacy, built on the foundation of the former Millard Hall after it had been destroyed by fire, which was officially designated Wulling Hall by the University Regents in 1942. Part of the medicinal plant laboratory can be seen on the right. The building was the home of the College of Pharmacy from 1916 to 1961.

Fires Bring Progress

During the first two decades of the 20th Century, the chronic space problem that had plagued the College of Pharmacy from the very beginning was also finally solved—but here again, not without major setbacks that included, improbably enough, not one, but two fires.

Frustrated by the Regents' failure to provide adequate facilities for pharmacy, Wulling resorted to one of the tactics that he'd used before to break logjams. In 1909, he again submitted his resignation to President Northrop (himself on the verge of retirement) but withdrew it when, shortly thereafter, the Board of Regents voted to request funds from the state to construct two new medical buildings and to

bequeath Millard Hall to the College of Pharmacy; in a twist of fate or perhaps poetic justice, Millard Hall would be renamed Wulling Hall in 1942.

Although Millard Hall did not have the layout or space pharmacy needed, Wulling accepted the arrangement, especially since it was considered to be a temporary fix until a new permanent facility could be constructed in the next few years. The move from Medical Sciences into Millard was set to go when a fire on Christmas Eve 1912 broke out in the building, causing extensive damage and gutting the top floor. A temporary metal roof was erected on top of Millard Hall. Then just three months later, another fire gutted the interior of the rest of the structure. Ironically, the "temporary" roof did not collapse, but during the conflagration all the inside floors collapsed into the basement, leaving behind nothing more than the shell of the four sandstone and brick exterior walls.

In the end, the successive fires were probably a godsend for the College. By now plans had already been announced

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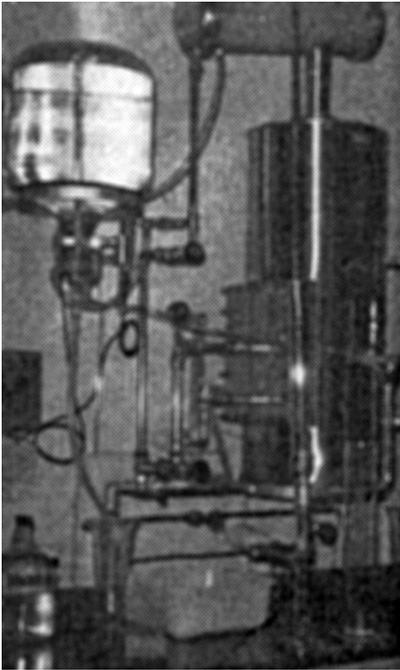
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The "still" was said to be used only for preparing distilled water during Prohibition, 1920-33.

to turn Millard Hall, whose interior floors were made of wood, into a fireproof building. Using a legislative appropriation of \$75,000, plus \$8,000 in insurance money from a fire that had destroyed yet another campus building, the Regents approved the idea of not only renovating Millard but also building a modern greenhouse and plant laboratory right next to it. The structures to be connected by a tunnel (Netz, 1971, 40-1).

Wulling Hall finally opened its doors to the College on September 17, 1913. It had begun as Medical Hall, underwent a name change to Millard Hall, and then called the Pharmacy Building before eventually being named after its most ardent supporter. The building featured four stories and a sub-basement. It was fireproof, with an outer shell of steel and concrete. Dedicated solely to pharmacy teaching and research, it was thoroughly modern and offered state-of-the-art features like equipment to produce distilled water, steam heat

controlled by thermostats in every room, maps, charts, 5,500 microscope slides, prescription and analytical balances, compound microscopes for every student, centrifuges, refrigerators, drug-drying ovens, animal cages, sand and water baths, refractometers, and more. Connected by tunnel to the building was the medicinal plant laboratory where plants were propagated before transplantation to the outdoor garden. Both the medicinal garden and the new buildings made a splash, with articles appearing in American, European and Latin American drug journals (*ibid.*,

31). Ultimately Pharmacy/Wulling Hall would serve as home for the College of Pharmacy until the 1960s.

The budget for the school likewise climbed. For the academic school year of 1898-99, the Regents appropriated a meager \$1,500 for supplies and equipment; another \$200 for books and

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CHARLES H. ROGERS

B.S. 1913; M.S. 1915 University of Michigan
Sc.D. 1918, University of Minnesota

Associate Professor, 1914-17, University of
West Virginia.

Instructor, 1913-14; Assistant Professor, 1917-
21; Professor and Head of Pharmaceutical
Chemistry, 1917-36; Dean of Pharmacy, 1936-
57, University of Minnesota.

Born, Bellville, Illinois, 1889; died, Fargo, North
Dakota, 1963.

journals and a stipend for a clerical assistant for Dean Wulling. A little more than a decade later, the school received \$15,000, by which time, Wulling's annual salary had finally reached the \$3,500 that he'd been expecting to receive when he joined the University in 1892. From that time forward, appropriations for the College remained adequate to pharmacy's needs (*ibid.*, 446).

The College was advancing on other fronts as well. By 1907, the school had 99 students enrolled; about a third of them were women. During World War I, the percentage of female students would climb even higher as young men enlisted or were drafted into the military. By the middle of the 1920s, the number of students would climb to almost 150. New faculty members were added slowly, relieving some of the burden on Dean Wulling's shoulders.

In addition to Professor Newcomb, perhaps the most significant new hire took place in 1913. John Handy, an instructor in pharmaceutical chemistry, resigned and was replaced by Charles Rogers. In 1936, Rogers would succeed Frederick Wulling as Dean of the College of the Pharmacy. In doing so, he would finally departmentalize the College—creating, for the first time at the University, a stand-alone department of Pharmaceutical Chemistry (College of Pharmacy, 1992).

Rogers joined the University as an instructor in 1913 and resigned in 1914 to accept a position as assistant professor at the University of West Virginia. He returned to Minnesota in 1917 as assistant professor of pharmaceutical chemistry and completed his doctorate in 1918.

By then, Rogers had already enhanced his own and the University's reputation in pharmaceutical chemistry with publication of his textbook, *Inorganic Pharmaceutical Chemistry*, only the second textbook published by a member of the pharmacy faculty—the other being an earlier book on pharmaceutical chemistry written by Dean Wulling (Minnesota State Pharmaceutical Association, 1930-40).

A Graduate Program is Born

In 1915, pharmacy came out ahead on another bone of contention going all the way back to 1892, when, as Wulling had advocated from the very beginning, a high school diploma became a prerequisite for enrollment in pharmacy. The year before, the University had also instituted a system of optional three- and four-year programs—until then, students only had to go for two years to get their degree; two years later, the programs were no longer optional, but mandatory. Both the two- and three-year programs demonstrated the critical role of pharmaceutical chemistry at the College of Pharmacy; the three-year curriculum, for example, required students to take four quarters' worth of pharmaceutical chemistry, for a total of 19 of 67 credits.

In 1926, the three-year program was eliminated and the University became only the second school in the country to adopt a mandatory four-year degree program. The move laid the groundwork for the next major advance for pharmaceutical chemistry at the University.

In 1923 the Minnesota State Pharmacy Association passed a resolution calling on the University to place graduate study in pharmacy under the auspices of the University's Graduate School—a move that had long been pressed by Dean Wulling as well.

But for that to happen, it was necessary that the Regents first approve a minimum four-year course in pharmacy leading to a B.S. in pharmacy, which it did in 1926. The following year—1927—the Regents took the next logical step and approved graduate programs for both pharmacognosy and pharmaceutical chemistry to be offered through the University's Graduate School (Netz, 1971). The first Master of Science in pharmaceutical chemistry was awarded only two years later, in 1929, to a student named Louis Maynard (*ibid.*, 67).

Thus was a true graduate program in pharmaceutical chemistry born. The next big step would be the formation of the Department of Medicinal Chemistry. §

Chapter 2

RESEARCH COMES OF AGE

The Great Depression affected the College of Pharmacy as it did every other institution in the country. But even so, the period between 1929 and the Second World War was a time when the stature of the department would continue to rise.

When the stock market crashed in 1929, that same year 27 students graduated from the College with an undergraduate degree in pharmaceutical chemistry. The medicinal plant garden bloomed with some 500 species. Charles Rogers, a faculty member in pharmaceutical chemistry who was long-seen as the eventual replacement for Dean Frederick Wulling, was putting the finishing touches on his textbook, *Inorganic Pharmaceutical Chemistry*, to be published the next year. The book was the first-ever published by a member of the College of Pharmacy faculty, although Wulling had written a textbook before coming to Minnesota. Rogers's book quickly became a standard text in the field for some 20 years, and was then only superseded by another text written in collaboration by University faculty members in medicinal chemistry (Wulling Collection, folder 65, undated; Netz, 1971, 69).

Numerous research projects in both pharmaceutical chemistry and pharmacognosy were underway during this time. Earl Fischer, who had just been appointed to replace Edward Newcomb as head of pharmacognosy, was overseeing studies on the effect of propylene gas on medicinal plant growth, as well as research on one of the staples of the natural products field—digitalis—and in particular investigating the effects of different methods of drying and storing the substance (Minnesota State Pharmaceutical Association, 1930). Fischer was busy in other areas, too, such as analysis of ash derived from 300 drugs then on the market. That year the pharmacognosy program was also the beneficiary of research-related gear, including 15 compound microscopes, additional drying racks, cameras, and more (Wulling, 1930; Minnesota State Pharmaceutical Association, 1930).

During this period, Rogers led research into, among other things, the hydrolysis



EARL B. FISCHER

B.S., 1919, Ph.D., 1940, University of Minnesota

Assistant Professor 1922-26; Associate Professor 1926-36; Professor and Head 1936-61, University of Minnesota

Born, Winona, Minnesota, 1893; died, 1961.

of some smoke-producing medicinal compounds and creosote distillation; the latter work would eventually bear fruit in the following decade when he and Ole Gisvold, a new pharmaceutical chemistry instructor, isolated a powerful anti-oxidant that for many years was the standard ingredient added to lard to prevent spoilage (Minnesota State Pharmaceutical Association, 1931).

Gisvold, who had just received his Ph.D. at the University of Wisconsin, was actively recruited by Rogers. Rogers made the drive to Madison to convince him



Microscopes acquired in the 1930s were as essential to research back in those days as nuclear magnetic resonance spectroscopy is an important tool in research from the 1970s to the present day.



OLE GISVOLD

B.Sc. 1930, M.Sc. 1932, Ph.D. 1934, University of Wisconsin

Assistant Professor 1935-40, University of Minnesota

Associate Professor 1940-41, The Ohio State University

Professor and Head 1941-69, University of Minnesota

Born, Stanley, Wisconsin, 1904; died, St. Paul, Minnesota, 1977.

Awards

- APhA Ebert Prize Medal, 1942
- APhA Ebert Prize Medal, 1953
- APhA Research Foundation Award in Natural Products, 1962

to come to Minnesota because of Gisvold's potential as a researcher. As it turned out, Roger's foresight proved correct, as Gisvold ultimately emerged as one of the department's most prominent scientists from the time he arrived at the University until well into the 1960s.

By 1935, Rogers could report to the MSPhA that there were 12 research projects underway at the College of Pharmacy, all of them in the field of pharmaceutical chemistry or pharmacognosy. This included work he himself was leading that was investigating wood alcohol and another collaboration involving him, Fischer, and Gisvold (*ibid.*, 1935). Over the next several years, research projects came to include studies of both natural and synthetic products, including sleepy grass, ergot, and, of course, digitalis. To help with these studies, the pharmaceutical chemistry department acquired a piece of equipment known as a Barnstead Extractor.



Barnstead Extractor.

Two factors helped create additional impetus to pharmaceutical research during this period before the federal government undertook large-scale funding of projects. One was volunteer work by faculty members on the committee responsible for updating the *U.S. Pharmacopoeia*. University of Minnesota participation with the Committee of

Revision began with Frederick Wulling, and continued on under Edward Newcomb of pharmacognosy, and later further advanced under Charles Rogers of pharmaceutical chemistry.

The other factor was the intense activity leading up to and following the adoption of the Food, Drug, and Cosmetic Act of 1938, which greatly expanded and detailed the powers of the Food and Drug Administration (FDA), created in 1906 by the Food and Drugs Act. Among other things, the act gave the FDA regulatory power over the labeling of medical and cosmetic products. Perhaps even more significantly, the act required drug manufacturers to prove that their products were safe for recommended usage before they could be released to the market, a provision that placed a new premium on determining not only what products a medication contained but also how those products might interact with each other in the human body (Anderson & Pennigton, 2005, 23-4).

To keep up with the research load, the number of graduate students admitted had climbed during the decade, even as in the early years the number of undergraduates enrolled in the College of Pharmacy had declined. From 10 graduate students in 1934, enrollment climbed to 29 by the end of the decade, with the first Ph.D.



Karl John Goldner, who was the first graduate student to receive the Ph.D. degree in pharmaceutical chemistry.

in pharmaceutical chemistry awarded in 1938 to Karl Goldner, who later went on to serve as dean of the College of Pharmacy at the University of Tennessee. During this time, the University also began funding for up to seven graduate teaching assistants (Anderson & Pennigton, 2005, 28).

A few years later, the graduate program got another, albeit belated, boost in funding with the establishment of the Melendy Fund. Samuel W. Melendy was one of the founders of the Minnesota State Pharmaceutical Association, a supporter, and eventually a close friend of Frederick Wulling. Melendy was one of the leaders in the drive to establish the College of Pharmacy in the late 19th Century.

Shortly after the College was founded, Melendy let Wulling know that he intended to donate part of his personal fortune to the College. Melendy, however, died unexpectedly in 1916, and the promise of his bequest remained until 1941 when his widow died and left a total of \$100,000 to pharmacy. The money was directed towards several purposes, including undergraduate scholarships, a lecture series, and two \$750 graduate assistantships (Anderson & Pennigton, 2005, 31; Netz, 1971, 88-9).

Of course by far the biggest news of the 1930s at the College was the retirement of Frederick Wulling in 1936, a year after he'd reached mandatory retirement age. The Board of Regents had granted him a special one-year extension in recognition of his contributions to the University. As expected, he was succeeded as dean by



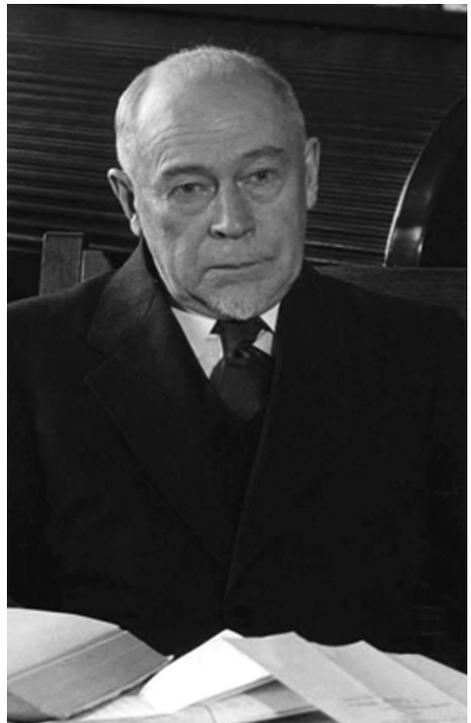
Exhibit of the College of Pharmacy at the Minnesota State Pharmaceutical Association annual meeting, 1934.

University of Minnesota
College of Pharmacy

With affectionate regard and sincere congratulations upon his birthday, this volume is presented on December 24, 1935 by his entire Staff to

Dean Frederick John Wulling
Rt

Waldie Foremost Pharmaceutical Educator	Traver Larson
Frank H. Allen	Charles V. Mey
Ragnar Almén	Edward Park
Eduard Sachman	Nelen Pederson
George Balok	Phyllis Sanchez
George Coasen	Kenneth M. Redke
Carroll B. Fisher	Charles A. Rogers
Oslo Gisvold	Lewis D. Savage
Paul Goldner	Chas. E. Smjith
William Janacek	Ralph F. Veit
Franklin D. Johnson	



An autographed page of a book was presented to Dean Frederick Wulling on his birthday by his staff, 1935.

Charles Rogers, who immediately instituted significant changes to the structure and curriculum of the College.



The faculty and their spouses at the Christmas Lake cottage of Dean Emeritus Frederick Wulling and Mrs. Wulling after a luncheon in honor of Dean Charles Rogers and Mrs. Rogers in September 1936. Left to right, top row: Gustav Bachman, Earl B. Fischer, Ragnar Almin, Mrs. Netz, Ole Gisvold, Frances Larson, Mrs. Johnson, George Crossen, Helen Pederson, Mrs. Smythe. Middle Row: Hallie Bruce, Dean Emeritus Wulling, Mrs. Wulling, Dean Rogers, Mrs. Rogers, Mrs. Fischer, Mrs. Almin, Mrs. Bachman; Lower row: George Balok, Ralph Voight, Frank Johnson, Edward Pavek, Charles V. Netz.

Perhaps the most important change Rogers made was the separation of the College into three departments: the Department of Pharmacognosy, headed by Earl Fischer, who'd been a faculty member since 1922; the Department of Pharmacy, headed by Gustav Bachman; and the Department of Pharmaceutical Chemistry (renamed 30 years later to the Department of Medicinal Chemistry), led by newly recruited faculty member Glenn Jenkins. Jenkins would only remain at the University for five years before leaving Minnesota to become the dean of Purdue's College of Pharmacy. Jenkins was a prolific researcher and a superb administrator as head of the Department of Pharmaceutical Chemistry at Minnesota and later as dean of pharmacy at Purdue University. He published more than 200 research papers largely dealing with the phytochemical and synthetic medicinal chemistry and was the recipient of the APhA Ebert Medal in 1936. Following his departure to Purdue, Jenkins would be succeeded by Ole Gisvold.

By then, Gisvold was head of the Department of Pharmaceutical Chemistry at The Ohio State University, but once again Rogers made his high opinion of Gisvold's abilities clear, tracking Gisvold down while he and his wife were on a fishing trip in



GLENN J. JENKINS

B.Sc. 1922; M.Sc. 1923; Ph.D. 1926, University of Wisconsin

Assistant Professor 1927, University of Maryland

Professor and Head of Department, 1936-41, University of Minnesota

Born, Sparta, Wisconsin, 1898; died, 1979.



Students enjoying sodas in Coffman Memorial Union, 1940.



In 1939-40, Coffman Memorial Union was built to house facilities for student recreation and relaxation. The photograph above shows the building under construction in 1939.

northern Minnesota. Rogers convinced him to return to the University to lead the department.



Research laboratory in Wulling Hall, 1942.

With Gisvold in charge and the addition of new faculty, including Frank DiGangi, Charles Wilson, and Taito Soine, pharmaceutical chemistry at the University continued to rank as one of the top programs in the country.

In addition to projects initiated by the members of the department, a program inspired by the national war effort also provided funding and research material for the University. Sponsored by the Bureau of Plant Industry in the U.S. Department of Agriculture, a phytochemical and pharmacological study was carried out by several institutions of Indian medicinal plants. The University's portion of the project was under the direction of the Pharmacology Department in the College of Medical Sciences, but it involved researchers from other departments, including pharmaceutical chemistry, where research was initially directed by Glenn Jenkins and then by Ole Gisvold after he succeeded Jenkins as department head.

Interestingly, the Indian medicinal plants study did not involve fieldwork by University researchers *per se*. Rather, government representatives interviewed Indian healers in Nevada about what plants they used and why. Armed with this information, these representatives gathered samples of the plants in season, dried them, and shipped them to the University for study where staff members in pharmaceutical chemistry would subject the material to extraction using solvents. The resulting residues were examined for their pharmacologically active components, which



Ole Gisvold in the greenhouse.

were purified and their structures mapped out through a combination of processes.

The program was certainly not on the scale or scope of something as critical as the Manhattan Project, but it yielded research that became the basis for numerous Ph.D. dissertations at the University as well as other important economic benefits.

Gisvold was part of a research team that identified a compound—nordihydroguaietric acid (NGDA)—found in the creosote bush. It proved to have potent antioxidant properties in even small quantities when added to animal fats. A Chicago company, W. J. Stange, was interested

enough in NGDA's commercial applications to enter into a royalty agreement with the University for use of the product. While isolating and producing NGDA was never easy, the compound appeared in lard and other products sold in the United States for nearly 20 years. The money was used in part to fund a post-doctorate fellowship for NGDA research supervised by Gisvold; Gisvold went on to hold a number of patents on the processes of isolating and producing the antioxidant. Still later, NGDA was shown to have effect in combating certain kinds of malignancies, although it did not emerge as a major weapon in the fight against cancer.

Gisvold's stature as a gifted researcher earned him the coveted Ebert Prize, an award given annually for the most outstanding research paper published in the *Journal of Pharmaceutical Science*, not once, but twice: the first time in 1942, the second in 1953. Gisvold is one of the few medicinal chemists to have received the prize more than once (College of Pharmacy, 1977, 5).

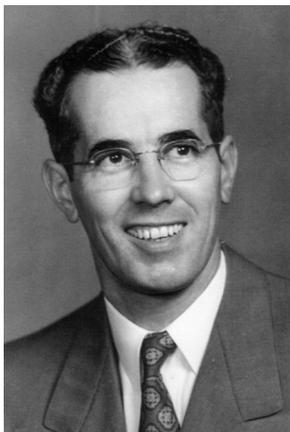
With increases in enrollment and number of research studies, the size of the faculty in the College rose as well, and in a way that reflected the College's changing priorities.

Although the change in absolute numbers was slight—from 10 faculty in 1940 to 11 in 1950—there were critical alterations in a few areas. First, and most impor-

tantly, the faculty recruited to the school were better qualified to carry out research. Secondly, the balance in the College shifted from an almost exclusive emphasis on teaching toward a broader combination of teaching and research on the part of faculty in both pharmaceutical chemistry and pharmacognosy. Research in the 1940s and 1950s continued to focus largely on natural products—isolating and analyzing the structure of their components and determining their pharmacological properties.

After the additions to the faculty of Ole Gisvold and Glenn Jenkins (whose hiring in some ways indicated a new emphasis on research as his first Ebert Award was awarded prior to his joining the College as the head of pharmaceutical chemistry), the College during this period took on several new faculty members with strong research agendas.

In 1940, Charles O. Wilson was appointed to the faculty in pharmaceutical chemistry. Although he would leave Minnesota in 1948 to eventually become dean



CHARLES O. WILSON JR.

B.Sc. 1934; Ph.D. 1938, University of Washington
 Assistant Professor 1938-40, George Washington University
 Assistant Professor 1940-44, University of Minnesota
 Associate Professor 1944-48, University of Texas
 1948-59, 1959-75, Dean and Professor, College of Pharmacy, Oregon State University
 Born, Bothell, Washington, 1911; died, 2002.

of the College of Pharmacy at the Oregon State University in Corvallis, he published numerous research articles while in Minnesota and served in the Anti-Malarial Synthesis Program, a project initiated by the Federal Office of Scientific Research Development during the war years. He was also chief chemist for the Minnesota State Board of Pharmacy (Wilson, 2008).

In another sign of the new trend toward research, the departure of George Crossen to become dean of pharmacy at Drake University led to the appointment of Taito Soine to succeed him. Although Soine's initial appointment was in pharmacy, he would emerge as one of the faculty mainstays of medicinal chemistry over the next 35 years (Netz, 1971, 91). His research interests were primarily on alkaloids, coumarins, local anesthetics, and anticholinergics.

With Charles Wilson's departure in 1948, the College appointed Frank DiGangi as assistant professor in pharmaceutical chemistry to replace him. At the time, Di-



TAITO SOINE

B.Sc. 1938; Ph.D. 1943, University of Minnesota
 Assistant Professor 1944-47; Associate
 Professor 1947-50; Professor 1950-78;
 Head of Department, 1970-74; Director of
 Graduate Studies (DGS) in Medicinal
 Chemistry, 1970-74, University of
 Minnesota

Born, Virginia, Minnesota, 1915; died, 1978.

Awards

- APhA Research Foundation Award in Natural Products, 1964



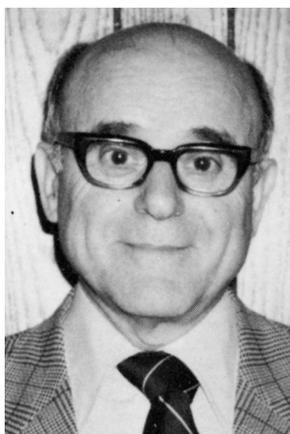
L to R: Charles Wilson, Ivy Magrath, Charles Rogers, and Taito Soine, who points to a coumarin compound isolated from plant material, 1946.

Gangi was completing his doctorate under Ole Gisvold, and finished his degree a few months later. During the next decade, DiGangi would join Soine and Gisvold as one of the triumvirate of faculty members who helped create a tight-knit, highly collegial department. While Soine and Gisvold maintained a very active research program, DiGangi spent much of his career in administration, initially as assistant dean for student affairs (1969-76), and then as associate dean for the College ad-

ministration from 1978 until his retirement in 1985.

DiGangi was known for his exceptional memory of names and faces. There was hardly a pharmacist or friend of pharmacy in Minnesota whom he did not know and about whom he couldn't provide at least a brief history. DiGangi was heavily involved with the Minnesota State Pharmaceutical Association, serving as president in 1971-72. He was the recipient of the Lawrence C. and Delores M. Weaver Medal and the Harold R. Popp Award for his outstanding service to the profession.

During the war years and into the rest of the decade, the Indian medicinal plant project was far from the only research program undertaken by College faculty. Reports submitted to the MSPhA during these years make it clear that the scope of scientific investigation continued to expand.



FRANK E. DIGANGI

B.Sc. 1940, Rutgers University

M.Sc. 1942, Western Reserve University

Ph.D. 1948, University of Minnesota

Assistant Professor 1948-51; Associate

Professor 1951-57; Professor 1957-85,

University of Minnesota

Born, West Rutland, Vermont, 1917; died, 2010.

Awards

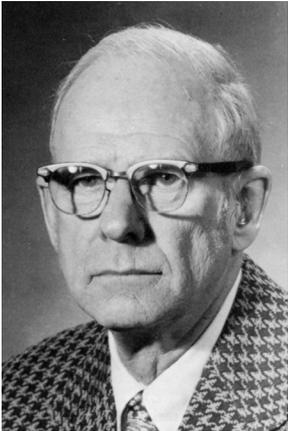
- Lawrence C. and Delores M. Weaver Medal, 1997
- Harold R. Popp Award, 1979

Indeed, by 1947, the College had 14 graduate students in pharmaceutical chemistry, all pursuing research projects (Minnesota State Pharmaceutical Association, 1947, 42).

During this time investigations included potential anesthetic and antibiotic properties of natural products in addition to the antioxidant products found in creosote, as well as investigations into the potential for these products as well as barbiturates from synthetic compounds. After completing his doctorate, for example, Soine attempted to prepare synthetic local anesthetics. Besides working on the Indian plant project, Gisvold pursued research into the venerable digitalis; later in the decade, he and Soine collaborated on a project that sought to synthesize compounds that would prove effective as antispasmodics.

Meanwhile, in pharmacognosy, Fischer continued his studies of medicinal plants, contributed research to developing standards for the *U.S. Pharmacopeia*, and collaborated with Charles Rogers on study of the adaptability of Minnesota peat for

use in cultivating different species of mint (*ibid.*, 1940-50). In 1948, Wallace White was hired as an associate professor of pharmacognosy, although he had no background in that discipline. His undergraduate training was in biological sciences, and he held a Ph.D. from Yale in pharmacology. He did not conduct research or teaching in pharmacognosy as his research interests were in the area of programmed instructions in pharmacology. Wallace's appointment most likely was to establish a role of pharmacology teaching at the College of Pharmacy. At that time pharmacology was—and still is—taught by faculty from the Department of Medicine.



WALLACE WHITE

B.S. 1930, Butler University, Indiana

M.S. 1932, State University of Iowa

Ph.D. 1949, Yale University

Instructor to Associate Professor 1937-49,

University of Connecticut

Associate Professor 1949-55; Professor 1955-

76, University of Minnesota

The role of research at the College of Pharmacy was highlighted by an exchange that took place in 1944 between Gisvold, the head of the Department of Pharmaceutical Chemistry, and the head of the Committee on Pharmaceutical Research, which was a group that had recently been created by the American Association of Colleges of Pharmacy.

Committee chair E. V. Lynn, a faculty member at the Massachusetts College of Pharmacy, noted in a report issued by that committee in September 1944 that most of the truly significant breakthroughs in materia medica, medicine, and pharmacy during the previous 50 years—like the development of sulfa drugs, insulin, and the discovery of vitamins and hormones—had taken place outside pharmacy colleges, pointing to a shortage of research by such colleges. The committee's goal was to “devise an arrangement whereby the individual and collective efforts at research in our schools could be stimulated, directed, and coordinated toward a goal of highest quality” (Lynn, 1944). In the absence of any other body in the profession available to carry out this task, Lynn volunteered the committee to serve, at least for the interim.

Toward that end the committee would collect “ideas” for research projects to be used to stimulate research—under some kind of unspecified “direction” from the AACP committee on research.

The report went on to state that, in the interest of discovering what faculty

at pharmacy colleges might direct or perform future research, deans at member schools had been sent a letter asking for the names of “research-minded” faculty, together with their curriculum vitae. By the time of the report, the committee had already collected the names, research interests, and publication information on about 250 faculty around the country.

A reading of submitted papers, however, had led Lynn to conclude that the quality of the work evidenced by the papers was “not been very impressive as a whole.” He argued that colleges must have adequately trained faculty to conduct research, proper equipment and laboratory space for the work, and sufficient time free from teaching to devote to their scientific investigations. Furthermore, Lynn felt that each college should have a research program and that graduate students should be given the opportunity for research fellowships, scholarships, and assistantships. Colleges also needed adequate libraries, he said. He noted that of 59 member institutions, 28 did not have a graduate program and offered no advanced degree. Of the remainder, only 15 offered master’s degrees and only 12 offered Ph.D. degrees (American Association of Colleges of Pharmacy, 1944).

As the chairperson of the leading research department at the College of Pharmacy—which, in addition to offering graduate degrees and fellowships also housed a pharmacy library created much earlier by Frederick Wulling—Gisvold took issue with Lynn’s report and the committee’s intent. He wrote to the committee early in 1946, outlining his objections: “Those who are actively engaged in doing and directing research may not want to divulge any problems they think are worthwhile or that they may want to use, however distant in the future” (Gisvold Collection, 1952, box 2). The priority placed on research in the pharmaceutical chemistry and pharmacognosy departments made itself known in other ways as well.

During the period between Wulling’s retirement and the 1950s, faculty members published dozens of articles in numerous journals. But that was not all. This was also a productive time for the publication of textbooks—some of which became the standards in their field—written or edited by members of the College faculty.

Wulling, of course, led the way with publication of *Inorganic Chemistry and Pharmaceutical Chemistry*, published in 1894. Charles Rogers’s textbook, *Inorganic Pharmaceutical Chemistry*, was the next book published by a faculty and appeared in 1930 after Rogers took the first-ever sabbatical by any member of the College of Pharmacy. Eventually the book went through two revisions and included contributions by Soine and Wilson before finally going out of print in 1967. An outgrowth of that book, *Inorganic Pharmaceutical and Medicinal Chemistry*, was published in 1974, with contributions from Soine, Wilson, and others.

In 1941, meanwhile, Rogers and pharmacy faculty member Charles Crossen published *A Laboratory Manual of Inorganic Chemistry*; the manual was later reissued as a collaboration between Rogers and Soine. As early as 1938, Gisvold and Rogers

co-produced *The Chemistry of Plant Constituents*, which was written primarily by Gisvold, with Rogers serving as consultant on the project (Netz, 1971, 84).

Gisvold followed this up with *Organic Chemistry in Pharmacy*, published in 1952 by J. B. Lippincott. Co-edited with Soine, it was a collection of three dozen papers gathered from researchers around the country. Several were written by Gisvold and Soine (Gisvold Collection, 1952, folder 6, Box 3). In 1949, the department also published a tome that went through several editions as *Textbook of Organic Medicinal and Pharmaceutical Chemistry*, edited by Wilson and Gisvold (College of Pharmacy, 1964). Currently Wilson and Gisvold's *Textbook of Organic Medicinals and Pharmaceutical Chemistry* is in its 12th edition.

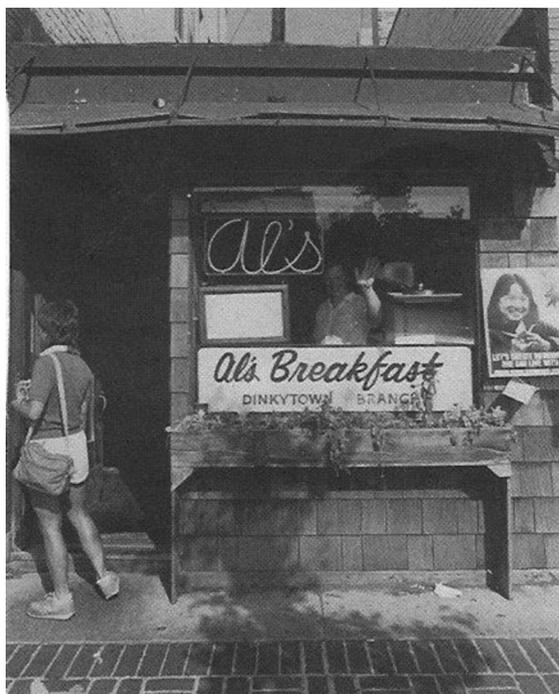
A Community of Faculty

With the appointment of Frank DiGangi in 1949, the faculty makeup of the department of pharmaceutical chemistry was set for the next decade. Ole Gisvold served as chair and continued his research in natural products, as did Taito Soine. Over the course of the 1950s, the number of graduate students continued to grow slowly. Laboratory and office facilities in Wulling Hall were limited at best; both Soine and Gisvold maintained small laboratories in their offices, which faced each other across the workbenches of a communal laboratory.

The cramped space, the small number of faculty (during this period, the entire academic field of pharmaceutical chemistry in the United States was confined to a handful of schools), and the type of time-consuming, labor-intensive research that was standard of the day were conducive to engendering a working atmosphere that was informal, collegial, collaborative, egalitarian, and even family-like where faculty and graduate students worked side-by-side almost as equals.

A graduate student during the latter part of this decade, K. H. Lee, who is now professor of medicinal chemistry at the University of North Carolina, recalls how Soine offered guidance to Lee on how to complete his studies. Lee, who took his master's degree at Kyoto University, also found himself the object of DiGangi's concern as the professor frequently asked the slender graduate student whether he was getting enough to eat (Lee, interview, November 2009).

The casual tone in the department—and indeed, throughout the College—was set by Dean Rogers who was known to keep a can of Coke mixed with a little alcohol on the windowsill of his office during winter months for a handy chilled drink. Faculty members who visited Rogers in his office often found the Dean's Golden Retriever lounging on the rug, and children accompanying a parent faculty member were invariably offered a candy bar from a stash Rogers kept in his desk (Kier, interview, November 2009; Soine, interview, January 2010). In the laboratory area, those same children would often also be allowed to shine their dimes in a little



Al's Breakfast in Dinkytown as it stands today came into being in 1950. It still has the same 14 stools and is still serving almost the same menu for the past 60 years.

puddle of mercury poured out by Soine (Soine, 2010). Beginning in the late 1930s and continuing into the 1960s, faculty and graduate students attended an annual picnic at Loring Park in Minneapolis, which was a potluck featuring burgers and hotdogs grilled by male faculty members and side dishes provided by their wives. Rogers also had a “shack,” as it was invariably referred to, in northern Minnesota, where he and faculty members would go once a year on a fishing trip (*ibid.*).

Socializing was also a regular feature of life at the departmental level. Gisvold had been Soine's Ph.D. adviser, and the two remained colleagues and friends for the rest of their lives.

An avid gardener who specialized in growing strawberries, Gisvold held regular dinner parties during growing season featuring his prize crop—parties where Soine would point out to his son, Bill, that it was Gisvold who isolated the antioxidant found in his son's favorite candy bars. Once a year, in turn, Soine hosted a faculty dinner at his house as well.

The department was both collegial, then, and very informal—a virtual “Belle Epoque” in the words of one graduate student, Lemont Kier, at the time (Kier, 2009). Kier, who is now a professor emeritus at Virginia Commonwealth University and a senior fellow at its Center for the Study of Biological Complexity, arrived at the University of Minnesota in 1954 and completed his doctorate in 1957 in medicinal chemistry. In the department's communal laboratory space, the graduate students would sometimes drop-kick empty milk cartons over the benches or pitch pennies down the length of the floor as ways to pass time while awaiting the outcome of chemical reactions.

The egalitarianism and informality of the department were perhaps best typified by Soine, whose office door was always open to graduate students. Swinging around from his desk, Soine would make inquiries in a student's ongoing research, offer advice, hand out recent articles germane to the subject at hand, and make fre-

quent—and enthusiastic—visits to the common laboratory where he would check on progress. He was also known for pushing graduate students to go out on a limb in their research, to think conceptually and creatively about their investigations, and to step back and see the big picture (Kier, 2009).

Department research continued to focus on natural products, with DiGangi, whose specialty was analytical chemistry, pursuing inquiries similar to those of Gisvold's, and Soine developing studies into alkaloids. "By present-day standards, research facilities and instrumentation were rudimentary and there was no UV analysis," recalls Kier. Everything had to be measured chemically through reactions,



Chemistry research laboratory, 1956.

which were then studied to analyze the structure of products.

Meanwhile, the communal laboratory space smelled strongly of green plants being dried for study and stored until use in bags and boxes stacked up in every available space. In his office, Soine kept a gold-chain balance and was very proud of the fact that he could measure out a tenth of a milligram in just five to ten minutes, or about as fast as could be achieved using that particular instrument. Soine sometimes enlisted his son, now a retired faculty member in medicinal chemistry at Virginia Commonwealth University, to help prepare research equipment (Soine, 2010).

Not surprisingly, the time frame for even simple research projects was considerably longer than today. It also meant that much research was carried out in a way that would now be considered fragmentary, with researchers publishing observations that, over time, might lead to a breakthrough in the understanding of a substance's ultimate structure. It was a trial-and-error method, and it could take years

before any definitive conclusions could be reached.

“Researchers would have to take a compound under study and, by means of analyzing by-products created by heat or exposure to acids or alkali, deduce structural facts about the original substance,” Kier said. “Sometimes it was a matter of simply heating a substance up with an acid or an alkali. A battery of two or three dozen chemical tests might be needed to eliminate, one at a time, all other possibilities except the right one” (Kier, 2009). It was no wonder that a faculty member like Soine would openly express joy when he’d finally nail down the structure of a product after earlier proposing two or three incorrect structures (Soine, 2010).

This is not to say that there wasn’t a keen interest in both pharmaceutical chemistry and pharmacognosy in the latest techniques and instrumentation. Despite his cherished gold-chain balance, Soine was fascinated by the possibilities of ultraviolet and infrared for chemical analysis, which began coming on stream in the Chemistry Department located not far from Wulling Hall; until the move to Appleby Hall, most of the analysis of products requiring more sophisticated techniques were carried out in the Chemistry Department’s laboratories (Soine, 2010).

Meanwhile, Herb Jonas’s expertise in employing radioisotopes to analyze chemical structure explains his appointment as assistant professor of pharmacognosy in 1958 despite the fact that his training was in plant physiology, not pharmacognosy (Schramm, interview, 2009). By this time, plans were also already in the works for an isotope research laboratory in Appleby Hall, and Frank DiGangi attended courses in the field, including one four-week seminar at the Oak Ridge Institute in Tennessee, as preparation for a wider application of isotopes both to research and teaching at the College (Netz, 1971, 121).

In perhaps one of the most important signs of the coming revolution in research, at the initiative of Dean George Hager, who’d become familiar with data processing during his years working in industry, Glen Hamor, a faculty member at the University of Southern California who took his doctorate in pharmaceutical chemistry in Minnesota, spent the 1959-60 academic year at the College. He was tasked with coding information about medicinal products so it could be entered into computer systems (Netz, 1971, 123).

The Physical Plant Grows

As from the very beginning, issues of space and facilities continued to dog the departments—and the College of Pharmacy as a whole. By the end of the 1930s, pharmacy had long outgrown Wulling Hall but it would take several more decades before the problem was rectified.

Dean Charles Rogers initiated efforts to alleviate the ever more pressing problem with his 1940 Biennial Report to the President in which he called for a \$175,000

allocation to add space and equipment to Wulling Hall (Netz, 1971, 95). In 1949, the Board of Regents finally followed up on Rogers's call with a legislative request for some \$450,000 to upgrade Wulling Hall, but the proposal went nowhere, in large part because it appeared far down the list of priority projects. The following year, the MSPhA pointed out that Wulling Hall was now home to three times the number of undergraduate and graduate students than it had been designed for—almost 450 as opposed to 150. By 1951, the legislative request had moved up the list of Board of Regent priorities but was once again overlooked by the state.

In the next round of funding requests, the Regents dropped the idea of adding space to Wulling Hall and decided to ask the state for \$150,000 to remodel Appleby Hall, the home of the School of Mines and Metallurgy, asking for an additional three-quarter million dollars to build a new structure to house the mining school. That request also went nowhere. In 1955, however, the University finally convinced the state to appropriate money for both projects. Minnesota appropriated more than \$800,000 for a new mining and metallurgy building and more than \$200,000 to retrofit Appleby Hall.

In addition, the College raised money on its own from private and corporate donors and landed a \$76,000 grant from the U.S. Department of Health, Education, and Welfare to help with construction and equipment (Anderson & Pennigton, 2005, 45-6).

By then, there had been a change in the leadership at the College of Pharmacy, as well as in its administrative structure. Both would help pave the way for the rise of a new era in the department that would begin early in the 1960s.

In March 1956, Rogers's wife died after an accident in which she slipped on street ice and fractured her skull. Distraught over his loss, Rogers soon announced that he would be leaving the University (Netz, 1971, 113). After a lengthy search for a replacement, the following year George P. Hager was appointed dean to replace Rogers, a position he took over in June 1957. Once again, the appointment reflected the College's emphasis on research; in turn, this emphasis would benefit from the launch of the Soviet Union's Sputnik satellite in October of that year, an event that led to an immediate surge in federal funding available to researchers in almost every discipline around the country.

Hager came to Minnesota from the University of Maryland, where he obtained his Ph.D. in 1942 and went on to serve as a faculty member in the School of Pharmacy and later the head of the Department of Medicinal Chemistry where he earned a reputation as an expert in pharmaceutical manufacturing and synthetic chemistry. Not long after arriving in Minnesota, Hager announced plans to create a new associate dean position in the College to help administer the increasingly complex needs of teaching, research, and outreach.

At first, then-President James Morrill balked at the idea, but in 1960, the new



GEORGE P. HAGER

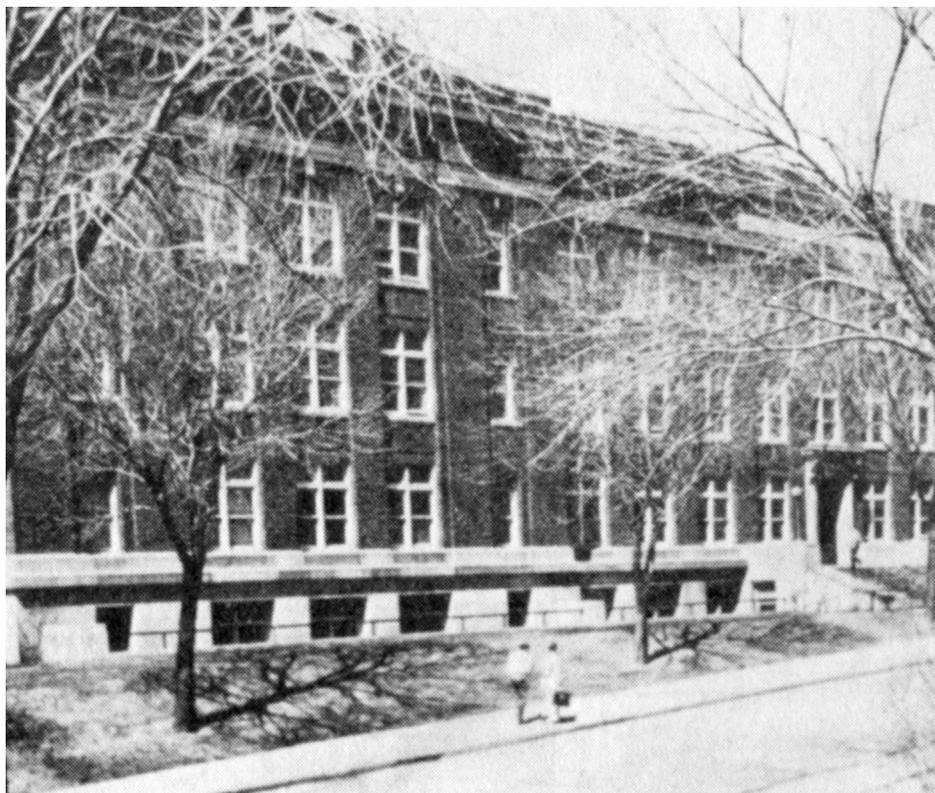
B.Sc. 1938; M.Sc. 1940; Ph.D. 1942, University of Maryland

Professor and Head 1945-55, University of Maryland

Professor and Dean 1957-66, University of Minnesota

Born, 1916; died, 2000.

position was finally established and Charles Netz, head of the department of pharmaceutical technology, was given the job. Hager revitalized the College's alumni association by leading an effort to renovate Appleby Hall, home to the College of Pharmacy and the School of Mines and Metallurgy. State funding wasn't available



Appleby Hall, the fourth home of the College of Pharmacy, from 1961 to 1981.

for the renovations, so with the support of University leaders, Hager secured a \$76,000 grant from the U.S. Department of Health, Education, and Welfare to construct and equip research buildings. Hager left Minnesota in 1966 to become dean and professor of medicinal chemistry at the University of North Carolina.

That set the stage for the next development. §

Chapter 3

FROM THE NATURAL TO THE SYNTHETIC

The two decades between 1960 and 1980 brought about the transformation of the Department of Medicinal Chemistry beyond recognition. The department moved into new quarters once again—this time to its current home. But this pivotal era began, as it did in the country as a whole, as little more than a continuation of what had gone before in the 1950s and even earlier. Indeed, new faculty and students arriving at the College of Pharmacy in the first few years of the 1960s would have found little that might have surprised Dean Charles Rogers—or possibly even Dean Frederick Wulling.

The departments were still fashioned after the traditional pharmaceutical chemistry and pharmacognosy programs of the old school: vertically integrated and featuring almost no interdisciplinary, or even interdepartmental, collaborations beyond a continued reliance on the Chemistry Department to carry out chemical analysis of isolated products. That dependency, in turn, reflected a continuation of the relative lack of instrumentation within the department itself (Abdel-Monem, interview, 2009).

While research was a key activity for faculty in both pharmaceutical chemistry and pharmacognosy, one of the three pharmaceutical chemistry faculty members, Frank DiGangi, was not involved in research as the decade dawned: his focus was primarily on coursework for undergraduate pharmacy students (*ibid.*). Undergraduate students had to take credits amounting to between three and three-and-a-half years of coursework. Most of the department's 15 graduate students were preparing themselves for a life of teaching, not research. Although it was not unusual for students to obtain an M.S. degree and leave after two years, it was also not uncommon for some students to take seven or eight years to earn their Ph.D.

Facilities and physical resources were still spartan, at least by contemporary standards. Students and faculty had access to office laboratories as well as shared

space in a community laboratory; at the time, there was no postdoctoral staff in the department. The laboratories offered microscopes and balances, but little else: learning how to use the Lloyd Extractor (now on display in Weaver-Densford Hall) was considered a rite of research passage (*ibid.*). On summer evenings anyone working in the un-air-conditioned laboratory had to contend with mosquitoes as well as scientific questions. Faculty and students continued to rely on the Chemistry Department—located across the street from pharmaceutical chemistry—to

carry out more sophisticated analytical procedures (Kier, interview, 2009).

But the single greatest dimension of continuity in both the pharmaceutical chemistry and pharmacognosy departments was the exclusive focus on natural products, with Gisvold and Soine leading the way in the pharmaceutical chemistry program, and Earl Fischer, Herbert Jonas, and Lee Schramm, a faculty member hired in 1961 who left the department in 1968, heading up pharmacognosy investigations (*ibid.*). That continuity, however, was about to be broken, at least in pharmaceutical chemistry, and replaced by what would become the dominant focus for the rest of the 20th Century—synthetic medicinal chemistry.



Ole Gisvold and Taito Soine collect a plant extract from the Lloyd Extractor, 1964.

Even before the change took place, it was heralded by a misguided announcement by Gisvold one day to faculty and graduate students working in the common laboratory. Gisvold had just learned that his application for a new National Institutes of Health grant had been turned down. Bemused, he came into the laboratory and solemnly announced that the NIH was simply not going to fund any more grant applications for natural product chemistry.

What the NIH rejection actually signaled, however, was a change already underway elsewhere in the country, if not as yet within the College of Pharmacy. Fortunately, given the department's reputation, the College was in a position to catch that wave in its early stages, thanks to the recruitment of new faculty members—



Craig's Counter Current Distribution Apparatus, 1962.

some of whom were former graduate students at the University—who would go on to become leading researchers in their fields. One such person was Herbert Nagasawa, a research scientist at the Veterans Administration Hospital, was recruited to join the department as a research assistant professor in 1959. A 1955 Ph.D. graduate of the Chemistry Department at the University of Minnesota, Nagasawa was trained as a synthetic organic chemist. He'd started his career by investigating the bioactivation mechanisms of drugs that inhibit the metabolism of acetaldehyde;

his goal was to synthesize second-generation, alcohol-deterrent drugs for the treatment of alcoholism. Nagasawa rose through the ranks and continued as a member of the department until his retirement in 2005.



HERBERT T. NAGASAWA

B.Sc. 1950, Case Western Reserve University

Ph.D. 1955, University of Minnesota

Assistant Professor 1959-63; Associate Professor 1963-72; Professor 1973-2005, University of Minnesota

Born, Hilo, Hawaii.

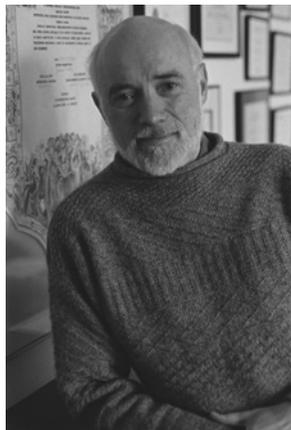
Awards

- Fellow, New York Academy of Science, 1983

In turn, it was primarily Nagasawa's and Soine's research interests that led to the creation of a new faculty position specifically geared toward investigating the relationship between molecular structure and biological activity at the University of Minnesota. Although Soine was interested in this area of research, he was at this time more focused on the chemistry of natural products rather than on exploring novel chemical structures to optimize biological activity.

That position was filled by Philip Portoghesi, who, in 1961, became the first

departmental medicinal chemist faculty member to use synthetic organic chemistry for the specific purpose of studying the architecture of receptor binding-sites. He pursued this goal by designing, synthesizing, and biologically testing different shaped molecules.



PHILIP S. PORTOGHESE

B.Sc. 1953, Columbia University

M.Sc. 1958; Ph.D. 1961, University of Wisconsin

Assistant Professor 1961-64, Associate

Professor 1964-69, Professor 1969-

present, Distinguished Professor 2000;

Director of Graduate Studies in Medicinal

Chemistry 1974-86, University of Minne-

sota

Born, New York, New York, 1931.

Awards

- ACS Medicinal Chemistry Hall of Fame, 2007
- Nauta Award in Pharmacochimistry, 2006
- AHC Academy for Health Excellence in Research, 2003
- Lawrence and Delores Weaver Medal, 2001
- Alfred Burger Award in Medicinal Chemistry, 2000
- The Oak & the Tulip Medal, 1999
- Edward E. Smismann-Bristol-Myers-Squibb Award, 1991
- Nathan B. Eddy Award For Excellence in Drug Abuse Research, 1991
- Research Achievement Award in Medicinal Chemistry, AAPS, 1990
- Medicinal Chemistry Award, Division of Medicinal Chemistry, 1990
- Ernest H. Volwiler Award, AACP, 1984
- Research Achievement Award in Medicinal Chemistry, APhA 1980
- Fellow, American Chemical Society, 2010
- Fellow, American Association for the Advancement of Science, 1986
- Fellow, Academy of Pharmaceutical Sciences, 1974

Meanwhile, the sequence of events leading to his appointment provides an insight into how departmental culture—especially when it comes to hiring new faculty—has changed over the past 50 years. Portoghese's Ph.D. thesis advisor, Professor Edward Smissman, had heard of an opening for an assistant professorship in pharmaceutical chemistry at the University of Minnesota College of Pharmacy through his friend George Hager, who was currently dean of the College. Smissman suggested Portoghese as a candidate; there were no search committees at that time. Hager then invited Portoghese to Minnesota to present a seminar on his Ph.D. research. Originally reluctant to interview at a Midwestern university because he wanted to return to his native East Coast, Portoghese was unenthusiastic about considering the University of Minnesota for a faculty position. In fact, he had already applied for a position at the University of Rhode Island. However, because of Smissman's convincing salesmanship on the merits of Minnesota as a venue for doing research, along with his successful lobbying of Portoghese's wife, Portoghese decided to accept the invitation to visit the University (Portoghese, interview, 2009).

After accepting Hager's invitation, Portoghese visited Minnesota and presented his research to the pharmaceutical chemistry and organic chemistry faculty. He soon received an offer from Hager for a position as an assistant professor, which he accepted with a starting date of September 1961. The fact that he was offered the position without even having applied for it or screened by a search committee would be unusual enough today; even more unusual is that he was funded through an NIH grant for which he applied prior to arriving at the University of Minnesota. Shortly after his arrival, his grant application was funded. Since then, he has been funded continuously by the NIH.

Portoghese brought with him a keen interest in stereochemistry, which originated in an equally strong interest in graphic art. In fact, prior to enrolling in college he had to make a decision on whether to pursue a career in art or science. The connection is clear in his first funded grant, which was related to the synthesis of molecules with well-defined geometry in an effort to define the three-dimensional shape of the receptor sites for morphine and related analgesics located on nerves in the central nervous system. The area of analysis was not related to his Ph.D. research: his interest in analgesics stemmed from a seminar topic Smissman had suggested he present as a graduate student (*ibid.*).

After four years of research on the stereochemical requirements for opiates that produce analgesia, Portoghese had amassed a large amount of data strongly suggesting the presence of multiple opioid receptor sites in the central nervous system. This concept was counter to the prevailing dogma of the day that proposed that there was a single type of receptor that binds an analgesic molecule in a manner similar to a key that fits a lock. Ten years passed before evidence published by biologists confirmed Portoghese's concept of multiple opioid receptor sites (Portoghese,

1965).

With more than 360 scientific publications over the past 50 years, Portoghese has made a significant impact both on the field of opioid research and medicinal chemistry research in general. A recurring theme in his research has been the utilization of novel concepts in the design of biologically active compounds. Most notably, in addition to his work relating to multiple opioid receptors, his research has included the design of highly selective opioid antagonists based on the message-address concept. Some of the compounds developed through this concept are standard research tools used in the field today. Presently, eight of his compounds are available through a number of commercial vendors and through the NIH. Through his bivalent ligand approach developed in 1982, his group first proposed the concept of opioid receptor dimers nearly two decades before they were demonstrated to exist in cultured cells. Most recently, he has led his group to design compounds that are selective for such dimers as a new approach to developing analgesics devoid of tolerance and dependence.

Portoghese's research has been highly cited, as reflected by his listing in the "Institute for Scientific Information's Highly Cited" database of researchers. He has been recognized both nationally and internationally with numerous awards from major scientific societies. In addition to being honored with numerous research recognitions from scientific and professional societies and the NIH, he has received

honorary doctorate degrees from two universities.

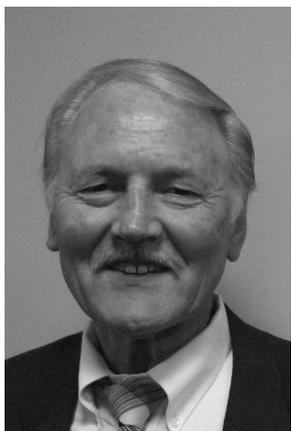


Philip Portoghese working to delineate the three-dimensional structure of one of the opiate analogs.

Following his doctoral studies at the University of Minnesota, Dennis Larson continued working as a postdoctoral research fellow in the Department of Medicinal Chemistry on research projects involving the synthesis of radio-labeled opiate compounds and study of their pharmacokinetics

in mice, and the synthesis of prostaglandin F₂ derivatives. During this period he also served as an interim professor during one of Portoghese's sabbatical leaves.

As research assistant professor, Larson continued research projects involving design and synthesis of varied unlabeled and radio-labeled opioid derivatives, as well as synthesis of substance P derivatives and synthesis of multifunctional opiate-



DENNIS LARSON

B.S. 1961; Ph.D. 1969, University of Minnesota
 Postdoctoral Research Fellow 1970-77,
 Research Assistant Professor 1978-2004,
 University of Minnesota
 Born, Minneapolis, Minnesota, 1939; retired,
 2004.

containing dendrimers for potential long-acting biological action. These research efforts are associated with about 10 compounds now being employed as principal pharmacological tools in research activities conducted by laboratories throughout the world. During this time, Larson also served as laboratory manager and operational adviser for Portoghese's research group. Additionally, he served on the College safety committee and as departmental controlled substances unit registrant. He also participated in the maintenance of departmental instrumentation, such as



ROBERT VINCE

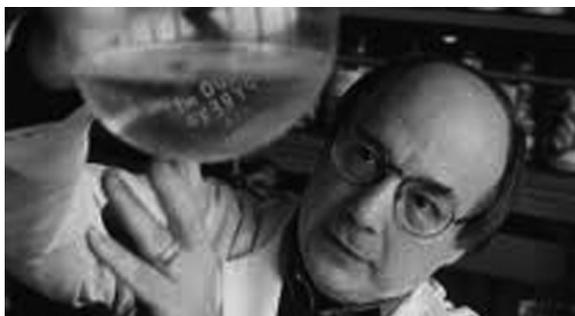
B.Sc. 1962, University of Buffalo
 Ph.D. 1966, SUNY at Buffalo
 Assistant Professor 1966-67, University of
 Mississippi
 Assistant Professor 1967-71; Associate Profes-
 sor 1971-76; Professor 1976-present,
 Director, Center for Drug Design 2003-
 present, University of Minnesota
 Born, Auburn, New York, 1940.

Awards

- Minnesota Science and Technology Hall of Fame, 2011
- Imbach Townsend Award, 2010
- ACS Medicinal Chemistry Hall of Fame, 2007
- AHC Academy for Excellence in Health Research, 2007
- Fellow, American Association for the Advancement of Science, 2000
- Outstanding Contributions to Research and Development—Medical Alley, 1994
- Certificate of Commendation by Governor Rudy Perpich, 1989

departmental FTIR, radioactivity scanners.

The department's growing reputation in synthetic medicinal chemistry research attracted other young research-oriented faculty, like Robert Vince, who trained under Howard Schaffer at the State University of New York in Buffalo where he worked on the design of acyclonucleosides. That work subsequently served as the basis for the development of an anti-viral drug for herpes simplex, marketed as Acyclovir. After taking a faculty position at the University of Mississippi, Vince joined the University of Minnesota in 1966



Robert Vince at work in search of a new antiviral.

where his research continued to explore the creation of compounds that would prove effective for fighting cancer and viruses, like those that can cause herpes.

During the early 1970s Vince's group developed the lactam, 2-azabicyclo[2.2.1]hept-5-en-2-one, dubbed "Vince's lactam," which has

become the major intermediate for the synthesis of carbocyclic nucleotides. That work laid the groundwork for his later investigations into anti-AIDS compounds. An exciting achievement in the anti-viral area has been the successful design of a



Medicinal Chemistry graduate students, 1967.

compound called cyclaradine, which has been found to possess significant activity in treating viral infections but lack of worldwide patent coverage prevented the backing for clinical development. Ultimately, Vince's legacy at the University will be his development of drugs effective in the treatment of cancer and a late 20th Century scourge, AIDS (Vince, interview, 2008).

In 1967, new faculty and the spirit of innovation they brought to the University, led by Portoghese, resulted in the adoption of a new departmental name that more accurately reflected the realities of the times, with the Department of Pharmaceutical Chemistry becoming the Department of Medicinal Chemistry.

Fueling the change in nomenclature was the fact that the term "pharmaceutical chemistry" did not mean quite the same thing in the pharmaceutical industry as it did at the College, giving rise to confusion. The connotation conferred on the phrase from long industry usage was of a problem-solving approach based upon pharmaceutical formulations. Nationally, the name change was catalyzed by an informal discussion of pharmaceutical chemistry participants at the 1965 AACP Teacher's Seminar in Toronto. The name change from pharmaceutical to medicinal chemistry was also indicative of the shift that took place in the department's research emphasis from research based on the isolation and characterization of medicinal agents from natural products to an emphasis on rational drug design based on an understanding of cell biology. The term "medicinal chemistry," then, was much more consistent with what was actually going on in the department as well as in industry and the discipline as a whole. Within the College, there was no resistance to the name change. In the end, all faculty members in the department voted to replace the old name that had been in use since 1892 (Portoghese, interview, 2009).

Another of the young faculty members was Patrick Hanna, who began his career at the University in 1969. Hanna, who obtained his Ph.D. in medicinal chemistry from the University of Kansas, was recruited to the University as a non-tenure track



PATRICK E. HANNA

B.Sc. 1963, Creighton University

Ph.D. 1969, University of Kansas

Assistant Professor 1970-75; Associate

Professor 1975-84; Professor 1985-present;

Director of Graduate Studies in Medicinal

Chemistry 1988-97, University of Minnesota

Born, Little River, Kansas, 1940.

Awards

- Fellow, American Association for the Advancement of Science, 1988
- Morse-Amoco Foundation Outstanding Teaching Award, 1979

faculty member of Professor Gilbert Mannering's Center for Drug Metabolism. Initially, his primary appointment was as an instructor in the Department of Pharmacology in the Medical School, with a joint appointment in medicinal chemistry. Although Hanna, whose background was in synthetic medicinal chemistry, initially focused his research on structure-activity relationships of histamine antagonists, he shifted his emphasis within a few years to the metabolism of carcinogens and investigations of arylamine N-acetyltransferases (NATs), which play important roles in the metabolic detoxification and activation of both arylamine drugs and arylamine carcinogens found in tobacco smoke. His early studies led to the acquisition of NIH and American Cancer Society research grants, and to his nomination by Portoghesi for tenure in the College of Pharmacy. Hanna's research on NATs and arylamine bioactivation yielded seminal contributions to the field and continued for more than three decades.

For some 25 years Hanna maintained research space in the departments of pharmacology and medicinal chemistry; he taught courses in both departments, was involved extensively in departmental and University committee service, and trained graduate students in both programs. He served as co-director of the joint

pharmacology-medicinal chemistry training grant and was director of graduate studies in medicinal chemistry for nine years. Hanna was an associate editor of the *Journal of Medicinal Chemistry* for 18 years, and was elected chair of the Division of Medicinal Chemistry of the American Chemical Society in 1986.

Hanna has been the recipient of several teaching awards. Students in the College of Pharmacy nominated him for the Morse-Amoco Foundation (now Morse-Alumni) Award for outstanding contributions to undergraduate education, which he received in 1979. He also was inducted into the University's Academy of Distinguished Teachers. In July 2010,



Patrick Hanna tells a story.

after 41 years as a faculty member, Hanna began a two-year phased retirement (Hanna, interview, September 2009).

One of the most notable hires during this period was of Mahmoud Abdel-Monem, who did his graduate work at the University, obtaining his doctorate with Taito Soine serving as his mentor. After returning to Egypt for several years, Abdel-Monem came back as a postdoctoral research associate working for two years with Portoghese. He then joined the faculty of the College of Pharmacy at the University of Illinois before he was recruited to Minnesota as assistant professor and appointed to the faculty in 1971. Later, Abdel-Monem would go on to play important roles in the College's administration.

One of his roles was to assist in revising the courses offered by the depart-



MAHMOUD M. ABDEL-MONEM

B.Sc. 1959, Cairo University

Ph.D. 1966, University of Minnesota

Assistant Professor 1970-71, University of Illinois

Assistant Professor 1971-75; Associate Professor 1975-80; Professor 1980-87; Head of Medicinal Chemistry 1983-84, University of Minnesota

Dean of Pharmacy 1987-98, Washington State University

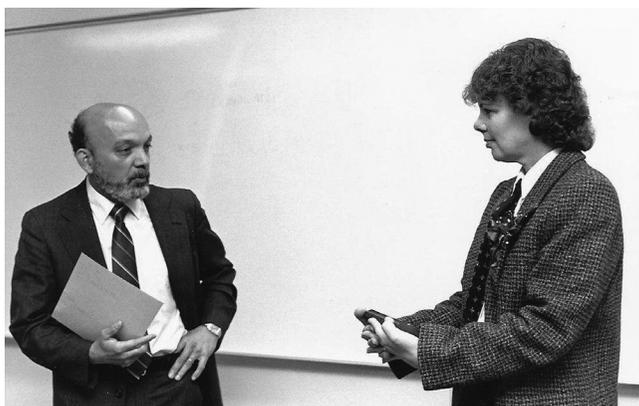
Born, Cairo, Egypt, 1938.

Awards

- Morse-Amoco Foundation Outstanding Teaching Award, 1985
- University of Minnesota Outstanding Achievement Award, 1999

ment designed to prepare graduates for the changing practice of pharmacy. Abdel-Monem modernized the two-course sequence in pharmaceutical analysis and was recognized by the students and colleagues as an exceptional teacher. In recognition of his contributions to undergraduate education he was nominated by professional pharmacy students and received the Horace H. Morse-Amoco Foundation Award in 1985.

In the research phase of his career at the University, Abdel-Monem's program focused on drug disposition and the examination of the chemical mechanisms of the enzymatic biotransformation of biologically active substances as well as studies on the metabolism and physiological function of the polyamines. His studies led to the discovery of two potent inhibitors of the enzyme ornithine decarboxylase. One of the compounds became available and was marketed by Calbiochem and was utilized by researchers for studies on cell proliferation and the prevention of induction



Mahmoud Abdel-Monem congratulates Judith Parker for her selection as Employee of the Year, 1987.

of cancer by chemical carcinogens (Abdel-Monem, interview, 2009).

With a rising level in research activity and directed funding, the department also generated increased funding from federal agencies. A major example was the five-year NIH training grant submitted by Soine in 1966 and fund-

ed in 1967 to support five pre-doctoral candidates, two postdoctoral fellows and one assistant professor.

At the termination of the fourth year of the grant, College of Pharmacy Dean Lawrence Weaver, together with the chairs of medicinal chemistry, pharmacognosy and pharmaceuticals, applied for and secured a five-year grant encompassing the



Medicinal Chemistry faculty, 1972, left to right, back row: Philip Portoghese, Ole Gisvold, and Patrick Hanna; front row: Mahmoud Abdel-Monem, Herbert Nagasawa, Frank DiGangi, Taito Soine, and Robert Vince.

three basic pharmaceutical science fields (Anderson & Pennigton, 2005, 86-7).

A renewal of this grant was approved but not funded in 1976, which led the medicinal chemistry faculty to submit a proposal in 1976 as a departmental unit rather than as a coalition of the pharmaceutical sciences; this second proposal was approved for an additional five years. Soine was the principal investigator for the grant but following his untimely death in 1978, the grant was transferred to Portoghese. When time came for an additional renewal in 1981, NIH was putting pressure on both departments of medicinal chemistry and pharmacology to submit a joint application; the new NIH guidelines would limit the number of similar pre-doctoral training grants at any one institution to only one. This new training grant was submitted to establish a multidisciplinary approach that not only incorporated features of both existing programs but also included members of the Department of Pharmacognosy. Fredrick Shideman, from pharmacology, was the program director and Portoghese its co-director. Following the retirement of Shideman, Akira Takemori from pharmacology and Hanna from medicinal chemistry assumed the director/co-director positions of the training grant which continued to be funded until 1996.

Following the retirement of Gisvold in 1973, the department hired Dwight Fullerton, who at the time was doing postdoctoral research studies with Morris Kupchan at the University of Wisconsin.

Fullerton assumed Gisvold's teaching responsibilities and carried out research on cardiac glycosides. He was expected to continue to build on the discoveries made by Gisvold. However, after three years at Minnesota he decided to accept a faculty position in 1976 at the University of Oregon.

Attempts to hire a replacement for Fullerton were not supported by the College administration. But Portoghese, who was heading the department of graduate studies in medicinal chemistry, convinced the College administration to hire a new faculty member in medicinal chemistry.

This led to the appointment of Rodney Johnson in 1978 as assistant professor to



DWIGHT (PETE) FULLERTON

B.A. 1966, University of Oregon
Ph.D. 1970; Assistant Professor 1973-76,
University of Minnesota

teach, among other things, nuclear pharmacy. Johnson received his Ph.D. in medicinal chemistry from the University of Kansas where he worked with Ed Smissman and Gary Grunewald. He was an assistant professor of pharmacology at the University of Kansas Medical Center prior to his position at the University of Minnesota. Although



The 50th anniversary of the establishment of the graduate program in medicinal chemistry, 1976. Left to right, back row: Patrick Hanna, Robert Mason, Herbert Nagasawa, Ole Givold, and James Henkel; front row: Frank DiGangi, Robert Vince, Mahmoud Abdel-Monem, Taito Soine, and Philip Portoghese.

it was expected that Johnson would also do research in radiopharmacy, he started his research career by working on the design, synthesis, and pharmacological evaluation of polypeptide and peptidomimetic inhibitors of renin. This effort evolved into



RODNEY L. JOHNSON

B.Sc. 1972, University of Minnesota

Ph.D. 1976, University of Kansas

Instructor 1976-86; Assistant Professor
1978-79, University of Kansas

Assistant Professor 1979-81; Associate
Professor 1981-89; Professor 1989-present;
Director of Graduate Studies in Medicinal
Chemistry 1986-88 and 1997-2003,
University of Minnesota



Rodney Johnson asks Abigail Fisher to obtain a crystalline compound from an oily mixture.

a well-funded research program on the design and synthesis of peptidomimetics and constrained analogues of neuropeptides as well as excitatory amino acid related to the neurotransmitter glutamic acid. In recognition of his outstanding overall achievements as a teacher and researcher, the College appointed Johnson in 2010 as Dis-

tinguished Professor of Medicinal Chemistry (Johnson, interview, 2009).

Other faculty added to the department during these years included Thomas Holmes. Following the sudden death of Soine in 1978, the department approached Weaver for a faculty replacement, which led to the appointment in 1980 of Thomas Holmes as assistant professor of medicinal chemistry. A graduate of medicinal chemistry program at the University of Michigan, Holmes did postdoctoral research associate at the University of Chicago and then went on to become a research scientist at Ortho Pharmaceutical Corporation before coming to the University. Holmes's research focused on synthesis of electrophilic derivatives of known anti-inflammatory and anti-tumor agents for use as affinity labels for cellular receptors and elucidation of specific molecular mechanisms of drug action. He had also great interest in teaching, which ultimately led him to take a new position at Campbell University in 1987 where he served as associate dean for 20 years.



THOMAS J. HOLMES JR.

B. Sc. 1971, Duquesne University

Ph.D. 1975, University of Michigan

Assistant Professor 1980-87, University of
Minnesota

Born, Pittsburgh, Pennsylvania, 1948.

Awards

- Fellow, American Association for the Advancement of Science, 1985

A Time of Transition

While not as dramatic as it was for medicinal chemistry at the University, the 1960s and '70s were also a time of transition in pharmacognosy from purely descriptive work to product extraction and the role of plant and microbial cells to product isolation.

Hired in 1958 as an associate professor of pharmacognosy to work alongside the long-time head of the department, Earl Fischer, Herb Jonas had not been trained as a pharmacognocist, but rather as a plant physiologist with extensive experience using radioisotopes in research. When Fischer, who had been ill for several years, died in 1961, Jonas took over as chair of the program. Later that year, the program added a new faculty member, Lee Schramm, who would work at the University until taking a position at the University of Georgia in 1967. During his time at the University, Schramm did research on fungi, plant cell cultures, and ergot; he and Jonas also completed an extensive revision of the pharmacognosy curriculum to reflect the changing research focus (Netz, 1971, 130). Other pharmacognosy projects investigated the effects of pesticides, insecticides, herbicides, and plant growth regulators on medicinal plants (Schramm, interview, 2009).

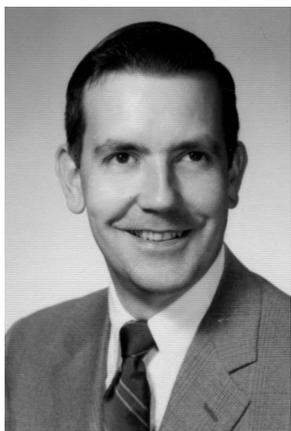
In 1968, Jonas transferred from pharmacognosy to the College of Biological Sciences where he accepted an appointment as an associate professor of botany. That same year, John Staba, head of the Department of Pharmacognosy at the University



HERBERT JONAS

B.S. 1941, University of California at Davis
 Ph.D. 1950, University of California at Berkeley
 Assistant Professor 1958-62; Associate
 Professor and Head of Pharmacognosy 1962-
 68, University of Minnesota
 Associate Professor/Professor 1968-85, De-
 partment of Botany, University of Minnesota
 Born, Dusseldorf, Germany, 1915; died, St. Paul,
 Minnesota, 2002.

of Nebraska, was appointed chair of pharmacognosy at Minnesota. A nationally recognized expert in plant cell culture, Staba was brought in by the new Dean of the College of Pharmacy, Lawrence Weaver, to reinvigorate the program, in particular by strengthening research activity. Staba continued his studies on plant cell cultures where he carried out investigations to experimentally establish the environmental and biological factors necessary for aseptic higher plant cells and organ cultures to



LEE C. SCHRAMM

B.Sc. 1957, The Ohio State University

M.Sc. 1959; Ph.D. 1962, University of
Connecticut

Assistant Professor 1961-67, University of
Minnesota

Born, Portsmouth, Ohio, 1934.

produce and/or transform substrates into new medicinal agents. Over the years he studied cell cultures for production and transformation of digitalis, ginseng, opiates, quinine, and artemisinin. Large-scale production of the active compounds produced by the plant cells were grown in 20-gallon fermenters.

Staba held many positions in various scientific societies and was elected in 1971-72 as president of the American Society of Pharmacognosy.

Despite that ambition, it turned out that Weaver's determination to build a clinical pharmacy program would have less than positive ramifications for both pharmacognosy and medicinal chemistry. In the absence of major increases in College funding, Weaver was forced to divert resources from medicinal chemistry and



E. JOHN STABA

B.Sc. 1952, St. John's University

M.Sc. 1954, Duquesne University

Ph.D. 1957, University of Connecticut

Assistant Professor 1957-60; Associate
Professor 1960-65; Professor 1965-68,
University of Nebraska

Professor 1968-94; Head of Pharmacognosy
1968-74; Director of Graduate Studies in
Pharmacognosy, 1968-82; Assistant Dean
for Professional Education 1974-76,
University of Minnesota

Born, New York, 1928; retired, 1994.

Awards

- Fellow, American Association for the Advancement of Science, 1981

pharmacognosy, making it difficult to accomplish the task of expanding research in those areas.

At the same time, Weaver had an interest in strengthening biological research



Graduate student Blanca Martinez works on the propagation of plant cell cultures.

in pursuing a career in the pharmaceutical industry. However, Weaver explained the advantage of academia and encouraged Abul-Hajj to consider the position at Minnesota.

In 1968, Abul-Hajj was hired. Although he had no training in pharmacognosy, his ability to deepen the biological expertise of the pharmacognosy program, in



New Brunswick 3-tier shaker for growth of plant and microbial cells.

at the University. As a result, he contacted Arthur Uhl, former dean of pharmacy at the University of Wisconsin, who arranged for a meeting with Yusuf Abul-Hajj in Madison. At the time, Abul-Hajj, who studied with Charles Sih and was involved with bioorganic research for his doctoral work, was primarily interested

in pursuing a career in the pharmaceutical industry. However, Weaver explained the advantage of academia and encouraged Abul-Hajj to consider the position at Minnesota. In 1968, Abul-Hajj was hired. Although he had no training in pharmacognosy, his ability to deepen the biological expertise of the pharmacognosy program, in particular through his work using enzymes from microbial cell systems to bring about biochemical transformations, were seen as necessary components for a strengthened program. But to work with enzymes, researchers need access to a cold room, which the College of Pharmacy did not possess. One of Abul-Hajj's first contributions to the pro-



Plant cells growing in a Petri dish.

Robert Vince and others, to use this facility extensively.

Upon discovering that in the days prior to passage of the National Cancer Act it was difficult getting money to fund research in microbial transformations, Abul-Hajj shifted his focus toward cancer and steroids. His research interests involved a variety of areas related to steroid chemistry and biochemistry. The principal focus of his



A fermenter was used by Staba's research personnel for the production of large scale plant cells.

research in the mid-1970s was on the enzymatic mechanisms and stereochemical aspects of steroid hydrogenations and dehydrogenations in both mammalian and microbial systems. He continued throughout his career working on the design, synthesis, and evaluation of aromatase inhibitors, steroidal anti-estrogens, and estrogen-linked cytotoxic agents for the treatment of breast cancer. He also carried out extensive investigations studying the underlying mechanism(s) involved in the genotoxicity/carcinogenicity of estrogens. His laboratory was the first to show the formation of estro-

gram was to raise money from Smith, Kline, & French, a pharmaceutical firm that is now part of Glaxo Smith Kline, to install a cold room in the department. This addition would prove to have far-reaching implications not just for the department or College but for the University as a whole, since it made it possible for researchers working with enzymes, like

Robert Vince and others, to use this facility extensively. Upon discovering that in the days prior to passage of the National Cancer Act it was difficult getting money to fund research in microbial transformations, Abul-Hajj shifted his focus toward cancer and steroids. His research interests involved a variety of areas related to steroid chemistry and biochemistry. The principal focus of his research in the mid-1970s was on the enzymatic mechanisms and stereochemical aspects of steroid hydrogenations and dehydrogenations in both mammalian and microbial systems. He continued throughout his career working on the design, synthesis, and evaluation of aromatase inhibitors, steroidal anti-estrogens, and estrogen-linked cytotoxic agents for the treatment of breast cancer. He also carried out extensive investigations studying the underlying mechanism(s) involved in the genotoxicity/carcinogenicity of estrogens. His laboratory was the first to show the formation of estro-



YUSUF J. ABUL-HAJJ

B.Sc. 1962, M.Sc. 1964, American University of Beirut

Ph.D. 1968, University of Wisconsin

Assistant Professor 1968-72; Associate Professor 1972-79; Professor 1972-present; Head of Medicinal Chemistry and Pharmacognosy 1984-87; Head of Medicinal Chemistry 1987-94, 1996-2005; Director of Graduate Studies in Pharmacognosy, 1982-85, University of Minnesota

Born, Jerusalem, Palestine, 1940.

Awards

- Lawrence and Delores Weaver Medal, 2005
- Fellow, American Association for the Advancement of Science, 1990

gen-nucleic acid adducts, which led his group to propose a new paradigm for the mechanism of estrogen carcinogenicity.

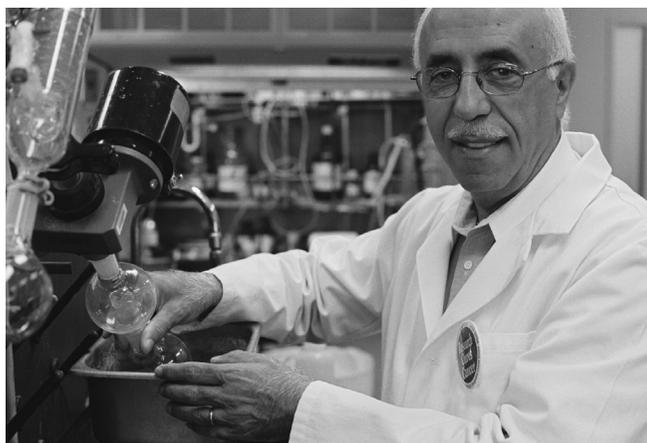
In 2005, Abul-Hajj was selected to receive the Lawrence and Delores Weaver

Medal. Meanwhile, changes in the pharmacy curriculum necessitated hiring a faculty member in pharmacognosy who could teach immunology. As a result, the program got the green light to add Orval Mullen in 1971. Mullen stayed at the University for only three years and focused his energies exclusively on teaching. When Mullen left, he was replaced by Daniel Miller, from the University of Wisconsin, in 1976, as an assistant professor. Described as an entrepreneurial thinker, Miller initiated an ambitious research program in the area of immunological



The cold room acquired in the mid-1970s was moved in the 1980s and is still currently used in Weaver-Densford Hall.

mediators, but became frustrated by the lack of resources available to the pharmacognosy program and left in 1980 to join a group conducting similar research at Riker-3M. He subsequently held positions of vice president for research and development at Dianon Systems, a start-up company involved in perfecting the clinical use of cancer biomarkers, and president of Excorp Medical, which is engaged in the commercial development



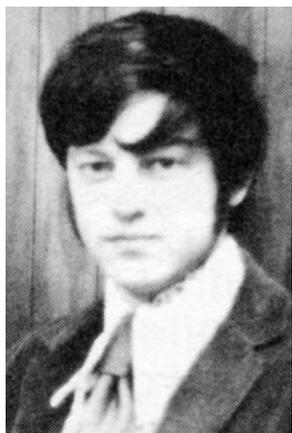
Yusuf Abul-Hajj relaxes in the lab after a stressful day at Central Council.

development of bioartificial liver technology.

Following the departure of Daniel Miller, the College hired Thomas Shier to assume Miller's teaching responsibilities and to embark on research in areas new to the College. Shier initially taught immunology to pharmacy students as Dan Miller had, but added the teaching of

biotechnology as that field developed. When Carston R. Wagner was hired, the immunology teaching was turned over to him, and Shier continued with teaching biotechnology and added the teaching of nutrition. Shier helped found the Toxicology Graduate Program at the University of Minnesota and served as its director of graduate studies for three years.

When Shier came to the College he had 10 years of research experience at the Salk Institute where he worked on mechanisms of cell killing by phospholipase

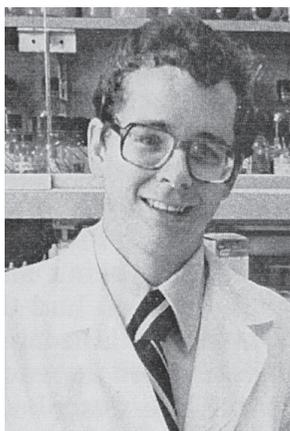


ORVAL L. MULLIN

Ph.D. 1971, The Ohio State University
Assistant Professor 1971-74, University of
Minnesota

activation, but his greatest research achievement was as a graduate student when he developed mutasynthesis, a novel way for making new antibiotics. In Minnesota he continued his studies on cell killing mechanisms including studies on cell killing in ischemic disease such as myocardial infarction and stroke using mammalian cell culture systems and explored the use of ionophores and chelators as tools to study mechanisms of cell killing.

The skills he brought in the use of mammalian cell cultures as a research tool was something new for the department. Mammalian cell culture techniques pro-



DANIEL G. MILLER

B.Sc. 1971, Bucknell University

Ph.D. 1976, University of Wisconsin

Assistant Professor 1975-80, University of
Minnesota

Born, Cambridge, Massachusetts, 1949.

vide important tools for understanding cellular mechanisms, as well as *in vitro* evaluation of drug candidates early in the drug discovery process. Shier quickly set up his laboratory and established the technique in the department. After a few



W. THOMAS SHIER

B.Sc. 1966, University of Waterloo

M.Sc. 1968; Ph.D. 1970, University of Illinois

Assistant Research Professor 1972-80, Salk
Institute for Biological Studies

Associate Professor 1980-85; Professor 1985-
present; Director of Graduate Studies in
Pharmacognosy 1985-90, University of
Minnesota

Born, Harriston, Ontario, Canada, 1943.

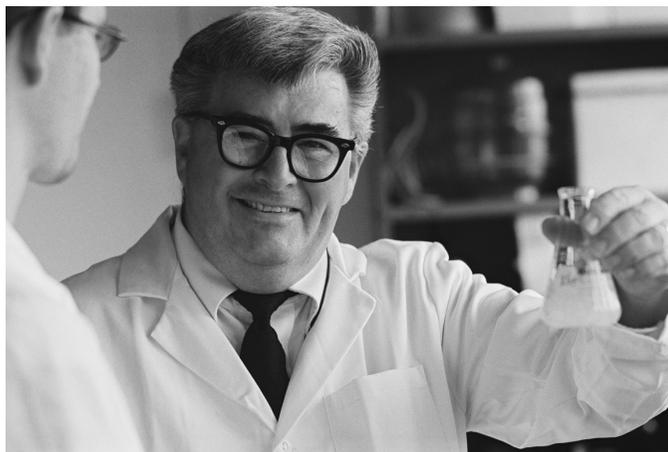
Awards

- Fellow, American Association for the Advancement of Science, 2002

years working with cell cultures, the techniques of mammalian cell culture became an important research tool in medicinal chemistry. Shier's research program has subsequently developed into several related areas. The largest part of the program has been devoted to studies on mycotoxins, which cause cancer, carried out in collaboration with scientists at U.S. Department of Agriculture laboratories. These studies have focused mainly on mycotoxins with significant commercial and health impacts, aflatoxins, fumonisins, and botryodiplodin. Other areas studied have included cryopreservation, single cell protein and most recently the development of novel approaches to drug delivery for human gene therapy.

Some of the major accomplishments of these studies were the first determination of the complete chemical structure of fumonisin B1; elucidating the role of phospholipase activation in cell killing mechanisms; determining the mechanism of action of fumonisins; the discovery of novel inhibitors of tyrosine-specific protein kinases; the discovery of novel food processing-induced structural alterations in contaminating mycotoxins, some of which increased their toxicity; and the discovery that the toxin which facilitates infection of plants by fungi in soil is botryodiplodin, not phaseolinone, as had been widely believed. Shier has also edited, authored, or co-authored three books as a faculty member, one on the study of toxins, one on mammalian cell culture methods, and one on the education system of the Philippines. He is the founding editor of the journal *Toxin Reviews*, which he established in 1980 and has continued to edit for more than 30 years. A co-editor has been added to help with manuscript flow, but the main base of editorial activities has remained housed in the Department of Medicinal Chemistry.

The changes that took place in faculty hires in the 1960s and 1970s in both medicinal chemistry and pharmacognosy led to decreased emphasis on natural product



Thomas Shier shows a big smile for finally getting the compound.

research resulting in an erosion and lack of interest for support of the medicinal plant garden and the green house. At that time, the College had two gardeners, Onie Benson and Clarence Stoltman, who spent many years working with Professors Fischer and Gisvold to maintain a state-of-the-art



Clarence Stoltman, medicinal plant gardener, 1977.

medicinal plant garden. With the decreased emphasis in teaching and research on natural products coupled with the emerging clinical pharmacy education to pharmacy students provided the opportunity for the College of Pharmacy administration to phase out its support for the green house and the medicinal plant garden. Following the retirement of Onie Benson, Clarence Stoltman left the University

two years later. Both positions were not replaced, and their salaries were redirected to support the expanding programs in clinical pharmacy.

The period between 1960 and 1980 had many advances. However, during the same two decades, Dean Lawrence Weaver continued to drain resources from the program, a move accelerated by his decision to de-departmentalize the College in 1974. As part of that move, for the first time in the history of the College, he initiated efforts to merge pharmacognosy into medicinal chemistry. Following the consolidation of the departments, both continued to operate as individual graduate programs, although there was some overlap between the two, particularly in the training of graduate students. Weaver's aim was to eliminate faculty lines in one or both programs, and to open up lines for clinical pharmacy. As it turned out, the merger did not occur until late in the 1980s, by which time the College had moved into new quarters, and Weaver had been replaced by a new dean.

Developments in Publishing & Community

Medicinal chemistry's growing renown as a research-oriented department helped usher in two other significant developments at the College during this time.

In 1972 the department became the new home of the *Journal of Medicinal Chemistry*. The publication began life in 1959 as the *Journal of Medicinal and Pharmaceutical Chemistry*. In 1962, it was acquired by the American Chemical Society with its name shortened to the *Journal of Medicinal Chemistry*.

For the first decade of its life, the journal was edited by co-founder Alfred Burger, a faculty member at the University of Virginia. When Burger retired in 1971, the ACS selected Philip Portoghesi to become editor-in-chief. Portoghesi immediately instituted structural changes that helped turn the journal into the field's leading publication. Setting up offices in the basement of Appleby Hall (the journal is now

housed in Weaver-Densford Hall), he expanded the editorial staff, enlisting associate editors Patrick Hanna (1972-89), Mahmoud Abdel-Monem (1972-83), and Herbert Nagasawa (1972-2004). Over the years, several other faculty members from the department served as associate or senior editors including Rodney Johnson (1984-88) and Yusuf Abul-Hajj (1995-present) (Portoghese, interview, October 2009). As of January 2012, Gunda Georg from the University of Minnesota and Shoameng Wang from the University of Michigan have been selected as the new editors-in-chief of the *Journal of Medicinal Chemistry*.

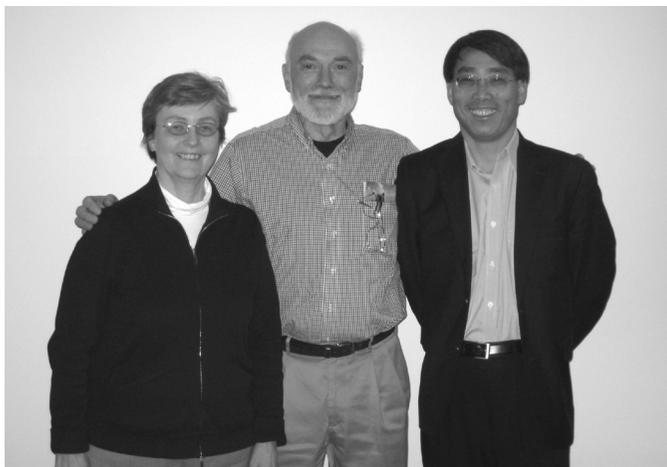
Ultimately, the journal has helped not only the discipline, but also the department by making it more visible to researchers around the world. In turn, this has possibly had an impact on grant funding, increasing the likelihood of success in grant applications and the recruitment of both new faculty and top-quality graduate students.

The second development that came out of the critical period of transition was the establishment of close relationships with four other universities to foster graduate studies in medicinal chemistry.

In 1962, the universities of Minnesota, Iowa, Kansas, and Illinois—all institutions with strong medicinal chemistry programs—created the “Medicinal Chemistry Meeting in Miniature,” or MIKI for short, to provide a forum for graduate students in medicinal chemistry to present papers and to network with faculty and graduate students from other institutions.

Joseph Cannon, a faculty member at the University of Iowa, proposed and hosted the first MIKI meeting. The faculty who oversaw the Iowa graduate students and who helped put together the first MIKI meeting at the University of Iowa in

1963 included: Ole Givold, Taito Soine, and Philip Portoghese from Minnesota; Edward Smissman, Matt Mertes, and Robert Wiley from Kansas; John Gearian, Ludvig Bauer, R. Coviello, and Ralph Daniels from Illinois; and Joseph Cannon and Donald Witiak from Iowa.



The longest serving editor-in-chief (1972-2011) for an ACS publication, Philip Portoghese (center) is flanked by the new editors-in-chief Gunda Georg (left) and Shoameng Wang (right).

In 1966, the host university (the site

for the weekend meeting rotates among the four participating schools) began inviting an eminent researcher—who may or may not be associated with one of the four founding universities—to deliver a keynote address, giving students the chance to meet and socialize with a top scientist in medicinal chemistry (Hanna, interview, November 2009). Over the decades, graduate students have been given increasing responsibility for organizing and managing the event, from arranging accommodations, choosing the venue for the scientific program and selecting the keynote speaker to arranging the opening night reception and a banquet that takes place the second day of the event. Graduate students now also bear the burden of fundraising money to support MIKI meetings. So important is MIKI to graduate education that medicinal chemistry graduate students at the University of Minnesota are required to attend at least four MIKI meetings before taking their Ph.Ds. The MIKI meeting served as a model for similar meetings elsewhere in the United States (MIKI, 2009).



MIKI faculty at its 25th anniversary in 1978. Back row (left to right): Patrick Hanna, William Dunn, Jack Rosazza, Charles Woodbury, Charles Barfnecht, Robert Hanzlik, Michael Duffel, William Rousch (keynote speaker from Indiana University), and Gary Grunwald. Center row (left to right): Lester Mitscher, Rodney Johnson, Rory Remmel, Yusuf Abul-Hajj, Matthias Liu, Thomas Holmes, Gunda Georg, Jeffrey Aubey, and Michael Doherty. Front row (left to right): Donald Witiak (guest faculty member from Ohio State University), Joseph Cannon, Philip Portoghese, James Gearian, Robert Wiley, and Matt Mertes.

Raising the Research Profile

The transformation between 1960 and 1980 of the department from classically-oriented, natural products research into a medicinal chemistry department supported by state-of-the-art instrumentation and increased federal funding was dramatic and played an important role in raising the research profile of the department both nationally and internationally.

These two decades also saw dramatic changes in the College's administrative structure. The change got underway with the resignation of Dean George Hager at the end of 1965 and his replacement by Lawrence Weaver in March 1966, after a brief interim when faculty member Charles Netz served as acting dean.

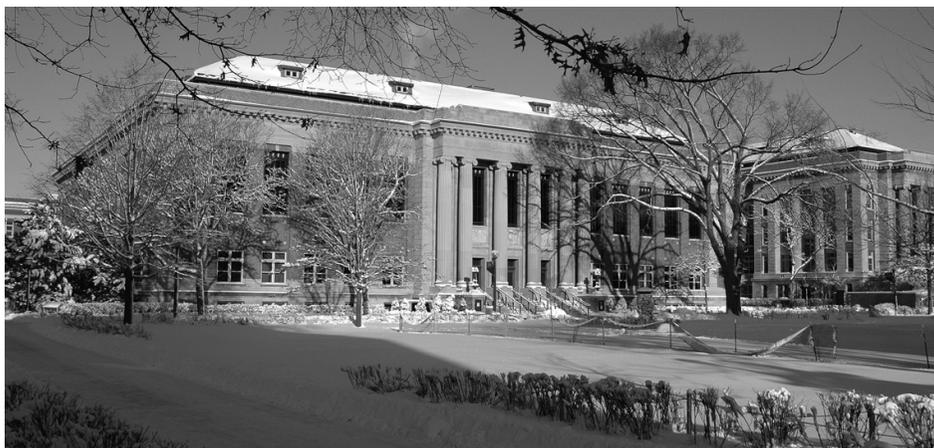
The new dean of the College of Pharmacy would go on to serve two terms in that capacity, totaling nearly 20 years. In the end, his policies would have an impact on the College second only to Frederick Wulling. Unlike every previous pharmacy dean, Weaver came to the University not from academia but from industry, and he brought with him a spirit of innovation and visionary leadership designed to place the College at the top of the pharmacy profession.

For his first eight years as dean, however, Weaver didn't make many dramatic changes to the existing administrative structure, which had changed little over the decades; his predecessor as dean, for example, operated with just one assistant dean for support. By 1974, Weaver continued to rely on just one assistant dean, augmented by a single new staff position reporting to him: assistant to the dean and director of continuing education.

Early that year, though, he took the first real steps toward altering the College's administrative structure, creating three new assistant deanships to join the already extant job of dean of student affairs, to which he appointed Frank DiGangi after Charles Netz retired in 1966. Hugh Kabat, a faculty member in pharmacy administration, became assistant dean for administration. Taito Soine was appointed assistant dean for research and graduate studies, and John Staba as assistant dean for professional education.

Not long after, Dean Weaver initiated even more far-reaching administrative changes designed to advance his goal of putting the College at the forefront of pharmacy education.

Weaver was convinced that clinical pharmacy was the wave of the future. But the path forward was challenging, to say the least. Since money to expand the number of faculty in clinical pharmacy was not available from the University's central administration, the only option was to reallocate resources from other departments within the College. At the time, medicinal chemistry commanded the most resources, but faculty in both that department and in pharmacognosy resisted the idea of diverting any of their resources in order to fund a beefed-up clinical pharmacy undertaking.



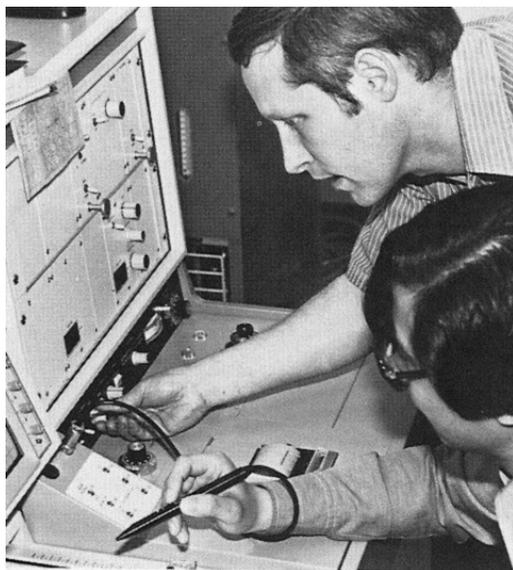
Walter Library was built in 1924 and renovated to its present condition in 2002.

Until 1974, Weaver had administered the College with the help of a faculty council, later called the Administrative Advisory Committee. The council consisted of the assistant deans and the chairs of the College's four departments: medicinal chemistry, pharmaceuticals, pharmacognosy, and pharmacy administration.

In order to free up resources—in which allocations were tied to the departments—Weaver made the bold move of dissolving the departments. He replaced them with an administrative structure of four units organized along functional lines. There was now a Drug Action Unit, which included medicinal chemistry and pharmacognosy; a Drug Delivery Unit, which included pharmaceuticals; a Professional Practice Unit, which encompassed clinical pharmacy and related activities; and a Continuing Education Unit. Operating alongside these units was the College's graduate program, which continued to function like a department (Anderson & Pennigton, 2005, 98-104).

To head up these new units, Weaver bypassed the former departments and appointed other faculty members, some of whom, like Abdel-Monem, were relatively new to the College. Dissolving the departments was a way of reducing perceived resistance to change by department members while at the same time uncoupling the undergraduate curriculum (and resources to underwrite that curriculum) from departmental control (Abdel-Monem, interview, 2009).

Within medicinal chemistry, de-departmentalization brought about dramatic changes in undergraduate curriculum. For example, prior to the transition the department had two large laboratories designated for exclusive use for undergraduate courses. By the end of the transition to the new functional unit structure, those laboratories were gone. In addition, the department moved from a chemistry-based focus to a focus on therapeutic applications—a shift that brought medicinal chemistry more into synch with the pharmacology unit. As director of the Drug Action



Tom Holmes training a student on the use of the 100MHz nuclear magnetic resonance spectrometer housed in Appleby Hall.

Unit, Abdel-Monem spearheaded a faculty effort to develop an integrated multidisciplinary course sequence with faculty in medicinal chemistry (Hanna), pharmacognosy (Abul-Hajj), and pharmacology (Dunham). The main objective of these courses was to avoid duplication and provide a better way of integrating the course content. This innovative approach continued throughout the years spanning from 1975 through 2012.

Dunham joined the University as an instructor in the School of Medicine, teaching and coordinating the pharmacology courses to pharmacy students. He played a key role in the integration of medicinal chemistry,

pharmacognosy, and pharmacology courses and continues in this regard. He joined the Department of Medicinal Chemistry in 1982 as an associate professor. His research has focused on the biosynthesis and pharmacology of endogenous vasoactive



EARL W. DUNHAM

B.S. 1965, Drake University

Ph.D. 1971, University of Minnesota

Instructor, 1971-72; Assistant Professor, 1972-79;

Associate Professor 1979-present, University of Minnesota

Born, Peoria, Illinois, 1942.

mediators and their role in hemodynamics and hypertension. During the 1970s, he instructed several medicinal chemistry graduate students in the application of methods for biological evaluation of their target compounds and has participated in collaborative research with Professors Portoghesi, Vince, and Nagasawa.

Weaver continued to evolve the administrative structure, eventually adding a layer of assistant deans to oversee the four functional units. But budgetary decisions lay firmly in the hands of the dean. Under the new administrative structure, then, the fight for resources became a matter of individual faculty dealing directly with the dean without the intermediary of a departmental head (Anderson & Pennigton, 2005, 98-104).



Autoclave used by pharmacognosy and medicinal chemistry researchers.

But in medicinal chemistry, faculty found a novel way to band together and sustain a departmental identity, even in the face of de-departmentalization.

During the transition, Portoghese was named director of graduate studies in medicinal chemistry. In that position, he rallied his colleagues by creating a “shadow” department of graduate studies in medicinal chemistry, complete with its own letterhead and regular departmental meetings but devoid of any budgetary support by the College administration. Such was the esteem Portoghese enjoyed in the eyes of the University’s central administration that the dean’s office simply turned a blind eye toward this small, but nonetheless critical act of defiance (Hanna, interview, 2009).

Finding A Home on Campus

The College’s move from Wulling Hall to Appleby Hall in 1960 brought new laboratory and office space to the department. The change, however, was barely three years old before discussion got underway about a larger, comprehensive change in University facilities that would eventually see medicinal chemistry move again, into its present headquarters.

In 1964, University President Charles O. Wilson created the Committee for the Study of Physical Facilities for the Health Sciences, to take a comprehensive look into the facilities needs not just of the College of Pharmacy, but of all the health sciences at the University. At the time the University’s five-year facilities plan called for a modest expansion of Appleby Hall.

Then in 1966, Dean Lawrence Weaver was added to the facilities committee and given the task of canvassing the faculty and administrators in the College of

Pharmacy on whether or not the College should be included in a larger comprehensive health sciences complex of facilities (Netz, 1971, 148).

Early in 1967, Weaver submitted his report to the committee. In it, he said that the College had determined that it must be part of the integrated health care complex because of a number of critical issues, including the prospect of steadily rising undergraduate enrollment and additional space needed for faculty and research facilities. At that time, the College of Pharmacy had some 31,000 square feet of space but was projected to need more than four times that much—133,000 square feet—by the middle of the 1980s.

As a result Weaver soon let faculty members know that the College was now part of the planning process for the proposed health sciences center. In 1969, the Legislature appropriated \$14 million for construction, with most of that money devoted to dentistry and the basic sciences. The University also requested federal matching funds. At this stage, neither the Legislature's appropriation nor the request for matching grants included funding for a new facility to house pharmacy (College of Pharmacy, 1977).

Dean Weaver now took the initiative in appointing a task force to prepare a direct College of Pharmacy request to the Minnesota Legislature. Although that request was withdrawn, the Legislature did approve additional funding that included money to initiate planning and purchase land for "Unit F," a part of the health sciences facility that would house both pharmacy and the School of Nursing (*ibid.*).

Groundbreaking on the first of the buildings took place in 1971. It would house the School of Dentistry and the School of Public Health, along with parts of the School of Medicine. Three years later, by which time work had also begun on a second building that would become the Phillips Wangensteen Building, funding for the pharmacy and nursing complex was still no closer to hand.

But Weaver was undaunted. He and the dean of the School of Nursing resubmitted the request for federal funding, proposing in return a big jump in the number of students enrolled each year into the pharmacy program even though projections of employment trends didn't really justify that kind of increase. In any case, the federal government went ahead and appropriated almost half of the projected \$21 million cost of the pharmacy/nursing building in 1975.

Next, Dean Weaver was faced with the need to raise matching funds from the state, which he coupled with a drive to raise money from private sources. In approaching the state he combined direct lobbying with legislators by himself and other officials at the College with pressure from the Minnesota State Pharmaceutical Association.

The efforts proved to be of little avail, at least in the short-run. Instead of matching the \$8.7 million federal grant, state legislators offered up a meager \$300,000 to pay for a study of ways to answer the needs of nursing and pharmacy for more space



Preparing the site of the new pharmacy building after demolition of the Fenwick apartments (these university-owned apartments housed some pharmacy departments including social and administrative pharmacy).

raise a matching grant. Together, the Regents, Dean Weaver, and the dean of School of Nursing returned to the state capitol to try again.

This time, Dean Weaver succeeded. After a spring visit to the campus by members of the Senate Finance Committee and a change of heart on the part of Gov. Rudy Perpich—who had initially opposed the idea of putting state money into a new pharmacy/nursing facility—the Minnesota Legislature passed a measure on the last day of the session approving money to help move the College and build a new facility to house it.



Groundbreaking for Unit F, left to right: C. Peter McGrath, President of the University; Irene Ramey, Dean of Nursing; Lyle French, Vice President for Health Sciences; Rudy Perpich, Governor; and Lawrence Weaver, Dean of Pharmacy.

without constructing a new building.

Despite the rejection, Weaver pushed on. He fought suggestions that Appleby Hall be upgraded and expanded to meet pharmacy's space needs, and continued lobbying hard at the Legislature.

In 1977, he won a breather when the federal government granted an extension on the time limit to raise a matching grant. Together, the Regents, Dean Weaver, and the dean of School of Nursing returned to the state capitol to try again.

Groundbreaking on what would become, fittingly enough, Weaver-Densford Hall, took place in fall, 1977, and the new building was ready for its new tenants by the end of the summer in 1980 (Anderson & Pennigton, 2005, 94-8). Not only did the move greatly increase and modernize the space



Unit F, later named Weaver-Densford Hall, was occupied with the College of Pharmacy from 1981 to the present day.

department as it provided an avenue with increased research collaborations with researchers in the medical school (*ibid.*, 94-8). §

available for the College, but for the first time in the school's history, it fully integrated the College into the University's multi-departmental college Academic Health Center. Although most faculty members in medicinal chemistry and pharmacognosy were not in favor of the move, in retrospect, this change was the best thing that happened to the department

Chapter 4

INTO THE FUTURE

In 1981, the College of Pharmacy moved into what was then called simply Unit F. The building is now known as Weaver-Densford Hall, in part to honor the deans who were the driving force in getting it built. But instead of this milestone marking the onset of a period of stability and manageable development, the 1980s would, like the preceding decade, be a time of transition and turmoil, not just for the department but for the University as a whole.

One of the sources of that turmoil was financial. The same year the College moved into its new facilities, the American economy took a nosedive into the worst recession to hit the country since the end of World War II.

Accompanying the recession was the inauguration of President Ronald Reagan and the rapid ascent of a new—or even radically different—conception of the proper relationship between the private and public sectors. President Reagan was a champion of a specific form of free market capitalism and shared that philosophy with Margaret Thatcher, who was elected Prime Minister in the United Kingdom at about the same time: the belief that anything government can do, private enterprise can do better. This led, not surprisingly, to a nationwide emphasis on privatization—the shifting of responsibility to private entities not only for implementing the tasks previously assigned to the public sector but for funding those tasks as well.

In higher education, that shift meant steep reductions in federal support, followed in time by reductions in state funding. In short order, a combination of a shrinking tax base caused by the recession and sharp increases in military spending led to mushrooming federal deficits that made the impulse to reduce funding from Washington even more urgent. In the five years ending in 1983, state funding for the University dropped almost 20 percent while federal funding shrank by an alarming 56.7 percent during the same period.

These cutbacks led to mandatory budget reductions throughout the University,

including the College of Pharmacy, which had to find ways to reduce expenditures (Anderson & Pennigton, 2005, 153-4).

The cuts led to suggestions by Dean Lawrence Weaver to merge the Department of Medicinal Chemistry with Pharmacognosy, folding the smaller program into the larger medicinal chemistry program—a suggestion that ultimately was carried out, though only several years later. Less predictably, the belt-tightening also led to a reversal of the previous decade's most radical innovation: de-departmentalization of the College.

De-departmentalization had never sat well with faculty, particularly for the faculty in medicinal chemistry with its long history of strong departmental identity and autonomy.

The return to a department structure had been broached in faculty meetings with the dean as early as 1981. Although efforts by several faculty groups to convince Dean Weaver about the need for departmentalization were not well received, he eventually appointed a committee that year, with Mahmoud Abdel-Monem as chairperson and Yusuf Abul-Hajj representing the medicinal chemistry/pharmacognosy faculty. The committee addressed the issues of reorganization and the reestablishment of academic departments and submitted its recommendation to Weaver late in 1982. In March 1983, he announced plans to reinstate departments, in order to better achieve targeted cuts and assign clear lines of accountability for cost-containment and spending. By the following fall, the College had four formal units: pharmaceuticals; pharmacy practice; social, administrative, and hospital pharmacy; and medicinal chemistry and pharmacognosy, headed by Abdel-Monem.

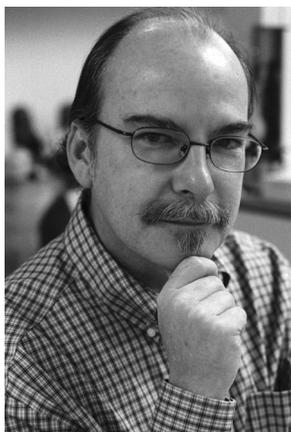
Although the former departments of medicinal chemistry and pharmacognosy were administratively one unit, the professional pharmacy curriculum was integrated and the graduate programs were completely autonomous and had their own curriculum and director of graduate studies.

The move was significant but not quite the return to the autonomy previously enjoyed by faculty over the governance of their departments. Under the new plan, the four new units would be run by department heads rather than department chairpersons. The department heads, meanwhile, would be appointed by the College dean, rather than elected by faculty with voting rights within the departments. That structure, however, was offset to some degree by the establishment of a permanent advisory council of faculty, also created by Weaver, which would include elected members as well as those appointed by the dean (Abdel-Monem, interview, 2011).

Dean Weaver did not have much time to place his personal stamp on the new order of things. At a faculty meeting early in 1984, he announced that he was resigning at the end of June to become vice president of what is now the Pharmaceutical Research and Manufacturers of America (Anderson & Pennigton, 2005, 156-7).

Weaver left before a permanent replacement could be found. Upon his departure, Abdel-Monem, recently appointed head of the Department of Medicinal Chemistry and Pharmacognosy, was made interim dean. During his year in the position, Abdel-Monem was able to unite the faculty and maintain the momentum for continued progress.

The search for a permanent replacement was a long process, and it was not until early in 1985 that the College announced that Gilbert Banker had been chosen to take over as the new dean (Anderson & Pennigton, 2005, 116). Abdel-Monem was appointed Associate Dean for Academic Affairs, a position he held until 1987 when he left Minnesota to assume the position of Dean of Pharmacy at Washington State University.



RORY P. REMMEL

B.Sc. 1976, University of Wyoming-Laramie

Ph.D. 1982, University of Washington

Assistant Professor 1984-91; Associate

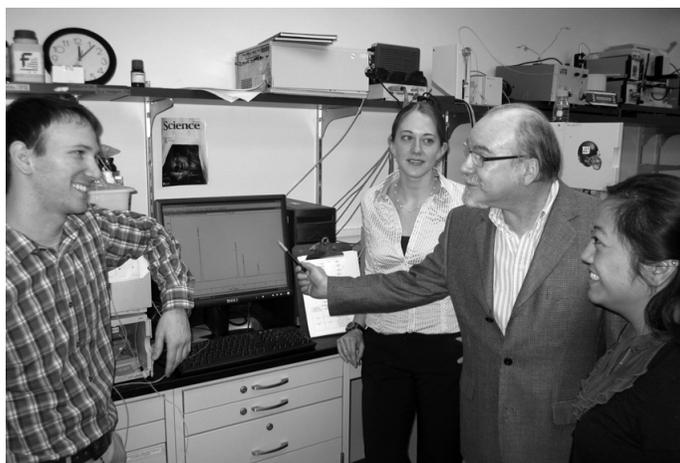
Professor 1991-98; Professor 1998-present,
University of Minnesota

Born, Colorado Springs, Colorado, 1954.

Awards

- Award for Outstanding Contributions for Professional and Graduate Education, 2010

Although Abdel-Monem continued teaching, his increased administrative responsibilities made it difficult for him to continue his courses. Dean Banker, therefore, approached the department and requested the appointment of Rory Rimmel as an assistant professor to assume Abdel-Monem's teaching responsibilities. At that time, Rimmel was working as a postdoctoral research associate with Abdel-Monem and was already giving a few lectures to pharmacy students. Rimmel brought a wealth of experience to the department in the use of modern analytical techniques for identification and measurement of drugs and their metabolites in small quantities of biological fluids. He spearheaded a departmental initiative in acquiring state-of-the-art instruments including gas chromatography, high pressure liquid chromatography, and mass spectrometry. Rimmel's research included investigations on the metabolism and chemical mechanisms of hepatotoxicity of antifungals and antiviral agents, the mechanisms of metabolic interactions between investigational antiepileptics and standard antiepileptic drugs using *in vitro* and *in vivo* animal models, and the role of glucuronidation and cytochrome P450 enzymes in drug-drug inter-



Rory Rimmel discusses HPLC results with graduate students Aaron Teitelbaum, Kathy Nelson, and Amy Doan.

actions. In collaboration with Robert Vince, Rimmel and Cheryl Zimmerman conducted the first animal pharmacokinetic studies on (+)-carbovir and (-)-carbovir in rats, leading to a National Institutes of Health (NIH) grant on prodrugs of carbovir.

From 1992 to 2002, Rimmel and Courtney Fletcher from the Department of Pharmacy Practice were co-investigators on a National Institute on Allergy and Infectious Diseases (NIAID) contract as one of five national sites for a combined pediatric and Adult AIDS Clinical Trials Group (ACTG) Laboratory that supported multi-site clinical trials of AIDS drugs. Rimmel directed the analytical laboratory and several novel assays, including one of the first simultaneous assays for protease inhibitors were developed and validated. In collaboration with several surgeons and chemical engineering professors at the University, Rimmel was instrumental in the development of a bioartificial liver utilizing collagen-entrapped hepatocytes in a hollow-fiber reactor. This effort was begun by Frank Cerra, a critical care surgeon, and Wei-Shou Hu, a faculty member in the Department of Chemical Engineering. The result was a licensing agreement with Regenerex.

Rimmel also excelled as a teacher and was the recipient of several teaching recognitions including the semester and teacher of the year awards. He also was recognized in 2010 with the Award for Outstanding Contributions for Professional and Graduate Education from the Academy of Distinguished Teachers. In the same year, he was awarded the first Outstanding Faculty Award from the Council of Graduate Students.

At the collegiate level, the administration's philosophical break with Weaver following the new dean's appointment was distinct. Banker, who'd received his doctorate from Purdue University where he went on to serve as a faculty member in pharmaceuticals, came to the University of Minnesota with a formidable record in research and writing, including a book he authored, *Pharmaceutics and Pharmacy Practice*. At his very first meeting with College faculty he made it clear that one of his top priorities would be to increase efforts to garner external funding, principally

through research grants, and to strengthen the departments, which now would have chairpersons rather than department heads. He also announced that he planned to have monthly meetings with the faculty.

In the meantime, Banker's inclination toward strong departments and enhanced research was reinforced by implementation of a new University-wide initiative called "Commitment to Focus," introduced by Kenneth Keller, who took over as president of the University of Minnesota only a few months before Banker was appointed dean of the College of Pharmacy.

As part of this new University-wide effort, each unit at the University identified internal goals. For the College of Pharmacy one such goal was to double outside research funding by the end of the 1980s. At the time, the majority of federal research money, principally from the NIH, was coming to medicinal chemistry and pharmacognosy—a little less than \$1 million per year at the time Commitment to Focus was launched. In response to the ambitious goal to double that figure, the department more than doubled the amount of outside research funding in just four years, reaching a total of \$2.3 million by 1989, with average funding per faculty member rising from \$78,000 to \$193,000 during that time. The increase, in turn, reflected trends already at work within medicinal chemistry, such as the acquisition of increasingly sophisticated equipment and techniques like NMR (nuclear magnetic resonance) and molecular modeling (Anderson & Pennigton, 2005, 156-69).

The emphasis on research and funding in Commitment to Focus, as well as Dean Banker's own research orientation, proved beneficial to medicinal chemistry with its long tradition of research orientation and strong departmental identity. In 1984, when Abdel-Monem was appointed interim dean, Abul-Hajj was appointed interim department chairperson. With Banker in the driver's seat, Abul-Hajj was offered the job on a permanent basis. Abul-Hajj seized the opportunity as a chance to put the department's fiscal house in order.

According to observers, at the time the College of Pharmacy was, for a variety of reasons, in a shambles financially. Funding allocated by the College to the four departments was not sufficient to meet expenses, and the Department of Medicinal Chemistry had been running a deficit for several years. One of the conditions that Abul-Hajj outlined for accepting the job of department chair was that the structure by which the departments were funded be changed. Banker, in consultation with Abdel-Monem, concurred and the necessary reforms were implemented.

When Abul-Hajj became the department chair, the dean's office under Weaver was keeping 100 percent of the indirect cost recovery (ICR) funds that faculty in medicinal chemistry were awarded as part of their federal research funding; no faculty outside the department was bringing in any ICR at that time. To make matters seem even less fair, Weaver refused to approve any grant application that did not seek ICR. If he was going to run the department, Abul-Hajj stipulated that this par-

ticular inequity would have to be rectified as would salary offsets—another chunk of indirect savings coming in by way of research grants. When Banker came on board the dean's office was keeping the savings in salary from faculty in medicinal chemistry who were winning outside funding. That, too, would have to change.

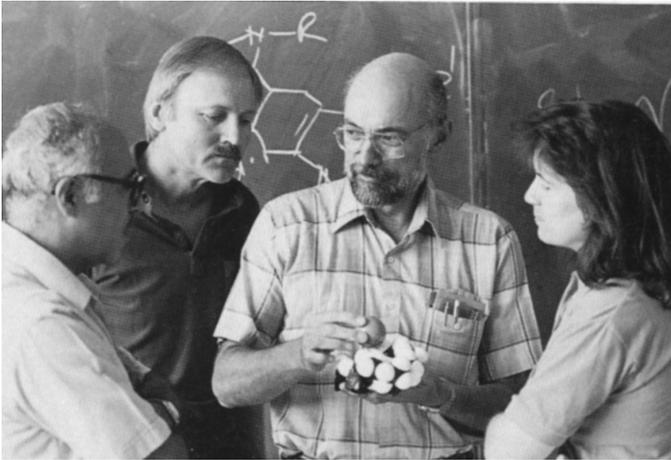
In a major signal of the new era ushered in by Dean Banker and the University's Commitment to Focus, the College acceded to Abul-Hajj's requests. Banker agreed to pass on 80 percent of the ICR and salary offset money to medicinal chemistry, with the College holding the balance.

Suddenly, the department, which had been operating in the red, now had abundant resources with which to proceed. Abul-Hajj approached the medicinal chemistry and pharmacognosy faculty to gather their ideas on how best to use the funds. For his part, he proposed that all of it be used over the next few years to build the department's infrastructure and acquire instrumentation. Because of the faculty's success in more than doubling the amount of research funding coming to medicinal chemistry, the department began to build up a reserve within only a couple of years. Abul-Hajj and the faculty agreed to a plan in which individual researchers would now receive half of the ICR and salary offset money grants generated.



Graduate student Mike Genin helps another student on the proper use of the GE 300 MHz NMR spectrometer.

In retrospect this transformation from a resource-starved to resource-rich department marked a turning point in the history of the department, at least in modern times. With the new departmental structure, medicinal chemistry regained its autonomy over coursework. With the new financial policies, it gained a high degree of autonomy over resources as well. By the end of the 1980s as the department reserve kept build-



Philip Portoghese discusses the interaction between ligand and a receptor model with Yusuf Abul-Hajj, Dennis Larson, and graduate student Eileen Larkin, 1985.

ing, eventually 75 percent and finally 100 percent of the ICR and salary-off-set money was reverted to individual faculty. For example, 80 percent of Philip Portoghese's salary came from outside the University, a situation that allowed him to place the funds he would have received from the University into a

reserve fund to underwrite future research projects.

The department's research muscle was further enhanced by faculty hires during this period. Immediately following his appointment as dean, Banker discovered that the College had no program in radiopharmacy. Coming from Purdue University,



MARK A. GREEN

B.Sc. 1978, Rose-Hulman Institute of
Technology

Ph.D. 1982, Indiana University-Bloomington
Assistant Professor 1985-88, University of
Minnesota

Born, Sidney, Ohio, 1956.

which had a strong research and teaching focus in radiopharmacy and radiochemistry, Banker arranged with the department to hire a faculty member with a joint appointment in radiology and medicinal chemistry. Following a national search, Mark Green was hired with 90 percent of his appointment in radiology and 10 percent in medicinal chemistry.

Green brought a strong background in organometallics with a primary focus

on the use of metal radionuclides in imaging with positron emission tomography (PET). He conducted research on gallium and copper PET radiopharmaceuticals for mapping perfusion in the heart, brain, and kidneys, as well as the application of gamma imaging techniques in the evaluation of novel therapeutic dosage forms. His stay in Minnesota, however, was cut short after accepting a faculty position in 1988 at Purdue University.



SIMON MBUA NGALE EFANGE

B.A. 1979, State University College Geneseo,
New York

Ph. D. 1984, State University of New York at
Buffalo.

Assistant Professor 1988-93; Associate
Professor 1993-99; Professor 1999-2003,
University of Minnesota

Born, Nigeria, 1952.

Following Green's departure, Banker pressed for an immediate replacement, which led to the hiring of Simon Efange. Trained as a medicinal chemist with a focus on biochemical pharmacology, Efange used his synthetic chemistry skills, preparing novel receptor specific activity agents aimed at regional mapping of the living brain and their involvement with the cholinergic systems. These studies were designed to better understand neurological disorders in AIDS, Parkinson's, and Alzheimer's diseases. After spending 14 years at Minnesota, Efange decided to go back to his native Cameroon to help in building that country's educational institutions.

New Directions

Even while resources were opening up for the department, the College continued to move toward implementing Commitment to Focus. At a meeting with college deans, President Keller announced that one of the goals of the new initiative would be to phase out smaller departments. Since both medicinal chemistry and pharmacognosy were relatively small departments, their viability suddenly became an issue. Unless one or both could be made to grow, each would lose faculty lines, especially since the curriculum of the two programs at both the undergraduate and graduate level had significant overlap. Although he'd been hired as a faculty member in pharmacognosy, Abul-Hajj came to the painful conclusion that the best solution

for meeting the Commitment to Focus objectives was to fold pharmacognosy into a single enlarged and strengthened Department of Medicinal Chemistry.

Initially the faculty in medicinal chemistry and pharmacognosy wanted nothing to do with the proposed merger. At a meeting shortly after Abul-Hajj announced his intentions, the faculty rejected all three options he presented. To avoid an impasse—and any appearance of high-handedness—Abul-Hajj appointed a committee composed of two members each from medicinal chemistry (Philip Portoghese and Rodney Johnson) and pharmacognosy (John Staba and Thomas Shier) and charged it with studying the dilemma and returning a recommendation. Three months later, the committee returned its verdict. The proposal to merge the departments was the best, albeit, painful solution. In 1987, the name pharmacognosy was dropped, and there would only be one combined entity operating under the name of Department of Medicinal Chemistry.

Transformation Continues

The late 1980s were a period of transformation in other areas as well.

During the 1960s and 1970s the discipline of medicinal chemistry was grounded in synthetic organic chemistry guided primarily by *in vitro* and *in vivo* pharmacological testing to generate “hand-crafted” molecules that provided the knowledge base for the advancement of medicinal chemistry. However, the 1980s brought new advances in molecular biology and computational sciences, which helped to focus medicinal chemistry. These advances provided an increased awareness of structure-activity relationships, greater inputs from target structures and *in silico* modeling, new discovery techniques, as well as the necessity to integrate pharmacokinetics, metabolic, and toxicological considerations into molecule design and synthesis. They also brought about an ever-more detailed knowledge of disease mechanisms and pathologies. Furthermore, as synthetic chemistry was itself increasingly influenced by the paradigms of molecular biology—diversity, evolution, replication, and self-organization—the medicinal chemist had become increasingly linked with molecular- and cell-based biological disciplines.

All these changes at the interface between chemistry, biology, and disease necessitated a closer look at the new requirements for educating and training future medicinal chemists. The combined impetus of Dean Banker’s appointment and President Keller’s Commitment to Focus led the College of Pharmacy to begin the process of long-range planning, requiring each department, in turn, to develop a strategic plan.

Through intense faculty discussion, the Department of Medicinal Chemistry adopted an ambitious strategic plan that won strong support from the College administration. The plan called for strategic hires over the following five years to

support the trends focusing medicinal chemistry research on structure-based drug design. Although the plan was lauded by the College administration, no funds were made available to support appropriate hires.

In the meantime, Portoghese was offered an endowed professorship in 1986 at the University of Tennessee that would provide him with considerable space as well as new faculty hires in computational chemistry and substantial resources for research. He was seriously thinking about accepting the offer, but was willing to consider remaining at Minnesota if the College hired a computational chemist; Portoghese's research program required such skills. Abul-Hajj, with the help of Associate Dean Abdel-Monem, worked hard to convince Banker to make a counteroffer and provide the necessary funds for retention of Portoghese. Funds from the College, Graduate School, and the office of Vice President for Health Sciences were committed and were sufficient to convince Portoghese to stay.

Portoghese's need for computational science assistance was also fulfilled. Following a national search for an assistant professor in computational modeling, an offer was made to Terry Lybrand in July 1986 to join the Department of Medicinal Chemistry, which he decided not to accept on the grounds that the start-up package offered by the College was insufficient to establish a strong research effort in computer modeling and computer-assisted drug design.

Later that year Lybrand informed Abul-Hajj that he received a National Science Foundation Young Investigator Award, which required matching funds from industry. Abdel-Monem, Portoghese, and Abul-Hajj put a request for matching funds (\$137,500) into the Riker-3M company to set up and support the equipment needs for a computer-assisted molecular modeling center to be housed in Weaver-Densford Hall. With these funds in hand, Lybrand accepted an offer to join the department in April 1987 as assistant professor of medicinal chemistry and was also appointed as a fellow of the University's Supercomputer Institute. In addition, he set up a computer-modeling center in Weaver-Densford Hall equipped with silicon

**TERRY P. LYBRAND**

B.Sc. 1980, University of South Carolina-Columbia

Ph.D. 1984, University of California-San Francisco.

Assistant Professor 1986-90, University of Minnesota

Born, Fort Gordon, Georgia, 1957.

graphics and other computers to carry out molecular modeling and dynamics studies.

Although Lybrand was on his way to establishing a highly visible and productive program in molecular dynamics and computational chemistry, he decided to leave the University in 1990 to accept a position at the University of Washington. Following his departure, it was agreed during discussions between Banker, Abul-Hajj, Portoghese, and Leo Furcht, head of the Department of Laboratory Medicine and Pathology, that not only would medicinal chemistry hire a replacement for Lybrand but, in addition, Furcht would hire a technical support person, with both positions to be housed in Unit F. Furcht, however, decided instead to hire his own computational scientist.

Abul-Hajj then negotiated with Donald Truhlar, director of the Supercomputer Institute, to provide an annual budget to support the acquisition of software and hardware as well as funds for a 50 percent appointment of a technical support staff person. This ultimately led to the establishment of a visualization and computer-



The Center for Simulations and Visualization was initially equipped with three interactive Silicon Graphics 4D/30 TG and a 4D/310 VGX workstations and one 240 S supercomputing server. Faculty member Dennis Larson and graduate student Scott Moe run a molecular dynamic simulation experiment.

modeling center as a satellite of the Supercomputer Institute. It was housed in Weaver-Densford Hall where it served the computational needs for scientists in the Academic Health Center plus the engineering and chemistry departments. The center was instrumental in helping many research staff begin to learn and apply the techniques of molecular modeling and dynamics to advance studies in the design of molecules that would have better binding with their target protein. The center is cur-

rently housed in a building at 717 Delaware Street Southeast and is still supported in part by the Supercomputer Institute.

In addition to Lybrand, there were several other strategic hires in the closing days of Banker's tenure as dean of the College.

With the acquisition of a new 500 MHz NMR instrument by biochemistry, the Department of Medicinal Chemistry hired Deborah Kallick in 1991 to establish and develop the area of drug design using high resolution NMR spectroscopy.

Kallick was the first of several high-resolution NMR specialists at the University to develop the art of drug design using high resolution NMR spectroscopy. During the next few years the University acquired several high resolution NMR spectrometers including the 600 and 800 MHz instruments. Kallick used these instruments to look at biomolecules, especially proteins and DNA, and to investigate the interaction of ligands with the macromolecules. Kallick left the university in 1999 for a position at Incyte Genomics.

David Ferguson joined the department in 1991 after spending two years as a postdoctoral trainee in Peter Kollman's laboratory at University of California at San



DEBORAH A. KALLICK

B.A. 1980; Ph.D. 1986, University of Illinois-Chicago

Assistant Professor 1991-97; Associate Professor 1997-99, University of Minnesota

Francisco. During the 1990s, Ferguson focused his research program on employing quantum mechanics, molecular mechanics/dynamics, and computer graphics to look at structural models of opioid receptors in order to delineate the molecular basis for ligand binding, selectivity, and receptor activation. In recent years, Ferguson has focused his research on the design and discovery of new therapeutics, as anticancer and antiviral agents, using both traditional structure-based drug design methods and high throughput screening techniques.

To continue strengthening the department and consistent with the departmental strategic plans, the department convinced Banker to provide funds to hire a new faculty member with expertise in molecular biology and site-directed mutagenesis.



DAVID M. FERGUSON

B.Sc., Bucknell University
 Ph.D. 1989, University of South Florida
 Assistant Professor 1991-97; Associate
 Professor 1997-2007; Professor 2007-
 present; Director of Graduate Studies in
 Medicinal Chemistry 2011-present,
 University of Minnesota
 Born, Philadelphia, Pennsylvania, 1961.

A national search led to the hiring of Carston Wagner.

Wagner came to the Department of Medicinal Chemistry in 1991 after completing a Ph.D. in chemistry at Duke University and an NIH Post-Doctoral Fellowship with Stephen J. Benkovic at Penn State University. Wagner was hired by the department in an effort to broaden and enrich the department with the techniques for recombinant protein expression, molecular biological analyses, and site-directed mutagenesis.

Wagner quickly started a program in targeted catalytic antibody nucleoside prodrug activation, which led him to discover that nucleoside phosphoramidates could be useful antiviral and anticancer agents. After further study, his laboratory in collaboration with Cheryl Zimmerman of the Department of Pharmaceutics determined that nucleoside phosphoramidates improved the pharmacokinetic parameters of nucleotides. Animal studies conducted in collaboration with Abul-Hajj showed that



David Ferguson asks John Goodell to purify the topoisomerase inhibitors.

phosphoramidates of AZT were potent anti-breast cancer agents. Wagner continued to work on the mechanism of cellular uptake and metabolism, subsequently discovering phosphoramidases responsible for the bioactivation of nucleoside phosphoramidates.

In 2004, Wag-



CARSTON R. WAGNER

B.Sc. 1981, University of North Carolina-Chapel Hill
Ph.D. 1987, Duke University
Assistant Professor 1991-97; Associate Professor 1997-2004; Professor 2004-present; Director of Graduate Studies in Medicinal Chemistry 2002-09 & 2011, University of Minnesota
Born, Burlington, North Carolina, 1959.

ner began to branch out into a new area—the study and design of small molecules that are capable of dimerizing proteins. His laboratory discovered the first chemically directed method for the self-assembly of proteins to defined nanostructures. He has applied this approach to the design of unique nanostructures that have been fused to targeting single chain antibodies and peptides. These structures are being evaluated for their ability to carry out drug delivery and as tools to understand the behavior of cellular receptors.

Wagner has been a highly collaborative researcher, engaging in projects with members of the department faculty, medical school, chemistry, mechanical engineering, and the University's Biotechnology Institute. In collaborations with Patrick Hanna and his long-standing interest in N-Arylamine acyltransferases (NAT), Wagner and Hanna cloned and developed the first recombinant expression systems for eukaryote NATs. They uncovered key features of their catalytic and kinetic mechanism as well as mapped their substrate specificities, especially for common environmental aryl amine carcinogens and established key features of their behavior in cells.

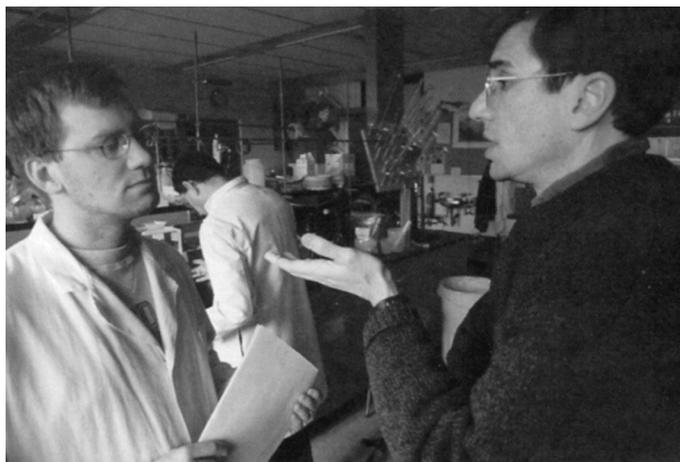
Wagner has had an impact on the department and the University in many other ways. Most importantly has been his interest



The Weisman Art Museum was designed by Frank Gehry and completed in 1993.

in developing interdisciplinary initiatives to facilitate research at the interface of chemistry, biology, and engineering. Early on, he recognized the value of bringing faculty, students, and researchers together from around the University who are working at the interface of chemistry and biology. After a year of study, he spearheaded the chemical biology initiative, which was initially funded by the Office of the Vice President for Research within the University. Wagner became the first director in 2003 and continues to serve in that position.

In this area, Wagner was also instrumental in championing the emerging area of bionanotechnology. With funds provided by the vice president of research, he and colleagues in the College of Science and Engineering and Medical School devel-



Carston Wagner (right) asks graduate student Dan Dronle to interpret results.

oped a Bionanotechnology Initiative (BI) that brought researchers from engineering, chemistry, developmental biology, medicinal chemistry, and medicine together to work on a number of projects. Most of these projects subsequently received substantial NIH funding. Wagner has served as associate

director and director of the BI. In 2010 Purdue University offered Wagner an endowed professorship to head their emerging Nanotechnology Institute. Quickly, the department countered the offer by establishing a new endowed professorship in the department and offered Wagner the position as the first Medicinal Chemistry Endowed Professorship.

Wagner has also been an active disciplinary leader, serving on several organizational boards for the ACS Medicinal Chemistry Division and as a founding editor of the American Chemical Society Journal of Molecular Pharmaceutics (Wagner, interview, 2011).

Changes Afoot

Although in many respects the 1980s ended and the following decade began with much promise for the department, difficult times lay ahead.

Challenges began in 1991 with the sudden announcement by Dean Banker—whose tenure at the College had been so beneficial to the Department of Medicinal Chemistry—that he planned to move to the University of Iowa as the dean of the College of Pharmacy. There followed a long and tumultuous period as the University struggled to find a suitable replacement. And once it did, a new wave of turbulence and hardship erupted with implementation of the re-engineering initiative in Academic Health Center (AHC).

Upon Banker's resignation, the AHC administration appointed Associate Professor Robert Cipolle, a faculty member in the Department of Pharmacy Practice, as interim dean to run the College while the University conducted a national search for Banker's replacement. More than a year after Banker resigned, the University offered the position to Craig Schnell, an applicant who was then serving as dean of the Graduate School at North Dakota State University. Schnell accepted the offer and then, a few days later, declined to take the job.

The reasons Schnell withdrew his acceptance have never been firmly established, but a rumor at the time—that a faculty member in pharmacy had contacted a state legislator to try to keep Schnell from being offered the position—symbolized to some a growing level of discord within the College of Pharmacy.

Whatever the case, Schnell's withdrawal set off a long period of uncertainty as University officials debated whether, given the large number of people who had already applied for the dean's position, a new national search would even succeed in turning up other candidates. The situation was made even worse because at the same time several other pharmacy colleges were also recruiting new deans.

A new internal search was undertaken and the job offered permanently to Cipolle, who not only turned down the offer but asked to be relieved as interim dean. Faced with the loss of its interim dean and with no permanent replacement in sight, the University asked Lawrence Weaver to come back and serve as interim dean at the beginning of 1994. That same year, Yusuf Abul-Hajj stepped down as department chairperson and was replaced by Rodney Johnson on an interim basis. Weaver then gave the department the green light to search for a new department chairperson. Following a national search, the faculty identified three qualified candidates to bring to campus. However, Weaver decided that these candidates should not be brought to campus for a formal interview until the new dean for the College had been selected.

Another search for a new dean ensued but took longer than anticipated when Marilyn Speedie finally took over as dean in September 1995.

Prior to joining the University of Minnesota, Speedie was head of the Department of Pharmaceutical Sciences at the University of Maryland and had an active research program in several areas, including enzymology and molecular biology of antibiotic biosynthesis, the expression and secretion of recombinant proteins in streptomyces, and the microbial biodegradation of pesticides and other pollutants.

However, the demanding administrative responsibilities of dean upon arrival precluded her from carrying on an active research program.



MARILYN K. SPEEDIE

B.S. 1970; Ph.D. 1973, Purdue University
Assistant professor 1973-75, Oregon State
University

Assistant Professor 1975-80; Associate
Professor 1980-88; Associate Professor
and Chairperson, 1988-91; Professor and
Chairperson, 1991-95, University of
Maryland

Dean and Professor 1996-present, University
of Minnesota

Awards

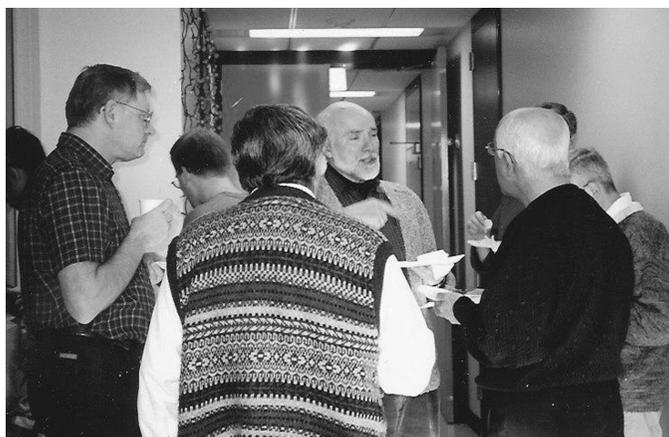
- Harold Popp Award, 2004
- Fellow, American Association for
Pharmaceutical Scientists, 1996
- AACP Paul Dawson Biotechnology Award,
1994

But no sooner was she in her new position than yet another wave of turmoil engulfed the College. This one was even more disquieting than the prolonged search for a new dean. For one, faculty relations had reached a stage where, just prior to Speedie's arrival, faculty from each of the College's departments formed an ad hoc group dubbed the SOS (Save our School) committee, with Abul-Hajj representing the interests of medicinal chemistry. The committee surveyed College faculty about problems and possible solutions and came up with a report. In response, Speedie formed three task forces to address a range of issues.

The work of those task forces, however, was superseded by still another wrenching change—a second round of de-departmentalization.

This round of College reorganization was prompted by the actions of the new Academic Health Center Provost William Brody to re-engineer the AHC. Henceforth, the entire AHC would be organized into three functional units intended to serve “customers.” Announced in January 1996, the re-engineering effort would lump individual departments and units into research, education, or clinical services groups.

Implementation of the effort was placed in the hands of 10 design teams charged with fitting the old departments and units into the new functional organization,



Monthly birthday parties were enjoyed by staff, students, and faculty.

which involved the establishment of centers and institutes and the elimination of departments and disciplines. At the College, Dean Speedie appointed a committee to oversee termination of the departmental structure.

To address this new initiative, the medicinal chemistry faculty established three subcommittees to assess the viability of a Center for Drug Design (CDD). In April 1995 this led to a report calling for the establishment of such a center. Both Dean Speedie and Frank Cerra, the senior vice president of AHC, were supportive of the idea.

Despite these efforts the CDD was not formally established until 2002, when a dispute over the royalties from Robert Vince's anti-AIDS drug, Ziagen, was finally settled with the company that had acquired the rights to produce it (Anderson & Pennigton, 2005, 229-33).

With the dissolution of departments, Medicinal Chemistry spent almost three years confronting conditions similar to those that prevailed during Weaver's first term as dean. Decisions about resources, curriculum, space allocations, and funding—including the ICR and salary offsets so providentially gained only a few years earlier—went through the dean's office. A College executive committee was formed consisting of three associate deans and two faculty members—one from basic pharmaceutical sciences (Abul-Hajj), the other from clinical pharmacy (John Rotschfer). It held a series of contentious meetings. Salary increases for faculty in medicinal chemistry, which had ranked in the top third of the College, tumbled to the bottom third; it was perceived, in part, because all of the College's new associate deans—

who evaluated the pay structure—came from clinical pharmacy.

Once again, medicinal chemistry carried on as a shadow department, led this time by Abul-Hajj, in the same manner as it had in the mid-1970s. Delegations of department faculty held meetings with Dean Speedie that were described by some attendees as “intensive”—intense enough so that at one meeting the medicinal chemistry faculty informed her that they wanted to have their unit removed from the College of Pharmacy and moved into the Chemistry Department. The dean refused to consider the suggestion.

Morale continued to sink, and faculty were up in arms—one even filed a grievance against the dean. But for the

most part, the changes were met with passive resistance, and there were occasions on which Dean Speedie could not raise a quorum at faculty meetings when decisions needing faculty approval were pending on curriculum and other matters.

The standoff finally came to an end late in 1996 when Dean Speedie decided to



The Department has held an annual potluck holiday celebration for many years.



Faculty joining in the holiday festivities in 2004, including (left to right) Rodney Johnson, Patrick Hanna, Robert Fecik, and Thomas Shier.

reinstitute the College's departmental structure. The move was made easier by the fact that Brody, the instigator of the re-engineering initiative, had unexpectedly left the AHC for a new position at Johns Hopkins University.

Brody was succeeded as provost of AHC by Frank Cerra. A new approach to internal College dissension was signaled by Dean Speedie's decision to hire outside consultants to gather input from faculty, staff, and administrators, and to recommend solutions. In September 1997, the consultants facilitated a two-day meeting. Nothing concrete came out of these gatherings, other than the observation that even as rancor within the College ran high, performance was just as high. In the end, all parties agreed to continue working on equitable solutions.

One of the organizations that was supposed to provide a forum for hammering out those solutions was the College's Constitution and By-Laws Committee, which now worked to develop an organizational structure that would meet with general approval.

In the end, however, the College's Executive Committee preempted the By-Laws Committee's deliberations by unilaterally deciding in April 1998 to move ahead with reinstating departmental structures, regardless of the outcomes reached by Constitution and By-Laws Committee. The plan proposed by the Executive Committee established a protocol in which all College faculty would have the chance to select membership in one of four departments: experimental and clinical pharmacology; pharmaceuticals; pharmacy practice; or medicinal chemistry (*ibid.*, 236-8).

The plan met with overwhelming faculty approval. Shortly thereafter, medicinal chemistry was reconstituted as a University department. At the time, there was



FRANK CERRA

Senior Vice President for the University of Minnesota Academic Health Center, 1997-2011.

no official head of medicinal chemistry and no money to hire anyone from outside the College. As part of her acceptance of the Executive Committee reorganization, Dean Speedie insisted that the new heads of each of the reconstituted departments had to have the backing of two-thirds of the faculty working in their units. Although Abul-Hajj, who previously led the department from 1984 until 1994, did not want to be named head of the newly reconstituted Department of Medicinal Chemistry, he reluctantly answered Speedie's request and was once again appointed department head.

Control of funding was one of the principal forces driving the continued push for re-departmentalization. In a de-departmentalized College, royalties for drugs developed by a member of medicinal chemistry would go to the dean's office rather than having a portion of the money directed to the department, as would normally

be the case. At this time the anti-AIDS compounds discovered by Vince seemed likely to end up on the market, with potentially rich royalties accruing to the University. Unless the College was re-departmentalized, where that money went would be entirely up to the discretion of the dean. Meanwhile, the re-departmentalization plan also addressed structural issues that had vexed the College prior to the 1996 de-departmentalization—some of the issues that Dean Weaver was trying to address in his de-departmentalization in the mid-1970s.

Under the new plan, the curriculum would continue to fall under the purview of the College's Central Administration and the system of associate deans assigned to functional groupings within the institution would continue. Most important of all, the plan addressed—and eliminated—the source of some of the worst friction within the College, assigning to each department responsibility for tenure and promotion of faculty only within a respective department. For example, faculty from clinical pharmacy would no longer have a say in tenure and promotion of faculty in medicinal chemistry or vice versa.

Soon after Abul-Hajj assumed the head position, he tried to fill Deborah Kallick's vacancy, but Dean Speedie had already spent half of that position's salary line to support another faculty member in a different department and could not fund a new hire in medicinal chemistry.

About that time, the University Cancer Center hired Stephen Hecht to establish the division of carcinogenesis and chemoprevention and had funds for hiring several faculty in this newly created division. In turn, medicinal chemistry had a long-standing interest in carcinogenesis with Patrick Hanna, Rory Rimmel, Herbert Nagasawa, and Yusuf Abul-Hajj carrying out investigations in several relevant areas of carcinogenesis/chemoprevention. In discussions with Hecht, Abul-Hajj indicated his willingness to have a joint hire between the cancer center and medicinal chemistry. Both Speedie and John Kersey, director of the cancer center,



Completed in 2000, the McNamara Alumni Center is on University property, but is owned by the University of Minnesota Gateway Corporation, made up of the Alumni Association, University of Minnesota Foundation, and Minnesota Medical Foundation.

supported this arrangement. Speedie, however, stipulated that the new hire would be assigned as the course director for a newly established Pharm.D. seminar course. Medicinal chemistry agreed to the proposal, which led to the hiring of Natalia Tretyakova with a 50 percent appointment in medicinal chemistry and 50 percent position in the cancer center.

To this joint position Tretyakova brought a unique set of strengths in chemical carcinogenesis. She set out to establish a research program that focused on the chemical modifications of nucleic acids by drugs and carcinogens. The effectiveness of her research was enhanced by her skill in employing biological mass spectrometry, along with organic synthesis, computational chemistry, and molecular biology, to study the interactions of carcinogens with nucleic acids, elucidate the structures of the resulting nucleobase adducts, quantify their concentrations *in vivo*, and identify DNA repair pathways responsible for their removal in cells. Tretyakova's contributions to the field were recognized by the University with her appointment as a McKnight Land-Grant Professor.

Re-Departmentalization Redux

In terms of funding, re-departmentalization of medicinal chemistry came in just the nick of time. When royalties from Ziagen began coming in (averaging approximately \$7.1 million a year to the department), the new College structure ensured that not only would a fair portion of that money come to medicinal chemistry but that the department would have a say in how it would be used. In turn, those funds helped underwrite several endowments and graduate fellowships and provided resources to pay for many other research and structural innovations.

In addition, during the past decade those royalties have played a critical role in the expansion and evolution of the Department of Medicinal Chemistry, eventually making possible the establishment of a new unit, the Institute for Therapeutics



NATALIA Y. TRETYAKOVA

B.Sc. 1988; M.Sc. 1990, Moscow State University

Ph.D. 1997, University of North Carolina-Chapel Hill

Assistant Professor 2000-05; Associate Professor 2005-11; Professor 2011-present, University of Minnesota

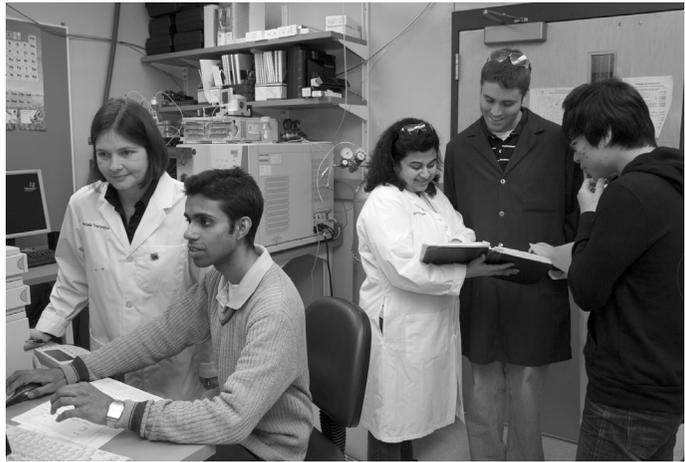
Born, Moscow, Russia, 1968.

Discovery and Development (ITDD) within the department and to create and to fund a new center within the Academic Health Center. But to reach the point where Ziagen could be created and marketed meant not just re-departmentalizing the College of Pharmacy. It also entailed persistence—and some luck—in navigating the vagaries of research funding and intellectual property rights. Failure to do so at any point could very well have resulted in failure for the whole project. That it didn't is testimony to the persistence of the lead researcher, Robert Vince, the foresight of the AHC, and even the willingness of then-President Mark Yudof, to undertake a multi-million dollar lawsuit for which the outcome was far from uncertain.

Ziagen is based on carbovir, an antiviral compound patented by Vince and his research associate, Mei Hua, in 1988. It inhibits HIV's ability to produce DNA and replicate itself. In turn that work was based upon Vince's previous research into compounds with potential antiviral and anticancer effects with the focus of his work influenced by the always evolving national research priorities.

Initially, Vince and Hua sent several related compounds to the NIH for study as potential anti-AIDS drugs, but were told that all of them fell outside the range of what the institute established as the parameters of potential effectiveness.

Soon the NIH contracted out the testing of several active compounds to research laboratories around the United States. One of them, the South-



Natalia Tretyakova discusses with graduate students the results from an LCMS chart.

ern Research Institute (SRI), happened to employ a researcher, William M. Shannon, who shared a close friendship with Robert Vince. At the friend's urging, Vince sent his compounds to the SRI. About two weeks later, Vince received a phone call informing him that five of the compounds were highly effective in combating HIV. Given that at the time there was only one medication available—AZT—that had much effect on HIV, SRI's findings pointed the way toward a tremendous potential for Vince's compounds.

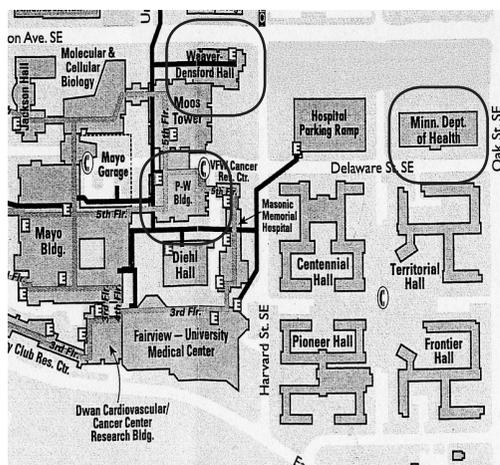
SRI sent the compounds to the NIH, and shortly thereafter, the institute contacted Vince and requested that he apply for patents on the compounds. The reason

was simple. NIH was willing to fund pre-clinical testing but no pharmaceutical company would be interested in pressing forward with the drugs unless they were patented.

After a presentation about his work at a conference, Vince was approached by researchers with the pharmaceutical company, Burroughs Wellcome, but ended up licensing the drug with another company, Glaxo. Two years later, Glaxo informed him that it was directing its attention to another anti-AIDS compound and was terminating its agreement with the University of Minnesota. In 1992, after further consultation, Burroughs Wellcome returned to the bargaining table and signed a licensing agreement with the University of Minnesota. Not long after, Glaxo bought out Burroughs Wellcome and, after a couple of more acquisitions, became GlaxoS-mithKline.

After several more years of testing, the most promising of Vince's compounds, now called Abacavir, was approved by the FDA in late 1998 and then marketed by Glaxo under the brand name Ziagen. Over the next 12 years—the average life of a patent—Ziagen was expected to yield some \$300 million in royalty payments. In actuality it yielded over \$510 million in royalties by 2011.

The only problem was that Glaxo claimed that on technical grounds it was not required to make any royalty payments. If the University was going to get anything out of the marketing of the drug, it would have to use legal channels. In consultation with Vince—who'd envisioned using his portion of the royalties to create a center dedicated exclusively to the development of new drugs—AHC and College of Pharmacy officials, legal counsel, and President Yudof made what, in retrospect, was a gutsy but logical decision to sue Glaxo. Glaxo countersued, but in October 1999 the



A map of the Minneapolis campus in 2002. Circled areas are the current sites for medicinal chemistry research.

company conceded, agreeing to pay royalties under a modification of the originally envisioned payments and schedule (Vince, interview, 2011).

According to a University of Minnesota Board of Regents policy, a third of the royalty funds would go to Vince and Mei Hua, a third to central University programs, 25 percent to the discoverer's department, and 8 percent to the discoverer's college.

Following the settlement there were questions in the minds of several administrators whether medicinal chemistry could make effective use of the new stream of funds. At an



New graduate students, 2003.

initial meeting, Frank Cerra, Vice President for Research Christine Mazier, Dean Speedie, Vince, and Abul-Hajj discussed the most effective ways of using the funds. This was followed by many meetings between Cerra and Abul-Hajj, and still other meetings involving Cerra, Abul-Hajj, and Vince and at times including Rodney Johnson.

For his part, Vince pressed forward with the establishment of a Center for Drug Design that reflected his own research experience. The University's Center for Drug Design, established on January 8, 2002, would differ from such centers located at other research universities in that it would not be completely dependent upon external funding—and thus driven by external research priorities—but would draw upon the bulk of Vince's royalties as unrestricted seed money for projects initiated by researchers appointed to faculty positions in the center (*ibid.*, 2011).

Following the settlement with Glaxo, President Yudof strongly supported the idea of establishing a drug center but the question arose of where it should be located. Discussions between the department and Cerra led to a proposal to build a new facility to house the Center for Drug Design, the Department of Medicinal Chemistry, and the Virtual Genomic Center. It was further proposed that this new facility be built, in part, with some of the royalty funds and should be located on East River Road behind the Children's Rehabilitation Center. President Yudof, however, did not approve of this site and suggested a location next to the Translational Research facility by Bierman Field. For its part, the department faculty did not accept this site and after further discussions with Cerra, approximately 3,000 square feet were allocated to the Center for Drug Design in the Phillips-Wangensteen Building with Vince appointed as its first director. Soon after the allocation of space, Vince, along with Ramaiah Muthyala (who became associate director of the center) began renovating the facility to accommodate the research programs in the center. Muthyala

was granted a research associate professor appointment in the department and graduate faculty status in the graduate program.

With the official grand opening symposium of the center held in May 2005 the hiring of senior and junior scientists began. Krzysztof Pankiewicz was appointed as a senior associate director of the center as well as a research professor in medicinal chemistry.

Pankiewicz had experience at Memorial Sloan-Kettering Cancer Center and Codan Pharmaceuticals and had a reputation as a talented nucleoside chemist with a good appreciation for biology. His major strength lay in structure-based drug design of nucleosides.

Since the establishment of the Center for Drug Design, the research funding and hiring of junior and senior scientists has proceeded at a rapid clip. Currently the major research at the center focuses primarily on developing new anticancer, antimicrobial, and antiviral drugs and therapies. The center is well equipped with state-of-the-art instrumentation to carry out the most sophisticated chemical and biochemical research. Looking toward 2013 when the Ziagen patent runs out—and with it, royalty payments—Vince established an endowment fund made up of royalty payments not directly needed to operate the center, which receives no University funding. Today, the endowment fund stands at \$60 million—enough to maintain operations long after Ziagen's patent ends (*ibid.*, 2011).

In addition to the direct boon brought into the department, Ziagen royalties

indirectly opened up additional resources when Vince requested that his teaching commitment be reduced in order to free up more of his time for research. By taking him off faculty salary, the department found itself with the funding to undertake the hiring of two new assistant professors, Robert Fecik and Chris Xing.



President George W. Bush meets with Robert Vince during a visit to Minnesota on July 11, 2002, and congratulates him for his success in the discovery of a new anti-AIDS drug.

The first faculty member who was hired using Vince's

former salary line was Fecik. Trained by Lester Mitscher at the University of Kansas and Dale Boger at the Scripps Research Institute, Fecik came to the department with a unique background in natural products and synthetic chemistry. His laboratory focuses on ways to combat antimicrobial and anticancer multi-drug resistance through the use of combinatorial biosynthesis and total synthesis of natural product.

The second of these appointments was Chengguo Xing. Trained as a synthetic medicinal chemist under Edward Skibo at Arizona State University and with post-doctoral training under the guidance of Andrew Myers at Harvard University, Xing has research skills in chemistry and biochemical and molecular biology to support



RAMAIAH MUTHYALA

B.Sc. 1964, Osmania University of India
 Ph.D. 1969, University of Sagar, India
 Ph.D. 1975, University of East Anglia
 Research Associate Professor 2000-05,
 University of Minnesota
 Born, Andhra Pradesh, India, 1946.

his research programs at Minnesota, which covers synthesis of natural and unnatural small-molecule based drug candidates and molecular probes, molecular/cellular biology to understand cancer development and the working mechanisms for cancer therapies, and various animal models for drug efficacy evaluation. During his initial



KRZYSZTOF PANKIEWICZ

Ph.D. 1979, Polish Academy of Sciences
 1983-95, Memorial Sloan-Kettering
 Cancer Center
 1995-98, Codon Pharmaceuticals
 Pharmacy Assistant, 1998-2004; Research
 Professor, 2004-present, University
 of Minnesota

years he had a strong emphasis on development of Bcl2 inhibitors, aiming to develop therapeutic candidates to eradicate drug resistance in cancer therapies, which is a common and serious problem for all malignancies. More recently his research focuses have expanded to cancer prevention and early diagnosis.

As with the faculty members hired in the late 1980s and early 1990s, strategic decision-making was applied to each of these new appointments, with an eye especially



Center for Drug Design Logo

toward enhancing medicinal chemistry's ability to work collaboratively with other departments and centers around the University and to enhance both synthetic capabilities as well as strengthen the ties with the cancer center.

During the search process that

led to the hire of Chengguo (Chris) Xing, one of the applicants was Shana Sturla. She was still early in her postdoctoral training with Hecht at the cancer center but was recognized as a promising faculty hire. While funds for a second position were not initially available, Speedie was willing to consider an additional faculty line and Abul-Hajj negotiated with the cancer center to create a joint appointment for Sturla. She was provided lab space in Weaver-Densford Hall by the department and salary by the cancer center to begin as an assistant professor one year later, at the conclusion of her postdoctoral work.

By the time she began in that posi-



The Center for Drug Design held an opening celebration and mini-symposium on May 17, 2005. Speakers included (left to right): Sydney Pestka (Robert Wood Johnson Medical School); Robert Vince; Ronald Breslow (Columbia University); and Jack Secrist (Southern Research Institute).


ROBERT A. FECIK

B.Sc., University of Iowa

Ph.D., University of Kansas-Lawrence

Assistant Professor 2001-07; Associate

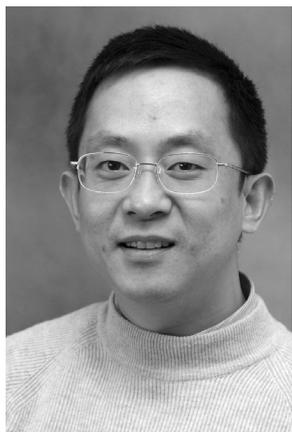
Professor 2007-present; Director of

Graduate Studies in Medicinal Chemistry

2010, University of Minnesota

Born, Wilmington, Delaware, 1971.

tion in 2004, Sturla had been awarded a National Cancer Institute Career Development Award to initiate research aimed at understanding the process of cancer initiation by dietary and environmental chemicals. Combining research strategies in organic synthesis and toxicology with a medicinal chemistry focus, Sturla's research also evolved to encompass efforts to understand factors that control the toxicity of natural product-derived potential chemotherapeutic or chemopreventive agents. Sturla, who is from the Dominican Republic, was recognized as an American Association for Cancer Research Minority Scholar in Cancer Research and as


CHENGGUO (CHRIS) XING

B.Sc. 1996, Dalian University of Technology

Ph.D. 2001, Arizona State University

Assistant Professor 2003-09; Associate

Professor 2009-present, University of

Minnesota

Born, Dalian, China, 1971.

a McKnight Land-Grant Professor. By 2009, she was poised to be awarded tenure the following year and was an ever-enthusiastic member of the department. An unexpected opportunity for a chaired professorship to lead a new Toxicology Program at the Swiss Federal Institute of Technology (ETH) in Zurich, however, lured Sturla and her research program to Switzerland.

The combination of the new departmental structure and increased revenues



Robert Fecik checks Annie Ngyunis results on the anticancer activity of the tubulysin analogs.

coming not only from royalties on Ziagen (which ultimately made possible perhaps the most significant hire in medicinal chemistry in several decades—the 2007 appointment of Gunda Georg as head of the Department of Medicinal Chemistry) but also

from sponsored research boosted the department's fortunes. The beginning of the new decade was not free, however, of a share of looming issues.

As had occurred time and again over the department's history, medicinal chemistry's growing roster of faculty and graduate students were running up against the



SHANA J. STURLA

B.Sc. 1996, University of California-Berkeley

Ph.D. 2001, Massachusetts Institute of
Technology

Assistant Professor 2004-09, University
of Minnesota

Born, Brooklyn, New York, 1975.

limits of space available at Weaver-Densford Hall. In addition, the department's emphasis on cross-disciplinary collaboration, sponsored research, and structure-based drug design—all requiring the most advanced instrumentation available—and the space to house that instrumentation. As the new millennium dawned there was also concern about the graying of medicinal chemistry's faculty, with seven of the department's 11 tenure track faculty having come to the University prior to 1980 (Department of Medicinal Chemistry, 2005). This led to a conscious attempt to recruit younger, top-notch faculty to the department.

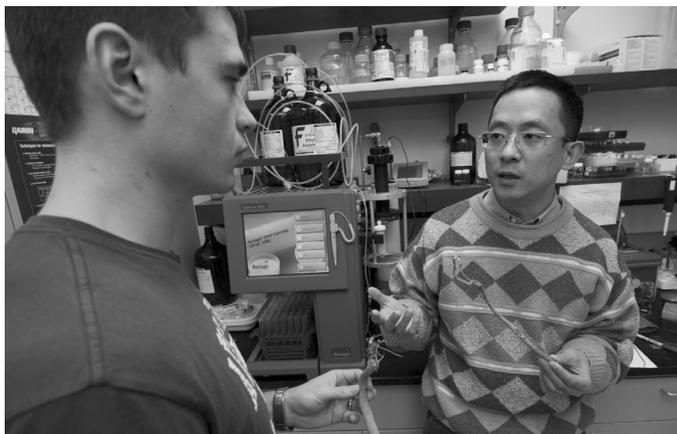
With Ferguson's shift of research emphasis towards synthetic medicinal chemistry and developing therapeutic agents for viral diseases and cancer, and the department's increased emphasis on

molecular modeling and computational chemistry for structure-based drug design, Elizabeth Amin was hired. Prior to joining the department she carried out investigations with Donald Truhlar in the University's Department of Chemistry and had been

collaborating with faculty members in medicinal chemistry. Amin's research program involves the development of new computational techniques to model transition metals in unusual coordination states with a focus on designing countermeasures to biological warfare agents, specifically anthrax toxin and organophosphates nerve gases (Amin, interview, 2011).

Other new faculty hires helped ease concern about an aging faculty base, while the University's 2005 acquisition of a 170,000 square foot building located two blocks from Weaver-Densford Hall opened up the possibility of answering the

department's space needs—and then some. The building, which belonged to the Minnesota Department of Health, had been constructed to accommodate offices and laboratories. Not surprisingly the sudden availability of so much space set off an intra-University scramble, especially



Chris Xing asks Dave Hermanson what should be done with the Kava roots.



Herb Nagasawa and Dennis Larson at their retirement party, 2005. L to R: Yusuf Abul-Hajj, Dean Marilyn Speedie, Herb Nagasawa, Dennis Larson, and Philip Portoghese.

within the Academic Health Center.

The building at 717 Delaware Street Southeast was purchased from the state of Minnesota in 2005 to accommodate the expanding research needs by AHC units. Frank Cerra approved the allocation of approximately 20,000



Shana Sturla is concerned about a small impurity in the acylfulvene sample.

square feet to house the expansions in medicinal chemistry and the establishment of the Institute for Therapeutics Discovery and Development. The facilities were renovated to house state-of-the-art instruments and to accommodate the large number of research personnel brought by Gunda Georg.

In the end, medicinal chemistry acquired the space it needed. But to do that entailed breaking with tradition and going outside the department to seek new leadership as well as the establishment of an innovative new research institute that would help advance the work of several other schools, departments, and research centers around the University.

Changes Continue

By 2002, Yusuf Abul-Hajj was ready to step down as department head. After a series of discussions, Dean Marilyn Speedie agreed to his proposal that the College look



ELIZABETH AMIN

B.Sc. 1996; M.Sc. 1998; Ph.D. 2002, University of Missouri-St. Louis

Assistant Professor 2006-present, University of Minnesota

Born, St. Louis, Missouri, 1966.

Awards

- ACS Hewlett-Packard Outstanding Junior Faculty Award, 2011



Elizabeth Amin explains the interaction between an anthrax inhibitor and the molecular structure of anthrax toxin.

outside for a candidate to replace him. After a year-long search failed to turn up a suitable candidate, the position was reposted and a new search committee formed.

This time, however, the committee also actively solicited candidates. One potential candi-

date Abul-Hajj brought to notice was a distinguished faculty member at the University of Kansas: Gunda Georg.

Abul-Hajj knew Georg from her research in medicinal chemistry of small molecule anticancer drug agents, in particular her focus on the development of both synthetic and natural products using the most advanced techniques. Although not an administrator per se, Georg had demonstrated strong leadership skills as principal investigator of a state-wide project funded as part of a larger NIH grant focusing on the research of junior faculty at schools around Kansas. In allocating the money, the NIH gave recipients broad latitude in exactly how they would structure their programs. The research infrastructure whose implementation she spearheaded was not only deemed the most effective of all the models adopted around the country, it also became the model for perhaps the most significant development in the recent history of the Department of Medicinal Chemistry—the Institute for Therapeutics Discovery and Development (ITDD) (Georg, interview, 2011).

Initially, Georg was not interested in being considered for head of the Department of Medicinal Chemistry in Minnesota. But Abul-Hajj persisted. Knowing her inter-



The building at 717 Delaware Street Southeast, Minneapolis.

est in cancer therapeutics, he approached the University's cancer center to see if there might be researchers there interested in expanding collaborations between the center and the department. With Masonic Cancer Center Director John Kersey and AHC Vice President Frank Cerra both interested in strengthening the Cancer Experimental Therapeutics Program at the University, it was thought that someone like Georg might be a good fit. Informed that the department was working on such a development, she agreed to submit her curriculum vitae. Around the same time, she visited the University to lecture about her work and to meet with faculty and administrators, including Cerra and Kersey. In 2005, two years after the initial search for a replacement for Abul-Hajj, she called and informed him that she was indeed interested in coming to Minnesota.

This led to a period of negotiations between Georg and the University. In August 2005, in response to a request from the provost's office, she wrote a 16-page proposal outlining both what she would personally accomplish if she took over the department but also the conditions the University would have to meet if she were to take

the job. These conditions went beyond the conventional issues of personal compensation and moving expenses. The heart of her memo was a detailed proposal for the faculty, staffing, instrumentation, space, and—most importantly—the operating philosophy of what would become the Institute



Students on the walkway to Coffman Memorial Union, which was originally built in 1940 and renovated in 2003 for more square footage to accommodate the rising number of students from 22,000 to more than 50,000.

for Therapeutics Discovery and Development (ITDD).

The key to the proposal—and to the institute that would come out of it—was to create a collaborative, translational research organization that would have an industrial approach to research taking place alongside a traditional academic approach. This meant focusing on application and commercialization of research projects from the outset. In turn, this meant that at least this portion of the ITDD's work would have to be carried out by researchers whose primary objective was creating procedures and products that might be eligible for patents rather than on publication in scholarly journals or the training of graduate students, although both of those out-



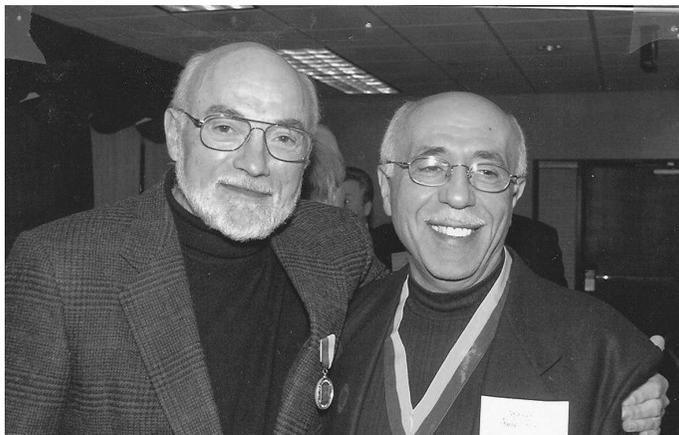
Coffman Memorial Union viewed from the rear, showing the top of the grand staircase that gives access to East River Parkway and the Mississippi River.

comes would also be included in the institute's operations (Georg, 2005).

In consultation with the dean and faculty, Cerra offered Georg the position as head of the department and director of the new research institute. Given the space and personnel such an organization would

need, Georg made it known that she planned to bring 25 people with her from Kansas as well as to recruit more staff and faculty when she arrived. Cerra also allocated some 20,000 square feet of space in the Delaware Street building just acquired as home to the ITDD. Georg, too, was offered the first Robert Vince Endowed Professorship in Medicinal Chemistry. To strengthen the offer President Robert Bruininks offered her a five-year McKnight Land Grant Professorship. Georg accepted the offer and began building on the already strong medicinal chemistry department.

Georg is best known in the medicinal chemistry community for her work with paclitaxel, a clinically important agent for the treatment of ovarian, breast, and other cancers. The work with paclitaxel eventually led her to investigate the hypothesis that tubulin-stabilizing agents could be used in the treatment of Alzheimer's disease. Her work on non-hormonal male contraceptive agents has resulted in the discovery of several new lead compounds. One of the lead compounds, named Gamendazole, has advanced to studies



Philip Portoghese, who was recipient of the 2001 Weaver Medal, congratulates colleague Yusuf Abul-Hajj for his selection as recipient of the 2005 Weaver Medal.

in primates in preparation for clinical trials. Her recent investigations, initiated at the University of Minnesota in collaborations with Ashok Saluja and others from the Academic Health Center, concerns a water-soluble prodrug of triptolide, named Minnelide, which showed potent cytotoxic activity across several cancers *in vivo*, displays potent antiangiogenic properties, and has been shown to be highly efficacious in animal models of several cancers, including an orthotopic animal model of pancreatic cancer. Other projects in the Georg group are centered on the development of novel synthetic methods in organic chemistry.

Architects met with Georg and Vadim Gurvich during the transition period between her accepting the position and her departure for Minnesota—the newly acquired facility had an insufficient amount of lab space, among other things. Two search committees were formed to look for ITDD core directors as soon as she arrived at the University, which included faculty from both within and beyond the Department of Medicinal Chemistry (Georg, interview, 2011).

Vadim Gurvich, who was working with Georg at Kansas, moved to Minnesota in 2006 to assume oversight of the construction of the research facilities in 717 Delaware Street Southeast to accommodate the needed space expansion in medicinal chemistry and for the creation of the ITDD. Since 2007, Gurvich has been the associ-



GUNDA I. GEORG

B.Sc. 1975; Ph.D. 1980, Philipps University of Marburg, Germany

Assistant Professor 1983-84, University of Rhode Island

Assistant Professor 1984-89; Associate Professor 1989-94; Professor 1994-2005, University of Kansas

Vince Professor, McKnight Presidential Chair and Head of the Department of Medicinal Chemistry, 2006-present; Director of Institute for Drug Discovery and Development, 2006-present, University of Minnesota

Born, Herborn, Germany.

Awards

- Sato Memorial International Award of the Pharmaceutical Society of Japan, 2000
- Fellow, American Association for the Advancement of Science, 1996



Georg suggests screening an additional 50,000 compounds from the special library in the ITDD.

ate director of ITDD, director of its chemical and API process development facility, and research assistant professor of medicinal chemistry. Gurvich mainly directs applied research in the areas of organic chemistry of drug candidates, their intermediates and metabolites,

chemical process development and scale up, manufacturing of small-molecule and protein-based active pharmaceutical ingredients to support clinical and translational research. He is also the associate director and one of the founding members of the National Institute for Pharmaceutical Technology and Education (NIPTe), a nonprofit national organization consisting of schools and colleges of pharmacy and chemical engineering engaged in pharmaceutical research (Institute, 2010).

Walters comes to Minnesota with both academic and industrial experience. After spending a few years as a professor of chemistry at Dartmouth College, he joined Warner-Lambert, which later merged with Pfizer, at its Ann Arbor laboratories. He worked in the area of second-generation atypical antipsychotics and subtype selective GABA positive allosteric modulators as novel anxiolytics. Additionally, he served as a leader in the Lead Discovery Group, a discovery team charged with hit-



Medicinal chemistry faculty and staff, 2008. The arrival of Gunda Georg to head the department led to doubling the space, as well as a significant increase in faculty and staff.

to-lead operations. He joined the University of Minnesota as a research associate professor in medicinal chemistry and as director of the Lead Discovery and Probe core group of the ITDD, where he is involved with multiple projects in the institute in the early process of drug discovery, especially in the stages involving active compound-to-lead optimization. He is currently working in the areas of the design and synthesis of new anti-fungals, the development of neuroprotective agents for the treatment of Alzheimer's, agents to treat ataxia, and anticancer therapeutics. Additionally, he is collaborating on computer methods to design compound libraries aimed at novel targets and fast algorithms to determine the synthetic accessibility of new compound scaffolds.

Derek Hook has spent almost all his scientific career working for pharmaceutical companies before joining Minnesota as research professor in medicinal chemistry and as director of the High Throughput Screening Core Facility at ITDD. His state-of-the-art laboratory is set up not only to provide a service function to the



VADIM J. GURVICH

M. Sc. 1987, Mendeleev University of Chemical
Technology

Ph.D. 1996, Hebrew University

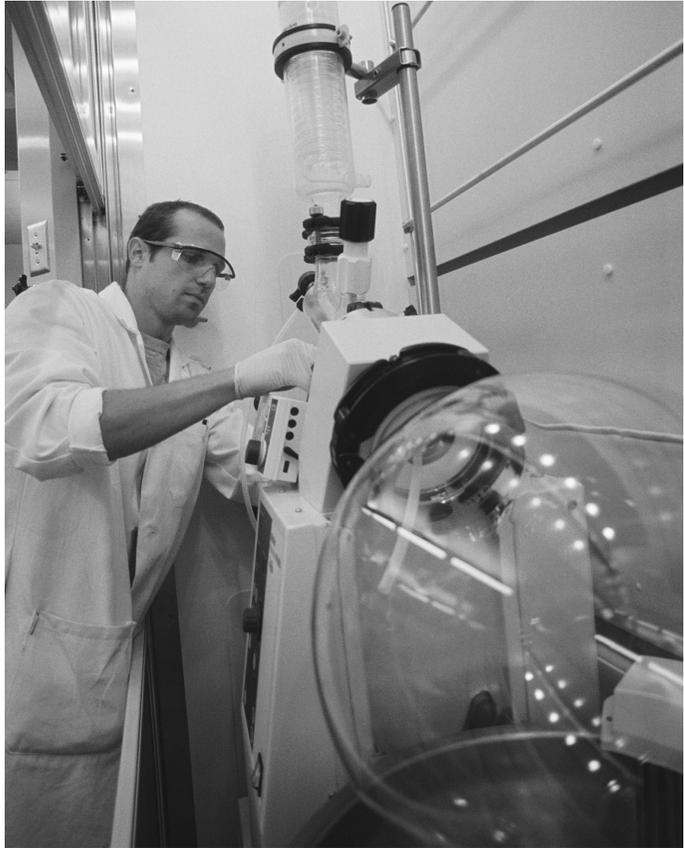
Research Assistant Professor 2007-present,
University of Minnesota

Born, Moscow, Russian Federation, 1964.

University of Minnesota but also to work collaboratively with other institutions and to provide an educational environment in which students, postdoctoral research associates, and faculty gain experience in modern industrial drug discovery technologies and philosophy.

As part of the agreement by which Georg was appointed head of the department, the College appropriated funds to hire a new assistant professor in cancer experimental therapeutics. A national search led to hiring Daniel Harki, who spent several years as a postdoctoral research associate at Caltech working with Peter Dervan before joining the Department of Medicinal Chemistry. Harki's research focuses on the synthesis and biochemical evaluation of small molecules for applications as chemical probes of biological processes and for development as potential anticancer agents. The Harki laboratory is particularly interested in tumor cell hierarchy, espe-

cially as it relates to cancer stem cells. One project in the laboratory aims to better understand the unique biology of cancer stem cells utilizing small molecule probes. Concurrently, the Harki laboratory is developing small molecule inhibitors of this population of tumor cells. A second area of research interest resides in the field of transcription factor-DNA binding and the development of small molecules that can be utilized to manipulate such processes.



Industrial scale evaporator at the new labs in 717 Delaware Street Southeast.



MICHAEL WALTERS

B.Sc. 1981, Hope College

Ph.D. 1986, University of Michigan

Assistant Professor 1989-97, Dartmouth
College

1997-2007, Pfizer Research

Associate Professor 2007-present, University
of Minnesota

Born, Dearborn, Michigan, 1958.



400 MHz NMR Spectrometer in the ITDD.

Dynamic Developments

The four years that followed Georg's appointment as chair of the department would prove to be among the most dynamic in the department's long history.

Space available for use by the department more than doubled—from 18,000 square feet in Weaver-Densford Hall to some 35,000 square feet shared between Weaver-Densford Hall and the building at 717 Delaware Street Southeast. The ITDD quickly evolved into a major organization that carries out interdisciplinary research



DEREK HOOK

B.A. 1968, Hull University
Ph.D. 1972, Dalhousie University
1974-77, Rayola Chemicals
1978-97, Bristol-Meyers Squibb;
1997-99, NPS Pharmaceuticals
2000-03, Psychiatric Genomics
2003-07, 3M Pharmaceuticals Research
Professor 2007-present, University of
Minnesota.

and offers scientific services to research and business communities in drug discovery and development and currently employs more than 30 scientists across a range of disciplines. It has acquired an array of instrumentation that gives it state-of-the-art capabilities in screening, synthesizing, and analysis of compounds.

Initially focused on small molecule research, it has evolved to include protein-based research. It has four scientific cores—medicinal chemistry, directed by Gunda Georg; lead and probe discovery, directed by Michael Walters; high throughput screening, directed by Derek Hook; and chemical process development, directed by Vadim Gurvich. In addition, the institute hired three experienced industrial scientists: Chris



High throughput screening at the ITDD.



Integrated laboratory HTS automation system for conducting assays in microplates at the ITDD.



Medicinal chemistry faculty sing Christmas carols at the annual holiday party in 2008.



DANIEL A. HARKI

B.A. 1999, West Virginia University
Ph.D. 2005, The Pennsylvania State University
Assistant Professor 2009-present, University
of Minnesota
Born, Morgantown, West Virginia, 1976.

Stenland, a protein chemist; Peter Dosa, a synthetic medicinal chemist; and Henry Wong, a pharmacologist.

Peter Dosa came to the University of Minnesota in June 2009 from Arena Pharmaceuticals. While at Arena, Dosa worked on several programs that reached the clinic, including an antithrombotic agent. Now part of the ITDD, Dosa is pursuing the development of water-soluble prodrugs of ursodeoxycholic acid, an antiapoptotic bile acid that has been shown in animal models to significantly reduce the damage caused by a heart attack or stroke. He has also been working on designing safer analogs of the dopamine agonist cabergoline, which could potentially be used to treat Parkinson Disease, Cushing's Disease, or sexual dysfunction.

Today, the ITDD is home to almost 60 projects, the majority of them interdisciplinary and involving partners within the University, like the Masonic Cancer Center, as well as partners outside the University, like the Mayo Clinic and University of Kansas, and sponsored by a wide array of institutions, including NIH, the Gates Foundation, the



Medicinal chemistry faculty at a 2009 picnic. Left row (front to back): Philip Portoghese, Barry Finzel, Chris Xing, Derek Hook, Dan Harki, Mrs. Harki. Right row (front to back): Yusuf Abul-Hajj, Gunda Georg, Rick Wagner, Pat Hanna, Natalia Tretyakova, Gregg Janis. Standing: Tom Shier. In the background: Mrs. Abul-Hajj, Mrs. Hanna, Peg Houck, and Peter Dosa. It is interesting to compare faculty attire with the 1936 faculty picnic (see page 34).

Mayo Clinic, the Minnesota Partnership, the University of Chicago, and the Northern California Institute for Research and Education (Institute, 2010).

In the fall of 2006, the Minnesota Partnership for Biotechnology and Medical Genomics, which had previously invested in research projects, research infrastructure, and new research facilities, launched a new initiative involving paired faculty hires between the University of Minnesota



New graduate students enjoy the 2009 medicinal chemistry departmental picnic at Como Park in St. Paul.

and the Mayo Clinic. The partnership planned to make available in 2006-07 approximately \$6 million for start-up packages for new faculty recruits to the two institutions.

Through the partnership, the department sought to capitalize on this opportunity to accomplish one of the strongly endorsed initiatives in its strategic plan. Rodney Johnson, interim chair, submitted a joint proposal for the paired hires between the Division of Oncology at the Mayo Clinic and the Department of Medicinal Chemistry. The Division of Oncology Research proposed to search for an established investigator of DNA damage-induced signaling, cell cycle regulation/checkpoint activation, and/or DNA repair while the Department of Medicinal Chemistry proposed to search for an established investigator with expertise in the



PETER I. DOSA

B.A. 1995, Princeton University

M.S. 1998, Massachusetts Institute of
Technology

Ph.D. 2002, University of California, Berkeley
2002-09, Arena Pharmaceuticals

Research Assistant Professor 2009-present,
University of Minnesota

Born, Manchester, England, 1973.



BARRY C. FINZEL

B.S. 1979, Eastern Michigan University

Ph.D. 1983, University of California at

San Diego

1983-86, Genex Corporation

1986-87, Dupont Company

1988-92, Upjohn

1992-2003, Pharmacia

2003-07, Pfizer

Professor 2008-present, University of
Minnesota

Born, Monroe, Michigan, 1956.

X-ray crystallography of drug-protein interactions that are identified as potential new targets for treating cancer. After a national search, Barry Finzel, a well-established X-ray crystallographer working for Pfizer for several years, was appointed as professor of medicinal chemistry.

Barry Finzel brings a strong industrial background and practical experience in the drug discovery process to the department. While working for nearly 20 years in large industry concerns, his research focused on providing timely, detailed experimental structural data to support medicinal chemistry, analog synthesis, and drug design. By applying X-ray crystallography to characterize targeted protein-ligand complexes, the molecular environment of drug action can be detailed and exploited



The Medicinal Chemistry Department, October 2010, showing faculty, staff, graduate students and research personnel. The department has doubled in size since 2006 as a result of the new faculty hires and the establishment of ITDD.

to help direct compound optimization and drug development. Since joining the department he has built upon the legacy of rapid structure delivery developed in industry to provide insightful experimental structural data to aid collaborators in the design of chemical probes with unique biochemical and pharmacological properties. Working in close collaboration with synthetic chemists and modelers, he is currently working to identify agents with antibacterial activity targeting anthrax, multi-drug resistant tuberculosis, vancomycin-resistant infections, and cancer and inflammation targets by utilizing structure-based drug design. He is also working to develop computational tools to mine existing databases for structural data and to simplify the way



Faculty and graduate students attend a luncheon for recruitment of graduate students for the 2010 academic year.

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CARRIE HASKELL-LUEVANO

B.S. 1990, California State University-Fresno

Ph.D. 1995, University of Arizona.

Assistant Professor 1998-2004; Associate
Professor 2004-08; Professor 2008-11,
University of Florida

Portoghese Endowed Professor, 2011-present,
University of Minnesota

Born, California, 1968.

collaborators who may not be experts in structural biology.

In recognition of Philip Portoghese's 50 years of teaching, research, and service (as the longest serving faculty member since the establishment of the College), the department held a symposium in his honor followed by dinner at the campus club. Faculty, Portoghese's family members, alumni, and friends were in attendance at the celebration.

Other additions to the faculty include Carrie Haskell-Luevano, who was selected by a search committee specifically to be the first faculty appointed to the newly formed Philip S. Portoghese Endowed Chair in Medicinal Chemistry.

Portoghese established the chairship as a way of marking his 50 years in the Department of Medicinal Chemistry and to express gratitude for the opportunity the College has provided him to conduct his groundbreaking research. The \$2 million endowment, half of it donated by Portoghese and half by the Permanent University Fund, ensures ongoing support for research in chemical neuroscience—Portoghese's principal area of work—at a time when the majority of faculty in medicinal chemistry are engaged in research focused on cancer.

In keeping with that goal, Haskell-Luevano was hired on the basis of her research focusing on the understanding of the melanocortin hormone endocrine systems in the brain, and their involvement in feeding behavior, obesity, exercise, diabetes, and energy homeostasis. Multidisciplinary approaches to study this pathway include medicinal chemistry, chemical biology, biochemistry, molecular biology, pharmacology, physiology, and neuroscience. Through the use of rational design approaches and combinatorial chemistry library screening, Haskell-Luevano works on developing pharmacologically distinct and receptor selective ligands (peptide and small molecule) to probe the physiological role or roles of the melanocortin pathway in mice. These ligand data will also be complimented by the generation and use of receptor mutations to probe putative ligand-receptor interactions and the molecular mechanisms of melanocortin receptor signaling in the brain.

Along with other interdisciplinary collaborations taking place involving department faculty outside ITDD's structure, the institute marks a step forward for medicinal chemistry. Many challenges, of course, still lie ahead. Many outstanding faculty are at or nearing retirement age and the es-



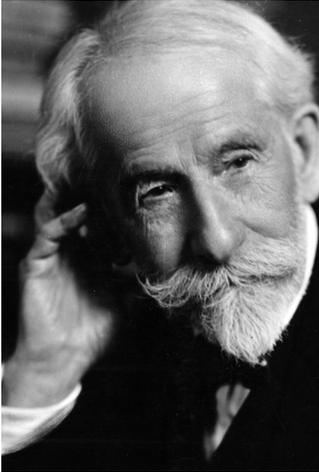
Speakers celebrating Portoghese 50 years of service (left to right): Lawrence Marnett (Vanderbilt University); Ivy Carroll (Research Triangle Park); Chris McCurdy (University of Mississippi); Dean Marilyn Speedie; Philip Portoghese; Gunda Georg; Yusuf Abul-Hajj; Alex Makriyannis (Northeastern University).

establishment of the multidisciplinary, multi-institutional ITDD, although it is part of medicinal chemistry, may foreshadow a long-term transformation of traditional departmental organization and structure. Nevertheless, at its centennial celebration in 2012, the Department of Medicinal Chemistry—whether measured by faculty achievements, research funding, innovation, or long-range prospects—is perhaps stronger today than at any time since the beginning of its evolution when Frederick Wulling arrived in Minnesota in 1892 to found the University's College of Pharmacy. §

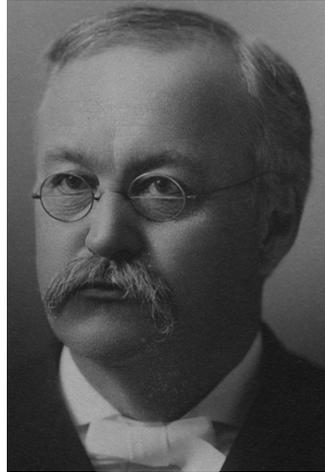
APPENDICES

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Appendix A.
UNIVERSITY OF MINNESOTA PRESIDENTS



William Watts Folwell
1869-1884



Cyrus Northrup
1884-1911



George E. Vincent
1911-1917



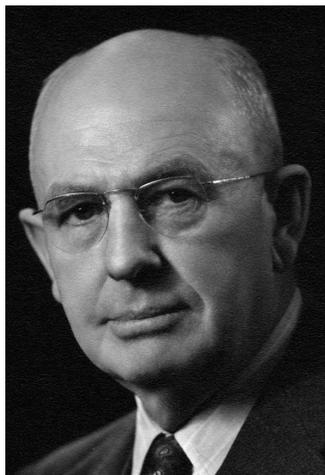
Marion L. Burton
1917-1920



Lotus D. Coffman
1920-1938



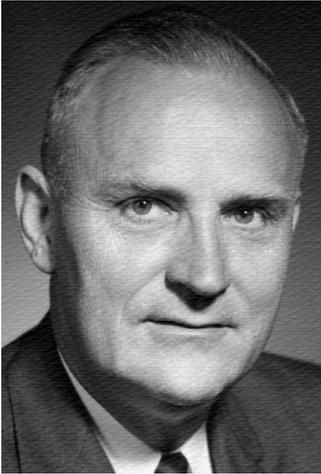
Guy Stanton Ford
1938-1941



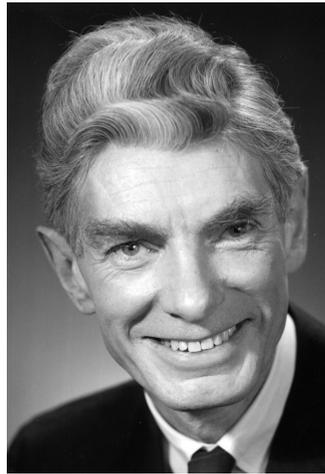
Walter C. Coffey
1941-1945



James Lewis Morrill
1945-1960



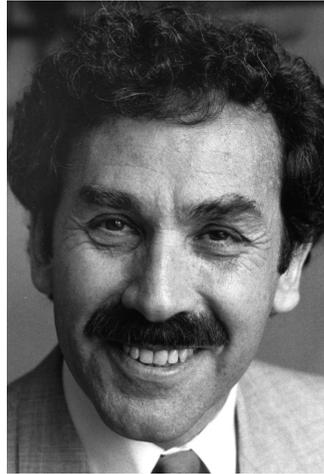
O. Meredith Wilson
1960-1967



Malcolm Moos
1967-1974



C. Peter McGrath
1974-1984



Kenneth H. Keller
1985-1988



Nils Hasselmo
1989-1997



Mark G. Yudof
1997-2002

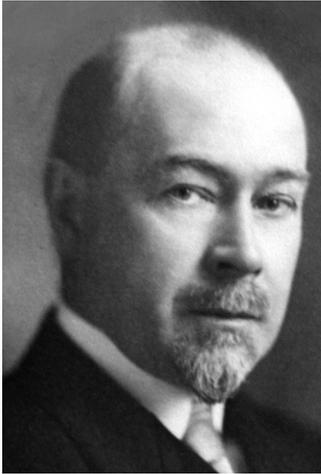


Robert H. Bruininks
2003-2011



Eric W. Kaler
2011-present

Appendix B. COLLEGE OF PHARMACY DEANS



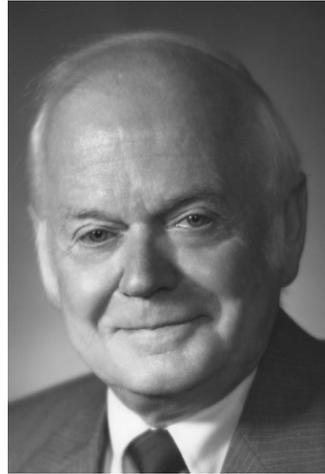
Frederick J. Wulling
1892-1936



Charles H. Rogers
1936-1956



George P. Hager
1957-1966



Lawrence C. Weaver
1966-1984



Gilbert S. Banker
1985-1992



Marilyn K. Speedie
1996-present

Appendix C.
MEDICINAL CHEMISTRY DEPARTMENT HEADS



Glenn L. Jenkins
1936-1941



Ole Gisvold
1941-1969



Taito Soine
1969-1974



Mahmoud M. Abdel-Monem
1983-1984



Yusuf J. Abul-Hajj
1984-1992; 1996-2005



Rodney L. Johnson
Interim, 1994-1996; 2005-
2006



Gunda I. Georg
2007-present

Appendix D. OUTSTANDING ACHIEVEMENT AWARDS

The Outstanding Achievement Award is the University of Minnesota's highest award to an alumnus. It is conferred upon former students of the University who have attained distinction in their chosen fields or professions or in public service, and who have demonstrated outstanding achievement and leadership on a community, state, national, or international level.



George E. Crossen

B.S. 1933, M.S. 1939, Ph.D. 1940, University of Minnesota.

Assistant Professor, University of Minnesota, 1940-43

Dean of Pharmacy, Drake University, 1943-45

Dean of Pharmacy, Oregon State University, 1945-58

Crossen was awarded the OAA in 1951 in recognition as an eminent author and administrator in pharmaceutical education. He was deemed to be worthy of special commendation for outstanding achievement.



Coy Webster Waller

B.S. 1937, University of North Carolina

M.S. 1939, University of Buffalo

Ph.D. 1942, University of Minnesota.

Instructor, State College of Washington, 1942-44

Head, Natural Products Chemistry, American Cyanamid, 1944-57

Director of Chemical Research, Mead Johnson and Company, 1957-66.

Waller was awarded the OAA in 1959 for his outstanding achievements in natural products research and was recognized for his success in the proof of structure and synthesis of folic acid, aureomycin, puromycin, and netropsin.



Charles Herbert Rogers

B.S. 1913, M.S. 1915, University of Michigan
Sc.D. 1918, University of Minnesota.
Instructor, 1913-14, University of Minnesota
Associate Professor & Head of Department of
Pharmacy, University of West Virginia, 1914-17
Professor and Head of Pharmaceutical Chemistry,
1917-36; Dean of Pharmacy, 1936-56; University of
Minnesota

Rogers was awarded the OAA in 1959 for his devotion to pharmaceutical education and the art and science of pharmacy. In his role as teacher, author, administrator, and researcher, he made many notable and lasting contributions to the instruction of students at both the graduate and undergraduate levels, to the practice of pharmacy as a vocation indispensable for the health of the public and the art of science of the apothecary in an era of “wonder drugs” and for his outstanding contributions as the second dean of the College of Pharmacy at the University of Minnesota.



James H. Boothe

B.S. 1939, Washington State College
Ph.D. 1943, University of Minnesota
Senior Research Scientist, Department of Medicinal
Chemistry at Lederle Laboratories Division, American
Cyanamid Company, 1943.

Boothe was awarded the OAA in 1962 for his outstanding work in medicinal chemistry and the chemistry of natural products. His initial contributions were on the synthesis of folic acid and its degradation of products as well as the first total synthesis of pteropterin. He is renowned for his work on the structural elucidation of aueromycin, the structure activity relationship between aueromycin and tetracycline as well as the first total synthesis of chlorotetracycline analogs.



Chauncey I. Cooper

B.S. 1934, M.S. 1935, Ph.D. 1938, University of Minnesota
Instructor, 1935-38; Associate Professor and Acting
Dean, 1938-41; Associate Professor and Dean, 1941-51;
Professor and Dean, 1951-72; Howard University

Cooper was awarded the OAA in 1964 in recognition of his energetic pursuit of higher educational standards for African Americans and greater opportunities for African Americans in pharmaceutical education and for his significant activities that led to the founding of the National Pharmaceutical Association.



Olav Johan Braenden

B.S. 1942, University of Oslo, Norway
Ph.D. 1950, University of Minnesota,
Social Affairs Officer, United Nations, New York,
1951-55
Chief, United Nations Narcotics Laboratory, Geneva,
1955-68
Chief, Scientific and Technical Section, Division of
Narcotic Drugs, United Nations, Geneva, 1968-76

Braenden was awarded the OAA in 1974 for his outstanding contributions to the control of drug abuse internationally and for his training of numerous scientists from all over the world in methods pertinent to drug abuse.



Michael J. Martell

B.S. 1954, Ph.D. 1958, University of Minnesota
Research Chemist, Lederle Laboratories, 1960-69
Manager for Product Development, American
Cyanamid, 1969-75
Director, Medical Products and Process Chemistry,
American Cyanamid, 1975-85

Martell was awarded the OAA in 1976 for his outstanding contributions to the tetracycline antibiotic, minocycline, which proved to be useful for the treatment of a broad spectrum of diseases.



Aubin Heyndrixcks

B.S. 1948, University of Ghent
M.S. 1952, University of Minnesota
Ph.D. 1953, University of Ghent
Professor and Director, 1958-70; Dean of
Pharmaceutical Sciences, 1970-85; University of
Ghent
Project Director, United Nations Industrial
Development Organization.

Heyndrixcks was awarded the OAA in 1980 in recognition of being a gifted scholar who improved the teaching and research of the department and made its laboratory one of the best in the country. He is a worldwide advisor on toxicology, drug abuse, and poison control centers and is an internationally recognized expert in toxicology and forensic science.



Jack R. Cole

B.S. 1953, University of Arizona
Ph.D. 1957, University of Minnesota
Assistant Professor, 1957-58; Associate Professor,
1958-62; Professor, 1962-87; Head, Department of
Pharmaceutical Sciences, 1975-79; Dean, 1977-87;
College of Pharmacy, University of Arizona

Cole was awarded the OAA in 1983 in recognition of his superb administrative skills of attracting quality faculty and improving curriculum and obtaining a new building for pharmacy at the University of Arizona. He is recognized as a expert in the field of medicinal chemistry involved in the isolation and structural elucidations of pharmacologically useful agents from plants.



Allen I. White

B.S. 1937, M.S. 1938, Ph.D. 1940, University of Minnesota
Assistant Professor, 1943-45; Associate Professor,
1945-48; Professor, 1948-79; Dean of Pharmacy,
1960-79; Washington State University

White was awarded the OAA in 1985 for his contribution and innovative leadership in the pharmacy practice and education and for implementing a clinical pharmacy program that became a model for other schools. He was also recognized for his leadership as Dean of Pharmacy at WSU and as president of the American Association of Colleges of Pharmacy.



Raymond Ernest Counsell

B.S.P. 1953, University of British Columbia

Ph.D. 1957, University of Minnesota

Senior Research Chemist, G. D. Searle and Company, 1957-64

Associate Professor, 1964-69; Professor, 1969-72;

Professor of Pharmacology and Medicinal Chemistry, 1976-99; University of Michigan

Counsell was awarded the OAA in 1989 for his outstanding contributions in medicinal chemistry, especially in the area of tumor-imaging agents and inhibitors of steroidogenesis. One of his compounds is licensed to Cellectar and is in early clinical trials for cancer therapy. He is a fellow of AAAS and has received several awards including the Horner Gold Medal in Pharmacy, American Cancer Society Research Associate Award, the Eleanor Roosevelt International Cancer Fellowship, the Fogarty Senior International Fellowship, and the Genia Czeraniak Prize in Nuclear Medicine and Radiopharmacology.



Kuo-Hsiung Lee

B.S. 1961, Medical College of Taiwan

M.S. 1965, Kyoto University, Japan

Ph.D. 1968, University of Minnesota

Assistant Professor, 1970-74; Associate Professor,

1974-77; Professor, 1977-present; Chair of Medicinal

Chemistry and Natural Products Division, 1998-2008;

Director of Natural Products Laboratory,

1983-present; Keenan Professor of Medicinal

Chemistry, 1992-present; University of North Carolina

Lee was awarded the OAA in 1999 for his outstanding contributions as an international leader in medicinal and natural products chemistry and was recognized for his discovery of more than 1,000 new compounds, including several to treat cancer and HIV. As of 2010, Lee has discovered more than 3,000 novel bioactive natural products and synthetic analogs.



Mahmoud M. Abdel-Monem

B.Sc. 1959, Cairo University

Ph.D. 1966, University of Minnesota

Assistant Professor 1970-71, University of Illinois

Assistant Professor 1971-75, University of Minnesota

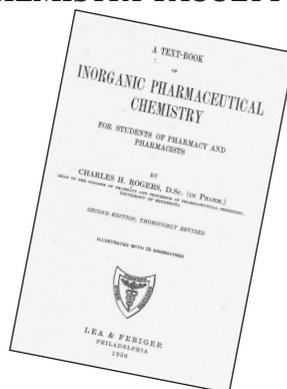
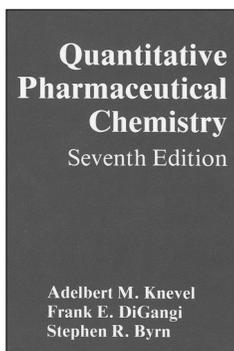
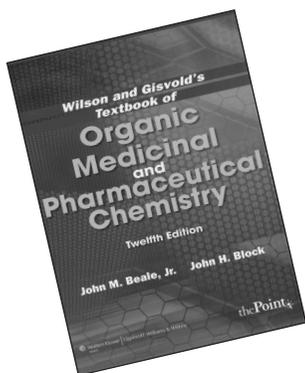
Associate Professor 1975-80; Professor 1980-87; Head
of Medicinal Chemistry 1983-84; University of
Minnesota

Dean of Pharmacy, 1987-98; Washington State
University

Abdel-Monem was awarded the OAA in 1999 for his overall accomplishments in teaching, research, and service. He performed admirably as an administrator at Minnesota while serving as Department Head, Interim Dean, and Associate Dean. His administrative experience helped him tremendously when he became Dean of Pharmacy at WSU.

Appendix E.

BOOKS AUTHORED BY MEDICINAL CHEMISTRY FACULTY

**Frederick J. Wulling**

The Evolution of Botany (Evolution Series)
1891

Frederick J. Wulling

Inorganic and Pharmaceutical Chemistry
Wiley & Sons, 1894

Frederick J. Wulling

Pharmacy Forward
Sumac Press, Lacrosse, WI, 1948

Charles H. Rogers

Textbook of Inorganic Pharmaceutical Chemistry, 1st-7th Editions,
Lea & Febiger, 1932-1961

George E. Crossen and Charles H. Rogers

Laboratory Manual of Inorganic Pharmaceutical Chemistry
Burgess Publishing Co., 1946

Charles H. Rogers and Taito O. Soine

Laboratory Manual of Inorganic Pharmaceutical Chemistry
Burgess Publishing Co., 1948

Ole Gisvold and Charles H. Rogers

The Chemistry of Plant Constituents
Burgess Publishing Co., 1938

Charles O. Wilson and Ole Gisvold

Organic Chemistry in Pharmacy
Lippincott, 1949

Charles O. Wilson and Ole Gisvold

Textbook of Organic Medicinal and Pharmaceutical Chemistry, 1st Edition
Lippincott, 1949
Currently in its 12th Edition

Taito O. Soine and Charles O. Wilson

Roger's Inorganic Pharmaceutical Chemistry, 8th Edition
Lea & Febiger, 1974

John H. Block, E. Roche, Taito O. Soine and Charles O. Wilson

Inorganic Medicinal and Pharmaceutical Chemistry
Lea & Febiger, 1974

Albert K. Knevel, Frank E. DiGangi and Stephen R. Byrn

Quantitative Pharmaceutical Chemistry, 7th Edition
McGraw Hill, 1977

Mahmoud M. Abdel-Monem and James G. Henkel

Essentials of Drug Product Quality: Concepts and Methodology
Mosby, 1978

W. Thomas Shier and D. Mebs

Handbook of Toxinology
Marcel Dekker, 1990

W. Thomas Shier

Mammalian Cell Culture on \$5 a Day, A Laboratory Manual of Low Cost Material
University of The Phillipines, Los Ballos, 1991

Yusuf J. Abul-Hajj and Richard Broderick

From Digitalis to Ziagen, The University of Minnesota's Department of Medicinal Chemistry
University of Minnesota, Minneapolis, 2012.

Appendix F.
GRADUATES OF THE DEPARTMENT OF MEDICINAL CHEMISTRY

Master's and Doctorate Degrees in Pharmaceutical Chemistry

1929		1941	
Mayrand, Louis Philippe	MS	Jack, Laurine Davison	PhD
		Lloyd, William Reese	PhD
1932		Urist, Harold	PhD
Goldner, Karl John	MS	Waldon, Curtis Henry	PhD
		Dennard, Turner Harrison	MS
1934		Janecek, William Leonard	MS
Betts, Loel Howard	MS		
Brecht, Edward Armnd	MS	1942	
		Hadley, Willard Jesse	PhD
1935		Voigt, Ralph Ferdinand	PhD
Cooper, Chauncey Ira	MS	Waller, Coy Webster	PhD
Fostvedt, Gerald Anderson	MS		
Souch, John Kennedy	MS	1943	
		Boothe, James Howard	PhD
1937		Buelow, Donald William	PhD
Brewster, Phyllis May	MS	Horn, Gertrude Mary	PhD
Crossen, George Edward	MS	Soine, Taito Olaf	PhD
Jack, Laurine Davison	MS	Benica, William Steinhart	MS
Voigt, Ralph Ferdinand	MS	Carlson, Edward Henry	MS
Waldon, Curtis Henry	MS	Klug, Silas Aloys	MS
		Small, Laverne Doreyn	MS
1938			
Goldner, Karl John	PhD	1945	
White, Allen Ingolf	MS	Small, Laverne Doreyn	PhD
		Asano, Akira	MS
1939			
Brecht, Edward Armond	PhD	1947	
Buelow, Donald William	MS	Almin, Ragnar	MS
Fredell, Walter George	MS	Bay, Gail	MS
Hansen, Harriet Eleanor	MS		
Keyes, Winifred Alice	MS	1948	
Soine, Taito Olaf	MS	Asano, Akira	PhD
		Benica, William Steinhart	PhD
1940		Bope, Frank Willis	PhD
Crossen, George Edward	PhD	DiGangi, Frank Edward	PhD
Fischer, Earl Britzius	PhD	King, Robert Edward	PhD
Netz, Charles Vail	PhD	Chang, Yu-Chung	MS
White, Allen Ingolf	PhD	Kuhlen, Lois Marie	MS
Hadley, Willard Jesse	MS		

1949

Doerge, Robert Fred PhD
 Kleber, John William PhD
 Schermerhorn, John Watson PhD

1950

Braeden, Olav Johan PhD
 Chow, Alfred Wen-Jen PhD
 Hopponen, Raymond Ellwood PhD
 Murty, Gollakota Gopala K PhD

1951

Abu-Shady, Hamed A PhD
 Buchdahl, Myron Robert PhD
 Chiang, Li-Chin PhD
 Patel, Ramanbhai Kishorbhai MS
 Zagelow, Leonard Paul MS

1952

Hamor, Glenn Herbert PhD
 Miller, Robert Herman PhD
 Putney, Blake Fuqua PhD
 Rost, William Joseph PhD

1953

Appel, Robert Martin PhD
 Boblitt, Robert Leroy PhD
 Gregg, David Henry PhD
 Rhodes, Harold Jesse PhD
 Heyndrick, AubinMarie Achille MS
 Ramarao, Maddury VenkataMS

1954

Bay, Paul G PhD

1955

Petersen, Robert Virgil PhD

1956

Ecanow, Bernard PhD

Schwartz, Samuel Meyer PhD
 Fiedler, Klaus Reiner MS

1957

Cole, Jack Robert PhD
 Counsell, Raymond Ernest PhD
 Batra, Karam Vir MS
 Yun, Tuk Sik MS

1958

Kelly, Clark Andrew PhD
 Kier, Lemont Burwell PhD
 Martell, Michael Joseph PhD

1961

Liebman, Arnold Alvin PhD
 Patel, Ramanbhai Kishorbhai MS
 Rao, Padukone Krishna MS

1962

Takebe, Yoshiko Higoshi MS

1963

Issacson, Eugene Ivan PhD

1964

Maulding, Hawkins Valliant Jr. PhD
 Prasad, Vadlamani Kali PhD
 Jawad, Fuad Hasan MS

1965

Gupta, Prem Kumar PhD
 Kriesel, Douglas Clare PhD
 Stubbins, James Fiske PhD

1966

Abdel-Monem, Mahmoud PhD
 Mikhall, Adel Ayad PhD
 Zoglio, Michael Anthony PhD

2004

Guo, Zhijun
 Jorvig, Erik C
 Kalyanaraman, Natarajan

2005

Carlson, Jonathan C T
 Fisher, Abigail Louise
 Li, Xingnan
 Rao, Priyanka Arvind
 Tang, Ye
 Wang, Haiqing
 Wong, Hansen L

2006

Argikar, Upendra Arvind
 Chou, Tsui-Fen
 Daniels, David John
 Kane, Brian Edmund
 Lao, Yanbin
 Goodell, John Robert
 Raghavan, Bhooma
 Steele, Terry William Joseph
 Vartak, Ashish
 Giraldes, John W

2007

Lu, Ding
 More, Swati Sudhakar

2008

PhD Balasubramanian, Ranganathan
 PhD Doshi, Jignesh Mahesh
 MS Loeber, Rachel Lea
 Kending, Cory Shawn
 Addo, Sadiya Noor
 PhD Johnson, Thomas Edwin
 PhD Norton, Jolanna Alikeh
 PhD Steele, Jaeson Charles
 MS

2009

PhD Bhagwanth, Swapna
 PhD Goggin, Melissa Mary
 Liu, Li
 Liu, Xiaodan
 PhD White, Brian Richard
 PhD Zhang, Siyi
 PhD Meng, Lei
 PhD Pietsch, Kathryn E
 MS

2010

PhD Bardaweel, Sanaa Khaled
 PhD Zhou, Jin
 PhD Zhou, Xin
 MS Michaelson-Richie, Erin Denise
 MS Aliwarga, Theresa

2011

PhD Das, Sonia Goutam Kumar
 PhD Ming, Xun
 MS

Appendix G. WORKS CITED

- Abdel-Monem, Mahmoud. Interview by Richard Broderick, Minneapolis, MN, 24 September 2009.
- Abul-Hajj, Yusuf. Interviews by Richard Broderick, Minneapolis, MN, 4 March 2010, 5 May 2010, 3 September 2010.
- American Association for Colleges of Pharmacy. Proceedings, Alexandria, VA. 1944.
- Amin, Elizabeth. Interview by Richard Broderick, Minneapolis, Minn., 19 November 2009.
- Anderson, Lee & Pennigton, Kathy. "The University of Minnesota College of Pharmacy, 1982-2004." University of Minnesota, Minneapolis, 2005.
- College of Pharmacy. "A Century of Challenge and Change." Pharmacy Record. University of Minnesota, Minneapolis, Spring 1992.
- _____. Pharmacopa. University of Minnesota College of Pharmacy, Minneapolis, 1964.
- _____. Pharmacy Review. University of Minnesota College of Pharmacy, Minneapolis, 1977.
- Department of Medicinal Chemistry. Presentation of Strategic Plan, 2000-05. University of Minnesota College of Pharmacy, Minneapolis, 2000.
- Dosa, Peter. Personal notes, 22 November 2010.
- Eccles, R. C. Education of a Pharmacist. [Pamphlet.] American Pharmaceutical Association, Philadelphia, PA, 1885.
- Gisvold, Ole. Gisvold Collection. University of Minnesota Archives (Folder 10, Box 2; Folder 6, Box 3), 1952.
- Gunda, Georg. Interview by Richard Broderick, Minneapolis, MN, 15 October 2010.
- Gunda, Georg. Letter to Frank Cerra, 25 August 2005.
- Hanna, Patrick. Interview by Richard Broderick, 10 October 2010.
- Harki, Daniel. Personal notes, 14 March 2011.

Haskel-Luevano, Carrie. Personal notes, 16 December 2010.

Higby, Gregory J. "Introduction," *American Pharmacy before 1852*. Edited by Gregory Higby and Elaine Stroud, American Institute of the History of Pharmacy. Madison: University of Wisconsin College of Pharmacy, 2005, ix-xi.

Institute for Therapeutic Drug Development. Update and Overview. Minneapolis, MN, September 2010.

Johnson, Rodney. Interview by Richard Broderick, Minneapolis, MN, 7 July 2009.

Kier, Lemont. Telephone interview by Richard Broderick, 17 December 2009.

Kohler, Robert. *From Medical Chemistry to Biochemistry: The Making of a Biomedical Discipline*. Cambridge: Cambridge University Press, 1982.

Lee, K. H. Interview by Richard Broderick, 3 December 2009.

Lynn, E. V. Report of Committee on Pharmaceutical Research, American Association of Colleges of Pharmacy. Arlington, VA, 1944.

MIKI. "Welcome to MIKI 2009" [Annual meeting handout.]. Department of Medicinal Chemistry, University of Minnesota, Minneapolis, MN, 2009.

Minnesota State Pharmaceutical Association. Proceedings [research committee report], 1930-40, 27, 29, 30-31.

_____. Proceedings, 1942, 1947 and 1950.

Netz, Charles V. *History of the University of Minnesota College of Pharmacy 1892-1970*. Minneapolis: University of Minnesota College of Pharmacy, 1971.

Portoghese, Philip. Interview by Richard Broderick, Minneapolis, MN, 1 October 2009.

_____. "A New Concept on the Mode of Interaction of Narcotic Analgesics with Receptors," *Journal of Medicinal Chemistry* 8 (1954): 609.

_____. "Drug Architecture," *Pharmacopa*. Minneapolis: University of Minnesota College of Pharmacy, 1965.

Rommel, Rory. Personal notes. 16 November 2011.

Schramm, Lee. Telephone interview by Richard Broderick, 10 November 2009.

Shier, Thomas. Interview by Richard Broderick, Minneapolis, MN, 19 August 2009.

- Soine, William. Telephone interview by Richard Broderick, 10 January 2010.
- Speedie, Marilyn. Interview by Richard Broderick, Minneapolis, MN, 7 October 2010.
- Tretyakova, Natalia. Interview by Richard Broderick, Minneapolis, MN, 12 August 2009.
- Vince, Robert. "A Brief History of the Development of Ziagen," *Chemtracts-Organic Chemistry* 21 (2008).
- _____. Interview by Richard Broderick, Minneapolis, MN, 1 February 2011, 24 February 2011.
- Wagner, Carston R. Interview by Richard Broderick, Minneapolis, MN, 19 August 2009.
- Walters, Michael. Personal notes, 6 March 2011.
- Wilson, Heather. Letter to Yusuf Abul-Hajj, 14 November 2008.
- Worthen, Dennis B. "Frederick John Wulling 1866-1947: Fighter for Professional Educational Standards," *Journal of the American Pharmaceutical Association*, September-October 2007.
- Wulling Frederick. *Pharmacy Forward*. Ed. Emerson G. Wulling. La Crosse, WI: Sumac Press. 1948.
- _____. Autobiography, Wulling Collection, University of Minnesota Archives, (Folder 65), [undated].
- _____. Letter to Dean Perry Millard, 10 May 1895.
- _____. Report to the President. University of Minnesota, College of Pharmacy, Minneapolis, 1930.
- _____. Second Melendy Lecture, University of Minnesota College of Pharmacy, Minneapolis, 1944.

