

American Society of Pharmacognosy

ASP Newsletter: Spring 2023, Volume 59, Issue 1

Spring 2023

Discovering Nature's Molecular Potential

ASP Mourns the Loss of Major Figures



In Memoriam: Heinz G. Floss

By Taifo Mahmud, PhD and Bradley Moore, PhD

n December 19, 2022, Heinz G. Floss, a world-renowned natural product chemist and a former president of the American Society of Pharmacognosy (ASP) and ASP Fellow, died at his home in Bellevue, Washington following a fall. He was 88 years old. Floss was a highly regarded mentor, proponent of natural product research, valued member of the ASP, and, to many of us lucky enough to work and study with him, he was an inspiration and a dear friend.

Floss was born on August 28, 1934 in Berlin, Germany. He grew up in a city ravaged by the Second World War and experienced the misery of the postwar era. He completed his *Diplomarbeit* (master's thesis) (1958) in chemistry at the Technical University of Berlin and his PhD (1961) at the Technical University of Munich, both under the guidance of Prof. Friedrich Weygand. Weygand was a student of Richard Kuhn (Nobel Prize 1938), who was a student of *continued on page 4*

Heinz G. Floss: PHOTO: UNIVERSITY OF WASHINGTON, DEPARTMENT OF CHEMISTRY, 1988



In Memoriam: Robert J. Krueger

By Jack Rosazza, PhD, Marcy Balunas, PhD, John Cardellina, PhD

he ASP and the ASP Foundation (ASPF) have lost a major force in its leadership for nearly five decades. Robert J. (Bob) Krueger died on January 1, 2023 after a valiant standoff with acute myeloid leukemia for almost two years. He, along with his wife Beth, were cheerful, ever-present fixtures at ASP annual meetings. His role as ASP Foundation treasurer further boosted annual meeting attendees' spirits since he was responsible for handing out many checks to ASP awardees from students to senior scientists.

Krueger played a major role securing the financial future of the ASP, thereby allowing the society to distribute a remarkable number of awards over the years. In his decades-long tenure as ASPF treasurer, he managed to guide the treasury from a startup of about \$300,000 and an annual outlay of about \$22,000 in awards and grants to a corpus of \$2,500,000 and an annual expenditure approaching \$150,000 for a continually expanding array of recognitions.

Robert Krueger: PHOTO: WILLIAM BITZINGER, FSU, 2011

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Robert J. Krueger



Barbara C. Sorkin

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By Edward J. Kennelly, PhD

s I write this, spring has officially begun, and in New York City, people are out in force in public venues from museums to parades. It is hard to believe that it is almost three years to the day that lockdowns began due to the coronavirus epidemic that swept through the world in 2020. While much has changed, thanks to vaccines and greater knowledge of the virus, things have not returned to pre-pandemic ways completely, and they may never. We also remember that last year, Russia invaded Ukraine, and our colleague Dr. Oleh Koshovyi provided the Newsletter with a compelling first-person account of the impact of the war on his family and colleagues. We have heard that he is well at his university and even invented a botanical medicine used by the Ukrainian army to stop bleeding and prevent frostbite. On February 6, parts of Turkey and Syria were devasted by a 7.8 magnitude earthquake. ASP has six members in the directory listed in Turkey. ASP President Amy Wright has reached out to the six and is offering them free ASP renewal through 2024.

ASP mourns the loss of two members who have greatly shaped our society over their decades of dedicated service. Professor Heinz Floss was former president and ASP fellow who highly valued research and helped mentor many scientists, including the authors of the expansive and moving tribute to him, Professors Brad Moore and Taifo Mahmud. Former ASP Foundation Treasurer Dr. Bob Krueger worked tirelessly for decades to improve the financial health of the ASP. This resulted in establishing an endowment and growing it through careful investment strategies. A favorite part of the annual membership business meeting was when Bob would give his assessment of the ASPF stock purchases over the last budget year. These wise investments have enabled the ASP to provide countless awards and travel grants. Bob would typically attend ASP meetings with his wife, Beth, and their devotion to ASP and each other was clear to everyone who interacted with them.

ASP received additional sad news that <u>Priscilla Farnsworth</u>, the wife of Founding Member and second ASP President Dr. Norman Farnsworth, died last October. Our condolences are extended to the family and friends of all these colleagues.

The ASP Annual Meeting will be held in the Washington, DC metro area from July 22-26. Please read the latest information about the topics that will be covered, and upcoming deadlines, including the <u>abstract submission</u> deadline of April 15.

ASP Vice President Dr. Tawnya McKee continues the second half of her "Taking Action" series about grant writing and tips and tricks for securing federal funding. If you have not read her first article in the winter 2022 ASP Newsletter, I encourage you to look at both. Tawnya provides excellent insights into putting together a competitive NIH application. I recently attended a webinar by Melissa Nickell at the University of Kentucky about the new NIH-NIGMS program known as Support for Research Excellence (SuRE). I think many ASP members who qualify for AREA grants may find this program of interest as well. I was glad to learn that at least one ASP member, Dr. Paul "Skip" Price, was funded in the first round of this new program, and he speaks glowingly of this funding opportunity in the article I wrote about the SuRE program.

Our regular columns continue to provide insights into pharmacognosy new and old. Dr. Dave Newman's "Hot Topics" provides important musings about antibiotic structures from the past and how they are being used nowadays. Lloyd Library archivist Christine Jankowski's fascinating "From the Archives" delves into the history of the Plant Science Laboratory Seminar some 100 years ago, hosted by Professor Edwin Leigh Newcomb, and how that led to the formation of ASP. In "Meet a New ASP Member," Dr. Neha Garg discusses her extensive training in microbial metabolomics and new training in Orangetheory fitness.

I hope you have a wonderful spring!

In Memoriam: Heinz G. Floss

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Richard Willstätter (Nobel Prize 1915), who himself was a student of Adolf von Baeyer (Nobel Prize 1905). Baeyer was a student of August Kekulé, the principal founder of the theory of chemical structure and the Kekulé structure of benzene. Kekulé himself studied with Justus von Liebig. This illustrious scientific pedigree was very near and dear to Floss who prominently displayed a photo of Weygand in his office at the University of Washington. Like his mentors before him, Floss cultivated a pioneering spirit in his more than 150 students and postdocs, many of whom became university professors and leaders in industry.

One of his early graduate students, Laurence Hurley (PhD 1970 Purdue), recently recalled, "I once asked Heinz if he had any advice for an aspiring scientist and he answered, 'Life is too short to drink cheap wine.' After I thought about this, I realized this went much deeper than choosing the wine but represented Heinz's philosophy about research too and unconsciously the



John Cassady, Varro Tyler, Heinz Floss, and James Robbers (I to r) at the 2000 ASP Annual Meeting in Seattle.

PHOTO: COURTESY OF THE FLOSS FAMILY

Floss was a highly regarded mentor, proponent of natural product research, valued member of the ASP, and, to many of us lucky enough to work and study with him, he was an inspiration and a dear friend.

most important lesson I had learned as a graduate student in his lab – choose important research questions to address."

Floss's exposure to the field of natural products began when he worked on the biosynthesis of ergot alkaloids in fungi for his PhD thesis. This work was done in collaboration with plant biochemists Prof. Kurt Mothes and Dr. Detlef Gröger in Halle, East Germany. The work on ergot also acquainted him with Prof. Varro E. (Tip) Tyler, a prominent ergot researcher and one of the founders and the first ASP president. When Floss spent some time in Prof. Eric E. Conn's laboratory at the University of California, Davis from 1964 to 1965, he and his family drove up to Seattle and visited with Tyler at the University of Washington. Subsequently, when Tyler became Dean of Purdue University's School of Pharmacy in 1966, Floss joined its Department of Medicinal Chemistry as an associate professor.

Floss's close relationship with Tyler and his love of natural product research placed him among active members and leaders of the ASP community. He was the ASP president from 1977-1978, during which time he played a major role in expanding the ASP Newsletter. A decade later in 1988 he was the second recipient of the ASP Research Achievement Award, which years later was renamed in honor of ASP's second president, Norman R. Farnsworth. "As a recipient of the award he (Floss) became one of the first ASP Fellows in 2006," reflected Gordon Cragg, former Chair of the ASP Fellows. "Among his many other

honors, he held honorary doctorates from Purdue University and the University of Bonn in Germany." In 2000, Floss organized a memorable ASP conference in Seattle where, as young Pls, we helped him set up one of the first ASP symposia on natural product biosynthesis during the early days of microbial genomics. He was always pushing the limits of his biosynthetic studies to incorporate the latest technology and trends and, as such, helped challenge and shape the ASP to be a progressive Society. In his 1977 address as the incoming ASP president, he wrote these prophetic words: "We have to look to the future and define new goals and frontiers. Areas like the genetics of microorganisms producing natural products, the development of economically viable systems for the production of higher plant constituents by single cell culture, or ultimately even by bacterial fermentations using recombinant DNA technology, for example, are all highly significant and legitimate research areas in Pharmacognosy." Floss ends with saying that "the opportunities which this field offers are truly boundless, but whether they are realized depends entirely on each and every one of us."

ASP President Amy Wright noted, "Dr. Floss was truly a pioneer in natural products research whose work and mentoring has touched all of us in the natural products community. His dedication to defining and rigorously addressing ground-breaking and challenging questions will remain an inspiration.

Floss's close relationship with Tyler and his love of natural product research placed him among active members and leaders of the ASP community.

In Memoriam: Heinz G. Floss

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Although he is gone, his continue through his publications and in the hands of the many researchers who had the opportunity to learn from him and who in turn are passing along this legacy of excellence to the next generation. The ASP will greatly miss this giant of natural products research."

Floss's approach science was ingenious and thorough. He was intrigued by how plants and microbes construct their bioactive and often complex chemical structures. Using his unique ability to solve intricate biochemical problems, he illuminated many of the



Left: A Floss birthday at work. Right: Floss in lecture mode.



foundational metabolic processes that we take for granted today in natural product biosynthesis. He was also fascinated by the stereochemical control and the catalytic mechanisms of enzymes.1 Floss was a master of combining chemical and biochemical approaches to solve questions in biology. To understand the control of chirality in enzyme-catalyzed reactions, he and his team stereoselectively synthesized methyl groups, labeled with the three hydrogen isotopes, and used them in biochemical assays to tease apart the intricate fate of a substrate during the course of an enzymatic reaction.2

His former graduate student Ming-Daw Tsai (PhD 1978 Purdue) noted, "In addition to natural product chemistry, biosynthesis, and pharmacognosy, Heinz Floss was a world leader in using chiral methyl groups to probe the mechanism of enzymatic reactions. I had the chance to work on such problems as his PhD student during 1975-78, which set the foundation for my future career in stereochemistry and enzymology. Even more importantly, I learned from Heinz to give students a great deal of freedom in research, to treat them as friends, and to explore

interesting problems with new methods."

Floss was among scientists of his generation that used interdisciplinary approaches. employing sophisticated isotope labeling studies and a variety of state-of-the-art biological methods including molecular genetics study the biosynthesis of bioactive natural products. After 16 years at Purdue, he moved to Ohio State University to become Chair of the Department Chemistry. There he started molecular incorporating genetics into his research, often with his microbiology colleague William Strohl. At

the time he also published an iconic paper in Nature with the groups of Sir David Hopwood and Nobel Laureate Satoshi Omura on the "Production of 'hybrid' antibiotics by genetic engineering."3 That paper is regarded as one of the earliest demonstrations of mixing and matching genes from biosynthetic gene clusters to engineer the production of new to nature natural products. In 1988, he moved to the University of Washington in Seattle, where his group continued to study the biosynthesis of a variety of important natural products, such as acarbose, ansamitocin, asukamycin, rifamycin, ⁴ Taxol, thiostrepton, ⁵ and validamycin.

What made Floss's lab such an exciting place to work and study during his Seattle years was how he approached projects, often matching chemists with biologists. Not only did this approach allow for projects to be examined in detail from a variety of perspectives but also allowed for the transfer of knowledge and training between group members. Sunghae Park (PhD 1999 Washington) reminisced, "Looking back on my time at Dr. Floss's lab, I feel extremely lucky that I had a chance to be continued on page 6

"We have to look to the future and define new goals and frontiers. Areas like the genetics of microorganisms producing natural products, the development of economically viable systems for the production of higher plant constituents by single cell culture, or ultimately even by bacterial fermentations using recombinant DNA technology, for example, are all highly significant and legitimate research areas in Pharmacognosy."

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"The opportunities which this field offers are truly boundless, but whether they are realized depends entirely on each and every one of us."



Celebration of Heinz Floss's 75th birthday in Xiamen, China, August 2009.
Sitting (I-r) - Jürgen Rohr, Isao Fujii, Inge and Heinz Floss, Lutz Heide and son.
Standing (I-r) - Linquan Bai, Kenji Arakawa, Chang-Joon Kim, Jae Kyung Sohng, Taifo Mahmud,
Yuemao Shen, Bradley Moore, Lutz Heide's wife and other son.

PHOTO: COURTESY OF YUEMAO SHEN

trained as an independent thinker. The lab was full of brilliant postdocs and senior grad students with diverse expertise, from organic synthesis to molecular biology. He encouraged us to learn from each other and come up with our own solutions."

While Floss excelled in science and commanded excellence, he was often most proud of the independent achievements and careers of his former students and postdocs. He thus took great pleasure in helping his mentees achieve and surpass their career goals. He was respected and appreciated for his never-ending encouragement of their scientific curiosity and independence, as well as for helping them navigate challenges in their careers. Andreas Kirschning, a postdoc from 1989 to 1991 in Seattle, recalled a defining conversation with Floss that set him off to his successful 30+ year academic career in Germany where he is now a professor of organic chemistry at Leibniz University Hannover. Kirschning reflected that Floss's "genuine personal interest for his coworkers led to large academic natural product schools around the world. I remember a brief conversation with him, a 'click' moment of my life. He asked, 'Andreas, what do you plan to do after your postdoc time in my lab?' And I responded that I'd probably go into the pharmaceutical industry. He then asked if that was what I really wanted to do, and I recall saying that I'd prefer going into university but that I didn't think that I was good enough for that. Heinz responded, 'You have what it

takes, I believe in you! Do it!""

One of his early postdocs John Vederas put Floss's contributions to mentorship well when he said, "The legacy of a professor is in the education and long-term inspiration of new researchers, who then transmit this in their own way to the next generation. In this regard especially, Heinz has been a true grandmaster who has educated a host of accomplished scientists and profoundly influenced the way a very large field of science has developed."

Floss enjoyed traveling the world and regularly visited his former group members and his many collaborators who often became

close personal friends. One of his long-time collaborators and friends Professor Eckhard Leistner from the University of Bonn remarked, "Heinz was an exceptional natural product scientist. In addition, he was also a very friendly and modest person. It was easy to approach him and to talk to him. This may be one of the reasons why he was an outstanding educator, teacher, and a friend I am proud to have had."

In summer 2005, soon after Floss closed his lab at the University of Washington, he gave an inspiring symposium lecture at the ASP annual meeting in Corvallis, Oregon, summarizing his 45 years of natural product biosynthesis research. In his lecture, not only did he elegantly describe the depth and breadth of his decades of exceptional research, but also humbly shared how he set himself up to a highest standard by trying to follow the almost impossibly rigorous standards of Prof. Duilio Arigoni at the ETH Zürich. In his words, "I would always ask myself whether a particular experiment or proof would meet Arigoni's standards. If you choose a role model, you might as well pick a challenging one, even if you can never live up to it." A review article describing his life-long scientific career entitled "From Ergot to Ansamycin – 45 Years in Biosynthesis" can be found in *J. Nat. Prod.*⁶

A special side of Heinz Floss that many of us marveled was his remarkable and magical relationship with his beloved wife continued on page 7

Floss was a master of combining chemical and biochemical approaches to solve questions in biology.

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Floss was among scientists of his generation that used interdisciplinary approaches, employing sophisticated isotope labeling studies and a variety of state-of-the-art biological methods including molecular genetics to study the biosynthesis of bioactive natural products.





Above left: Celebration of Heinz Floss's 88th birthday in Bellevue, Washington, August 2022, just a few months before he passed away. Left to Right: Heinz Floss, Inge Floss, Shinta Muljani, Reika Mahmud, and Taifo Mahmud. PHOTO: COURTESY OF TAIFO MAHMUD.

Above right: Heinz and Inge Floss (center) with Brad Moore and his wife Sonia Teder-Moore in May 2019, at the Scripps Institution of Oceanography Pier at UC San Diego. PHOTO: COURTESY OF BRADLEY MOORE

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of 66 years, Inge. They were inseparable and regularly traveled together on work trips that took them across the globe. Their admiration of Native American art, Asian culture, and the great outdoors were some of their passions that they enjoyed together. After his full retirement in 2005, they regularly visited friends and colleagues in Europe and Asia as well as drove around the country to visit historical sites and enjoy the natural beauty. One of their favorite places was Kyoto, Japan,

where they visited nearly every November (except during the COVID-19 pandemic) to enjoy the red-tinted maple leaves in the fall (*momiji*). Just weeks before his death, they were finally able to return to Kyoto, Japan, together, for the last time.

Floss is survived by his beloved wife, Inge, his sons, Peter (Barbara) Floss and Helmut Floss, his daughter Hanna (Tony Andrews) Floss, nine grandchildren, and four great grandchildren.

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Krueger played a major role securing the financial future of the ASP, thereby allowing the society to distribute a remarkable number of awards over the years.

"Bob was one of the pillars of the Society and Foundation. Friendly and perennially upbeat. [He] worked tirelessly and steadily for ASP. [He was] a true gentleman and friend."

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Through it all, Krueger was a sterling example of a kind, caring human being. As attested to by ASP Fellow Tad Molinski, "Bob was one of the pillars of the Society and Foundation. Friendly and perennially upbeat. [He] worked tirelessly and steadily for ASP [He was] a true gentleman and friend." ASP Vice President Tawnya McKee stated, "He was a devoted member of ASP and the Foundation and a truly kind human." And ASP Fellow Cindy Angerhofer remarked, "Bob was a special person with tireless enthusiasm for natural products."

ASP President Amy Wright spoke for many in the Society when she noted, "Bob Krueger will be greatly missed. Not only for his long-term service to ASP, the field of pharmacognosy, and his sound financial and investment skills, but also for his cheerful attitude and caring friendships with so many members of the ASP."

Krueger was born and grew up in Milwaukee, Wisconsin, graduating from Wauwatosa West High School in 1966. His precocious interest in pharmacognosy began very early when, as a high school sophomore, he read Margaret Krieg's 1964 book, *Green Medicine: The Search for Plants That Heal.* She described the years-long efforts of the late ethnobotanist and ASP Honorary Member Richard Evans Schultes, who studied the uses of plants by indigenous peoples; how Mexican yams provided precursors for steroid semi-synthesis; discoveries and uses of quinine, digitalis and others; ongoing searches for antineoplastic drugs from *Catharanthus* spp. and psychotropic principles from ergot mushrooms. Included among the photos in *Green Medicine* was one featuring the late ASP member and *Journal of Natural Products* editor Arthur E. Schwarting and the pharmacognosy group at the University of Connecticut (UConn),



Krueger with his daughter Allison and granddaughter Linden at the Ann Arbor March for Science in 2017.

PHOTO: COURTESY OF ROBERT KRUEGER

College of Pharmacy. Krueger took notice and was hooked. He enrolled in Pharmacy at UConn in the Fall of 1966 and went on to earn his BS in Pharmacy in 1971. It was at UConn that he met Beth Lindberg, and they married right after his graduation.

At the time, Pharmacognosy at UConn was roughly divided into "higher Pharmacognosy" with an emphasis on plants and natural products, and "lower Pharmacognosy" that emphasized microbiology and natural products. Prof. Bill Kelleher led the latter, with an emphasis on all aspects of the fermentation production of lysergic acid derivatives by an ergot fungal species, *Claviceps paspali*. Kelleher, who had received his PhD in Biochemistry from the University of Wisconsin, accepted Krueger as an undergraduate research assistant to work on an aspect of *C. paspali* that Jack Rosazza had begun a few years earlier while a graduate student working with Kelleher. The result was Krueger's first publication in *Lloydia* (now *Journal of Natural Products*).²

At UConn, Krueger was mentored by one of the top pharmacognosy programs at that time. Schwarting, Kelleher and Mike Edwards were all past ASP presidents, with Schwarting also one of the founders of ASP. Krueger was also exposed to more of the best natural products/pharmacognosy people - Dick Hutchinson, Ralph Collins and Anna Rother. Schwarting, Kelleher (both Pharmacognosy), Ralph Collins (Botany, Mycology) and Jim Bobbitt (Chemistry) had previously received the first NIH Training Grant in Natural Products, supporting the field of pharmacognosy. ASP Executive Committee member Dr. Marcy Balunas had her first academic appointment at UConn and recollected, "I was so connected to both Bob and Beth since they were UConn alums – I even kept a four-leaf clover continued on page 9

In Memoriam: Robert J. Krueger

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he picked when he visited UConn in 2012 – he called it my tenure four-leaf clover and it meant the world to me! Bob will be sorely missed!"

Krueger chose to attend the University of Iowa, College of Pharmacy in Iowa City as a graduate student in pharmacognosy. He worked in Professor Dave Carew's laboratory. which was actively studying plant tissue culture with an emphasis alkaloid production, other products, natural and enzyme activities by Catharanthus roseus. Carew and Rosazza were former and future ASP presidents, respectively, and Carew was also a founding member of the Society. Krueger was an exemplary graduate student; he assumed, among other activities, the maintenance of the greenhouse on the College of Pharmacy rooftop, where C. roseus and a handful of other medicinal plants were grown. Kreuger's thesis work resulted in the characterization of anthocyanidins in C. roseus cultures,3 and he evaluated the capabilities of callus cultures of C. roseus to metabolize the alkaloids

vindoline, catharanthine and vincaleukoblastine.4

He continued his interests in plant tissue culture long after leaving lowa to accept an assistant professorship in the College of Pharmacy at Ferris State University in Big Rapids, Michigan. Over the years, through excellent collaborations, he and his coworkers evaluated *Sanguinaria canadensis* cell cultures for dihydrobenzophenanthridine oxidase, an enzyme catalyzing the last step in the biosynthesis of the alkaloid sanguinarine, identified anthocyanins in *Strobilanthes dyeriana* callus cultures, and characterized a monoterpene hydroxylase from cell suspension cultures of *C. roseus*. Krueger contributed numerous book reviews and chapters on various aspects of natural products and pharmacognosy during his long tenure at Ferris State.





Above: Bill Baker, Thomas Prisinzano and Krueger at the 2008 ASP Annual Meeting in Athens, Greece.

PHOTO: AMY KELLER

Below: Marcy Balunas, the late John Cassady and Krueger at the 47th ASP Annual Meeting in Washington, DC, 2006.

Krueger served on numerous university committees and was the chair of the Ferris Arts and Lectures Committee, bringing speakers and performing artists to the community for several years. In 1988 he was honored by the Michigan Association of Governing Boards of Colleges and Universities as Ferris State's Distinguished Faculty Member and was an active member of the Ferris Faculty Association. He served as a member and president of the Michigan Wildflower Association and was recognized as a 50-year member of the American Chemical Society in 2022. Krueger was a member of the American Botanical Council, the Michigan Botanical Club, and Sigma Xi. He shared his knowledge of plants and herbs with audiences at conferences across the world.

Krueger took great pride in his public service to the community of Big Rapids. He was elected to Big Rapids Board of Education and was involved in the passage of the millage proposal to build the new high school. He was a proud member of the Big Rapids Rotary Club and served a term as its president. He was selected to lead a team of young Rotarians to Germany in 2011 on a sixweek exchange program. He was an active member of Immanuel

Lutheran Church and served on various committees within the church. He was elected by the residents of Big Rapids to represent them on the City of Big Rapids Charter Revision Commission. He truly lived a life of service, not only to his profession but his community as well.

Krueger's own words from his reaction to being selected for Honorary Membership in the ASP provide unique and accurate insight into his character and commitment to our Society and its Foundation. "My philosophy, based on my Rotary motto 'Service above self,' has always been to help wherever needed, whether it is via my employment, my community, or the ASP, where I have been a member of almost every standing committee in our Society. In 1992 I was named treasurer of continued on page 10

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the ASP Foundation, having been mentored for this position by David Slatkin, a former Society President and long-time Society Treasurer. As ASPF treasurer, I served at the pleasure of the Society's Executive Committee under many Presidents and ASPF Chairs. 'Mentoring' is what the ASP does best. It is a 'family of scientists' who excel in producing good science. Its members unselfishly help younger members to achieve that principle [of good science and service to others]. As I have prospered from my membership in the ASP, I consider it an honor to serve it through a kind word of encouragement, the handing out of an award check, or a direct helping hand. I intend to continue my service as long as the ASP needs my help."

And continue to serve he did, even into the last waning months of his life. Despite his illness and resulting fatigue, he worked feverishly with current ASPF Treasurer Kirk Manfredi



Krueger, in his role ASPF treasurer, presents an ASP Travel Grant Award to Dr. Esperanza Carcache de Blanco at the 2008 joint annual meeting in Athens.

to bring him up to speed on both the day-to-day and big picture operations of the ASPF Treasury.

Krueger will be greatly missed by his many ASP colleagues and friends. ASP member Ben Naman stated, "Bob made a lasting impression on many people in the society and the foundation, and I am glad to have known him." Former ASP President Barry O'Keefe wrote, "Bob was a stand-up guy and a leader in the ASP who made tireless contributions. He was also a fun person to be around and always had a great attitude." ASP Fellow Douglas Kinghorn ranked him among the seminal figures in ASP history, "Bob represented the heart of ASP for so many years. He will be very greatly missed."

Krueger is survived by Beth, his wife of 51 years ("the love of his life"), daughters Laura and Allison, grandchildren Linden, Leah, and Samuel, and his sister Jacque. ■

"Bob was a special person with tireless enthusiasm for natural products."

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By Craig Hopp, PhD and Nandakumara Sarma, PhD

The meeting program is developing very nicely with most of the invited speakers confirmed. Visit the meeting program page for the sessions and invited speakers. Abstracts submission is open for contributed talks and proposals for poster presentations. (The **April 15** deadline is rapidly approaching.) Submissions are invited for the following broadly inclusive topics of the ASP membership interests:

- Where Chemistry and Biology Meet
- Natural Products that Modify Macromolecular Interactions: PPI, RNA-Prot, DNA-Prot, etc.
- Old Molecules / New Purposes
- Microbiome/Probiotics Interactions
- Bridging the Gap: Collaborations with Predominantly Undergraduate Institutions
- Public/Private Partnerships
- Unique Environments
- Fungal Biosynthesis and Chemodiversity
- Natural Products: Who's Your Partner: Symbiosis and Natural Products
- Cannabis and Cannabinoids
- Recent Advances in Traditional Herbals Quality/ Authenticity and Analysis
- Natural Products and Infectious Diseases

The meeting will begin with a series of informative workshops on Saturday, July 22. Pending confirmation of details, the following workshop topics are being evaluated:

- FDA IND/Botanical Drug Review
- Botanical Safety Consortium
- Cell-free Screening Methods
- Fungal Identification and Taxonomy
- Public Speaking

The meeting will feature several continuing themes, such as the Younger Members symposium, jobs fair, and various

awards symposia, including the Norman R. Farnsworth Research Achievement Award, Varro Tyler Prize, and Matt Suffness Young Investigator Award.

Thanks to Local Organizing Committee member Emily Mevers for submitting an NCCIH grant proposal for \$30,000 to support registration costs for students, postdoctoral fellows and junior investigators with the goal of promoting diversity based on the guidelines established by the NIH NOT-OD-20-031: Notice of NIH's Interest in Diversity. If the grant is awarded, a request for a registration waiver may be made by qualifying attendees. You may watch out for updates in the meeting landing page.

Come with family! North Bethesda / Rockville is in a populated neighborhood well connected to the regional attractions in DC, Maryland and Virginia through metro trains. Monday afternoon and evening are free to spend time with friends, family and colleagues. A couple of local favorites for things to consider include free Smithsonian museums, the National Mall and associated memorials, US Botanical Gardens, and other historic sites. Rockville is about a 45-minute commute to DC (by road or train) and well served by three major international airports (IAD, DCA and BWI). All these airports are about equal distance from the meeting venue. You may check WAS as the airport code for all these airports and select the best price based on which airlines you take. DCA is well connected to the meeting venue by Metro train. Uber or Lyft are available from BWI and IAD airports. ASP updated the 2023 meeting Health and Safety Policies to facilitate safe and productive in-person interactions. An outdoor event is planned at the **Smokey Glen Farm** to provide for ample networking and team building opportunities.

The ASP annual meeting presents a wonderful opportunity for interested companies to network with about 600 attendees through exhibits of their product offerings and sponsorship of the meeting's events. The career fair and young member events at the annual meeting are also opportunities to hire talent.

We are looking forward to welcoming ASP members and families to the 2023 annual meeting for an intellectually stimulating opportunity for **INNOVATION THROUGH INTERACTION!** We encourage you to register early and book your hotel room at the meeting venue, Bethesda North Marriott Hotel & Conference Center - Rockville, MD, at a preferred rate.

See you in July!

Taking Action Part 2:

Writing Applications, the Review Process and Summary Statements —How to Approach and Respond Effectively to Them

By Tawnya McKee, PhD

ontinuing from the last newsletter, by now you have become an expert on finding and identifying appropriate funding opportunities for your research. Now, you should be poised to write your application. For NIH the current application is Forms H. General instructions are found here. There are numerous pages, webinars and classes that cover all the parts of an application and will teach you how to write an application. Use these resources to help write your application. Given the limited space, I cannot cover all the important aspects of writing an effective application. Instead, my advice will focus on three things I think are critical. The first is to make sure you fill out form P-600 Assignment Request Form. This form allows you to request specific study sections, Institute and, most importantly, scientific expertise required to review your application. Use this instead of a detailed cover letter.

Second, several weeks before submitting, give it to your least experienced graduate student or trusted colleague in another field to read and write down any questions they have while reading it. Why? Remember, although your application's assigned study section will have at least one reviewer with specific expertise for your application, the rest of the panel are not experts in your field. Instead, you should think of them as generalists. Having someone else with different or less expertise (another generalist) review it will identify what parts of the application still need clarification or more details. After working for weeks on it intensively, you often stop seeing what is written, and this outsider review will help identify those parts that need additional work.

Third, plan to spend as much time on the other tasks as you do on writing the main research portions of the application. This includes the biosketches, budget, letters of support, human and/or animal welfare, and the new required data

sharing plan. Keep in mind not only the NIH submission deadlines, but also your institute's internal deadlines. It takes a lot of time to get all the required information gathered and organized for submission. Do not forget to double check the funding opportunity announcement (FOA) for additional requirements like performance measures. These are not found in the general instructions, but, if not included in your application, your application will be administratively withdrawn as non-responsive. Submit your application early so you have time to sort out any issues. If there is a problem, contact the eRA Helpdesk only. Program directors (PDs) cannot see your screens, and we cannot help with these issues.

Once your application is submitted, you enter a waiting period. At the NIH, the application arrives and is sent for Receipt and Referral, that is, the application is assigned an Institute (or more) and a study section. On our end, we are assigned applications based on our assigned areas as well. Once we accept the application into our portfolio, we are able to listen to the study section when it meets. We only have access to those study sections where we have assigned applications. Personally, I try to listen to the review of as many applications as I can, but since each is scheduled by the scientific review officer (SRO) and the study section members, inevitably there are multiple study sections meeting simultaneously or conflicting with other standing meetings I have each week. Usually, the scores are released within two days of completion. PDs do not have access before they are released. They are released simultaneously to you and your PD. Even when the score is released, you still need to wait until the summary statement (aka pink sheet) is released before contacting your PD. Again, we do not have access before you do, and since the summary statement is the official record of the review, only continued on page 13

Third, plan to spend as much time on the other tasks as you do on writing the main research portions of the application. This includes the biosketches, budget, letters of support, human and/or animal welfare, and the new required data sharing plan.

Taking Action Part 2:

Writing Applications, the Review Process and Summary Statements —How to Approach and Respond Effectively to Them

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once it is released (generally within six weeks) can we discuss the review. If it has been more than eight weeks, go ahead and reach out to the SRO. They are the only ones who can release the summary statement.

Once you have the summary statement, please reach out by email and set up an appointment to discuss; do not just pick up the phone and call out of the blue. Why? It is simple really, I want our discussion to be as efficient and fruitful as possible, and it will not be unless: 1) I have time to prepare, and 2) you have time to really think about what the reviewers have to say and how you can address their concerns. For me I want to reread your application after reading your summary statement. That allows me to identify what I think the most significant issues are and how they might be addressed. Also, it is important to think about whether it is in the correct study section: did they really have the expertise or is there a different type of expertise needed? You will also need some time to think about the summary statement and talk to your team, and perhaps gain a little perspective. The reviews can seem very personal and can trigger lots of different strong emotions. And, while it may seem productive to get me on the phone and scream or cry for an hour, it is not a constructive use of anyone's time. Even if it is within the payline and will be funded, I may still need to talk to you prior to funding.

I approach my review of the application and summary statement from the point of view that the study section and your application's reviewers are offering their best advice on where the application needs to improve to be funded. Remember, study section members are volunteers, and the vast majority are really working to identify the best applications and provide constructive critiques to all their assigned applications. You should too, at least to the best of your ability. It can be very cathartic to draft your first response with all the emotion that it brings up. Then find a way to destroy it, taking all the negative emotions with it. Finally, walk away from your summary statement and application for a week or so. This break will, hopefully, allow you to view it with a less emotional, clearer perspective.

If you are going to revise and resubmit, remember that there is the extra introduction page. Use this page to thank the reviewers for their review and then take the two or three most significant concerns and address them on this page. Other critiques can be responded to by changes within the application itself. I recommend the changes be indicated with a vertical mark in the margin where substantial changes have been made. If you resubmit without responding, that will absolutely decrease your score as it is a score driving criteria for resubmissions. Also note, revised application success rates generally hover around 35%.

Quickly, two other comments. There is often an exception process for applications just outside the payline. At NCI, each division gets an allotment for this and decides how they will allocate the money. This is another reason to speak to your PD. They can tell you if it is an option for your application or not. Lastly, a word about appeals. (Note: this is my personal opinion, not the NCI's, and based on my 10 years as a PD.) You have the right to appeal for a new review. You should carefully decide if it is worthwhile. At NCI only 5-10% of appeals succeed. More importantly, however, you should know that if you do win an appeal, your original application goes back to the same study section for re-review. You have no opportunity to see or alter your application. It is critical that you look at the summary statement and decide if the issue that allowed the appeal to be successful is the only thing that lowered your score. If the error for which you obtained appeal is corrected in the rereview, if there are enough additional score-driving problems, the re-review will still result in an unsuccessful application. You must carefully consider whether revising and resubmitting, coupled with asking for additional expertise, is a better option.

Remember, there are many different organizations that provide grants for research. Regardless of the organization(s) you apply to for money, perseverance and understanding the organization's process and culture are key to successful grant writing. Investing the time it takes to adapt your ideas to the culture of the funding organization and to learn their unique process will be time well spent. Finding a way to accept and depersonalize the critiques will allow you to respond respectfully, even when you disagree, and to persevere until successful. If you have comments or questions, you can reach out to me directly at mckeeta@mail.nih.gov.

Remember, there are many different organizations that provide grants for research. Regardless of the organization(s) you apply to for money, perseverance and understanding the organization's process and culture are key to successful grant writing.

Do You Qualify for This NIH-NIGMS Funding Opportunity with a Remarkably High Success Rate?

EDITOR'S NOTE: Much of the information for this article is based on a presentation given by Melissa Nickell, MA, of the <u>Sure Resource Center</u> on January 25, 2023 and is available to view <u>here</u>.

By Edward Kennelly, PhD

t a time when only about 20% of reviewed NIH grant applications receive funding, did you know that the National Institute of General Medical Sciences (NIGMS) has a program with more than double that success rate? In 2021, NIGMS Division of Research Capacity Building (DRCB) introduced a newly imagined program called Support for Research Excellence (SuRE) to strengthen the research capacity for faculty at institutions that have limited NIH research support and serve groups underrepresented in biomedical research. This program, which currently has a greater than 40% success rate and covers an extremely broad variety of biomedical and behavior sciences, is an attractive alternative to ASP members with tenure-track faculty appointments at SuREqualified institutions who may otherwise apply for Academic Research Enhancement Awards (AREA), R15 grants. Several natural products projects have already been funded in the first round of SuRE. The SuRE program replaces the NIHGMS Support of Competitive Research (SCORE) program.

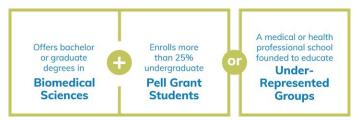
The SuRE program (PAR-21-169) provides direct costs of \$100,000 per year for up to four years and is renewable using the R16 activity code. The deadline is May 26 for standard submissions and September 7 for AIDS-related submissions. SuRE also offers a First Independent Research Award (PAR-21-173), provides direct costs of \$125,000 per year up to four years, requires a mentor, and is non-renewable. The deadline is September 28 for standard submissions and January 7 for AIDS-related submissions.

To qualify for this R16, your institution must offer a bachelor's degree in biomedical, behavioral, clinical, and social sciences and enroll greater than 25% undergraduates who receive Pell grants or be a medical or health professional school founded to educate underrepresented groups. Furthermore, your institution must have received less than \$6 million in NIH research projects in the past two years. Finally, for SuRE, but not SuRE First, your institution must have less than 20 active NIH SuRE, SC1, and SC3 awards, combined.

To see the percent of students receiving Pell grants in your institution, you can look at the <u>Integrated postsecondary Education Data System</u>. Using this new 25% baseline of Pell recipients means that institutions that enroll many economically disadvantaged students can qualify, no matter

In 2021, NIGMS Division of Research Capacity Building (DRCB) introduced a newly imagined program called Support for Research Excellence (SuRE) to strengthen the research capacity for faculty at institutions that have limited NIH research support and serve groups underrepresented in biomedical research.

1. Institutional Criteria



2. Funding Criteria

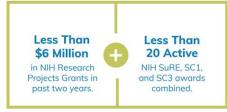


DIAGRAM: UNIVERSITY OF KENTUCKY

what the racial or ethnic composition of the student body. Certain institutions in West Virginia, for example, did not qualify for previous NIGMS DRCB funding opportunities but are now SuRE eligible. To determine if your institution brings in less than \$6 million in NIH research project grants is a little more challenging. You can look at the NIH RePORTER, but the types of grants that are counted toward the \$6 million include an alphabet soup of activity codes, so it is probably easier to discuss with your Office of Sponsored Programs or the Sure Resource Center at the University of Kentucky.

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Do You Qualify for This NIH-NIGMS Funding Opportunity with a Remarkably High Success Rate?

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Unique requirements of the SuRE application include a Student Involvement Plan of no more than a half page that must provide the recruitment and training strategy for underrepresented minority students. Two institutional letters are also required: a strategic plan for building research capacity and research excellence written by a provost or other senior administrator; and a letter from a dean or chair supporting the faculty's research and career development. For SuRE First, a letter of support from a research mentor is also required, along with the PI's Research Enhancement Plan.

SuRE (R16) is different than AREA (R15) grants in several respects. SuRE provides support for up to four years at \$100,000 per year for a total of \$400,000 direct costs, while AREA provides three years of support for a total of \$300,000 in direct costs. SuRE is focused on supporting faculty research, and student involvement is a secondary goal, while AREA is focused primarily on training students in research. Most SuRE qualified institutions are AREA qualified as well, but the reverse is not true, since the number of economically disadvantaged students is an important criterion for SuRE but not for AREA. AREA grants are managed individually by each NIH center/institution, and they review and make funding decisions at the center/institution level. SuRE is managed by NIGMS and it reviews most applications in special emphasis panels, and NIGMS makes funding decisions.

In 2022, the first year NIGMS began funding SuRE projects, there were a total of 75 funded projects, for a total funding of \$11,758,565. There were 50 regular SuRE grants and 25 SuRE First funded in this first round. The majority of the projects (67) were funded by NIGMS, but NIAID and NINDS also each funded four projects. Many ASP members conduct natural product research relevant to NCI and NCCAM, and they are both participating institutions/centers to this funding opportunity. Some institutions funded in the first round of SuRE include those with ASP members, like colleges of the City University of New York, Howard University, East Michigan University, and San Jose State University, so you may want to reach out to colleagues at these institutions for input.

ASP member Professor Paul "Skip" Price at Eastern Michigan University was awarded a SuRE grant in 2022 for his project entitled, "Redefining Fermentation Parameters in Natural Products Drug Discovery." He noted that the SuRE program is an excellent avenue for research funds for faculty teaching underserved student populations but reminded those interested, "There is only one submission deadline per year so make sure to put in your best effort each year." While not a requirement, collaborations with larger labs were viewed positively by his reviewers due to the exposure his students would have with other investigators. Price wrote that "receiving the SuRE grant was a great benefit

In 2022, the first year NIGMS began funding SuRE projects, there were a total of 75 funded projects, for a total funding of \$11,758,565.



for me and my students conducting natural products research. It now allows us to take our microbiology focused research to the next level and collaborate with a natural products chemist. Professionally, it was a very nice validation that the work we've been doing with cryptic/silent antibiotic production has finally some funding to support it." He encouraged others to apply and said that after not being funded after a number of submissions including AREA, the SuRE is his first NIH grant.

Many of the grantsmanship recommendations that ASP Vice President and NCI Program Director Dr. Tawnya McKee has written for the current ASP Newsletter and Winter 2022 issue are important for SuRE applications as well. The SuRE program is looking for creative, biomedically related topics, well-defined research plans, and clearly written applications. For help with this process, SuRE has awarded a U24 grant to the University of Kentucky to create a SuRE-specific resource center. The SuRE program director and the SuRE Resource Center are both important contacts for those interested in applying for the funding opportunity. The SuRE Resource Center provides virtual training, consultation, conferences, and, in an effort to enhance the administrative infrastructure at institutions's Offices of Sponsored Projects, seed grants. The next SuRE training will take place by Zoom on March 30, and you can register here.

Hot Topics in Pharmacognosy

Antibiotic Structures from the Past, and/or Novel Sources Now Being (Re)investigated

By David J. Newman, DPhil

INTRODUCTION (WITH SOME HISTORY)

he search for novel antibiotics by "interrogation" of the massive databases of compounds originally synthesized as part of the "conversion" of industrial chemical repositories to use compounds generated from combinatorial chemistry pipelines from the 1990s onwards has failed miserably (as documented by the GSK group in 2007¹ with further comments in 2015 by Blaskovich et al.2). Further documentation in publications from other groups is given in an excellent article by Scannell et al. in the December 2022 issue of Nature Reviews Drug Discovery.3 This article has an excellent "side bar box" showing how, from the title and contents, the 1930s "decision tool quality used by Domagk to discover and validate the sulfa drugs" beat the 1990 onwards decision tool quantity in antibacterial discovery, and no "synthetic chemistry substitute methodology" has risen since in industry.

Thus, what has become quite obvious (though whether the pharmaceutical industry has formally admitted it is an open question), is that the combinatorial chemistry techniques initially developed during those years have a well-defined place in the optimization of an active structure obtained from nature. An example of these techniques is shown in the later discussion on the oral antifungal agent ibrexafungerp.

LACK OF CONSISTENT ANTIBIOTIC DEVELOPMENT FUNDING BY INDUSTRY AND TO AN EXTENT BY GOVERNMENTS IN NORTH AMERICA AND THE EU?

The source(s) of funding for the initial discoveries, which today are almost without exception performed by academic groups either by themselves or as part of consortia (as in the EU), are from government grants. However, once potential agents are discovered and early promise is shown for a given structure, the current major problem is locating a viable and consistent funding source that is willing to cover the preclinical and clinical costs. These costs include the necessary infrastructure for production under GLP of adequate amounts to perform the necessary preclinical investigations, prior to consideration for clinical trials which might be stretched to Phase II using a GLP

product, but GMP level is required for Phase III. Unfortunately, the resources for GLP production, let alone GMP, are not areas that are performed or funded for by academic labs. In addition,

biotech

lack the infrastructure and funding that are necessary for further development.

companies

One can argue, and I will, that this state of affairs has developed due to the perceived costs in "Pharmaceutical Industry C Suites" of maintaining industrial research groups investigating natural product sources in order to find a suitable agent that may lead to an anti-infective drug candidate. Unfortunately, the days when the leaders of major pharmaceutical houses were scientifically and/or medically trained are long gone.

However, there are some bright spots on the "source horizons," particularly with academic consortia in the US / South America and the EU who have "attacked this problem from both directions": the modification of what one might call "gray-haired active molecules" and the investigation of "unusual sources often insects and small mammals," as sources of candidate molecules.

WHERE AND/OR WHY DO WE URGENTLY NEED NEW ANTIBIOTICS?

There are six bacteria identified by the WHO as the ESKAPE pathogens that currently do not have antibiotics consistently effective against them, due predominately from resistance profiles expanding as treatment continues. They are as follows: Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp.

However, what is noteworthy in the list above, is the total absence of pathogenic fungi, even though infections by these agents, both old and new, are increasing as can be seen by the rise of *Candida auris*. This fungus is treatable by the echinocandins (which were first approved in the early continued on page 17

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2000s), but strains resistant to these and the other two major classes of antifungal agents (polyenes and azoles) are now being recognized. Currently in the US and to a large extent in the EU, until very recently, only three NP-derived antifungal agents were approved in the last 20 years plus the odd synthetic azole. These were the three echinocandins: caspofungin in 2002, micafungin in 2005 and anidulafungin in 2006.

APPROVAL IN 2021 OF IBREXAFUNGERP

Then, very recently in the middle of 2021, ibrexafungerp [1-4], a novel orally effective β -1,3-glucan synthesis inhibitor derived from the natural product enfumafungin, was approved by the FDA. The final route to the agent is shown in Figure 1. However, it took more years than the nominal 21 to achieve this

agent, from the initial report by Schwartz et al.⁴ in 2000 to Apgar et al.⁵ published just before its approval by the FDA in the middle of 2021. The Apgar paper demonstrated the use of what can be considered combi-chem techniques to obtain subtly different structures at different stages of the optimization as shown in the referenced paper.

The reason why I used the term "nominal 21" above is that the first paper reporting the initial structure was by Pelaez et al.⁶ working in the then MSD laboratories in Madrid in 2000, where they isolated the compound from an endophytic *Hormonema* species isolated from leaves of *Juniperus communis* collected in Spain. The "sting is in the tail" of this paper is that only one *Hormonema* species produced this active agent, and by the time the article was published, the MSD scientists tested another 9000 fungal strains from their collection (from many different sources) plus another 8000 actinomycetes.

Unfortunately, today those biological resources are no longer available as the large, mainly US, pharmaceutical houses have "disposed" of their collections. They claim that they were not destroyed, but removal of these microbes and their associated high-cost support processes effectively means that they are no longer available.

CURRENT CHEMICAL MODIFICATION OF EXISTING NATURAL PRODUCT-DERIVED AGENTS

However, thanks to groups of talented chemists working with natural-product derived agents, there has been a significant amount of work reported as mentioned earlier, where combi-chem inspired processes have been applied to generate modifications of well-known antibiotic structures with the aim of overcoming microbial resistant processes. At the "risk" of pushing one of my own more recent editor-requested reviews, an open access article published in 2022 covered some of the potential molecules based on natural products that have used synthetic chemistry techniques (descendent of combicontinued on page 18

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chem perhaps?) to produce compounds with significant potential for future use.

BOGER'S VANCOMYCIN MODIFICATIONS

Of particular note, the vancomycin derivatives reported from the Boger laboratory in recent times have overcome the major vancomycin resistant microbes. In one of this group's variations, a simple modification within the dipeptide buried in the overall structure (number 2 in reference 7 in the DJN review), yields a molecule that is active against previously resistant Gram-positive bacteria. The further extension of this excellent chemical foray led to the compound (number 3 or CBP-G3 in reference 7 in the DJN review). Further structural variations are mentioned in that review.

VIRIDICATUMTOXINS

These agents contain the basic tetracycline nucleus with "interesting" extensions between the A and B rings of the tetracycline. The original molecules viridicatumtoxin A and B were first reported in 1973 from *Penicillium viridicatum*, and the B variant was synthesized by Nicolaou in 2013⁸ with a revision in 2014.⁹ A mixture of enantiomers was active against resistant strains of two of the ESKAPE pathogens (*E. faecalis* and MRSA) with activity also against *E. faecium*.

In contrast to the story on enfumafungin above, the biosynthetic gene cluster for these agents was found in a variety of fungi including A. nidulans, P. brasilianum and three other Aspergilli. The number of these toxins increased when it was realized from work by the Capon¹⁰ group in Queensland that a marine sourced endophytic Paecilomyces produced not only the A and B structures but also 4 more (C to F). Of the six compounds, B [5] and C [6] demonstrated a 15 to 40 fold difference in favor of antimicrobial activity versus cytotoxic activity in tested lines. The MoA of these compounds is "binding directly to the undecaprenyl pyrophosphate synthases (UPPS) of E. faecalis, S. aureus and E. coli with high affinity." Since this target is an essential one for growth, it is a target worth considering, particularly since the BGC has been identified; targeted fermentation is a possibility to produce enough materials for larger-scale investigations. "Provided monies can be located!"

MODIFIED PYRIMIDINES AS POTENTIAL ANTI-TB CANDIDATES

A very recent paper by Li et al. in the *Journal of Medicinal Chemistry*¹¹ demonstrated how, by utilizing intermediate [7] from the synthesis of ceritinib, the novel candidate LPX-16j [8] was synthesized. Ceritinib, though approved for use in

anaplastic lymphoma via inhibition of the relevant kinase (ALK), was shown to have moderate inhibitory activity against the *Mycobacterium tuberculosis* strain H37Ra with an MIC of 9.0 micromolar. Using a suitable SAR regime, the preliminary lead compound LPX-16j [8] had an MIC of 5 micromolar against H37Ra but had a higher cytotoxicity against human cells with an MIC of 1-2 micromolar.

Using now standard combi-chemistry techniques, a long series of successive syntheses and biological testing, converted LPX-16j (basically a substituted pyrimidine) into compound 5a [9] which had a significantly lower toxicity, better oral activity and (MIC 0.5 micrograms/ml).

ACADEMIC GROUPS SOMETIMES WITH GOVERNMENT FUNDING (NIH, NSF, EU, ETC.) INVESTIGATING "UNUSUAL RESERVOIRS" OF NOVEL ANTIBIOTIC STRUCTURES

Though there are a number of groups that have pursued what could be considered in earlier days as "unusual sources," three areas in particular have captured the "current scientific public eye." These are not in chronological order but cover sea and land sources.

In the first to be discussed, a micromonospora species isolated from a sea squirt collected off the Florida Keys yielded the antifungal agent named as turbinmicin [10]. This agent turned out to be very active against *Candida auris* with an MIC of 0.25 micrograms per ml,¹² and in a later paper Zhao et al.¹³ demonstrated the "killing mechanism" was inhibition of the biofilm vesicle production thus eliminating the matrix assembly.

The second source of novel antimicrobials against bacteria and/or fungi are the antibiotics expressed by microbes existing in the fungus gardens of fungus-growing ants. Granted the agents initially identified are protective agents against extraneous fungi that want to consume the ants' food supplies, their "fungal gardens." This work was pioneered by Clardy at Harvard Medical School in conjunction with Currie at the University of Wisconsin, with a publication in Nature Chemical Biology in 200914 identifying the novel antifungal agent dentigerumycin [11]. This work was part of a specific program funded by NIH in conjunction with other USG grant sources under a grant system that required participation with source country scientists, known by the acronym NCDDG. This system funded a very fruitful relationship with Monica Pupo and colleagues at the Pharmacy School at the University of Sao Paulo, Ribeirao Preto in Brazil, that permitted access to fauna in Brazil that has continued after the initial USG-sourced funding by

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utilizing a number of funding sources, including Brazilian. Two recent papers that aptly demonstrate the interplay between these researchers and their sources should be required reading in this field. $^{15,\,16}$

In addition to those mentioned above, another group, this time at the University of Oklahoma, have "pioneered" the study of what can be best described as the "microbiomes of roadkill." Granted the Cichewicz group have been studying many other sources, but this one yielded some very interesting bacterial sourced agents. (In particular, a pseudomonad and a Serratia species, both isolated from an opossum's ear, inhibited drug-resistant *C. albicans* biofilm formation.)

FINAL COMMENTS

Though some of the compounds shown above and those I have described in earlier columns may well have potential against microbial diseases that now are (or are becoming) major problems, the amount of funds available are nowhere near sufficient to develop a new antibiotic in spite of the requirement for such agents. As can be seen from comments above, significantly more than 20 years were necessary for the latest orally active antifungal agent to be approved. In earlier columns I have covered antibacterial agents uncovered by novel techniques by academic groups in the US, and a fair number have now had academic and/or small biotech companies synthesizing modified structures based on the originals, but to date, as far as I can tell, none have progressed to preclinical studies.

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Meet a New ASP Member

Professor Neha Garg



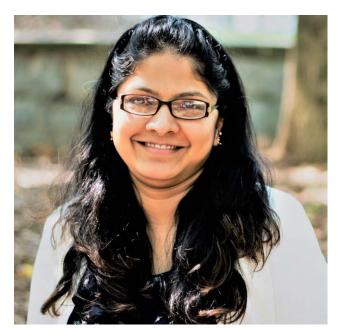
Professor Neha Garg is our featured new member in this issue of the Newsletter. After receiving her PhD with Professor Wilfred van der Donk at the University of Illinois at Urbana-Champagne and completing postdoctoral research with Professor Pieter Dorrestein at University of California, San Diego, she is now an assistant professor in the School of Chemistry and Biochemistry at Georgia Tech. Her multidisciplinary research focuses on developing fundamental understanding of the role of natural products in structuring of mucus-associated microbial communities that live in human lungs and marine corals. We are pleased to be able to officially welcome Dr. Garg to the ASP!

By Wendy Strangman, PhD

What is your scientific background?

My research training began in Technische Universität Berlin, Germany where I was optimizing the activity of enzymes called laccases to detoxify chemical dye waste from the textile industry. Through this work on chemical dyes, I was introduced to the world of natural dyes and natural products and how they play an important role in our everyday life. I wanted to understand how these small molecules are made by nature. To fulfill this desire, I joined the lab of Prof. Wilfred van der Donk at the University of Illinois Urbana-Champaign where I spent my time understanding how enzymes decorate ribosomally synthesized peptides with dehydrations and cyclization and how we can fine tune these decorations to enhance their biological activity. Here, I was using mass spectrometry to solve structures and identify peptides in extracts from novel bacteria.

During this time, Prof. Pieter Dorrestein was leading the development of methods to image these molecules using mass spectrometry on bacterial plates, human skin, and surfaces. We would often discuss his papers in journal clubs, and I was always attracted to how we can decipher the function of molecules by visualizing where they are. This was also the time where we were really beginning to



Professor Neha Garg

PHOTO: GEORGIA INSTITUTE OF TECHNOLOGY

appreciate how natural products produced by bacteria on our skin and in our gut affect our mood and our health. So, I wanted to apply the power of mass spectrometry to understand how microbial communities are structured continued on page 21

I now combine my training in microbiology, enzymology, molecular biology, biosynthesis, small molecule mass spectrometry and structure elucidation to discover mechanisms that govern microbe-microbe, microbe-drug, microbe-host and microbe-environment interactions with the goal of enabling establishment of stable ecosystems.

Meet a New ASP Member: Professor Neha Garg

continued from page 20

by the presence of natural products, how molecules produced by one bacterium trigger the production of natural products by others and how they tag team to create a molecular ecosystem around them. I joined Prof. Dorrestein's lab to develop mass spectrometry-based methods to visualize production of natural products in diverse communities including human lung, human mouth and environmental lichens, to name a few.

I now combine my training in microbiology, enzymology, molecular biology, biosynthesis, small molecule mass spectrometry and structure elucidation to discover mechanisms that govern microbe-microbe, microbe-drug, microbe-host and microbe-environment interactions with the goal of enabling establishment of stable ecosystems. We apply these methods to study microbial communities that infect human lungs and marine corals. When we think of infections, we often think of human infections, but marine corals are devastated by secondary opportunistic infections by marine pathogens leading to loss of over 80% of coral reefs. The governing principles of how microbial communities are structured in the mucus of human lungs and in the mucus of marine corals have a lot of parallels. Thus, we are motivated to extend our methods to understand chemical communication between communities that live in the mucus of marine corals with the hope of contributing to the preservation of this pristine marine organism.

What are your research interests in pharmacognosy?

All lifeforms communicate via biomolecules. Specialized metabolites, aka natural products, are a subset of these biomolecules that play important roles in growth, structuring and homeostasis of an ecosystem. For example, these molecules enable coral larvae to settle, microbes to communicate with kin to coordinate behavior, with each other, with their host and even swim towards nutrition. My research focuses on developing fundamental understanding of the role of natural products in structuring of mucus-associated microbial

communities that live in human lungs and marine corals. This knowledge base will allow us to understand what makes an organism resilient or susceptible to a disease and how we can reconfigure microbial makeup in the mucus promoting health-like state.

How did you hear about the ASP?

Having worked on natural products since 2007, I have always known about ASP. I very much appreciated the natural products webinar series during COVID as a way to stay in touch with my scientific family and still do. Graduate students in my lab have attended ASP and raved about it. I have been a member of the American Chemical Society, the American Society for Microbiology and the American Society for Mass Spectrometry. It was high time I also officially joined ASP.

Why did you decide to join ASP?

ASP is truly an interdisciplinary society bringing scientists from different disciplines working on different ecosystems together. My own research training has been interdisciplinary involving molecular biology, enzymology, chemical biology, bioinformatics and omics. Thus, I cannot think of a better society that fits my research interests.

What would you like to achieve through your membership?

To understand natural product synthesis, function, and application through the eyes of multidisciplinary scientists that ASP brings together. To interact with and contribute to the mentoring of our student body.

What do you like doing in your spare time – movies, activities, etc.?

Reading books with my six-year-old and splashing in the pool. Our favorite book is *Zobi and the Zoox: A Story of Coral Bleaching*. Additionally, the last few years have brought to the forefront the importance of staying healthy. I am a new member of Orangetheory fitness classes, and I love making time for these classes.

My research focuses on developing fundamental understanding of the role of natural products in structuring of mucus-associated microbial communities that live in human lungs and marine corals.



ASP would like to welcome our new members. The Society's main objectives are to provide the opportunity for association among the workers in pharmacognosy and related sciences, to provide opportunities for presentation of research achievements, and to promote the publication of meritorious research. New members include 8 full members and 39 associate members. We look forward to meeting you and learning more about you and your work.

FULL MEMBERS

Dr. Mamadou Saliou Telly Diallo Guinea

Dr. Petrea FaceyTrinidad and Tobago

Dr. Scott LongUnited States

Dr. Fabricio Medina-Bolivar United States

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Dr. Balasubramani Subramani ParanthamanUnited States

Dr. Joshua Torres Denmark

Mr. Ahmad Alif Danial Zailan Malaysia

Ms. Liana Zaroubi Canada

Dr. Laila Ziko Egypt





The Newsletter is pleased to announce the following upcoming conferences and meetings.

The events portrayed here reflect what listings and notices the Newsletter has specifically received.

For a more extensive calendar, please visit the ASP website at www.pharmacognosy.us. If you have a conference or event you would like mentioned, please send us relevant information, including any graphics, at asp.newsletter@lehman.cuny.edu.

2023 ASP Annual Meeting
July 22-26, 2023
Rockville, Maryland

aspmeetings.pharmacognosy.us

ASP Natural Product Sciences Webinar
Bimonthly Zoom Seminars
Thursdays 4 PM ET / 1 PM PT

www.pharmacognosy.us/natural-productsciences-webinar/

C&EN Webinars
Various Days and Times

cen.acs.org/collections/webinars.html

21st Annual Oxford ICSB
April 24-27, 2023
Oxford, Mississippi
www.oxfordicsb.org

Society for Economic Botany and Society of Ethnobiology Joint Meeting

June 4-9, 2023

Atlanta, Georgia

econbot.org/home/meetings/economicbotany-2023.html 71st International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA)

July 2-5, 2023

Dublin, Ireland

www.gadublin2023.com

Gordon Research Conference: Natural Products and Bioactive Compounds

July 30-August 4, 2023

Andover, New Hampshire

www.grc.org/natural-products-and-bioactivecompounds-conference/2023/

31st International Symposium on the Chemistry of Natural Products / 11th International Congress on Biodiversity

October 15-19, 2023

Naples, Italy

www.iscnp31-icob11.org



By Barbara C. Sorkin, PhD

GLOBAL NEWS



Theobroma cacao

♦ Coffee drinkers and chocoholics beware! Changes in rainfall and unaccustomed variability in temperatures in regions as far flung as the US, Europe, Pakistan, India and China are damaging supply chains for the botanical and herbal industry according to a January 30 story in Natural Products Insider. Among the crops affected: Theobroma cacao and Coffea species.

ELSEWHERE IN THE AMERICAS

Brazilian President Luiz Inácio Lula da Silva made campaign pledges to reverse Amazon deforestation policies implemented by the previous administration. He has appointed Marina Silva as the head of the environmental ministry. When she last served in that role, from 2003-2008, Amazon deforestation declined by 53%.



Luiz Inácio Lula da Silva

NEWS FROM THE US

♦ Funding News:

- President Biden signed an omnibus spending package for the 2023 fiscal year (FY '23) on December 29, 2022. FY '23 began on October 1, 2022. The package includes a 10.3% increase for federal research and development spending. You can find more details on how these funds are allocated on this American Association for the Advancement of Science dashboard.
- The US hit its **debt ceiling** on January 19. The US Treasury Department has begun implementing "extraordinary measures" to meet US obligations, but these are not expected to suffice beyond early June. Congressional passage of an increase to the debt ceiling is needed to avoid default. Negotiations on raising the debt ceiling are ongoing and involve proposed cuts to discretionary spending (e.g., for the US Department of Health and Human Services' Centers for Disease Control and Prevention and National Institutes of Health (NIH), and the US Department of Agriculture and the National Science Foundation).

News from the National Institute of Standards and Technology (NIST)

The NIST **Dietary Supplements Laboratory Quality Assurance Program** (DSQAP) is a collaboration between NIST and the NIH Office of Dietary Supplements (ODS). The latest NIST DSQAP Exercise (1) has concluded. The participating labs analyzed:

- · Withanolides in Withania somnifera (ashwagandha), at right
- Vitamins B₁, B₂, B₃, B₅, B₆, B₇, B₉ and B₁₂ in liquid and powdered drink mixes
- Ash, carbohydrates, fat, protein, solids, starch, total dietary fiber, calories, niacin, vitamin K1, Cr, Mg, I, Na, K, As, Cd, Cu, Zn, Se, I, S, Hg, phenolics and per- and polyfluoroalkyl substances in kelp
- Phenolics in green tea.

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Capital Communiqués: Natural Product-related News from NIH and Beyond



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The Final Report from this Exercise will be available in spring 2023. When published, a link to the digital object identifier (doi) assigned to the report will be added to the NIST DSQAP website.

Enrollment for DSQAP Exercise 2 will open soon. Potential studies include toxic elements in botanicals (botanicals not yet selected), folates in dietary supplements, fatty acids in fish oils, and marker compounds in black cohosh- and ginger-containing materials.

- · You can read more about DSQAP here.
- To receive email announcements for upcoming Exercises, create an account on the QAP HUB site.

NIST, in collaboration with NIH ODS, continues to produce **reference materials** to support natural products and dietary supplements communities. New and upcoming materials include SRM 3289 Multivitamin Tablets and a suite of *Panax ginseng* standard reference materials (SRMs).

To search for other NIST SRMs click here.

UPDATES FROM NIH

- ♦ No more FOAs! Well, not quite yet. No, NIH has not stopped accepting grant applications. But Funding Opportunity Announcements (FOAs) are changing their name to NOFO, Notice of Funding Opportunity.
- ◆ NIH has published a Request for Information (RFI) for input on proposed changes to the **framework for the peer review** of research project grant applications submitted to NIH. The proposed changes aim to reduce the complexity of the review criteria, the reviewer workload, and the potential for bias. The RFI notice, NOT OD 23-034, details the proposed changes and how to submit comments by the March 10 deadline. You may also be interested in the "Open Mike" blog on the topic.
- ♦ NIH is also looking for input on postdoctoral research training and career progressions in biomedical science via another RFI, NOT-OD-23-084, with a deadline for comments of April 14. The Advisory Committee to the Director of NIH's Working Group on Re-envisioning NIH-Supported Postdoctoral Training held four virtual listening sessions in March:
 - Wednesday, 3/8 12:30 1:30 p.m. ET: Role, duration, structure, and value of the academic postdoc (including impacts on underrepresented populations).
 - Friday, 3/10 1:30 2:30 p.m. ET: International trainee concerns.
 - Friday, 3/17 12:30 1:30 p.m. ET: Compensation and benefits (including childcare and dependent care).
 - Monday, 3/20 1:30 2:30 p.m. ET: Job security, career prospects, and quality of life.

More information can be found <u>here</u>.

◆ The new version of the NIH Grants Policy Statement, consistent with longstanding federal regulations, now requires institutions receiving NIH support to have internal controls to assure compliance with the standard terms and conditions of award. These include behavioral codes of conduct to ensure safe and healthful working conditions for employees, for example, ensuring that information on application documents is true, complete, and accurate (GPS Section 2.3.7.6) and ensuring that work environments are free of discriminatory harassment and are safe and conducive to high-quality work. The December 29 issue of Extramural Nexus has more on this change.

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Capital Communiqués: Natural Product-related News from NIH and Beyond



continued from page 25

- ◆ The new NIH Data Management and Sharing (DMS) policy went into effect on January 25.
 - An expanded selection of sample DMS plans for different data sources is now available on the NIH Scientific Data Sharing website.
 - The NIH policy on hyperlinks and Uniform Resource Locators (URLs) applies to the DMS attachment of your application leave them out or your application may be returned without review. (See here on the Data Sharing website.) Planning to submit your first NIH application? Get an early start with this NIH "All about grants" podcast useful for fellowship or career award applicants, too.
- ◆ An NIH grants tip that may be useful for more experienced applicants as well if you're resubmitting an application to a later receipt date, check the Funding Opportunity Announcement (FOA) online for changes to receipt dates, application forms or participating Institutes (or Centers or Offices), or for notices on other new policy implementations.

EVENTS

- ◆ Coming soon (April 28): NCCIH's hot topic webinar series on emerging trends in natural products research: electron microscopy, ion channels and gut microbes. More here.
- May 22 24, the 2023 Mary Frances Picciano Dietary Supplements Research Practicum, organized by the NIH Office of Dietary Supplements. To be notified when agenda and registration are available: https://odspracticum.od.nih.gov/

FUNDING OPPORTUNITIES

◆ The NIH National Cancer Institute's (NCI) Board of Scientific Advisers recently gave the nod to a proposal from the NCI's Division of Cancer Prevention (DCP) to support the discovery and development of new natural products for cancer interception and prevention. See this blog and the linked PowerPoint to learn more about DCP's plans. This initiative is a collaboration with NCI's Division of Cancer Treatment and Diagnosis and NIH's National Center for Advancing Translational Sciences.

ODDS AND ENDS

Two things I did not know about plants:

- ♦ Plants generate electrical discharges during thunder storms here's a photo.
- Researchers at the University of California, Santa Barbara have estimated the annual total of evaporative energy plants leverage to raise water up to where they need it. They estimate that forests alone use 9.4 quadrillion watt-hours of energy annually, and that the total evaporative energy used is equivalent to 90% of the hydropower generated worldwide in 2019.





From the Archives: The Plant Science Laboratory Seminar —100 Years Ago

This year marks the 100th anniversary of the Plant Science Laboratory Seminar, the annual meeting which paved the way for the formation of the American Society of Pharmacognosy. We look back at the first conference held in Minneapolis and one of its organizers, Edwin Leigh Newcomb.

By Christine Jankowski, MA

hroughout the week of August 20, 1923, thirty-nine men convened at the University of Minnesota in Minneapolis for a week-long seminar full of discussions and demonstrations related to the topics within botany and pharmacology. Later referred to as the First Plant Science Laboratory Seminar, these events were hosted by the College of Pharmacy and one of the department's professors, Edwin Leigh Newcomb.

Born in New Jersey in 1882, Newcomb received his doctorate in 1905 from the Philadelphia College of Pharmacy. In 1910, he was invited to teach at the University

of Minnesota. He accepted the role and taught botany and pharmacognosy courses. While there, he was also the editor of *The Northwestern Druggist* from 1916 to 1920. He served as secretary of the Minnesota State Pharmaceutical Association in 1914 and later was president for the 1920-1921 term.

In 1922, Newcomb hosted a day-long seminar on medicinal plants for drug manufacturers and educators at the university. It proved to be so successful that Newcomb was selected to chair a meeting for the following year, the 1923 Plant Science Laboratory Seminar, and activities were extended for a whole week. As further described in volume 46, issue 7 of the *Journal of the American Pharmaceutical Association*, "The purpose of the Seminar is that each worker shall have the opportunity to pursue investigations in his particular field, to demonstrate his work and methods and to discuss the results with other workers."

The first activity at the First Plant Science Laboratory

PLANT SCIENCE LABORATORY SEMIMAR Minespolis, Minespolis, Minespolis, Minespolis, Minespolis, Minespolis, Minespolis, Seminar here at the Minespolis of Minespolis and the recent laboratory Seminar here at the Minespolis of Minespolis and the recent laboratory Seminar here at the Minespolis of Minespolis and the recent laboratory Seminar here at the Minespolis of Minespolis of the recent of th

After the First Plant Science Laboratory Seminar, Edwin L. Newcomb mailed out surveys to attendees. 1923.

COURTESY OF THE UNIVERSITY OF MINNESOTA ARCHIVES.

Seminar was a tour through the university's medicinal plant gardens and their greenhouses. Established by the first dean of the College of Pharmacy, Frederick Wulling, the garden grew over time with assistance from Newcomb and his classes. It became more important during World War I when medicines were rationed, and people turned to natural remedies as replacements.² Demonstrations were then given on drug harvesting and drying. Some

of the many discussions that were held were about the current studies of pharmacology and natural science and about establishing standards for testing natural products and medicines. Lectures included "The Future of Pharmacognosy" by Newcomb, who stated the following:

Pharmacognosy is one of the most attractive of sciences. It touches living things on the one hand and its problems are the riddles of the whole drug world. The work of pharmacognosists is at the basis of the administration of medicines. Human life ultimately depends in a very large measure on the standards and purity of drugs which they establish...The world is changing and the captains of industry are looking for men, who can detect the defects in established practices and who have the...understanding to find a way to improve methods and are willing to consider new ways and means of doing the old things.³

"The purpose of the Seminar is that each worker shall have the opportunity to pursue investigations in his particular field, to demonstrate his work and methods and to discuss the results with other workers."

From the Archives: The Plant Science Laboratory Seminar —100 Years Ago

The First Plant Science Laboratory Seminar showed to be impressive and successful. The following year, the second session was held in Buffalo, New York. Advertised for those "interested in medicinal plants, vegetable drugs and food products," attendees included botanists, pharmacognosists, retail pharmacists, and plant chemists.1 For two days, they were invited to present their research and work as well as discuss universal standards for testing and research of natural products. Conversations were even held on gathering plants and forest preservation.

Over the next three decades, the seminar sessions grew in attendees

and was hosted in many locations including St.

Louis and Washington, DC. The name of this annual meeting was shortened to the Plant Science Seminar by 1928. As

The first Plant Salence Seminar or as it was then called "Pirst Salence Leboratory Seminar" was held at the University of Kinnesota during the wesk of August 20th,1055. It was preceded by an one day meeting the previous year, also on the compus of the University of Kinnesota, br. Newcomb, then a member of the Department of Pharmacognesy at the College of Pharmacy at the University of Kinnesota, was instrumental in the preparation of both meetings. We wrote in the "Northwestern Druggist", 31:85,2933.

For a number of years there has been a growing demand for an opportunity where pharmacists, plant speaklists, bottomists, and others interested in medicinal plants, vegetable drugss and food products might pursue or-operative laboratory work together. A little ower a year age an one-day sentings of this kind was held at the interesty of Minnesota Moriers from the mitrovention, other educational institutions, federal and state laboratories, pharmaceutical and themical manufacturing plants were in attendance. The program consisted primarily of demonstrations of research nethods for determining the quality and value of vegetable drugs and of discussions on research, analytical and teaching methods and standards.

"The purpose of the seniner is that each worker shall have the opportunity to pursue investigations in his particular field, to demonstrate his work and methods, and to discuss the results with other workers,"

" While there will be lots of discussion, this is not a plan simply to get tegether and talk, but rather an opportunity for a week's period of intensive laboratory and field work on The first page of Dr. Anna Koffler Wannamaker's "Outline of the History of the Plant Science Seminar." She presented this history at the 1965 Annual Meeting held at the University of Rhode Island in Kingston, Rhode Island.

these gatherings were informal, requests about becoming a formalized society were on the rise: at the 1947 Seminar, attendee Dr. Elmer Wirth proposed to reorganize the group as a society. Unfortunately, he died shortly after, and his proposal fell through. Later, Arthur E. Schwarting echoed Dr. Wirth's request at the meeting at Big Rapids, Michigan in 1958. There, Schwarting proposed for the organization to become a

society, known as the American Society of Pharmacognosy, and handed out copies of a proposed constitution and by-

laws to attendees for their consideration.⁴ The following year in Chicago, the motions were passed and the American Society of Pharmacognosy was organized.

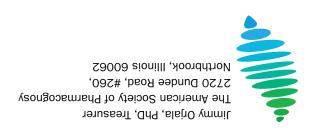
Even though Newcomb died in 1950, he is recognized as a founder and supporter of the ASP. Today, the ASP continues to operate and grow, with annual meetings held across the United States and the world. These meetings have similar agendas to past Plant Science Seminars, like gathering to discuss the latest advancements in pharmacognosy, learning about new natural products, and even touring nearby sites and affiliated universities. In an age of instant knowledge, conferences like these still host a purpose for learning, connecting, and growing.



Attendees and some family members at the Plant Science Seminar of 1958.

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Full Membership

Full membership is open to any scientist interested in the study of natural products.

Current membership dues and *Journal of Natural Products* subscription rates can be found at **www.pharmacognosy.us**.

Associate Membership

Associate membership is open to students of pharmacognosy and allied fields only. These members are not accorded voting privileges.

Current membership dues and *Journal of Natural Products* subscription rates can be found at **www.pharmacognosy.us**.

Emeritus Membership

Emeritus membership is open to retired members of the Society who maintained membership in the Society for at least five years.

Current membership dues and *Journal of Natural Products* subscription rates can be found at **www.pharmacognosy.us**.

Honorary Membership

Honorary members are selected by the Executive Committee of the American Society of Pharmacognosy on the basis of meritorious service to pharmacognosy.

Present Honorary Members are:

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Additional information about membership may be obtained by writing to the Treasurer of the Society:

Jimmy Orjala, PhD, Treasurer, The American Society of Pharmacognosy,

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