American Society of Pharmacognosy

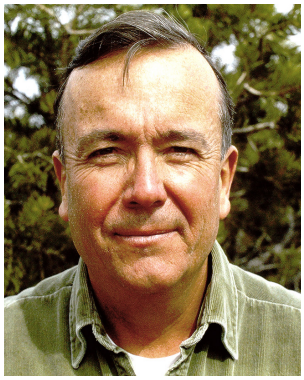
Winter 2021

Discovering Nature's Molecular Potential

ASP Newsletter: Winter 2021, Volume 57, Issue 4

In Memoriam: George Robert "Bob" Pettit II

By John H. Cardellina II, PhD, Gordon Cragg, PhD, Kevin G. Pinney, PhD and Sheo B. Singh, PhD



ASP Fellow and world-renowned natural products scientist Dr. George Robert Pettit II died September 21, 2021 in Scottsdale, Arizona at the age of 92.

Pettit was born June 8, 1929 in Long Branch, New Jersey and grew up on the Jersey Shore, less than a mile from the Atlantic Ocean. He spent much of his childhood visiting the beaches and exploring and studying invertebrates. He also developed an early interest in chemistry at the age of ten, dabbling in simple experiments with a friend who had a chemistry set. He began working in 1942 at the age of 13 as an apprentice to a pharmacist, and two years later, the principal of his high school, having observed his passion for chemistry, recommended a position in a medical laboratory of the Monmouth Medical Center.

There, he assisted the pathologist during postmortem examinations and noted for the first time the ravages of cancer. This experience upset him deeply and led him to think about all the creatures he observed on the New Jersey coast. Although seemingly vulnerable, these marine organisms managed to survive for millions of years without being decimated by predators or disease, and he conceived then that they must possess chemical defenses which also might be used to fight cancer. As noted by Dr. Laurent Meijer, research director at the CNRS Station Biologique de Roscoff in France, this set the stage for a lifelong career devoted to the "worldwide exploration of natural products, especially of

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In Memoriam: John M. Cassady

By John H. Cardellina II, PhD, A. Douglas Kinghorn, PhD, Rachel Mata, PhD, Kerry L. McPhail, PhD and Popat N. Patil, PhD

Dr. John M. Cassady, a leading member of the American Society of Pharmacognosy, passed away on September 29, 2021 at the age of 83. Known for numerous outstanding achievements, he was a prolific natural products scientist, an effective university administrator, a highly capable committee member, and an accomplished student athlete.

Cassady served ASP in many different capacities, including as a former president (1993-1994) and also as a long-term and highly successful chair of the ASP Foundation. He was elected to the ASP Executive Committee (1978-1981) and also served as the scientific program chair for the 1976 annual meeting of ASP, as well as being on the ASP nominating and publicity committees. In 2006, at the 47th An-

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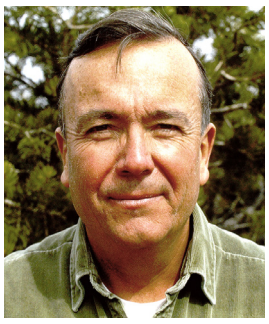

George Robert "Bob" Pettit II

Barbara Sorkin

John N. Cassady

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Editor's Corner

American Society of Pharmacognosy

By Edward J. Kennelly, PhD

I am writing this on the day of the winter solstice, and the shortest day of the year seems even darker with the onset of the omicron variant of the coronavirus. Almost two years into the pandemic, it seems that finding the light at the end of this long tunnel is harder than any of us may have imagined. Omicron is now accounting for about 70% of new COVID cases in the New York City area, and with holiday travels upon us, I fear rapid spread is almost impossible to avoid.

Sadly, three highly prolific ASP members, Drs. John Cassady, Bob Pettit, and Hildebert Wagner, have passed away recently. Each of these scientists contributed significantly to natural products research, helping to shape the future of single-entity as well as admixture drugs. They served unselfishly as leaders of the ASP and the *Journal of Natural Products*. They were leading academics, deans, institute heads; truly this marks a great loss for natural products. Their combined academic careers totaled more than 110 years, and they helped shape the fields in important and distinct ways. They will be missed, but not forgotten. Please take the time to learn about their contributions to our field in the significant tributes for each that are included in this newsletter.

Despite the challenges of this day and age, the society continues to move forward with its traditions. The 2021 Norman Farnsworth Research Achievement Award, the highest honor bestowed by our society, has been given to Dr. Brad Moore of Scripps Institute. His former mentor and current colleague, Dr. Bill Fenical, has contributed a beautifully written and extensive look at Brad's career, providing insights and perspectives on his contributions to natural products research. The 2021 Tyler Award focuses on excellence in botanical chemistry and was awarded to ASP Fellow Dr. John Cardellina. His career path has included stays in academia, government, and industry. John's service to the ASP on so many levels is truly remarkable.

I remember reading a very enlightening book "The Girls in the Balcony: Women, Men, and *The New York Times*" back in the early 1990s. The author, Nan Robertson, noted that if you relied on the *Times* for news, you would be under the impression that women never died because there were so few obituaries of women in that paper. Likewise, with the ASP, the history of women and other minorities in the leadership of ASP is often not highlighted or recognized formally. Dr. Esther Guzman, cochair of the Diversity and Inclusion committee, has done a great job lifting up issues and people that have often been overlooked in ASP and the pages of this newsletter. She has systematically looked at the composition of ASP leadership and awards by gender and race and provided context by looking at how the composition of the society has changed over six decades. I hope every ASP member will read this article, noting where we started and how we can move forward to further equity.

With regard to our regular columns, I am very pleased indeed to announce the return of the column that covers issues of Washington that impacts natural products research. ASP member Dr. Barbara Sorkin from NIH volunteered her services to the *Newsletter* a few months ago. Her new column, called "Capital Communiqués: Natural Product-related News from NIH and Beyond," is a treasure trove of information for anyone interested in how the federal government works to fund research. I sincerely thank Barbara for her commitment to this column that had been such a staple when it was penned by Dr. Georgia Perdue. Welcome, Barbara, and I look forward to your contributions for a long time to come.

I hope everyone keeps safe over this holiday season, and I wish everyone a happy, productive, and brighter 2022. ■

Pettit's career was devoted to the discovery and development of novel and more effective anticancer agents from natural sources, and those of us who have collaborated with Pettit knew him as an outstanding and resourceful scientist totally committed to improving the treatment and quality of life of cancer patients worldwide.

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marine origin, in search of promising anticancer leads, the discovery and structural elucidation of very potent drug candidates, their synthesis, and the launch of some of them into the pharmaceutical market."[1]

In 1952 he gained his BS in chemistry at Washington State University (Pullman) and then proceeded to Wayne State University, where he completed his MS in heterocyclic chemistry in 1954 and his PhD in steroid chemistry in 1956, both under the direction of Professor Carl Djerassi. In 1956, he joined Norwich Eaton Pharmaceuticals (now Procter & Gamble) as a senior research chemist, and in 1957 he transferred to the University of Maine as assistant professor, rising through the ranks to become full professor in 1965. After a brief stay as a visiting professor at Stanford University, he accepted a professorship in the Department of Chemistry at Arizona State University (ASU) in late 1965.

From 1966 to 1968, he served as chairman of the ASU Organic Division. In 1974 his research group was officially recognized as the ASU cancer research laboratory, and in 1975 he was appointed as the director of the newly established ASU Cancer Research Institute (ASU-CRI). In 1986, he assumed the position of Dalton Professor of Cancer Research and Medicinal Chemistry, and in 1990 he was appointed as Regents Professor of Chemistry, a position he held until his retirement in September, 2020. A new research building dedicated to the ASU-CRI, incorporating chemistry, biology of cancer, and microbiology laboratories was built between 1995 and 2001, thanks to income generated from patents, as well as from numerous donations.

In 2005, the ASU administration decided to repurpose the ASU-CRI, which then became part of the newly formed Biodesign Institute. These developments, which are discussed in Chapter 7 of the biography written by Dr. Robert Byars,[2] caused considerable friction between the ASU administration and Dr. Pettit, but he continued to pursue cutting edge research with a very much reduced research team until his retirement in September, 2020. It is gratifying to see how much he was appreciated and respected by his colleagues in the ASU School of Molecular Sciences (https://news.asu.edu/20200928-distinguished-asu-cancer-researcher-george-r-pettit-retires-after-55-years-service).

Pettit's career was devoted to the discovery and development of novel and more effective anticancer agents from natural sources, and those of us who have collaborated with Pettit knew him as an outstanding and resourceful scientist totally committed to improving the treatment and quality of life of cancer patients worldwide. During his distinguished and productive career of over 60 years, he authored or coauthored 14 books, 17 book chapters, and some 800 papers, and he was inventor and coinventor on 70 US patents. His papers have been cited over 30,000 times with an h-index of 89, and he was ranked number 3468 out of the top 100,000 most influential scientists with regards to their publication citations in a recent PLOS article.[3,4] His books included a series of six volumes on synthetic peptides published between 1970 and 1982 as well as a series of six volumes on *Biosynthetic Products for Cancer Chemotherapy* published between 1977 and 1989,[5] culminating in a volume on *Anticancer Drugs from Animals, Plants and Microorganisms*, published in 1993.[6]

Pettit's research encompassed all aspects of natural products chemistry, including the isolation of bioactive agents, structural elucidation, biological evaluation, biosynthesis, and chemical synthesis. He can truly be regarded as one of the great pioneers and giants in natural products drug discovery, and he was among the first to explore the realm

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He can truly be regarded as one of the great pioneers and giants in natural products drug discovery, and he was among the first to explore the realm of marine organisms as a source of potential antitumor agents.

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of marine organisms as a source of potential antitumor agents. His early research in this area developed into a marine natural products drug discovery program of exceptional productivity and achievement. Space does not permit the listing of the numerous bioactive molecules discovered through this program, but several stand out as agents of considerable promise in the area of cancer chemotherapy.

Foremost among these are the dolastatins, a family of peptides originally isolated from the marine mollusk, *Dolabella auricularia*. Of the more than 20 dolastatins reported, the linear peptide, dolastatin 10, and several of its synthetic analogues entered cancer clinical trials but failed to advance beyond Phase II (P II) due to toxicity and/or lack of efficacy. However, synthetic studies by the Pettit group yielded the analogues, auristatin E and F and some derivatives which have been linked to various monoclonal antibodies (mAbs) by companies, such as Seattle Genetics, to give a range of Antibody Drug Conjugates (ADCs) showing significant promise in clinical trials against a number of cancers. ASP Fellow David Newman has written a Hot Topic Review discussing these developments.[7] In 2011, the FDA approved the first such ADC (brentuximab vedotin; Adcetris®), in which monomethyl-auristatin E (MMAE) is linked to a monoclonal antibody (cAC10) directed against the CD30 epitope, for the treatment of certain lymphomas. Two other MMAE and one monomethyl-aurisatin F (MMAF) derived ADCs were approved by the FDA in 2019 and 2020.[7] Referring to the database *clinicaltrials.gov* (as of 10-5-2021), there are 285 clinical trials of MMAE-linked ADCs completed or in progress, showing the promise of these ADCs for the treatment of a range of serious cancers.

Another important marine-derived discovery from the Pettit group are the bryostatins, isolated from the bryozoan, *Bugula neritina*. The bryostatins are 20-membered macrocyclic lactones, and bryostatin 1, the major member of the 20 structures isolated thus far, has been in more than 80 cancer clinical trials to date. Currently (10-5-2021), there are 37 completed trials reported in *clinicaltrials.gov*, and while there have been some responses when used as a single agent, this is probably not the optimal application, while administration in combination with other cytotoxins, such as paclitaxel, cisplatin, vincristine and nucleosides, is demonstrating improved efficacy. Possibly of greater significance is a Phase II clinical trial in patients with advanced Alzheimer's disease (AD), where evidence of improvement in cognition has been observed in patients receiving 20 µg of bryostatin.[8] A long term clinical trial is being planned in collaboration with the NIH.[9] In addition, structurally simpler analogues, so-called "bryologs," synthesized by the Wender group at Stanford University, have been shown to flush out the latent HIV virus, making it sensitive to highly active antiretroviral therapy (HAART), which would permanently eliminate the virus from the patients.[10]

Other promising marine-derived compounds discovered by the Pettit group are the cephalostatins, isolated from *Cephalodiscus gilchristi*,[11] and the spongistatins, isolated from a sponge of the family Spongiidae.[12] Both agents show potent *in vitro* activity against various cancer cell lines as well as significant *in vivo* activity in xenograft models, but further development has been hampered by the very low yields obtained from their respective source organisms. The recent development of efficient total syntheses, however, could provide sufficient amounts to permit advanced preclinical studies and clinical development.[13, 14]

Another important marine-derived discovery from the Pettit group are the bryostatins, isolated from the bryozoan, *Bugula neritina*.

While Pettit's research has been focused primarily on the discovery of marine-derived anticancer agents, his group has also performed extensive studies of plants and has had considerable success in the isolation and identification of some promising agents. Most notable of these are the combretastatins, isolated from *Combretum caffrum*. Being members of the stilbene family, these are readily amenable to chemical synthesis. The most promising of these is combretastatin A-4 (CA4), which was converted to the water-soluble phosphate prodrug, combretastatin A-4 phosphate (CA4P; Fosbretabulin; Zybrestat). Following several clinical trials, CA4P was granted orphan drug designation by the FDA in 2003 for the treatment of anaplastic thyroid cancer, medullary thyroid cancer, and stage IV papillary or follicular thyroid cancer. In 2006, it was granted orphan drug designation for the treatment of ovarian cancer. Another promising analogue, combretastatin A-1 (CA1), as its diphosphate prodrug CA1P (OXI4503), has shown promising efficacy in the treatment of patients with relapsed and refractory acute myelogenous leukemia and myelodysplastic syndromes. In 2012, orphan drug designation for this compound was granted by the FDA for the treatment of acute myelogenous leukemia.[15] CA4 and CA1 function biologically as potent inhibitors of tubulin polymerization and also act as promising vascular disrupting agents (VDAs) that impart selective and effective damage to tumor-associated microvessels in a manner that is distinct from the

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Pettit's research received strong support over the years from the National Cancer Institute, which recognized his significant contributions to anticancer drug discovery through funding him as an Outstanding Investigator from 1989 to 2001.

well-studied angiogenesis inhibiting agents (AIAs). The relatively simple chemical structure of the combretastatin A-series of natural products coupled with their potent biological activity has inspired countless worldwide efforts directed towards the synthesis of analogues and derivatives. The synthesis and activity of bioreductively activatable prodrug conjugates (BAPCs) of CA1P and CA4P has recently been reported.[16]

Last but not least, as outlined in the tribute by Dr. Ernest Hamel, a leading world expert on tubulin inhibitors, he and Pettit collaborated for over 30 years on the determination of the mechanisms of action of a wide range of natural products. These studies led to the discovery that tubulin-based mechanisms of action can be determined by computer-assisted evaluation of differential cytotoxicity data[17,18] and the discovery of novel dolastatins, which stimulate actin assembly and were later shown to bind in a unique site on actin polymers.[19,20]

Pettit's research received strong support over the years from the National Cancer Institute, which recognized his significant contributions to anticancer drug discovery through funding him as an Outstanding Investigator from 1989 to 2001. In addition, his unbounded enthusiasm and commitment to improving the lives of cancer patients worldwide, and his outstanding record of achievement in addressing these goals, inspired generous support from several foundations and individuals.

Pettit with his wife, Jean

His contributions have also been recognized through the award of many honors and invitations to deliver lectures at national and international conferences. Among the honors are the Alumni Achievement Award by Washington State University (1983–1984), the Chemical Pioneer Award by the American Institute of Chemists (1988), the State of Arizona Governor's Excellence Award (1993), the ASP Norman Farnsworth Research Achievement Award (1995), the Mathias P. Mertes Memorial Lecture Award by the University of Kansas (1997), the Ernest Guenther Award in the Chemistry of Natural Products by the American Chemical Society (1998), the Nolan and Gloria Sommer Award by the University of Nebraska (2000), election to the NJ Long Branch High Schools Distinguished Alumni Academic Hall of Fame (2009), Laverne Weber Visiting Scholar, Hatfield Marine Science Center, Oregon State University (2009), Distinguished Lecture Series, School of Pharmacy, University of Pittsburgh (2009), and Washington State University Regents Distinguished Alumnus Award (2012). In March, 2008, a special issue of the *Journal of Natural Products* was dedicated to him, and in 2019 the French journal *Médicine Sciences* published a tribute to him.[17]

From 1970 he was a Fellow of the American Institute of Chemists and from 2007 an ASP Fellow. In addition, he was an Honorary Member of the ARCS Foundation (Achievement Rewards for College Scientists), the PAMM Group of the European Organization for Research and Treatment of Cancer (EORTC), and the International Cancer Advocacy Network (formerly the International Foundation for Anticancer Drug Discovery).

Pettit served on the editorial advisory boards of the *Journal of Natural Products, Synthetic Communications, Anticancer Drug Design*, and *Current Organic Chemistry*. Other services include as a member of the advisory boards of the NCI Division of Cancer Treatment (1971–1974), the Walter Reed Medical Research Institute (1985-1990), and the Clinical Trials Board, UK Cancer Research Campaign (1985-2006), as well as the American Chemical Society Awards Committee (1998–2002), the American Institute of Chemists Chemical

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Pioneer Award Selection Committee (1989–1997), and the Board of Directors of the American Society of Pharmacognosy Foundation. He also served for many years on NCI and NIH Special Study Sections, and from 2006-2011 was Research Vice President and President of Oregon State University. In 1973, he participated in US government negotiations for the exchange of drugs for the treatment of cancer, some of which took place in the then USSR. In 1974, he was a member of a group representing the US Academy of Sciences in a study of drug development and medicine in the People's Republic of China.

During his tenure at the University of Maine and Arizona State University, Pettit trained over 70 graduate students, while 200 postdoctoral fellows and visiting scientists, including professors on sabbatical leave, many of whom were from overseas, have carried out research in his program. Also included in his program have been 60 staff, research assistants, and undergraduate research students as well as over 100 undergraduates who have gained technical experience in the processing laboratories as work-study students. Most of his graduate students and colleagues have progressed to positions of influence in academia, government, and industry and have continued to promote the cause of natural products drug discovery that he so strongly advocated.

TRIBUTES

In memoriam: Regents Professor George 'Bob' Pettit | ASU News, Arizona State University.

Family/obituary:
https://www.azcentral.com/obituaries/par053089

John H. Cardellina II, Chair, ASP Foundation; Reeves-Group.

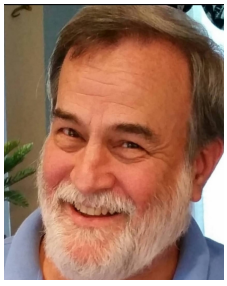

PHOTO: BERNADETTE CARDELLINA

I first met Bob in 1985 at an IUPAC meeting on marine natural products in Paris. I was still an assistant professor about to be considered for tenure and was presenting my first invited lecture at that meeting. Bob sought me out after my talk and was very complimentary, despite my obvious nerves; he asked me to have lunch with him and we talked well into the afternoon. Thus began our long friendship. Shortly after the Paris meeting, Bob and I "traded" seminars at each other's universities. I mention this because Bob so enjoyed talking natural products chemistry that he would lose track of time, despite numerous reminders that, for example, his plane was due to leave soon. Despite my setting what had to be a land speed record getting him to the airport, when we arrived at the gate, the door to the jetway was closed. Bob did not become agitated or angry; instead, I watched him calmly sweet talk the gate agent into talking to the captain of the flight, getting the jetway reattached, and letting him board the plane. I know this could never happen today, but I even marvel that it did in the 1980s. (I can even imagine him making St. Peter wait for him at the pearly gates!) Bob and I remained friends for the next 35 years. He always gave me excellent advice, genuine encouragement, and heartfelt support during my numerous career changes. In exchange, I reveled in his seemingly endless accomplishments and helped him fill in some gaps on his family tree. I certainly got the best of the deal, and I will sorely miss our long conversations.

Gordon Cragg, NIH Special Volunteer, NCI Natural Products Branch.

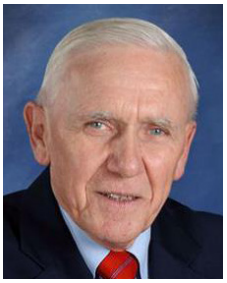

PHOTO: LIFETOUCH, INC

I first met Bob in 1972 when I spent a sabbatical year from the University of Cape Town (UCT) at ASU learning the details of natural products anticancer drug discovery. I returned to UCT keen to explore the rich South African biodiversity as a source of novel drug leads. In 1977, UCT invited Bob to deliver a series of lectures and research seminars, and the local chemistry community was inspired and motivated by his extensive knowledge and enthusiasm. He was accompanied by his daughter, Peggy, and we enjoyed showing them the scenic splendors of the Cape Town region. Bob invited me to join the ASU Cancer Research Institute (CRI), and in mid-1979 my wife, Jacqui, and I migrated to Tempe where I spent the next five years as a member of his outstanding team. In 1985, I joined the NCI Natural Products drug discovery program in Maryland, and I had the pleasure and privilege to continue close communication with Bob and his team. I regard Bob as one of the most outstanding and resourceful scientists I have known, and I am forever grateful to him for the indispensable role he played in guiding my professional career in anticancer drug discovery.

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Ernest Hamel, Molecular Pharmacology Branch, Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, National Cancer Institute.

My 32-year collaboration with Bob began as I was leafing through structures in a chemical abstract publication at NCI. I saw a diagram of the original combretastatin and thought, "That has to be a colchicine site compound." My hunch was correct, and combretastatin A-4 discussed in this Memoriam article turned out to be one of the most powerful inhibitors of colchicine binding to tubulin yet described. It turned out that Bob was harboring a treasure trove of structurally and mechanistically exciting tubulin inhibitors: dolastatin 10, dolastatin 15, halichondrin B and the spongistatins. In the case of halichondrin B, we found that it and homohalichondrin B bind to the vinca domain of tubulin, which led to the discovery that tubulin-based mechanisms of action can be determined by computer-assisted evaluation of differential cytotoxicity data.[17,18] This observation was a key element in the initial proof of concept of the COMPARE algorithm, and it was our comparison of the simpler synthetic analogue eribulin to halichondrin B that contributed to NCI's support of eribulin for advanced development over the scarce halichondrin B and ultimately to its clinical use. This development, and the development of dolastatin 10 analogues as the "drug" components of highly active antibody-drug conjugates (ADCs) used to treat a variety of cancers, achieved Bob's dream of treating cancer patients with drugs from the sea. The "fish that got away" was dictyostatin, a sponge-derived product that Bob's group was only able to isolate in minute quantities for cytotoxicity studies. Dictyostatin would have been the second drug discovered to have the mechanism of action of taxol (enhancement rather than inhibition of tubulin assembly), if enough had been isolated for tubulin studies. It was later repurified by ASP Fellow Amy Wright's group at Harbor Branch Oceanographic Institute, and the mechanism was determined by the Harbor Branch team. They referred to Bob's original isolation (as implied by the "statin" ending). But on compounds that enhance cytoskeleton component assembly, Bob's group had isolated dolastatins 11 and 12, both of which stimulate actin assembly and bind in a unique site on actin polymers.[19,20] Bob was a gracious and generous host when I came to Tempe to give seminars on tubulin. Although once when I walked out the airport door, I turned around and immediately walked back in, retreating from the extreme heat! These visits allowed me to see a part of the country, including the Grand Canyon, that I might never have seen. Thus, I am immensely grateful to Bob for both a challenging and rewarding scientific collaboration and for enriching my personal life.

Thus, I am immensely grateful to Bob for both a challenging and rewarding scientific collaboration and for enriching my personal life.

Kevin G. Pinney, Professor, Department of Chemistry and Biochemistry, Baylor University.

PHOTO: TRACY A. PINNEY.

I am honored to share a few thoughts and reflections regarding a true gentleman who defined excellence for a generation (and beyond) of research scientists and student scholars. Beyond his truly remarkable scientific productivity (which is absolutely extraordinary), Professor George R. (Bob) Pettit further embodied a set of characteristics and traits that cemented his status as a legend in science and society. Bob lived daily life in a manner that reflected the values of honor, service, family, friendship, respect, and integrity. His legacy is further defined by the attributes of diplomacy, nurturing mentorship, collegial encouragement, and voracious tenacity. These characteristics and traits resounded from head to toe in Bob's public and private persona and seemingly emanated from his very soul. From the first time I met Bob in person when I was a relatively young assistant professor at Baylor University through many continual years of meetings, adventures, and conversations, Bob always made me feel that I was uniquely important and valued (both scientifically and personally). Bob was over the top (in a good way) in con-

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His legacy is further defined by the attributes of diplomacy, nurturing mentorship, collegial encouragement, and voracious tenacity.

In Memoriam: George Robert "Bob" Pettit II

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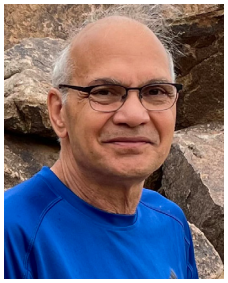
tinually providing this type of endless encouragement. He provided a constant voice that was always cheering me on and coupled with his wise counsel and sage advice, this type of mentoring and sense of scientific guidance proved instrumental in the early years of my career and remained steadfast with the passing of time. Long walks enjoyed with Bob provided wonderful opportunities to discuss science and life in general, and these conversations helped define my career-path and research goals. Those fortunate to be closely associated with Bob know how focused he could be on individual conversations, always to the betterment of the person he was speaking with. I recall Bob often telling me that when he awoke each new day, he hardly knew which direction to run first (since he had so many activities constantly ongoing) in regard to pursuing his passion for helping cancer patients. In every aspect of Bob's life that I observed, he always remained true to that goal of truly wanting to make a positive difference in the lives of cancer patients. Bob Pettit was a remarkable scientist as evidenced by seminal contributions to the natural products, organic chemistry, and medicinal chemistry communities and reflected in an amazing publication portfolio and an enduring legacy of research scholars who gained career-guiding mentorship while carrying out research in Bob's laboratory. His dedication to helping cancer patients at every opportunity offers lasting encouragement for other research scientists to follow in his giant footsteps. Of equal importance is the life that Bob led in regard to love for his family, respect for the preservation of our natural resources including forests and oceans, and friendship to so many individuals. While Bob is well known for his scientific excellence and career-long accomplishments, he was also a recognized statesman, naturalist, botanist, and humanitarian. He worked tirelessly toward the betterment of humankind. Bob was truly remarkable and while he will be sorely missed, his legacy will endure for generations to come.

His laser focus on bioactivity-directed isolation of new natural products was, and remains, unparalleled.

Sheo B. Singh, President, SBS Pharma Consulting, LLC (retired, Senior Principal Scientist, Merck Research Laboratories, 2013) and Adjunct Professor, Stevens Institute of Technology.



My first meeting with Bob took place in his office when I arrived to join his group in November of 1983. His soft spoken, charming, and welcoming nature put me at ease then and during my very successful stay at ASU. He assigned me the combretastatin project that day involving bioassay-driven isolation and total synthesis, followed by the total synthesis and absolute configuration determination of dolastatins 10 and 15 a couple of years later after the successful completion of the combretastatin project. For my six years at ASU, he blessed me with his absolute trust and provided me complete independence to perform work which allowed me to grow in confidence, making me what I am today. His laser focus on bioactivity-directed isolation of new natural products was, and remains, unparalleled. That learning was foundational for my career. While no one can predict the success of early projects as related to yielding a drug, he did assign to me two of the most successful projects of his group that led to clinical candidates and many FDA approved drugs. For that, I am deeply indebted to him. One of my fond memories was his organization of hikes, especially to the Grand Canyon, dubbed as "natural products in the wilderness," and ice cream runs. I met him in January, 2017 for a long lunch at his favorite restaurant in Scottsdale. He asked me details about my family and my sons by name, and their career progress. Regretfully that was the last time I met him. I found him very engaged, a dedicated, focused and outstanding scientist who wanted to cure cancer. I am so happy that he saw the fruits of his labor paying off with the approval of Adcetris™ in 2011, followed by approvals of other ADC drugs derived from dolastatin 10. He was very kind to me and my family. He played an outsized role, not only in my career success, but in encouraging me to stay in the US, and for that I am forever indebted and grateful to him. ■

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In Memoriam: George Robert "Bob" Pettit II

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...he was a prolific natural products scientist, an effective university administrator, a highly capable committee member, and an accomplished student athlete.

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nual Meeting of ASP held in Arlington, VA, he was named as an Honorary Member of the Society.

Cassady graduated in 1960 with a BA degree in chemistry from DePauw University, where he was also an outstanding baseball player, being a three-year letterman. In 1962 and 1964 he received MS and PhD degrees in organic chemistry from Case Western Reserve University. He went on to become a NIH postdoctoral fellow (1965-1966), where he worked with the late Dr. S. Morris Kupchan at the University of Wisconsin-Madison on the isolation and structure elucidation of plant-derived antitumor agents.[1] He joined the faculty of the Department of Medicinal Chemistry and Pharmacognosy at Purdue University in 1966 and was quickly promoted through the academic ranks. He became department head in 1980 and was named the Glenn L. Jenkins Distinguished Professor in 1987. While at Purdue, he collaborated with Drs. Heinz Floss and James Robbers on ergot alkaloids[2] and with Drs. Ching-jer Chang and Jerry McLaughlin on annonaceous acetogenins,[3] in addition to establishing a program on natural product cancer chemotherapeutic and cancer chemopreventive agents.[4]

In 1988, Cassady moved to Ohio State University, where he became Dean of the College of Pharmacy and served three consecutive five-year terms. During this period, despite having considerable administrative duties, he continued with his productive externally funded research program. Among those with whom he collaborated while at Ohio State were Dr. Gary Stoner from the College of Medicine[5] and Dr. Ken Chan[6] and one of the present authors (A.D. Kinghorn)[7] from the College of Pharmacy. He stepped down as dean in 2003 and left Ohio State in 2005 to become Vice President for Research at Oregon State University, where he remained until retiring in 2009. Altogether, Cassady co-authored about 150 research and review articles during his scientific career, and he trained some 70 MS, PhD, and postdoctoral investigators.

Present-day ASP Fellow Rachel Mata remembers Cassady from her time when she was a graduate student at Purdue University. "I met Professor John Cassady in 1974 when I arrived at Purdue University to pursue graduate studies. At the time, the Department of Medicinal Chemistry and Pharmacognosy at Purdue University was populated by some excellent researchers. Of course, he

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Below: ASP Foundation Chair John Cassady presenting Jerry McLaughlin with the 2007 Varro E. Tyler Award along with ASP President Roy Okuda at the annual meeting in Portland, Maine.

I will never forget that I learned from him how to apply circular dichroism to establish the absolute configuration of specific chiral molecules. He devoted time to any student who showed an interest in his subject. Indeed, he was a great teacher.

—Rachel Mata

His impact on research on antitumor compounds will remain forever —a legacy of excellence that has inspired several generations of scientific minds.

—Rachel Mata

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was one of them. He was very charismatic, and soon I noticed that he was a crucial figure in the department. It was wonderful to have known John Cassady, and I cherish many fond memories of him.

"Like many other students at the time, I had the pleasure of having Dr. Cassady as my teacher in two classes of natural products. Several faculty members team-taught these courses. One of these courses was 'Advanced Natural Products,' where the students had to present two seminars as designated by the academic staff. In both cases, I selected his chosen topics, so my experience in this class was very formative. I will never forget that I learned from him how to apply circular dichroism to establish the absolute configuration of specific chiral molecules. He devoted time to any student who showed an interest in his subject. Indeed, he was a great teacher.

"I also had the privilege and honor of having him on my PhD committee along with Professors Jerry McLaughlin (adviser), Graham Cooks, and James Robbers. He was always very critical in this endeavor and challenged me, but he played an essential role that helped me get to the end of the journey. It was a deep and rich learning experience to have him on my dissertation committee. I still remember how happy he was the day of my dissertation defense. He was confident of my future transformation into a promising scholar.

"After I left Purdue, I met Dr. Cassady in Monterrey, Mexico, at one of the natural product meetings organized by the late Professor Xorge Dominguez of the Technological Institute of Monterrey. It was a nice reunion. I was at the beginning of my career as an independent researcher. During an excellent dinner, I received from him both helpful criticism of my research and many words of encouragement. After that, I started to see John Cassady at each meeting of the American Society of Pharmacognosy we both attended. It was always a pleasure to see him. I have tender memories of all these periodic gatherings. His impact on research on antitumor compounds will remain forever —a legacy of excellence that has inspired several generations of scientific minds.

"Finally, I want to comment that,

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Below: The NCDDG Team, circa 2005: Norman Farnsworth, Steve Swanson, Jimmy Orjala, Geoff Cordell, John Cassady, Nick Oberlies, David Kroll, Mansukh Wani, A. Douglas Kinghorn, Bill Rose, Robert Wild, and Gordon Cragg.

...under Dean Cassady's leadership, the faculty approved the entry-level Pharm.D. program and a new B.S. degree in Pharmaceutical Sciences. As a result, the College was able to increase the size of its clinical faculty and student services without eroding the pharmaceutical sciences and faculty and graduate programs...

—Popat Patil

Having a VPR so knowledgeable about and invested in natural products research was unprecedented for the natural products faculty at OSU.

—Kerry McPhail

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coincidentally, my daughter Monica was born on precisely the same day as one of his children. Each time we met, we recalled this happening."

Two of us recall John Cassady's positive influence on research while at Ohio State University. Popat Patil, a pharmacologist and long-time collaborator of the late Dr. Jack L. Beal, was a senior College of Pharmacy faculty member for the entire time Cassady was dean. In his book co-authored with Dr. Robert A. Buerki, titled *A History of Drug Sciences at the Ohio State University College of Pharmacy* (Linus Learning, 2019), it is stated: "…under Dean Cassady's leadership, the faculty approved the entry-level Pharm.D. program and a new B.S. degree in Pharmaceutical Sciences. As a result, the College was able to increase the size of its clinical faculty and student services without eroding the pharmaceutical sciences and faculty and graduate programs. In 1994, the Vernal G. Riffe building was dedicated, creating more research space…The number of full-time faculty members was increased to 47 by 1999, and 124 graduate students were recruited."

Kinghorn (Emeritus Editor, *J. Nat. Prod.*) recalls: "John Cassady was extremely helpful to me when I made the move from the University of Illinois at Chicago to become the inaugural Jack L. Beal Chair at Ohio State in 2004. He took my wife, Helen, and me out to dinner when we were living in a rented accommodation in Columbus and provided much helpful information on possibilities for purchasing a home and on the other local amenities of the citand suburbs. Moreover, he very graciously agreed to join our National Cooperative Drug Discovery Groups (NCDDG) project team focused on the discovery of anticancer agents from plants during the period 2004-2005, and we were able to produce a number of collaborative publications from the work performed. In addition, earlier he was very supportive of my role as the then editor of the *Journal of Natural Products*, and came up with some practical suggestions as to how our two new annual awards for best paper (the Arthur E. Schwarting and Jack L. Beal Awards), could be funded for the first time in 2001 and thereafter annually."

From his time at Oregon State University, Kerry McPhail (the current president of ASP) recalls: "Dr. Cassady arrived at OSU to take up the position of Vice President for Research (VPR) shortly before I began my tenure-track assistant professor position in 2006. Having a VPR so knowledgeable about and invested in natural products research was unprecedented for the natural products faculty at OSU. I had the privilege of continual interactions focused on research until his retirement in 2009, including discussions of ideas and opportunities for new funding collaborations and advice on publications. I remember Dr. Cassady's enthusiasm for one project in particular. He connected my colleague Mark Zabriskie and myself with OSU Hatfield Marine Sciences Center (William Chadwick and others) and NOAA Pacific Marine Environmental Laboratory (David Butterfield) researchers involved in the NOAA Vents Program. This collaboration started with a NOAA-funded pilot project to review the state of knowledge on biological diversity at deep-sea hydrothermal vents and

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Below: Cassady was named an Honorary ASP Member at the 2006 ASP Annual Meeting, shown here with his wife Nancy, Taifo Mahmud, and Ching-jer Chang.

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to assess their potential as a source of valuable natural products. The extensive background research compiled by then graduate student Chris Thornburg in my research group (now senior scientist at the Frederick National Laboratory for Cancer Research) was discussed at an 'all hands' project meeting organized by Dr. Cassady that included the late Dr. George R. Pettit as consultant. What a memorable meeting for the expansive ideas and wonderful social interactions with both Drs. Cassady and Pettit! It was certainly a critical time in my career to receive such support and friendly encouragement. The NOAA pilot project led to a review published in *J. Nat. Prod.*,[8] in which the brief acknowledgment made of Dr. Cassady now seems inadequate, and laid the foundation for further funding from NOAA and an NIH/NIAID R21 award. I also will never forget Dr. Cassady's encouraging words that helped spur me to resubmit a disappointingly reviewed manuscript. The resubmitted manuscript[9] led to a joint *J. Nat. Prod.* Beal award for best paper to my USDA-ARS and OSU co-authors."

Above: John and his wife, Nancy, at the 2006 annual meeting.

Cassady should be lauded, in particular, for his term of service as Chair of the ASP Foundation (ASPF). John Cardellina, the present ASPF Chair explains: "John Cassady was the first Chair of the ASPF and unquestionably the critical element in transforming the Foundation from an idea to a functioning entity. To be sure, David Slatkin, long-time ASP Treasurer, proposed the idea of a foundation and provided the first infusions of cash from the ASP treasury, but John Cassady's insight and leadership took that humble beginning and made the Foundation a functioning reality. Two of his critical contributions were establishing a fundraising goal and seeking external funding. When John first proposed a fundraising target of one million dollars, the other members of the board were shocked. (We had about $250,000 at that point and a million seemed so far away.) Nonetheless, with modest but steady infusions from ASP, consistent donations from ASP members, and astute management of our money by ASPF Treasurer Bob Krueger, we reached that goal. Bequests from three members and more donations from members pushed us over the next goal (two million dollars), enabling us to fund far more awards than ever before without diminishing the corpus of the Foundation. Our annual outlays have gone from less than $20K to $75K or more per year.

"John Cassady was also a big proponent of finding external funding. He conceived the idea of establishing a 'flagship' award for career achievement in the area of commercial botanicals, and he wanted to name it for Varro Tyler of Purdue University. At the time, the mid to late 1990s, Varro Tyler was the most important and sought-after consultant, advisor, and board member in the botanical supplements/phytomedicine industry, both here and abroad. John chose Pharmanex (NuSkin) as a likely supporter of the idea and asked me to join him on a visit to the senior leadership of the company. It was an eye-opening experience! While the company leaders liked the idea of the

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John Cassady was the first Chair of the ASPF and unquestionably the critical element in transforming the Foundation from an idea to a functioning entity.

–John Cardellina

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award, there was hesitation about funding it. Each reason for resistance was met with a new angle, perspective, or direction from John Cassady. Of course, John wanted the company to fund the award permanently, giving us enough money so that the earnings on that sum would pay for the award. To me, that was only about $100K for a company that probably spent that much on lawyers' fees in a couple of weeks. The compromise reached was that Pharmanex would fund the award for one or two years and then revisit the idea of funding it in perpetuity. Sadly, the company later said their legal issues precluded their funding the award, but it planted a seed for the ASPF Board. We now realize that we need large sums to fund substantial new awards, like the Bingel Fellowships for Female Scientists, the minority Summer Research Fellowships, and the John Daly Grant for Field Research, and we are actively pursuing the 'Cassady Approach' in an effort to establish long-term funding for these and other awards. It has been a great honor for me to follow in John's footsteps as Chair of the ASPF. I do not think we would have achieved the level of success that we have without his inspirational leadership and guidance."

John Cassady was the recipient of numerous other awards and honors during his lifetime. In 1989, he received an honorary doctorate from his alma mater, DePauw University. He was the recipient of the 1990 Research Achievement Award in Natural Products Chemistry from the American Pharmacists Association. Moreover, he was a Fellow of the American Association for the Advancement of Science, the American Association of Cancer Research, and the American Society for Pharmaceutical Sciences. He was elected as a visiting professor at Xian Medical University in China in 1991 and was a visiting professor at the University of Bonn in Germany in 2002. In 2011, he was elected to the DePauw University Athletics Hall of Fame as a result of his outstanding undergraduate student baseball career.

Cassady's wife, Nancy, passed away after 57 years of marriage. He is survived by his four daughters (Betsy Anne, Kimberley Nelle, Susanna Lee, Patricia Nancy) and one son (John McDowell), as well as many grandchildren and great-grandchildren, to whom our deepest condolences are extended. ■

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In Memoriam: Hildebert Wagner

By Edward J. Kennelly, PhD

ASP Honorary Member Professor Hildebert Wagner died on November 5 at the age of 92. He was a pioneer in the field of modern pharmacognosy, published prolifically, headed the Institute of Pharmaceutical Biology at Ludwig Maximilian University in Munich (LMU) for over a quarter of a century and collaborated with many ASP colleagues. His service to ASP included membership on the *Journal of Natural Products* editorial advisory board for 25 years and organizing the first joint pharmacognosy meeting with American and European societies. He is remembered fondly as visionary in bridging medicinal plants and clinical medicine, as manifested in the journal he founded, *Phytomedicine*.

Professor Hildebert Wagner

Wagner was born on August 28, 1929 in Laufen, Germany, near the Austrian border. After completing his professional studies in pharmacy at LMU in 1953, Wagner went on at the same institution to receive his doctorate in 1956 under the direction of Professor Ludwig Hörhammer. He remained at LMU and completed his habilitation (1960) and was promoted to full professor in 1965. In 1970-71, he did a sabbatical as a Distinguished Visiting Professor at the College of Pharmacy, Ohio State University, hosted by the late Professor Jack L. Beal, former editor of the *Journal of Natural Products* (*Lloydia*). Wagner later went on to serve as the Dean of the Faculty of Chemistry/Pharmacy (1981-1983) and then to direct the Institute of Pharmaceutical Biology until his retirement in 1998.

ASP Honorary Member Dr. Ikhlas Khan received his doctorate with Wagner in 1987 and remembered his PhD mentor as "… a giant among pharmacognosists, as one who stands out for many of his outstanding traits — expertise, commitment to excellence, maintenance of the highest standards, and relentless pursuit of new and emerging research. He has influenced so many pharmacognosy graduates and others by his commitment and sustained energy to pursue the discovery of natural products. I had the pleasure to work with him as a PhD student at the Institute for Pharmaceutical Biology in Munich. I can say that he has the ability to evaluate, teach, motivate, and guide. He was not only a mentor but also a guardian for me. His legacy will remain alive for ages to come."

His research in pharmacognosy was expansive over the decades of his career and included almost 1,000 publications on bioactive phytochemicals, including anti-inflammatory and antiviral compounds. He conducted seminal research on well-known, evidence-based use of medicinal plants common in the European pharmacopeia, like *Echinacea* species and *Silybum marianum*.

ASP Fellow Dr. Guido Pauli stated, "Within the European pharmacognosy community, Bert Wagner was a pioneer, scientific trend setter, and a strong advocate for the shift from 'pharmacognosy' to 'pharmaceutical biology' in the education of young pharmacists in the 1970s. He spearheaded the development of modern analytical approaches for the characterization of traditional medicines, was the first to expand 'Western' research to Traditional Chinese Medicines, and talked about botanical synergy long before this hypothesis was embraced more broadly."

Wagner wrote dozens of review papers and seven books. Visually, one of the most impactful books on phytochemical analysis ever published was his 1992 *Plant Drug Analysis* coauthored with Sabine Bladt and Eva Maria Zgainski. This beautifully photographed collection of thin-layer chromatography plates made the chemical diversity of medicinal plants jump off the page in its stunningly colorful images. In the book's preface, Wagner and coauthors noted, "In order to make the documentation as realistic as possible, we have therefore attempted to make faithful photographic reproductions of thin layer chromatographic separations of drugs in visible and UV-light." They were indeed successful, and the book was translated into English by A. Scott. Comparing their glossy volume to Dr. Egon Stahl's classic encyclopedic *Thin-Layer Chromatography. A Laboratory Handbook* was like

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He is remembered fondly as visionary in bridging medicinal plants and clinical medicine, as manifested in the journal he founded, *Phytomedicine.*

"... a giant among pharmacognosists, as one who stands out for many of his outstanding traits — expertise, commitment to excellence, maintenance of the highest standards, and relentless pursuit of new and emerging research."

— Dr. Ikhlas Khan

Professors Wagner and Cordell surrounded by attendees at The International Conference on Bioscience and Biotechnology 2011 in Yogyakarta, Indonesia.

PHOTO COURTESY: GEOFF CORDELL

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watching Dorothy in *The Wizard of Oz* stepping from the black and white of her Kansas farmhouse into the technicolor of Oz. A second edition of Wagner's book was published in 1996 by Springer Verlag, and it can be found in many natural products laboratories worldwide.

Wagner served on the Editorial Advisory Board of the *Journal of Natural Products* for decades. Editor Emeritus Dr. A. Douglas Kinghorn wrote, "I am extremely sad to hear about the passing of Hildebert Wagner, a truly outstanding authority in the field of Pharmaceutical Biology (Pharmacognosy), not only in Germany but worldwide. As an expert in medicinal plants, he was on the Editorial Advisory Board of *J. Nat. Prod*. (*Lloydia*) from 1977 (Volume 40) through 2002 (Volume 65). In 1970-71, he was a Distinguished Visiting Professor at the College of Pharmacy, Ohio State University. I was privileged to give a seminar on my work on natural product sweetener research at the Institute of Pharmaceutical Biology of the University of Munich in July 1990, and I remember

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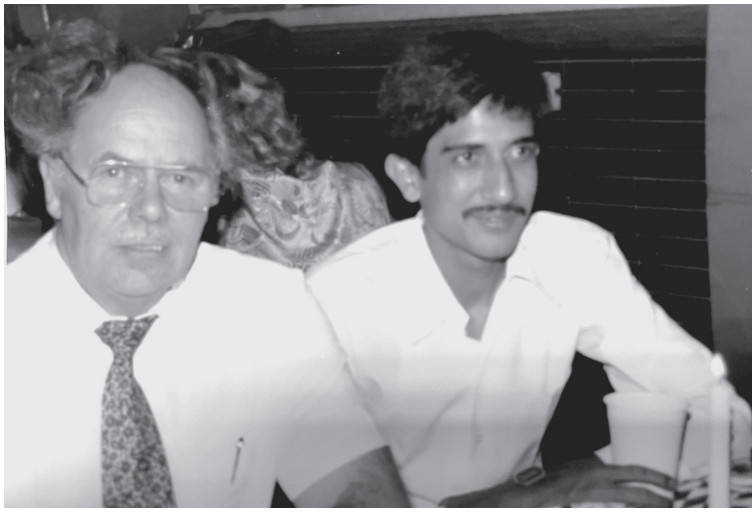
"He spearheaded the development of modern analytical approaches for the characterization of traditional medicines, was the first to expand 'Western' research to Traditional Chinese Medicines, and talked about botanical synergy long before this hypothesis was embraced more broadly."

—Dr. Guido Pauli



Professor Wagner with his doctoral student Ikhlas Khan in 1985.

PHOTO COURTESY: IKHLAS KHAN

Hildebert being a very welcoming host. The major impact he has had on phytomedicine research, including co-founding and editing the now-leading journal *Phytomedicine*, will be very long lasting."

Wagner had long-standing collaborations with many ASP members, especially those from the University of Illinois at Chicago, including the late Professor Norman Farnsworth, a founding member and first vice president of ASP. For the 1970 joint meeting between ASP and the Gesellschaft für Arzneipflanzenforschung (GA) in Vienna, Austria, Farnsworth was co-chair of the Scientific Program Committee, and Wagner hosted a pre-meeting International Symposium on Pharmacognosy and Phytochemistry at LMN. Farnsworth later did a sabbatical with Wagner. ASP elected Wagner as an honorary member in 1992. Over the course of three decades, Wagner and Farnsworth published dozens of papers together, beginning in 1967 with identification of n-alkanes from *Arctostaphylos patula*.

ASP member Dr. Guido Pauli, who holds the Norman Farnsworth Distinguished Professorship at University of Illinois at Chicago, wrote, "Bert Wagner and Norman Farnsworth met in the late 1960s and considered each other best friends. Their friendship led to highly productive joint work and was at no risk even during disputes where one of them argued that pharmacognosy was dead, while the other demonstrated why it was the future." ASP member Prof. Rudi Bauer echoed this sentiment, "Hildebert Wagner was an outstanding scientist, full of visions of how medicinal plant research should develop. I am very grateful that I was one of his students and that I could learn from him over so many years. I especially am grateful for the connection to the group in Chicago, and Norman Farnsworth has always been of extraordinary importance for him."

ASP Honorary Member Dr. Harry H.S. Fong knew Wagner for decades and remembered in 1968 cementing their long friendship with an epic drive across the United States. "An opportunity presented itself for Professor Wagner and me to drive together from Pittsburgh to attend the ASP meeting at Iowa City. During this ten-hour trip, we discussed many things, scientific and personal, including his desire to drive a 'big' American car not readily available to him in Germany. I was more than happy to accommodate his desire and shared the driving to Chicago, where we met up with Norman Farnsworth for the rest of the trip. We bonded during this long drive, resulting in Professor Wagner's being 'Bert' to my 'Harry' - the start of a long, long friendship."

Wagner's dream to start a peer-reviewed pharmacognosy publication was realized with Farnsworth when they became the founding editors of *Phytomedicine* in 1994. Wagner served as the editor-in-chief for 18 years and made it into a leading pharmacognosy journal with an emphasis on therapy-oriented research. This Elsevier journal now boasts an impact factor of 5.3 and is viewed as one of his many lasting legacies.

In addition to ASP, Wagner was honored by others, including in 2002 for Medicinal Plant and Natural Product Research (GA) for his outstanding lifetime achievements with the Egon Stahl Medal in Gold (2002), and apropos, the Norman R. Farnsworth Excellence in Botanical Research Award of the American Botanical Council (2007).

Wagner is survived by his wife, Ursel, and his three children, Christine, Thomas, and Michael. ■

Wagner's dream to start a peer-reviewed pharmacognosy publication was realized with Farnsworth when they became the founding editors of *Phytomedicine* in 1994.

Moore Receives the 2021 ASP Norman R. Farnsworth Research Achievement Award

By William Fenical, PhD

ASP Fellow Dr. Bradley S. Moore, distinguished professor at the Scripps Institution of Oceanography, University of California, San Diego, has been selected to receive the 2021 Norman R. Farnsworth ASP Research Achievement Award. His award lecture is slated to occur at the 2022 ASP Annual Meeting in Charleston, South Carolina in July.

ASP President Kerry McPhail stated, "The award to Dr. Moore of the 2021 Norman R. Farnsworth Research Achievement Award is timely recognition of his exceptional accomplishments. In striving to understand the biosynthetic machinery that enables 'life's biochemical prowess,' Dr. Moore continues to make outstanding and diverse contributions that elevate the natural products sciences and promote the application of natural products for human health and well-being."

Dr. Bradley Moore
UCSD PHOTOGRAPHY

Upon receiving news of the award, Moore stated, "I'm honored to join my many mentors, colleagues, heroes, and father who have been recognized with this prestigious award from the ASP. I would be remiss if I did not also acknowledge my amazing team of students and postdocs who continue to be such a joy to work with and learn from."

Moore hails from Hawaii and has a long history of interest in the chemical biology of natural products. While an undergraduate at the University of Hawaii, Moore started his career as an intern in his father's lab, the highly accomplished 2002 ASP Farnsworth Research Achievement Award winner, the late Professor Richard E. Moore. While an undergraduate, Moore made notable discoveries involving the structures of the cyanobacterial cylindrocyclophanes and the biosynthesis of anatoxin-a(s).

With these superb credentials, Moore moved on to the University of Washington to study for his PhD with Professor Heinz Floss, the 1988 ASP Farnsworth Research Achievement Award winner. It was with Professor Floss that Moore developed his in-depth training in the chemistry and biosynthesis of microbial natural products. After receiving his PhD, Moore accepted a postdoc position with the now emeritus professor John A. Robinson in Zurich. In Zurich, Moore broadened his background to include researching the stereospecificities of biosynthetic enzymes.

In his search for a career position, Moore returned to the University of Washington as a research professor where he undertook several independent investigations including his first marine biosynthetic studies of the salinamides, marine bacterial depsipeptides with potent anti-inflammatory properties. During these few years as an independent researcher at the University of Washington, Moore began his professorial career by working with postdocs who have themselves become well known in creative natural products research. This

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"In striving to understand the biosynthetic machinery that enables 'life's biochemical prowess,' Dr. Moore continues to make outstanding and diverse contributions that elevate the natural products sciences and promote the application of natural products for human health and well-being."

Moore Receives the 2021 ASP Norman R. Farnsworth Research Achievement Award

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includes Joern Piel and Christian Hertweck. Together, they were the first to sequence, clone and express the entire gene pathway for the bacterial production of enterocin, a unique polyketide antibiotic.

In 1999, Moore accepted his first tenurable career position as assistant professor of medicinal chemistry at the University of Arizona. There he made notable contributions that included sequencing the first bacterial genome (*Salinispora tropica*) of a natural product-rich marine microbe in the US.[1] His pioneering work in bacterial genomics helped to usher in the field of genome mining and provided the foundation for the development of genome annotation tools to predict the presence and identity of biosynthetic gene clusters.

Moore with his PhD mentor Heinz Floss on the SIO pier, 2019.

In 2005, Moore accepted a position as professor of marine chemical biology at the Scripps Institution of Oceanography at UC-San Diego (SIO). His appointment was noteworthy as he was also appointed to the Skaggs School of Pharmacy and Pharmaceutical Sciences. This joint appointment enabled Moore to further broaden his science, but this heralded an important intracampus collaboration that brought professors Ted Molinski and Pieter Dorrestein in close relationships with the marine natural products researchers, Moore, Paul Jensen, Bill Gerwick and Bill Fenical at SIO. Over the past 16 years, Moore's interests and capabilities have expanded enormously to include many innovative concepts that remain poorly explored. Following up on their detailed knowledge of the enterocin pathway, Moore and co-workers performed what was perhaps the most elegant example of enzymatic natural product total synthesis. Amazingly, they combined 12 recombinant enzymes, with the starter unit, in a single tube and observed the production of fully chiral enterocin in 25% overall yield.[2] Subsequently, using similar approaches involving total enzymatic synthesis, the Moore lab reported the enzymatic synthesis of napyradiomycin B1, and later the unique marine neurotoxin kainic acid. These are rare examples of the first synthetic use of biosynthetic enzymes and illustrate the enormous future potential of this approach.

At SIO, Moore's activities have continued to approach important concepts in spectacular ways. Genome mining has allowed Moore to discover new molecules and to explore their biosyntheses. New molecules include the taromycins, which are closely related to the clinically-utilized antibiotic daptomycin. Utilizing the genomic information derived from the salinosporamide biosynthetic gene cluster (BGC), observed in *Salinispora tropica*, Moore's group was able to bioengineer the production of the fluoro derivative, fluorosalinosporamide. Moore has become keenly aware of the utility of biosynthetic enzymes. One of Moore's group members, Michelle Moffitt (now a professor in Australia), isolated and defined a unique phenylalanine ammonia lyase enzyme from *Anabaena variabilis*, which has since become an FDA-approved drug called Palynziq (BioMarin) used as an enzyme substitution therapy to treat phenylketonuria (PKU).

One of Moore's most exciting discoveries is the production of the infamous didemnin class of marine cyclic peptides by the marine bacteria *Tistrella mobilis* and *Tistrella bauzanensis*. First discovered in the early 1980s, the didemins are potent cytotoxins that were the first marine natural products to enter human cancer clinical trials. In a collaboration with his colleague Pieter Dorrestein at UCSD and Pei-Yuan Quan

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at the Hong Kong University of Science and Technology, they showed, using genomics and time-course imaging mass spectrometry, the time-dependent extracellular conversion of the didemnin X and Y precursors to didemnin B in support of an unusual post-synthetase activation mechanism.[3]

Approaching untested boundaries never seems to phase Moore and his students and postdocs. Using all the tools of genomics and synthetic biology, he has explored areas of great importance in marine science. In response to the growing importance of diatom toxin-induced events in California and the Pacific Northwest, the Moore lab isolated the responsible gene cluster for domoic acid production in *Pseudo-nitzschia multiseries* and, in a landmark paper, decoded the full biosynthesis of this important toxin.[4] This discovery provided genetic markers as analytical tools to fully understand the distribution of this toxin. He also examined the biosynthesis of the poorly known cyanobacterial organophosphate toxin guanitoxin, previously known as anatoxin-a(s). Here, too, having the biosynthetic genes illuminated will allow their use as an analytical tool to quantitate this toxin that lacks UV absorbance and is thus difficult to evaluate by HPLC.

As time passes, Moore's interests and the focus of his lab have enlarged dramatically. He has invested heavily in halogenation processes especially as they relate to halogen-induced biosynthesis. His ground-breaking examination of the biosynthesis of the marine actinomycete produced merochlorins, for example, demonstrated a unique chloronium-induced terpene macrocyclization.[5]

As time passes, Moore's interests and the focus of his lab have enlarged dramatically. He has invested heavily in halogenation processes especially as they relate to halogen-induced biosynthesis. His ground-breaking examination of the biosynthesis of the marine actinomycete produced merochlorins, for example, demonstrated a unique chloronium-induced terpene macrocyclization.[5]

Moore collecting halogenating seaweeds in the La Jolla region.

Moore's interests in marine halogenation biosynthesis have been a recurring theme of his work for over a decade. At present, Moore and his students are capitalizing on the current capabilities to explore seaweed genomes, focusing on those that involve the halogens in their basic biosynthetic activities.

In more recent activities, based upon the availability of marine invertebrate genomic sequence data, Moore has ventured into areas of long-term debate in marine natural products chemistry. Marine octocorals, gorgonians (sea whips and sea fans) and alcyonaceans (soft corals) typically contain a diversity of terpenoids. Since the early days of marine chemistry, it was generally accepted that only plants can produce terpenoids, coupled with the fact that these octocorals typically contain large numbers of endosymbiotic algae (dinoflagellates of the genus *Symbiodinium*), led to the conclusion that the algae were the terpene source. Using genome sequence data, Moore's group identified numerous putative terpene synthases (cyclases), had these enzymes synthesized, and showed that they were able to convert

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sesquiterpene and diterpene precursors to the classic cyclic terpenes isolated. This is an exciting and very important contribution that lays to rest the suggestion that algal symbionts are responsible for terpene production. As more genomic data from other marine invertebrates become available, the identification of animal terpene synthases will likely be observed and confirmed.

Moore's achievements are clearly demonstrated by his large number of important publications (ca. 250) in the highest-level journals. What is particularly impressive is the diversity of his work, which is strong in basic organic chemistry, genomics, biosynthesis, and enzyme synthetic biology. Moore is widely respected for this diversity of capabilities and expanding interests in the fields of marine toxins, the origins of marine molecules and the utilization of marine genomics to solve biosynthetic challenges. Moore is widely sought as a speaker at national and international meetings and universities worldwide. Importantly, Moore is a superb colleague and collaborator with existing relationships outside and across the UCSD campus. He has a long history of producing quality young academics, recent North American examples of which are Jaclyn Winter (Utah), Alessandra Eustáquio (UIC), Amy Lane (UNF), Katherine Ryan (UBC), Avena Ross (Queens), Vinayak Agarwal (Georgia Tech), Jie Li (South Carolina), Roland Kersten (Michigan), Jonathan Chekan (UNC-Greensboro), and Shaun McKinnie (UC-Santa Cruz).

Moore in his typical attire discussing research with Shaun McKinnie (left) and Patrick Brunson.

As one of Brad's closest colleagues, I have had ample opportunity to experience his genuine concern for his students and postdocs. He has very high standards but fully supports his students and postdocs and is very aware and supportive of the career goals of those who associate with him. It gives me (and I'm sure his students and associates) great pleasure to know that the ASP will recognize his achievements and personal qualities by awarding him their highest honor. ■

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Cardellina Named 2021 Tyler Prize Recipient

By Nicholas Oberlies, PhD, Stefan Gafner, PhD and James Gloer, PhD

Dr. John H. Cardelina, II

Dr. John H. Cardellina, II has been awarded the 2021 ASP Varro E. Tyler Prize. The prize is given by ASP to researchers in botanicals and named in honor of the first president of ASP, Dr. Varro "Tip" Tyler. Like Tyler, Cardellina is a renaissance man who has worked across so many disciplines of natural products research and given considerable time to the service of the ASP.

Regarding the prize, Cardellina stated, "When I was first told that I had been selected to receive the Tyler Prize for contributions to the science of botanicals two and one half years ago (thanks, COVID), I thought, 'Is someone pranking me, I don't think I have reached the threshold of eligibility.' When the reality that this was not a cruel joke set in, I felt honored that someone(s) considered me sufficiently worthy of this award to nominate me. Then I had to grapple (and still am grappling) with the challenge of constructing an interesting, informative, and entertaining tale of my adventures with medicinal plants. So, my reaction went from shock/disbelief to a sense of honor to a new level of anxiety for me. I look forward to our meeting in Charleston, and hope to see many old and new faces there."

Cardellina's top two papers, both of which have been cited over 450 times according to Scopus, described natural products with inhibitory activity against HIV.

Cardellina was a chemistry major at Pennsylvania State University, and after four years of sea duty as an officer in the US Navy, he began his graduate work in chemistry at the University of Hawaii with the late Professor Richard Moore, a long-time member of ASP. He published nine papers as a graduate student, eight of which were first-authored and included prominent structure work on lyngbyatoxin, a causative agent of swimmer's itch in Hawaiian waters. After graduation, Cardellina conducted postdoctoral research at Cornell University with the late Professor Jerry Meinwald and wrote five additional manuscripts.

Cardellina was an assistant and later associate professor of chemistry at Montana State University and published over 50 papers ranging from marine, fungal, and plant natural product chemistry to natural product synthesis to separation and structure/stereochemical determination techniques. Included in this period were a series of studies of Native American medicinal plant metabolites, such as the isolation of parasorbic acid from the cranberry plant, *Vaccinium macrocarpon*[1] and falcarindiol and 3-*O*-methylfalcarindiol from *Osmorhiza occidentalis*, a medicinal plant.[2] This led to a series of papers on the phytochemistry of plants used by indigenous tribes. During this time, he also published one of the earliest papers on the use of step gradients in gel filtration as a new approach to isolation of natural products. This technique is still widely used in natural products research laboratories and the industry around the globe.

Cardellina then joined the National Cancer Institute and was soon named Head of the Natural Products Chemistry Section, a role in which he served for nine years. He was involved in some of the earliest screenings of natural products against HIV infections, which led to the discovery of several important compounds such as the michellamines and calanolides. An unusual paper from this time period was the paper on sustainable harvest of *Ancistrocladus korupensis* (Ancistrocladaceae) leaf litter for research on HIV,[3] taking into account the growing concerns about overharvesting of promising herbal materials. Cardellina's top two papers, both of which have been cited over 450 times according to Scopus, described natural products with inhibitory activity against HIV. He and his NCI team really championed the idea of examining how natural products could influence a wide range of targets, and this resulted in truly seminal research results.

Many compounds with anticancer potential were also discovered by Cardellina's group at NCI, including numer-

He and his NCI team really championed the idea of examining how natural products could influence a wide range of targets, and this resulted in truly seminal research results.

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Like Tyler, Cardellina is a true old-school gentleperson who exudes scientific talent but tempers it with a jovial, friendly demeanor and a great sense of humor.

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ous examples with unique cytotoxicity profiles, and considerable patent activity resulted from many of these studies. This was an amazingly fruitful period for Cardellina and his colleagues; well over 100 papers emerged during his time there in the 1990s. While some of these included papers from earlier work, or collaborations outside of NCI, the level of productivity during this time was extraordinary.

Cardellina at an ASP annual meeting poster session with Stefan Gafner and Jim Gloer. As the chair of the ASP Foundation, Cardellina has spearheaded the distribution of many student awards, like the ASP poster awards.

PHOTO COURTESY: JAMES GLOER

His next major career turn took him to a four-year position as Vice President for Botanical Science and Regulatory Affairs with the Council for Responsible Nutrition, leveraging his extensive chemistry experience and his knowledge of plant natural products and their medicinal use, and generating authoritative reports on botanical supplements. Subsequently, he returned to more chemistry-oriented work at the NCI and the USAMRIID. Throughout these periods, he continued to participate in and publish top-line natural product research leading to a variety of antimalarial, antibacterial, and anticancer agents, as well as specific disease-relevant mechanistic inhibitors including compounds with effects on Chk2 kinase, HIF-1α, key endonucleases and topoisomerases, NF-κB activation, and botulinum neurotoxin. The degree of versatility he has shown over the years is remarkable, as is the depth and breadth of his scientific knowledge.

He is a model of approachability and is equally respectful and comfortable talking with anyone from novice students he has never met to giants of the field.

Cardellina has been extraordinarily devoted to serving ASP on many levels. It is hard to think of a role that he has not embraced over the years. He is currently the chair of the ASP Foundation, whose corpus has more than tripled since he took over its stewardship. He has done an excellent job making sure that the money is being used for good purposes, particularly the funding of travel and research for our young members. He firmly believes that the future of ASP depends on fostering younger members.

He has served as ASP vice president and president and has repeatedly shown his dedication to the society, even when personal issues would have excused his participation. Under his leadership, the ASP Younger Members Committee was formed, which today serves in a great capacity to draw young scientists into the society. He has helped to organize many annual meetings, including the 50th anniversary meeting in Hawaii. He gladly serves as the parliamentarian for ASP business meetings and is known for his cool hand, assisting many ASP presidents with the proper and orderly conduct of these lengthy meetings, particularly when the issues were controversial and/or cantankerous. He also was the book reviewer editor for the *Journal of Natural Products* for many years.

Cardellina's career mirrors that of the prize's namesake, Varro Tyler. Tyler began his career with military service in WWII. He then returned to school for his PhD and began his academic career working with bioactive fungal natural products for a number of years before moving more into the herbal and plant chemistry realm. Cardellina began

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Tyler was "the consummate gentleman, always direct in his thoughts, words, and actions, deeply honest, and always respectful of others' views," and many would describe Cardellina in similar terms.

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his career with military service as an officer in the Navy in the Vietnam era, then returned to school for his PhD and began his academic career working with bioactive marine natural products before moving more into the herbal and plant chemistry realm.

Like Tyler, Cardellina is a true old-school gentleperson who exudes scientific talent but tempers it with a jovial, friendly demeanor and a great sense of humor. He is a model of approachability and is equally respectful and comfortable talking with anyone from novice students he has never met to giants of the field. Cardellina knew Tyler and had a great deal of respect for him. Tyler was "the consummate gentleman, always direct in his thoughts, words, and actions, deeply honest, and always respectful of others' views," and many would describe Cardellina in similar terms. ■

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Inés Cereijo Student Award

Nominate a student or colleague for an AOAC award recognizing their research by December 31, 2021!

AOAC International's Technical Division on Reference Materials (TDRM) sponsors an annual student award for the purpose of raising awareness of the need for method performance evaluation at an early point in a chemist's career. Nominees are evaluated based on a report describing either the use of a reference material for method performance evaluation or the development of a new reference material.

Undergraduate and graduate students are eligible. The award is based on a report that evaluates the use of a reference material for a specific application. The winner will receive $500 USD, a travel grant for the AOAC Annual Meeting, and a one-year AOAC and TDRM membership.

Please visit:

https://aoac.org/wp-content/uploads/2019/08/TDRM_StuAward_Policy.pdf

for more information about the award.

Please visit the AOAC website at:

https://www.aoac.org/wp-content/uploads/2019/08/Stud_Award_App.pdf

and nominate someone by December 31, 2021.

Crawford Receives Suffness Award

By Jon Clardy, PhD

The 2021 Matt Suffness Award has been awarded to Dr. Jason Crawford, an associate professor of chemistry and microbial pathogenesis at Yale University. ASP President Kerry McPhail remarked, "Dr. Jason Crawford is an outstanding recipient of the Matt Suffness Young Investigator Award. He has an inspiring talent for identifying and addressing key questions on mechanisms of natural products biosynthesis and function at the human-microbiome interface. His highly collaborative, interdisciplinary research illustrates the broad appeal and impact of natural product sciences."

Crawford spent his childhood in West Virginia and received his BS degree from Fairmont State University in 2001. His engagement with natural products began with his PhD research in Dr. Craig Townsend's laboratory at Johns Hopkins University. This early work, which dealt with the biosynthesis of fungal polyketides, established a theme that would be repeated: Crawford showed an affinity for tough problems that had resisted solution and an ability to employ multiple disciplines to solve them.

The pathway he studied was difficult to analyze because there appeared to be no easily identifiable intermediates – a substrate went in, lots of things happened, and a product came out. One review called it *Nature's Black Box*. Crawford's "deconstruction" of this pathway illuminated some previously hidden steps and featured a highly productive collaboration with mass spectrometry and structural biology laboratories. His research resulted in several highly influential papers (*Science,* 2008 and *Nature*, 2009). He then moved to my laboratory at Harvard Medical School, where he was supported by a Damon Runyon Foundation Fellowship whose stated mission is "identifying brave and bold scientists early in their careers and providing them with the resources to make the next breakthroughs in cancer research."

Crawford extended his skills in the mechanistic enzymology of natural product biosynthetic enzymes into structural and functional studies. He focused on the rich natural product chemistry of bacteria that preyed on insect larvae – *Xenorhabdus* and *Photorhabdus*. He explored "unculturable" bacteria in a collaborative project with Northeastern University microbiologists.

He began his independent career at Yale with a wildly ambitious project that was being pursued by multiple laboratories around the world: the structure of colibactin, a DNA-damaging small molecule produced by *Escherichia coli* and associated with colon cancer. While some important questions about colibactin chemistry remain to be answered, Crawford's research has made a major contributor to its solution. And he enlisted a top synthetic chemist (Dr. Seth Herzon) and structural biologist (Dr. Steve Bruner) as collaborators. Recently Crawford began publishing on the chemistry of the gut microbiome, a field in which natural product research skills can be highly productive.

Dr. Jason Crawford
PHOTO: MARISSA CRAWFORD

The Matt Suffness Award recognizes both Crawford's past contributions to natural products research and looks ahead to many future contributions. This award recognizes the contributions of younger natural products scientists and provides a forum for them to share their research. The award was created to honor the memory of Dr. Matt Suffness, who served as ASP President in 1989-1990. During his term he initiated the "Young Investigator's Symposium" and was a strong supporter of young investigators trying to establish successful research programs and careers.

Crawford commented that, "The Matt Suffness Award means quite a lot to me, as it is the first award that I have received in the field of natural products, a field that I have loved for more than 20 years now." ■

He has an inspiring talent for identifying and addressing key questions on mechanisms of natural products biosynthesis and function at the human-microbiome interface.

ASP Fellow Kingston Honored with Symposium

By Brian Murphy, PhD

Professor David Kingston
PHOTO: APRIL DOW

On November 6, 2021 the Virginia Tech (VT) Department of Chemistry hosted a symposium to honor the career of University Distinguished Professor David Kingston. The symposium, organized by VT Professor Paul Carlier and team, marked the retirement of Kingston from a 60-year scientific career (48 years of which were spent at VT). The 65 persons in attendance comprised former students, postdocs, colleagues, and loved ones, who all travelled to celebrate his illustrious career. This showing was symbolic of the legacy and lasting impact that Kingston had on so many lives, as the night was filled with a blend of both professional and deeply personal gratitude from former trainees.

The symposium opened with a series of short talks from past trainees. A former postdoc and current professor at the University of Hawai'i Hilo, Dr. Shugeng Cao, summarized a decade of his lab's efforts to discover bioactive natural products from fungi isolated from botanicals and marine sources. Dr. Liva Rakotondraibe, former postdoc and currently an associate professor at Ohio State University, discussed an innovative, one-dimensional, NMR-based dereplication pipeline designed to prioritize natural product collections. This was followed by a presentation from Professor Qiao-Hong Chen at California State University Fresno, a former Senior Research Fellow of the Kingston lab. Dr. Chen detailed her lab's efforts to optimize the microtubule stabilizing agent zampanolide for possible treatment of prostate cancer. Dr. Maria Belen Cassera, a previous VT assistant professor and currently an associate professor and Innovation Fellow at the University of Georgia, presented her screening efforts to discover novel antimalarial agents. As a former PhD student in the Kingston lab, I presented ongoing cultivation-dependent and independent research that documents distribution patterns of natural products in the environment.

At a break in the talks there was an opportunity for additional scientists to speak. Like the presenters before them, former PhD recipients of the Kingston laboratory Drs. Jason Clement and Russell Williams shared a heartfelt appreciation to Kingston for both professional, personal, and spiritual guidance over the course of their careers. This was a common theme of what was to be an intimate night of reflection and praise.

It is important to note that the aforementioned presenters, all trainees of the Kingston lab, spanned areas of expertise that were hallmarks of Kingston's research program over the course of more than a half century: synthetic chemistry, cancer biology, natural products drug discovery, neglected tropical disease research, and low-middle income country capacity building. As the night progressed, one of Kingston's greatest accomplishments was emphasized: the training of young scientists. Over 60 years of service he was advisor to 46 postdoctoral researchers, 29 visiting scholars, and 78 graduate students (27 MS, 51 PhD).

Carlier wrapped up the session with a presentation on Kingston's latest legacy, advocacy for the formation of a drug discovery institute both at the university and state levels. Kingston was instrumental in creating the Virginia Tech Center for Drug Discovery (VTCDD) (www.vtcdd.science.vt.edu). The center boasts greater than 40 affiliated faculty across eight colleges at VT. Since its inception in 2012, the effort to discover drugs has expanded to include a statewide effort titled the Virginia Drug Discovery Consortium (VaDDC)

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Kingston surrounded by his former trainees at Virgina Tech on November 6, 2021.

ASP Fellow Kingston Honored with Symposium

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(https://vaddc.org/). Founded in 2015, VaDDC includes VT, the University of Virginia, Virginia Commonwealth University, George Mason University, and Virginia Bio. Kingston served as the first chair of this organization.

The night concluded with a dinner and additional speeches from colleagues and family, who thanked Kingston for his years of service toward drug discovery, mentorship, and community building through his faith. In front of a backdrop of a picture collage that documented images of trainees over the decades, Kingston took to the stage to offer thanks to his team and personal reflection on his career: *"I get to sit in my office and come up with ideas. You get to go in the lab and actually execute them. So, everything I've been able to do is really due to you. To your help, to your hard work in the lab, to your drafting publications for me to fine tune and submit and everything else that you did in the lab…it's why I've been able to do what I did. Without you, who knows where I'd be, but I wouldn't be here giving thanks to you tonight."* ■

Report from First Audrey Bingel Fellow

By Nassifatou Koko Tittikpina, PhD

On December 10, 2019, I was informed I was awarded the first Audrey Bingel Fellowship, and it was indeed a happy day! The funds from the fellowship helped me to go further in my research work and my academic career. The fellowship allowed me to devote more time to research and teaching and to apply for other fellowships to further my career. The Bingel Fellowship was of tremendous help, especially with the COVID pandemic which brought on so many personal and professional challenges. I am greatly thankful to the ASP for this assistance.

Due to COVID-19, a visiting lecturer from Senegal, who was responsible for analytical chemistry, bromatology and analytical expertise courses with the faculty of health sciences at the

University of Lomé, was not able to travel to Togo. Consequently, I was obliged to take charge of the courses, including the practical labs and tutorials. Furthermore, due to COVID-19, I was not able to travel to France as planned to complete research I had started during my PhD. I also could not take part in the July ICNPR 2020 meeting in San Francisco, which was cancelled due to the pandemic. I was able to travel to Senegal as planned from October to December to work on my application for the next phase in my career, senior assistant professor, and I also conducted pharmacognosy research.

Upon my return to Lomé, I finalized my application and sent it to the University of Lomé which sent it to the African institution in charge of the applications evaluation by March 17 (CAMES: www.cames.org). The results were announced in September, and I am happy to report that I am now a senior assistant professor at this institution.

In addition, the Bingel Fellowship helped me to have time to apply for funding from other external sources, including:

- Organization for Women in Science for the Developing World Early Career Fellowship
- Fulbright African Scholar Fellowship
- International Foundation for Science basic research grant
- African Academy of Sciences Future Leaders African Independent Research program

I was awarded the first two fellowships! With the Fulbright fellowship, which began in October, I am working on metabolomics approaches for the investigation of two plants used against malaria in West Africa and their fingerprinting for standardization. In addition, I have submitted nine papers for publication, and seven have been accepted and published.

The Bingel Fellowship has been of tremendous help during a period which was chaotic for most of us around the world. I am grateful to have been the first recipient and would like to express my dearest gratitude to the American Society of Pharmacognosy for this support. ■

Dr. Nassifatou Koko Tittikpina
PHOTO:DOLAGBENOU KOFFI

2022 ASP Annual Meeting Update

Considering the significant challenges and "alone time" created by the virus, we have done some significant soul-searching in regard to how the ASP community can contribute to global issues including emerging viral infections and climate change.

By Mark Hamann, PhD

After two years of canceled meetings due to COVID-19, the local and scientific committees for the July 23-28, 2022 ASP meeting are anxious to provide a truly memorable experience in Charleston. Considering the significant challenges and "alone time" created by the virus, we have done some significant soul-searching in regard to how the ASP community can contribute to global issues including emerging viral infections and climate change. Thus, the special symposia this year include numerous contemporary approaches and applications for natural products without compromising the timeless role of natural products to human health.

ASP has secured rooms at the Embassy Suites by Hilton Charleston Airport Hotel and Convention Center for just $159 per night. This facility is conveniently located near Charleston International Airport which provides direct flights from most major cities in the country and is a short distance to the diverse attractions to be found in this vibrant and historical city.

Session chairs and plenary/invited lectures have been identified for most sessions, which include timely topics such as the emerging role of CryoEM and computational approaches in natural products-based drug discovery, innovations in cancer research, cannabinoids, the role of natural products in carbon sequestration and, of course, the role of unique prototypic natural product structures for the control of SARS-CoV2 and other emerging viral diseases, to highlight a few.

Due to the lapse of time since our most recent meeting, the conference will be extended for one day which will be dedicated to ASP award winners for 2021 and 2022. Financial support has been secured for students and new investigators in need of help with travel expenses and can be requested during abstract submissions. In addition, ample time has been provided to allow attendees to socialize and catch up with friends and colleagues.

Historic Old Charleston

The venue is just a ten minute drive to downtown Charleston's historical sites and restaurants. Shem Creek, just north of the peninsula (15 minute drive from the hotel), is a small shrimp-boat harbor featuring local fresh seafood restaurants, bars, kayaking, waterboarding and fishing. Just south of the peninsula is Folly Beach, a favorite of surfers and beach goers, and Kiawah Island, which provides first class golf, tennis and beaches as well as fine dining and the amenities of the Sanctuary, a five-star resort.

Charleston was made famous in part due to the development of the natural product indigo used as a dye as well as the unique diversity of food and fiber crops that grow well in the rich soil of the Lowcountry. In the past the city has been severely damaged by the Revolutionary and Civil Wars, a major hurricane, earthquakes, tornadoes and the Great Depression. However, during its 350-year history, it remains a timely model for resilience.

The organizing committee is looking forward to welcoming you to the Palmetto State, providing both an intellectually stimulating meeting as well as fresh and unique memories with your colleagues, friends and family. ■

Thus, the special symposia this year include numerous contemporary approaches and applications for natural products without compromising the timeless role of natural products to human health.

Taking Action: Reviewing ASP Diversity and Inclusion Over 62 Years

By Esther Guzman, PhD

With the end of my term as co-chair of the ad hoc Diversity and Inclusion Committee at the ASP, it seemed a good opportunity to look at diversity and inclusion at ASP through the years. *ASP Newsletter* editor, Dr. Edward Kennelly, shared a picture of the inaugural group that formed ASP in 1959. In a group composed of 89 people, there were 7 women, including one from the Philippines. He also shared a special edition of the *Newsletter* published in 2007 called "The Changing Face of ASP: The Role of Women" (volume 43, issue 4). This newsletter highlighted the achievements of women and their participation in ASP. I read this edition with interest. This issue highlighted the increased participation of women in the society, the fact that many awards received at the junior level seem to be equally distributed among male and female members, and the disparity in awards recognizing lifetime achievement as at that point there were no female Farnsworth Award recipients and no female honorary members. I also revisited the newsletters from 2017 (Vol 53, issue 4 and Vol 54, issue 1), when the lack of female speakers at the 2017 annual meeting called to attention the need to increase representation at the ASP annual meeting and the society as a whole, which led to the creation of this committee.

In 2007, graphs showing the number of awards by gender were generated by looking at the lists maintained on the website. I repeated this exercise and looked at the recipients of the main awards in our society, as well as our leadership. Honorary members, ASP fellows, and members of the executive committee reflect those who currently hold those titles. For the presidents and recipients of the Farnsworth, Suffness, and grant awards, the lists show all recipients through the years. We have had 62 presidents of ASP to date, of which only five are female. There are currently 39 ASP Fellows of which nine are female. Of the 35 recipients of the Farnsworth award, only one is female, and of the 24 Suffness Young Investigator Award Recipients, only four are women. Meanwhile, only two of the 16 current honorary members are female.

An encouraging sight was the current composition of our executive committee that has almost the same number of women and men. A graph was constructed showing these results as percentages (Figure 1a). Since our aim is to be more inclusive, not only with women, I went through the lists and marked how many Blacks, Latinx and Indigenous people have been in leadership positions or received awards in our society based solely on their pictures and last names, and sometimes a quick google search (Figure 1b). To provide perspective, I asked the excellent ASP business manager, Ms. Laura Stoll, for the composition of our membership as well as meeting attendance in the last few years and plotted this along with information contained in the above-mentioned newsletters (Figure 1c). While I expected to see a marked difference from the numbers shown in 2007, it was sad to see that, although we have improved, we still have a long way to go.

One of the points made in the 2007 special issue is that "we must be vigilant in encouraging and supporting our best students, regardless of their gender or other demographic." Dr. Brian Murphy took it a step further in the 2017 newsletter and called on the society to make a concerted effort to include more women speakers at the next annual meeting. I believe that Murphy is correct, and that this active effort to include individuals from underrepresented groups (women, Blacks, Latinx,

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One of the points made in the 2007 special issue is that "we must be vigilant in encouraging and supporting our best students, regardless of their gender or other demographic."

Taking Action: Reviewing ASP Diversity and Inclusion Over 62 Years

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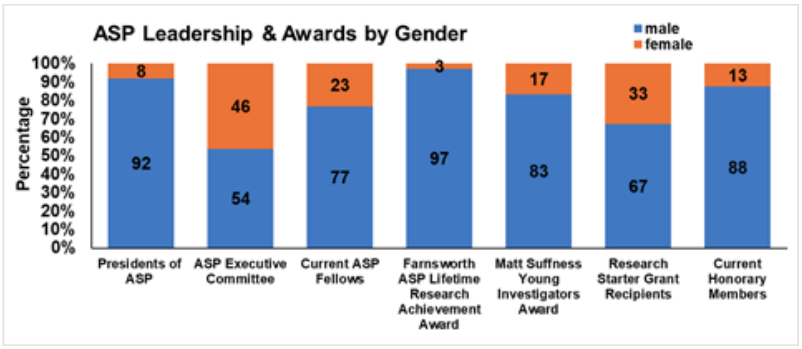

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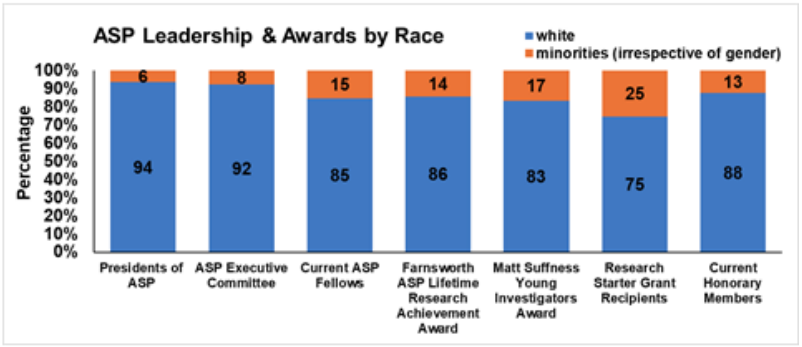

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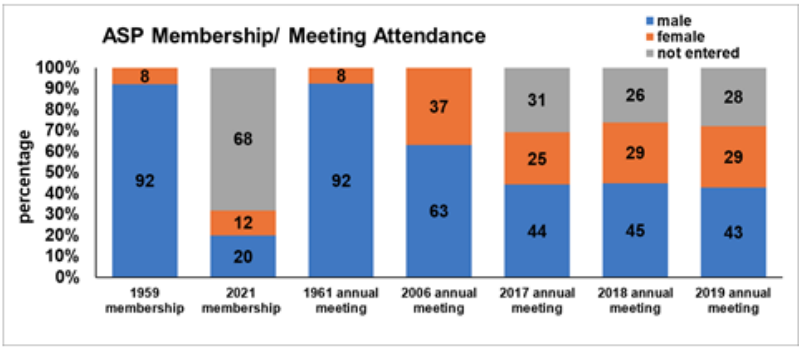

Figure 1a. ASP Leadership & Awards by Gender. The data for this figure was obtained from the lists with profile photos maintained at the ASP website. Honorary members, ASP fellows, and members of the executive committee reflect those who currently hold those titles. For the Presidents and recipients of the Farnsworth, Suffness, and Grant awards, the lists show all recipients through the years.

Figure 1b. ASP Leadership & Awards by Race. Using the photos and last names from the lists mentioned above, it was possible to get an approximation of awards and leadership positions held by Blacks, Latinx, or Indigenous People.

Figure 1c. ASP Membership/Meeting Attendance. 2021 Membership and 2018 and 2019 meeting attendance numbers were provided by ASP Business Manager. Data for older meetings and 1959 membership comes from past issues of the newsletter.

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I believe that Murphy is correct, and that this active effort to include individuals from underrepresented groups (women, Blacks, Latinx, Indigenous people, persons with disabilities, non-binary and transgender people) must be taken in all aspects of the society.

Taking Action: Reviewing ASP Diversity and Inclusion Over 62 Years

If we want our society to persist, then the speakers at our annual meeting, the leadership, and the awards recipients must be representative of the makeup of our membership.

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Indigenous people, persons with disabilities, non-binary and transgender people) must be taken in all aspects of the society. We must actively seek to make sure our awards and leadership are reflective of the current makeup of our society membership and that speakers and participants at our annual meeting are representative of the society membership makeup. The numbers show that this is of the essence. The time is past for passively hoping that the numbers will correct themselves.

Why is the diversity of our leadership and award recipients important? Because it matters to the future of the society. If we want our society to persist, then the speakers at our annual meeting, the leadership, and the awards recipients must be representative of the makeup of our membership. Women have been members of the society since its inception. They have contributed to our society and their fields of science. Clearly, more than one women member is worthy of a lifetime achievement award. The nine women fellows are examples for all of us women members of the next generation. Their presence shows me that it is possible for women to be as successful and accomplished in pharmacognosy as their male counterparts. Fellows and Farnsworth recipients Dr. Phil Crews and Dr. Rachel Mata are excellent examples for us all, but especially for those of us who come from underrepresented groups. Having people who look like us succeeding in their careers inspires the next generation of scientists. Having that success recognized by the society lets us know that this society welcomes us. Moreover, when we start inviting more women and individuals from underrepresented groups to present their research and when we consider more of them for awards, the whole society will realize that all of them are doing great science. That is why we want them in the society. Our gender, accents, or skin color do not affect our intellectual prowess. Once women and underrepresented scientists are given an equal opportunity to present their research to their colleagues, the need to go out of our way to include them will cease to exist, as their scientific achievements will speak for themselves.

We are making progress in our efforts to increase representation. The current ASP president is a very accomplished scientist who happens to be a woman and so will be our next president. The lack of representation of speakers at the 2017 annual meeting led to the formation of the ad hoc Diversity Equity and Inclusion (DEI) Committee. Dr. Kerry McPhail, president of ASP, is considering making the DEI Committee a permanent committee of ASP. I hope we will all support this decision, as this reflection shows us that there is more work to be done in this area.

The establishment of the Audrey S. Bingel Fellowship for Female Scientists should assist female scientists at ASP in career transitions or increase their likelihood of success in their current career. The COVID-19 pandemic has affected the careers of women (www.mckinsey.com/featured-insights/diversity-and-inclusion/seven-charts-that-show-covid-19s-impact-on-womens-employment) significantly more than

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Once women and underrepresented scientists are given an equal opportunity to present their research to their colleagues, the need to go out of our way to include them will cease to exist, as their scientific achievements will speak for themselves.

The fact that we care enough to form an equity and diversity committee and to reflect on our progress tells us we are on the right path.

Similarly, if we are choosing award recipients or considering nominating someone, we will try to make sure that the candidate pool is more diverse.

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those of men, probably because many have the lion's share of child rearing and, in some cases, housekeeping. Because of those same reasons, even in the absence of a pandemic, women sometimes leave their careers. Hopefully this award will assist some of those women, helping them be successful.

One of the biggest accomplishments of the DEI Committee to date was the creation of an ASP internship program for Black, Indigenous and Latinx undergraduates. The first cohort just completed their internships, and hopefully this experience will lead them to careers in one of the many disciplines encompassed by pharmacognosy. If these young people become members of ASP, having role models within the society may make them more likely to remain lifetime members of the society. A list of actions that will help create a more diverse annual meeting was also created by the DEI Committee to assist the organizers of future meetings. The fact that we care enough to form an equity and diversity committee and to reflect on our progress tells us we are on the right path. Hopefully, we will continue to put our collective efforts into giving more opportunities for members from underrepresented groups to be recognized for their work.

While these efforts as a society are great, we also need to make more efforts individually. Many members of ASP have very visually diverse laboratories as attested by the pictures shown in their presentations. I hope we will all aim at maintaining this trend and, if we notice that our labs could use more diversity, make a concerted effort to attract those members to our lab. If we serve on a hiring committee and notice that all applicants are white males, we will call attention to this to increase the diversity of the candidate pool. Similarly, if we are choosing award recipients or considering nominating someone, we will try to make sure that the candidate pool is more diverse. Because of biases in promotion committees (www.pewresearch.org/social-trends/2018/01/09/women-and-men-in-stem-often-at-odds-over-workplace-equity/), having women and individuals from underrepresented groups being recognized by their work in the society, or even being invited to present at the annual meeting, may also help them advance in their career. Such success will hopefully also mean keeping them as members of ASP. Finally, if we are serving as section leaders in a meeting, we should bring to the attention of our organizers when the session lacks diversity.

I hope that when we reflect on our progress in another 15 years, the growth in our diversity and inclusion will be more obvious. ■

I hope that when we reflect on our progress in another 15 years, the growth in our diversity and inclusion will be more obvious.

Hot Topics in Pharmacognosy

So What Do You Do When Microbes Are Resistant to Current Antibiotics?

By David J. Newman, DPhil

INTRODUCTION

Although the press commentary on lack of new antibiotics has tended to wane over the last 18 months or so due to the emphasis on CoV-2 and its manifold variants, there is still an absolute need for new (or even reworked) antibiotics due to the increased infections due to what are frequently known as the ESKAPE pathogens: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* spp. A paper by Mulani et al.,[1] though published in 2019 in the open journal *Frontiers in Microbiology,* is still valid and gives an idea of the difficulties in finding reasonable treatments against these organisms, to say nothing about multidrug resistant (MDR) and extensively drug resistant (XDR) bacteria, plus the extended spectrum β-lactamase (ESBL) and carbapenemase-producing Gram-negative bacteria. As of the time of writing (late September 2021) this paper has been cited by over 150 journals in PubMed. One area of drug structures that is often mentioned in the 150 citations are variations on antimicrobial peptides.

1. VANCOMYCIN PLUS COLISTIN/POLYMYXIN E TO PRODUCE VANCOMYXINS

In a very recent paper in *ACS Infectious Diseases*, van Groesen et al.,[2] from a cooperative relationship between Leiden University and Utrecht University in the Netherlands, described their successful "melding" of two peptidic antibiotics, though people often do not realize that vancomycin (**1**) is in fact based on a linear peptide core, coupled via variable linkers to a series of variations on colistin/polymyxin E (**2**) which is a true cyclic peptide.

By using different linkers between the two major components, with some linked to the sugar molecules at the "top" of vancomycin (as drawn) and others with variable spacings in the center of the molecules, a series of potential agents with activities ranging from 16 micrograms/ml to 8 nanograms/ml for MIC values were shown, where the individual parent antibiotics had values in excess of 128 micrograms/ml (effectively inert). A very useful control was also run where the two unlinked antibiotics were run. In a small number of cases, that combination was more effective than the linked molecules, but this was not the norm.

Thus, by simple chemical modifications, two old antibiotics were found to be excellent leads to potential drugs against the ESKAPE pathogens. Due to the many modifications by the Boger group, which were discussed in an earlier *ASP Newsletter,* the modifications of those compounds using the colistins shown here may well lead to very useful antibiotics.

2. CHEMICAL SOCIETY REVIEWS, 2021

A superb review of the possibilities surrounding both natural product peptidic antibiotics, whether pure NPs, modifications or totally synthetic but based upon peptide structures, was published in 2021 by the Spring[3] group from the University of Cambridge, UK. This 60-page review is full of information as to what can be "done" by talented chemists and biochemists when using amino acid moieties, from natural though partially synthetic to synthetic peptides with the aim of producing potent molecules against microbial infections. Due to the size of the review, I will only touch upon a couple of examples. It should be pointed out that *Chemical Society Reviews* was almost always covering the synthetic chemistry and physical chemistry aspects of chemistry, but over the last two to three years, very significant reviews around natural product-based chemistry have been appearing in this journal, mainly due to changes in the editorial board.

Though I cannot reproduce the table due to copyright restrictions, Table 4 in the article gives a non-exhaustive listing of 16 such agents that have entered clinical trials with some failing others currently in Phase 3. There are significantly more such agents in various stages of clinical trials, but the speed of such trials and

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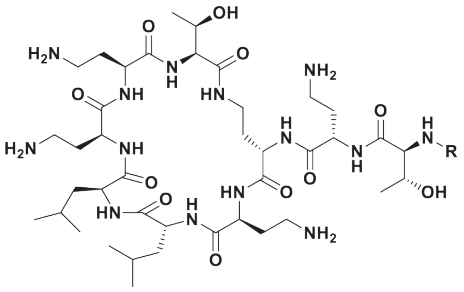
Structures



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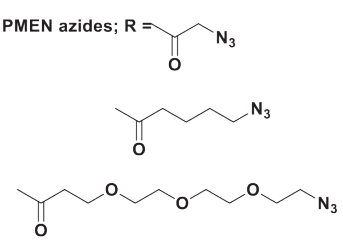
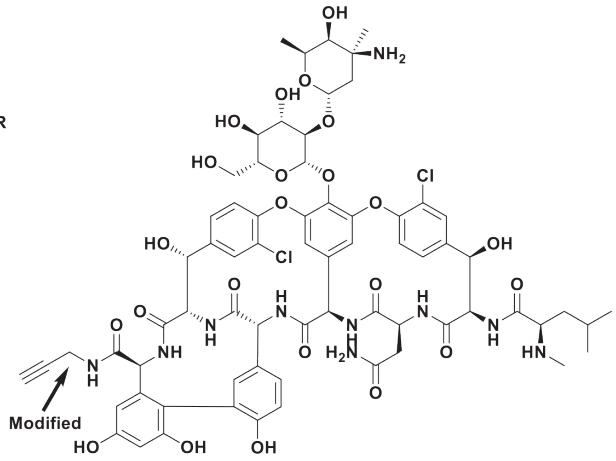
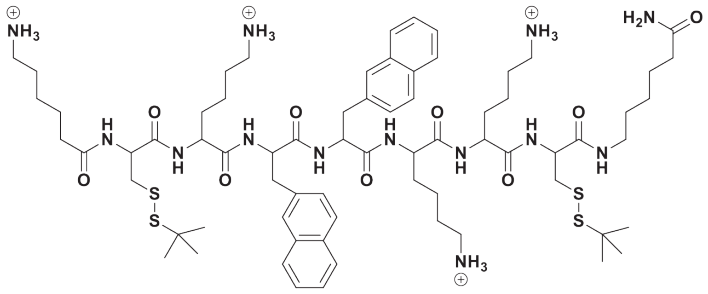


2. Colistin E Modifications



1; Slightly Modified Vancomycin

3. Cathelicidin-BF-15-a4 (ZY4)



4. P9Nal(SS)

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Thus, as can be seen from just these examples, the chemical, and at times biochemical and/or genomic, systems are available, and it is up to scientists (of multiple flavors!) to continue to investigate nature's "gifts" in order to overcome the current lack of antibiotics against a variety of significant diseases.

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their costs may well be a reflection of what happened a couple of years ago when the small molecule antibiotic fidaxomicin was approved but only produced sales of <$80 million versus development costs of more than 10 x that figure.

However, to show what can be done by relatively simple modifications of a base natural product, in 2019 Mwangi et al.[4] reported the formation of a cyclic peptide following the addition of two cysteine residues to a peptide cathelicin-BF-a3 derived from a component of the venom of the snake *Bungarus fasciatus*. This cyclized derivative was known as ZY4 (**3**). This cyclic peptide demonstrated excellent activity against *P. aeruginosa* and *A. baumannii* strains with MICs of between 2 and 4.5 micrograms/ml. In addition, it was not hemolytic nor did it cause inflammation. There is a table in the SI for this paper that demonstrates how efficient it is at inhibiting growth of highly resistant strains of the two microbes above, with their figures being comparable to colistin (which was highly hemolytic), but none of the "regular" antibiotics tested as controls (tobramycin, levofloxacin, kanamycin and carbenicillin) were between 13 and >200 times less potent in comparable *in vitro* assays.

Unnatural amino acids can be used to modify potential AMPs with examples being the use of ornithine, 2,4-diamino-butyric acid, or 2,3-diamino-propionic acid as substitutes for LYS, thus increasing the number of side chain methylenes. Or one can use 2-naphthyl_L-alanine and S-tert-butylthio-L-cysteines as shown by Petraccone and coworkers[5] where they produced a series of peptides with one example being the peptide P9Nal(SS) (**4**).

FINAL COMMENTS

Thus, as can be seen from just these examples, the chemical, and at times biochemical and/or genomic, systems are available, and it is up to scientists (of multiple flavors!) to continue to investigate nature's "gifts" in order to overcome the current lack of antibiotics against a variety of significant diseases. In this regard the short but pithy perspective by Hosisson and Seipke[6] in 2020 should be required reading for anyone aiming to aid in this process. Can these efforts be funded by traditional means? Probably not, as trying to fit these into classical NIH R01 applications in the USA is probably not going to work, but we have to push both government and industry (probably worldwide) to first recognize that there is a problem and then to adequately fund it. ■

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NIH-Sponsored Roundtable on Resilience

By Barbara Sorkin, PhD

At a recent meeting, senior researchers from the NIH Consortium Advancing Research on Botanicals and Other Natural Products (CARBON) Program led off a roundtable. The goal of the session was to describe policies, practices or approaches in place at each consortium component when the pandemic first affected their communities and their research, or policies, practices or approaches they developed in response to the pandemic that were more – or less – effective in supporting resilience of the research and the researchers, and to try to discover unifying themes among the effective approaches as well as share lessons learned.

The CARBON Program Centers all received new awards in July 2020, in the midst of a rising phase of the COVID-19 pandemic in most of the US. Many of the centers explored the potential of interventions for the prevention of COVID infection or treatment of infected patients; some received funding to pursue those projects. Centers on the West Coast were adversely affected not only by the pandemic but also by wildfires in both 2020 and 2021. Some researchers were evacuated during the 2020 California wildfire season, the greenhouse growing material for another Center was threatened by the summer 2021 heat wave in the Northwest, and all the centers were affected by pandemic-related supply chain disruptions, laboratory shutdowns and/or limitations in lab occupancy, as well as hard stops or major decreases of in-person interactions among project personnel and between personnel and clinical trial participants. Nevertheless, the work – and the publications – were resilient.

Prior to the roundtable discussion, Dr. LaVerne Brown, NIH Office of Dietary Supplements and Chair of the **Trans-NIH Resilience Working Group** (https://ods.od.nih.gov/research/resilience.aspx), presented resources developed by the working group for designing resilience studies. She highlighted the working group's conceptual graphic of resilience and demonstrated the use of the **Resilience Research Decision Tool** (https://ods.od.nih.gov/pubs/resiliencedesigntoolandkeyterms.pdf) for implementing key criteria for resilience study designs. During the roundtable discussions, some presenters referred to the Trans-NIH Resilience Working Group's definition of resilience: ***resilience encompasses the capacity to resist, adapt to, recover, or grow from a challenge.***

Major themes which emerged among the effective approaches to increase resilience were:

- preparation,
- flexibility,
- communication,
- teamwork and
- awareness of differences in response between individuals and research projects as well as differences in the way different aspects or types of resilience may respond to disruptions or mitigating approaches.

Dr. John MacMillan, University of California, Santa Cruz (UCSC) reported that UCSC is currently developing detailed disaster plans for the campus, with every lab required to have contingency plans for both known and potential disasters. The goal is to be prepared to protect institutional investments and resources and the precious resources assembled through significant

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The goal of the session was to describe policies, practices or approaches in place at each consortium component when the pandemic first affected their communities... and to try to discover unifying themes among the effective approaches as well as share lessons learned.

The question was raised during the discussion whether the lessons learned from the COVID-19 pandemic will be incorporated into individual, community and institutional practices or policies, or forgotten post-pandemic.

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investments of time, effort and funds by many researchers. These and the researchers, another critical resource reflecting substantial investment, should all benefit from having emergency plans in place when disruptions occur and through the reassurance of knowing what the emergency plans are.

The question was raised during the discussion whether the lessons learned from the COVID-19 pandemic will be incorporated into individual, community and institutional practices or policies, or forgotten post-pandemic.

Flexibility or adaptability in research foci, research approaches (both experimental and logistical) and researcher interactions were described by all the centers.

Research foci: Several centers were able to rapidly begin to explore applicability of interventions for the prevention or treatment of COVID-19.

The order or immediate focus of research within planned projects was shifted to adapt to COVID-related limitations, often via an initial focus on tasks that could be effectively accomplished remotely:

- training in methods to be used on return to the lab,
- other detailed planning for the return to the lab,
- resequencing of planned experiments to accommodate supply chain disruptions, or
- use of computational rather than bench approaches.

Flexibility in research approaches and the use of newer methods:

Dr. Gailen Marshall, University of Mississippi Medical Center, described how, when the pandemic shut down the center, ongoing clinical trials were rapidly divided into three groups.

- Those that could be paused without risk of significant adverse effects were paused.
- Those critical trials which could be continued using telemedicine were continued using telemedicine

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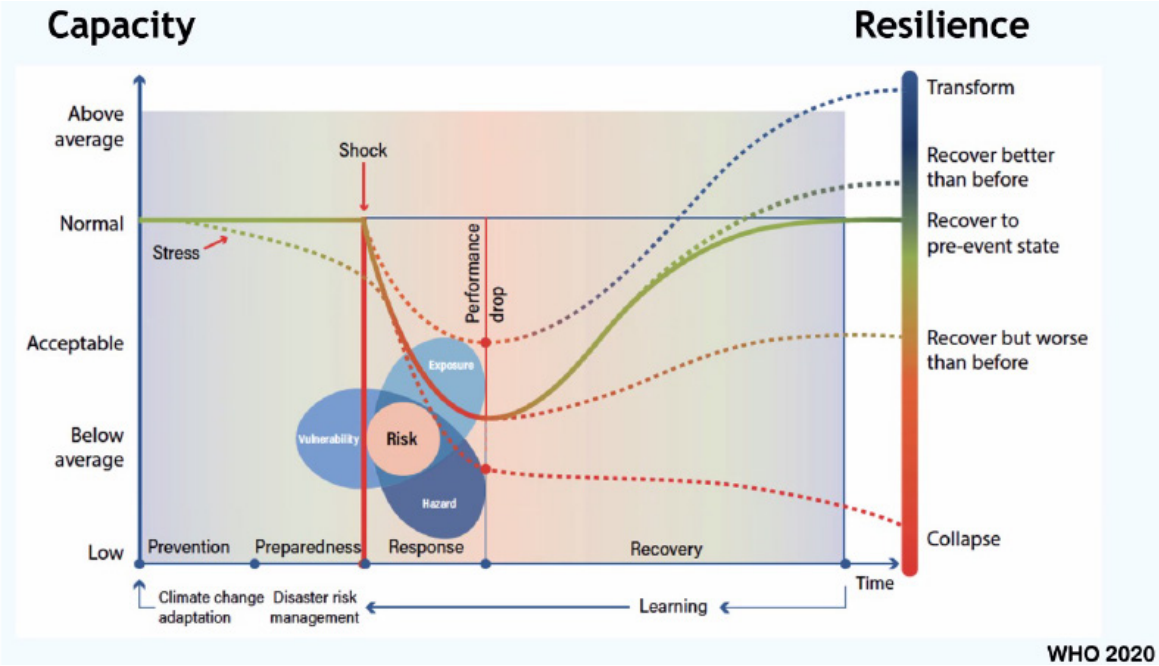
preparation · flexibility · communication · teamwork · awareness of differences



MacMillan noted that many research trainees deserve recognition for finding novel ways to increase and improve communication during the pandemic, such as through social media.

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(with appropriate approvals for changes in protocol). Prior preparation facilitated this flexibility.

- Those critical trials requiring in-person visits were converted to "scattered participation," with clinical coordinators essentially making house calls in full protective gear.

Flexibility in recruitment/hiring/promotion: MacMillan suggested that those who expect to hire junior researchers within the next five to ten years should be cognizant of the restrictions that COVID-19 has placed on these people's ability to conduct research at least during the 2020-2021 timeframe. MacMillan encouraged the CARBON meeting participants to think more holistically about the criteria used to evaluate such candidates, rather than only focusing on track records.

NIH policy flexibilities intended to mitigate pandemic-related delays are summarized here: https://nexus.od.nih.gov/all/tag/covid-19/

MacMillan noted that many research trainees deserve recognition for finding novel ways to increase and improve communication during the pandemic, such as through social media. He said he thinks that in their center communication is better now than ever before because of the efforts of these younger scientists. MacMillan suggested that principal investigators would benefit from giving trainees more latitude to communicate about science and their research and to interact on multidisciplinary teams in new, nontraditional ways.

MacMillan said that although NIH and other institutions are already addressing mental health resiliency, including by offering relevant workshops, additional efforts are needed to support the mental health of research trainees.

Online NIH resilience training webinars are available at this link: https://www.training.nih.gov/virtual_nih_activities_for_trainees_outside_the_nih

Marshall suggested that candidates' abilities to work as a team should be weighed along with their individual talents when building a research team. He added that senior researchers have a responsibility to make people feel like part of the team even if they are physically isolated.

Dr. Giulio Pasinetti (Icahn School of Medicine at Mt. Sinai) noted that clinical research requires teamwork as well as flexibility. Different types of resilience include:

Diversity: Pasinetti noted that ISMMS increased recruitment from disadvantaged communities during the pandemic, finding that this led to better adaption to the pandemic-associated disruptions.

Younger researchers: MacMillan noted that the pandemic is affecting trainees, such as graduate students and postdoctoral fellows, more significantly than other researchers. It has affected their career trajectories and job stability, for example. Metrics that are critical for career development are more difficult to achieve amid pandemic and other disruptions. Supervisors need to make every effort to make time available for trainees to do their research while observing COVID-19-related restrictions. Supervisors should apply flexibility, for example, considering computational projects when trainees cannot physically work in the lab.

Dr. Jacob Raber, Oregon Health and Science University, noted that it is important to avoid generalizations, that individuals respond differently to environmental stressors; consistent with the results seen in animal model studies, individual humans also vary in their responses to environmental stressors, including psychological and physical stressors, such as exposure to second-hand smoke and other environmental toxins, high-fat diet, radiation, surgery, pathogens, and pharmacological treatments. Some adapt extraordinarily well, others continue as usual, still others have a much harder time adapting. He believes it is possible to support people in becoming (more) resilient and that it is especially important to support those who live alone, for whom the social aspect of work in a laboratory with more people present may be disproportionally important.

Marshall noted that resilience requires a mutual support mechanism, even for people who live alone. He recognized, however, that some people prefer to be alone; respecting their preference is important.

Raber reported that their group observed differences in neuronal activation between cohorts of mice studied prior to and during the height of the pandemic (normal vs. personnel density-restricted (quieter) conditions). ■

MacMillan said that although NIH and other institutions are already addressing mental health resiliency, including by offering relevant workshops, additional efforts are needed to support the mental health of research trainees.

Behind the Scenes in Pharmacognosy

Antibacterial Peptides from Ghost Pepper

By Erin A. Conley, PhD Candidate

The August 2021 issue of the *Journal of Natural Products* featured an article from the Hicks lab at the University of North Carolina at Chapel Hill, which investigated antimicrobial peptides (AMPs) from a hot new source organism. Titled "Too Hot to Handle: Antibacterial Peptides Identified in Ghost Pepper," this article highlights the utility of complementing *in silico* predictions with peptidomics and bioactivity assays in the discovery and characterization of AMPs from plants. Following, Dr. Leslie Hicks and her graduate student Kevin Culver discuss their article, pets as lab mascots, and how Kevin came to be known as the "peptide whisperer." Full article here: https://pubs.acs.org/doi/10.1021/acs.jnatprod.1c00281

How did you become interested in investigating antimicrobial peptides from ghost peppers?

Culver: I'm a pretty big fan of spicy foods in general. I have a collection of hot sauces. There seems to be a history of medicinal use from peppers, and there are a few AMPs that have been published from peppers, but it seems like it's a little underexplored. I thought that trying ghost pepper would be interesting, and I got some really good data out of it.

Where did you collect your ghost peppers?

Culver: We have a greenhouse space where we typically will grow our plants, so we purchased the ghost pepper seeds and then grew them there.

Could you summarize for a broad audience the major takeaways of the paper?

Culver: We were able to do a lot of *in silico* AMP predictions and see a number of potential AMPs from the plant. We screened the extracts for bioactivity and were able to see exciting antibacterial activity against several different pathogens. We ended up attributing the activity to two novel AMPs that don't really classify into any of the known major plant AMP families. We were able to determine the full sequences and experimentally determine the disulfide bond linkages. We did a lot of additional characterization on one of the AMPs which was much more abundantly expressed. We looked at the mechanism of action and saw that it is membrane-lytic. We were able to determine that it is non-hemolytic, which was exciting. We did a lot of biological characterization. We have collaborators at USF that can screen against an ESKAPE pathogens panel, and we were able to see a lot of activity against those pathogens.

Who helped contribute to the success of this project?

Culver: Definitely our collaborators in the Shaw lab at the University of South Florida did a lot of the antimicrobial assays, so that was a big contribution. My lab mates in general helped to guide me with the data analysis.

Hicks: The PepSAVI-MS was established by one of my first

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The Hicks lab at University of North Carolina at Chapel Hill. Front row (L-R): Abigail Hall, Wenya Jian, Hailey Lewis, Conrad Hartman, Kevin Culver, Amanda Smythers, Megan Ford, Samantha Balboa. Back row (L-R): Saher Mubarek, Wyatt Schug, Holden Rogers, Tessa Moyer, Patric Sadecki, Anthony Iannetta, Nicole Parsley, Leslie Hicks.

PHOTO: ALICE ZHAO

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graduate students, Christine Kirkpatrick, and that pipeline enables detection of things that can't necessarily be predicted.

Who came up with the catchy title?
Culver: That was actually Nicole Parsley, a former graduate student.

What was the most exciting day in the lab when you were working on this project?
Culver: Probably the initial bioactivity screening. It's pretty rare to see so much activity when we screen plants like that, so that was pretty exciting.
Hicks: We had three [graduate] students on this project when Kevin came into the lab, and we had many undergraduates who had grown 80 plant species. We know cyclotides are in these *Viola* species, and we had done a lot of cool work in *Amaranthus.* We have screened a lot of plants, and they might have a little bit of activity or a little bit of a peptide trace. Kevin has the nickname the "peptide whisperer" because he came in and said, "I'd like to try ghost pepper," and boom! Massive signal in his SCX traces, massive activity, beautiful novel peptides, and this is just his first paper.

What was one of the biggest challenges with this work?
Culver: Experimentally determining the disulfide bonds was a little challenging. The spectra were a lot more complex, and, especially for CC-AMP2, we had to do a partial acid hydrolysis, which is a lot of non-specific cleavage, and it was a little challenging to comb through that data.

Were there any surprising findings in the course of this project?
Culver: Basically how unique these peptides seemed, and the fact that they seemed to be pretty broadly expressed, not just across other pepper species that have reference proteomes available but also other plants within the Solanaceae family, which is the family that the *Capsicum* genus is in, so I think that's pretty surprising.
Hicks: Kevin went back in the prediction process to see why these particular CC-AMP1 and CC-AMP2 don't make it through the process. It's because they're in the genome. I think as we discover new peptides that fall outside of these canonical classifications, we can improve those prediction algorithms because it is much higher throughput. Kevin undersells how much work it took to get the sequence and to know where any modifications were. Even with the reference genome, it's not matched to his sample so there can be residue differences that shift masses, so he manually interprets that data. It's not automated proteomics; the characterization is really challenging.

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Greenhouse at UNC Chapel Hill.
PHOTO: HICKS LAB

We screened the extracts for bioactivity and were able to see exciting antibacterial activity against several different pathogens.

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What are favorite social activities of the Hicks lab?

Hicks: Pre-COVID, in the summers, generally there is another mass spectrometry lab on campus, and we would have monthly group meetings and go out with them. Also in the summer we would have what we call the "Glicks Olympics," with the Glish and Hicks labs, so each month we play a sport and there is a trophy that we fight over. We would pick one sport each month, like kickball, or volleyball, or bowling. We would just go play and have fun.

Since COVID, we've had some happy hours online, and beginning last December we would meet at the park all masked up, but it's been less social than before, for sure. We have lab T-shirts, lab mascots on the wall...

You have a lab mascot? What is it?

Hicks: All of my students, we all have animals, so we have...

Culver: Like a pet wall, basically.

Hicks: And then when they graduate, they get a little graduation cap on their pet.

Ghost pepper plants analyzed in this study.
PHOTO: KEVIN CULVER

As someone who has spent time both outside and within academia, do you have any advice for students and early career scientists who are trying to decide which direction to go?

Hicks: I think it's good to keep your options open and keep your eyes open for opportunities. Being as productive as you can regardless of where you're at will leave doors open. [With my students] I try to make sure people know how to network and how to position themselves to open those doors, so people know what they're interested in and what the possibilities are. Keeping options open and continuing to show productivity wherever you are can be really good to leave you flexible in terms of where you can go.

Do you have any general tips for women who are pursuing these careers?

Hicks: I think that it's going to be difficult at times. But if we don't persist, there won't be role models that can change things for the better for later generations. No one is going to say, "Hey wait, this is unfair," if no one had to experience that.

Have you ever eaten a ghost pepper?

Culver: I have not!

Hicks:: You've tasted something with it in there though, right?

Culver: I've had things with ghost pepper, a lot of really hot, hot sauces, but I've never eaten the actual pepper. I've never really had the opportunity, I guess.

Hicks: We don't eat the ones we grow in the greenhouse. My tolerance for spicy is nil. We have a ghost pepper hot sauce, and I've tasted like 3 µL of whatever that substance was and that was sufficient. I have ordered some ghost pepper salsa and ghost pepper queso to have at our lab tamale party in December! ■

We ended up attributing the activity to two novel AMPs that don't really classify into any of the known major plant AMP families. We were able to determine the full sequences and experimentally determine the disulfide bond linkages.

Meet a New ASP Member

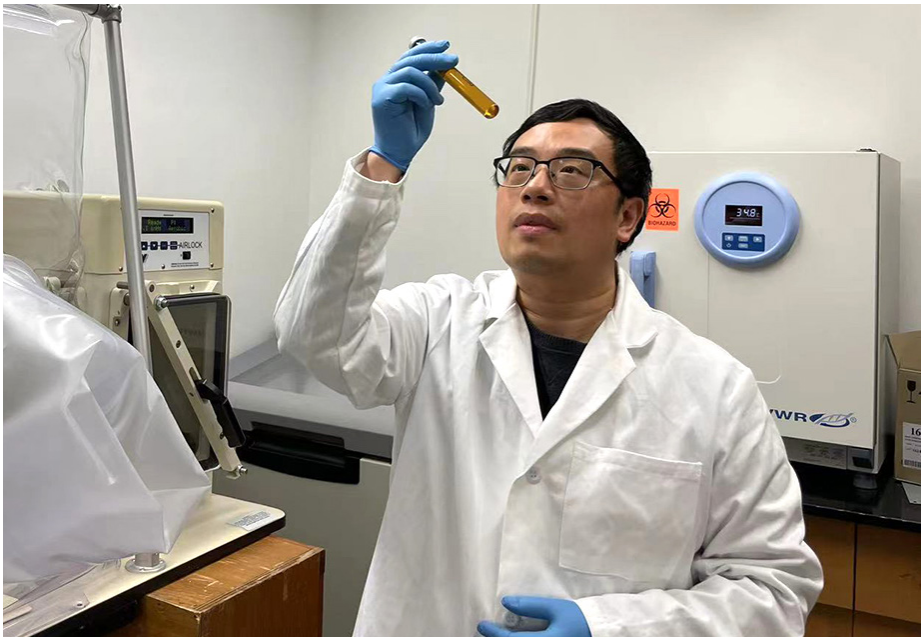
Dr. Jie Li

Dr. Jie Li *is our featured new member in this issue of the* Newsletter. *Dr. Li started his independent career as an assistant professor in the Department of Chemistry and Biochemistry at the University of South Carolina in January of 2019. He has co-authored more than 40 scientific papers and is a member of the planning committee for the 2022 ASP Annual Meeting in Charleston, South Carolina. In addition to the American Society of Pharmacognosy, he is also a member of the American Chemical Society. We thank Dr. Li for taking the time to talk with us and are pleased to officially welcome him to ASP.*

By James Fuchs, PhD

What are your research interests in pharmacognosy?

I have been fascinated with the sophisticated chemical structures of molecules made by nature as well as their biological activities. A major direction of my current research is to discover molecules produced by human microbiota. These microbes live in or on us, and their metabolites have been shown to have a significant impact on human health. However, these metabolites are produced in a very complicated environment and usually in trace quantities. In addition, many of these human microbes are not cultivable under laboratory settings. Facing these challenges, my research uses (meta)genomic and metabolomic approaches in combination with bioassays, aiming to link biosynthetic genes to molecules and further to biological functions.



Dr. Jie Li in his microbial culture room.

PHOTO: DAN XUE

A major direction of my current research is to discover molecules produced by human microbiota.

What is your scientific and educational background?

I received both my BS and MS degrees in pharmaceutical sciences at Sichuan University, a medical university in China, studying natural products chemistry and pharmacology. Then I moved to the College of Pharmacy at The Ohio State University and obtained my PhD in Pharmaceutical Sciences working with Dr. Doug Kinghorn to discover and assay anticancer and cancer chemopreventive natural products. During my almost five years of postdoctoral research with Dr. Bradley Moore at the Scripps Institution of Oceanography, University of California San Diego, I received a systematic training in microbial genetics and enzymology to study the biosynthesis of bioactive natural products, including some intriguing human microbial metabolites. This scientific and educational background strengthened my interests in natural products. I was fortunate enough to have great advisors at each stage of my education, leading me to my current position where I can continue studying natural products.

When did you first learn about the ASP?

My PhD advisor, Dr. Kinghorn, introduced me to ASP. The first ASP meeting I attended in Tampa, FL was an exciting and im-

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Facing these challenges, my research uses (meta)genomic and metabolomic approaches in combination with bioassays, aiming to link biosynthetic genes to molecules and further to biological functions.

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pressive experience. After that, I attended the ASP meeting every year during my PhD studies to present my research. I continued attending ASP meetings during my postdoctoral training and after I became an independent researcher.

What would you like to achieve through your membership in ASP?

I am very glad to be a member of the ASP family. The membership provides me with more opportunities to learn from my peers and senior researchers in my field. ASP provides fellowships and small grants for young investigators and their students, some of which my students and I aim to win in the near future. ASP also organizes a lot of webinars, workshops, and symposiums that help members grow. I am currently serving on the ASP Younger Members Committee, which also provides opportunities for me to learn how to organize and chair younger member symposiums.

What is your involvement in the planning of the 2022 ASP Annual Meeting?

I am currently serving on the ASP 2022 Organizing Committee. My role on the organizing committee is to help organize the scientific topics, overall logistics and accommodations for the ASP 2022 Annual Meeting. This has included initial weekly and now biweekly discussions with committee members to plan the theme and time of different sessions and identify potential session chairs. I have also been involved with communications with chairs of the sessions within my research direction to help organize the sessions and invite speakers, as well as helping to organize workshops, transportations, and exhibitions. The ASP 2022 Annual Meeting will be held in Charleston, South Carolina, a beautiful and historical coastal city. So far, this meeting has been planned to have very diverse and inspiring topics related to natural products, and we have invited many session chairs and speakers who are the leaders in their respective fields. The past two ASP annual meetings were unfortunately cancelled due to COVID, and the ASP 2022 meeting is envisioned to be a great opportunity for re-gathering all scientists loving natural products and studying natural products worldwide. We heartily invite everyone to attend the ASP 2022 Annual Meeting in Charleston, South Carolina!

What do you like doing in your spare time?

I enjoy spending my spare time with my family. My wife and I usually read books with our four-year-old daughter and play games with her. I used to play table tennis in a club and would attend competitions at different levels. I wish I had more spare time so that I could restart this hobby.

How has the COVID-19 pandemic affected your research, teaching, or how you work with your lab group?

My teaching was online during the worst time of COVID but has changed back to in-person since this semester. I used emails and weekly virtual meetings to communicate with my students when our university was locked down. COVID actually also brought a project to me: my lab received a small grant to screen our over 1000 in-house microbial extracts to look for potential inhibitors of SARS-CoV-2 main protease, an essential component for COVID virus' replication.

What has been your biggest adjustment during the COVID-19 era?

Getting used to wearing a face mask during all personal and professional interactions with colleagues and students. ■

COVID actually also brought a project to me: my lab received a small grant to screen our over 1000 in-house microbial extracts to look for potential inhibitors of SARS-CoV-2 main protease, an essential component for COVID virus' replication.

New Members of ASP Winter 2021

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 12 full members and 33 associate members. We look forward to meeting you and learning more about you and your work.

FULL MEMBERS

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Bruker Biospin
United States
Vice President

Mr. Jackson Baumgartner
University of California, Santa Cruz
United States
PhD Student

Dr. Sandipan Datta
University of California, Davis
United States
Assistant Project Scientist

Dr. Leslie Goldstein
NYIT College of Osteopathic Medicine
United States
Associate Professor

Dr. Espen Hansen
Marbio
Norway
Researcher

Dr. Sanem Hosbas Coskun
National Institutes of Health
United States
Biochemist

Dr. Stephen Lee
USDA-ARS Poisonous Plant Research Laboratory
United States
Research Chemist

Prof. David Pereira
University of Porto
Portugal
Assistant Professor

Dr. Chin-Soon Phan
National University of Singapore
Singapore
Postdoc

Mr. Robert Shepherd
University of North Carolina at Greensboro
United States
Undergraduate Research Assistant

Dr. Alexander Sherwood
Usona Institute
United States
Medicinal Chemist

Dr. Christine Theodore
University of Tampa
United States
Assistant Professor

ASSOCIATE MEMBERS

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Dicle Universitesi
Turkey
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Mr. Francisco Benitez
University of Puerto Rico Humacao
Puerto Rico
Undergraduate Student

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University of California San Diego
United States
Postdoctoral Researcher

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CSIR-Central Institute of Medicinal and Aromatic Plants
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Université Cheikh Anta Diop de Dakar
Senegal
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University of Uyo
Nigeria
Graduate Assistant

Ms. Katelyn Grenell
Duquesne University
United States
Graduate Student

Ms. Blessing Ishola
University of South Dakota
United States
Graduate Student

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Centera Bioscience
United States
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Istanbul University
Turkey
Research Assistant

Dr. Muqeet Kazmi
Novartis
Pakistan
Head QA

Ms. Mst Lutfa Khatun
Islamic University
Bangladesh
Graduate Student

Mr. Andrew Kim
University of Rhode Island
United States
Teaching Assistant

Dr. Mahendar Kotte
Jyothishmathi Institute of Pharmaceutical Sciences
India
Assistant Professor

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New Members of ASP Winter 2021

American Society of Pharmacognosy

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Prof. S. D. Shanmuga Kumar
Jyothishmathi Institute of Pharmaceutical Sciences
India
Associate Professor and Principal

Dr. Viqqi Kurnianda
Syiah Kuala University
Indonesia
Lecturer

Mr. Changyeol Lee
University of Wisconsin – Madison
United States
Postdoc

Ms. Hina Manzoor
Nusrat Jahan College
Pakistan
Lecturer

Dr. Carla Menegatti
University of São Paolo
Brazil
Postdoc

Mr. Md Al-Amin Milon
Islamic University
Bangladesh
Graduate Research Assistant

Dr. Aminata Nacoulma
University of Ouagadougou
Burkina Faso
Program Manager

Dr. Patrick Okechukwu
UCSI University
Malaysia
Associate Professor

Ms. Maribel Okiye
University of Michigan
United States
Graduate Student

Dr. Dimitri Perusse
University of Minnesota
United States
Postdoc

Mr. Roberth Riggs Rondilla
Southern Luzon State University
Philippines
Instructor

Mr. Kayode Salawu
University of Ilorin
Nigeria
PhD Student

Dr. Xavier Siwe Noundou
Rhodes University
South Africa
Research Scientist

Mr. Andrew Ssenyange
Santa Rosa De Lima Medical Centre
Uganda
Operations Manager

Mr. Suratno Suratno
Universitas Muhammadiyah Palangkaraya
Indonesia
Researcher

Dr. Talabi Temitope
University of Lagos
Nigeria
Lecturer I

Dr. Udaykumar Vegad
Gujarat Technological University
India
Assistant Professor

Mr. Bryan Walker
Indiana University
United States
Graduate Student

Mr. Joshua Welsch
University of South Florida
United States
Graduate Student

Conference Calendar

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**.
A number of scientific conferences have been delayed or canceled due to the COVID-19 pandemic.
Please check with conference organizers about the status of any in-person conferences.

2022 ASP Annual Meeting

July 23-28, 2022

Charleston, South Carolina

aspmeetings.pharmacognosy.us

ASP Natural Product Sciences Webinar

Bimonthly Zoom Seminars

Thursdays 4 PM ET / 1 PM PT

www.pharmacognosy.us/natural-product-sciences-webinar/

ACS Webinars

Every weekday 2 PM ET / 11 AM PT

https://www.acs.org/content/acs/en/acs-webinars.html

C&EN Webinars

Various Days and Times

https://cen.acs.org/collections/webinars.html

American Society of Pharmacognosy

NIH Office of Dietary Supplements Seminar Series

Sept. 15, 2021 – Jan. 12, 2022

Monthly via WebEx Webinars

ods.od.nih.gov/News/Conferences_and_Workshops.aspx

Environmental Roles, Biological Targets and Applications Gordon Research Conference: Marine Natural Products

March 6-11, 2022

Ventura, California

www.grc.org/marine-natural-products-conference/2022/

Oxford International Conference and the Science of Botanicals (ICSB)

March 28-31, 2022

Oxford, Mississippi

oxfordicsb.org

70th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA)

August 28-31, 2022

Thessaloniki, Greece

www.ga-congress.org

Capital Communiqués

Natural Product-related News from NIH and Beyond

By Barbara Sorkin, PhD

- The continuing resolution signed by President Biden on December 3, 2021, continues the operations of the US Government. The Department of Health and Human Services (including the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC)), and the US Department of Agriculture are among the agencies funded at Federal fiscal year 2021 (FY21) funding levels through February 18, 2022. The Appropriations bills released in October by the Senate for FY22 indicate increases for both the National Science Foundation (NSF; 11%) and the NIH (12%), and the House's increase in the NIH appropriation is even larger.

Dr. Robert Califf

- On November 12, 2021, President Biden nominated for FDA Commissioner **Robert Califf, MD**. Dr. Califf was the FDA Commissioner from 2016 to 2017.
- Following through on President Biden's January 27 directive, the **Office of Climate Change and Health Equity** (www.hhs.gov/ocche/about/index.html) was established in the Office of the Assistant Secretary for Health on August 30, 2021.
- At NIH, the Climate Change and Health Working Group has been re-activated and is now (among other activities) compiling responses to a recent request for information (grants.nih.gov/grants/guide/notice-files/NOT-ES-21-009.html).

- The NSF has posted a new grant opportunity on **Biodiversity on a Changing Planet** (www.grants.gov/web/grants/view-opportunity.html?oppId=336118) which will support both US-only collaborative proposals and collaborations with certain international partners.
- In August the National Institute of Standards and Technology announced **two new kudzu** (*Pueraria montana*, var. lobata) reference materials (www.nist.gov/news-events/news/2021/08/two-new-reference-materials-assist-supplement-makers-measurements), and in October they published values for over 70 analytes in an **avocado powder standard reference material** (www.nist.gov/publications/certification-standard-reference-materialr-2386-avocado-powder).

NEWS FROM NIH

- NIH Director Francis S. Collins, MD, PhD, announced on October 5, 2021 that he plans to step down as NIH Director at the end of 2021. He will continue to lead his lab in the NIH's National Human Genome Research Institute. Dr. Collins has served as NIH Director since 2009.
- NIH recently updated the "**Supporting a Safe and Respectful Workplace at Institutions that Receive NIH Funding**" webpages: (grants.nih.gov/grants/policy/harassment.html) with related definitions and data. Also linked from the website is information on finding help if you're experiencing harassment as well as relevant NIH policies and requirements for grantees.
- On October 25 NIH published a "**Notice of NIH's Encouragement of Applications Supporting Individuals from Underrepresented Ethnic and Racial Groups as well as Individuals with Disabilities**" (grants.nih.gov/grants/guide/notice-files/NOT-OD-22-019.html).
- COVID-19 effects on NIH research and researchers: In October 2020, 45,348 researchers at domestic, NIH-funded institutions and 224 research leaders from the top 1,000 NIH-funded domestic institutions

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responded to an NIH COVID-19 Impact on Extramural Research Survey. 55% said they expected the pandemic to have a negative effect on their career trajectory, 68% said social/political events negatively affected their mental health, and 78% reported lower levels of productivity during the pandemic.

✦ Ongoing NIH efforts to support the research community during the COVID pandemic (grants.nih.gov/policy/natural-disasters/corona-virus.htm#proposal) include:

- Flexibility may be available for extended early-stage investigator (ESI) eligibility and/or award extensions for those significantly affected by COVID-19.
- **NOT-OD -21-026** (grants.nih.gov/grants/guide/notice-files/NOT-OD-21-026.html) provides guidance for addressing potential pandemic-related limitations in grant applications and review, and in the conduct of clinical trials and other human subjects research.
- Post-award flexibility may be offered on some budgeting and reporting requirements for affected activities and institutions, including for financial reporting and Research Progress Performance Reports (RPPRs) – see Flexibilities Available to Applicants and Recipients of Federal Financial Assistance Affected by COVID-19 (**NOT-OD-20-086**) (grants.nih.gov/grants/guide/notice-files/NOT-OD-20-086.html).
- The NIH has posted a free, 9-seminar "**Becoming a Resilient Scientist Series**" (www.training.nih.gov/virtual_nih_activities_for_trainees_outside_the_nih).

✦ Some ongoing and some new NIH funding opportunities (FOAs) or Notices of Special Interest (NOSIs) that may be of interest:

- **Identification and Characterization of Bioactive Microbial Metabolites for Advancing Research on Microbe-Diet-Host Interactions** (grants.nih.gov/grants/guide/pa-files/PAR-21-253.html).
- The National Cancer Institute (NCI) has published a NOSI: **Dietary Effects on Nutrient Sensing Pathways in Tumor Etiology and Prevention** (grants.nih.gov/grants/guide/notice-files/NOT-CA-21-121.html).
- The NCI has re-issued the FOA **Exploratory Grants in Cancer Control:** (grants.nih.gov/grants/guide/pa-files/PAR-21-341.html).
- The National Center for Complementary and Integrative Health (NCCIH) is accepting applications for I**nnovation Grants to Nurture Initial Translational Efforts (IGNITE): Assay Development and Neurotherapeutic Agent Identification** (grants.nih.gov/grants/guide/pa-files/PAR-21-124.html) for receipt dates into 2024.
- NCCIH issued a new NOSI describing their priorities in innovative basic and mechanistic research and technology/method development research within their purview, including natural product research (grants.nih.gov/grants/guide/notice-files/NOT-AT-21-006.html). Among the areas of interest described as high program priorities: the development of targeted and untargeted bioinformatic approaches to identify active components in a natural product mixture.
- The next due date for the NIH Office of Dietary Supplements (ODS) Pilot Project (**PAR 20-228**) (grants.nih.gov/grants/guide/pa-files/PAR-20-228.html) R03 awards supporting collaborations with the **NIH Consortium Advancing Research on Botanicals and Other Natural Products** (CARBON) (ods.od.nih.gov/Research/Dietary_Supplement_Research_Centers.aspx) is February 15, 2022.
  - Certain NIH awards may be eligible for supplemental awards through one of the ODS FOAs with receipt dates in January and April 2022:

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- Validation Studies of Analytical Methods for Dietary Supplement Constituents (PA 20-252) (grants.nih.gov/grants/guide/pa-files/PA-20-252.html) and
- Administrative Supplements for Research on Dietary Supplements (PA 20-227) (grants.nih.gov/grants/guide/pa-files/PA-20-227.html).

Dr. Craig Hopp

Gingko

✦ A recent **NCCIH blog post from Craig Hopp, PhD** (www.nccih.nih.gov/research/blog/finding-answers-to-questions-about-drug-herb-interactions) highlighted their Center for Excellence in Natural Product-Drug Interaction Research and additional related research opportunities.

✦ The NIH **Office of Dietary Supplements (ODS) 25th Anniversary Scientific Symposium** (events-support.com/events/ODS_25th_Anniversary_Scientific_Symposium) was held in October. Botanical natural product research presented included:

- The ginkgo enhancement of memory study (Annette Fitzpatrick, University of Washington)
- *Hydrastis canadensis* (goldenseal) and mechanistic synergy (Nadja Cech, University of North Carolina Greensboro)
- *Centella asiatica* (Gotu kola) and resilience in aging (Amala Soumyanath, Oregon Health & Science University School of Medicine) and
- Curcumin metabolites (Claus Schneider, Vanderbilt University).

Dr. Nadja Cech

Video recordings of the entire symposium are available from the website.

✦ Upcoming **ODS webinars** include:

- **Wednesday, January 12, 2022, 11:00 a.m. (ET)**
  Nuisance Compound Behaviors in Biological Assays with Natural Products
  Jayme L. Dahlin, MD, PhD, FASCP — National Center for Advancing Translational Sciences, National Institutes of Health, Bethesda, MD
- **Wednesday, March 30, 2022, 11:00 a.m. (ET)**
  Preclinical Evaluation of Interactions Between Dietary Botanicals and Drugs
  Cassandra L. Quave, PhD — Emory College of Arts and Sciences, Center for Human Health, and Curator of the Herbarium
- **Viewing information** is available from **ODS@nih.gov**.

✦ ODS expects to offer the Mary Frances Picciano Dietary Supplement Research Practicum on May 23-25, 2022. The Practicum provides fundamental information on dietary supplements to faculty, students, and practitioners with a serious interest in this subject. The website is at ods.od.nih.gov/Research/dsrp.aspx and will be updated when new information becomes available.

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✦ Did you know that outgoing NIH Director Francis Collins is also an accomplished guitarist? Note the inlay behind the frets of his guitar in this video (directorsblog.nih.gov/2021/04/09/here-comes-the-sun/) of the multi-talented Dr. Collins accompanying himself while (virtually) serenading NIH staff last spring.

Dr. Francis Collins

FUNDING OPPORTUNITIES FROM THE NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)

The National Institute of General Medical Sciences (NIGMS) supports basic research that increases our understanding of biological processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. NIGMS welcomes applications that fall within its **mission:** (www.nigms.nih.gov/about-nigms/who-we-are/overview) to address fundamental research questions. Detailed descriptions about the areas NIGMS supports, including natural products discovery and analysis, can be found on the **NIGMS website** (www.nigms.nih.gov/about/pages/contactbyarea.aspx). The Institute places great emphasis on supporting investigator-initiated research grants.

The **NIGMS Maximizing Investigators' Research Award (MIRA)** provides support for the research in an investigator's laboratory that falls within the mission of NIGMS. The goal of MIRA is to increase the efficiency of NIGMS' funding by providing investigators with greater stability and flexibility, thereby enhancing scientific productivity and the chances for important breakthroughs. There are two NIGMS MIRA funding opportunity announcements (FOAs) with unique eligibility criteria for **established investigators:** (grants.nih.gov/grants/guide/pa-files/PAR-19-367.html) and **early stage investigators:** (grants.nih.gov/grants/guide/pa-files/PAR-20-117.html). Please review the **NIGMS MIRA webpage:** (www.nigms.nih.gov/research/mechanisms/mira/pages/default.aspx) for FOA details, FAQs, NIGMS staff points of contact, and relevant webinars.

The NIGMS Technology Development R21 and R01 FOAs encourage evaluation of technological hypotheses without the pressure to additionally test unknown biological questions. Please review the NIGMS technology development webpage: (www.nigms.nih.gov/grants/R21-R01/Pages/NIGMS-Technology-Development-Programs-R21-and-R01.aspx) for FOA details, FAQs, NIGMS staff points of contact, and relevant webinars. The three stages of technology development have distinct purposes: to demonstrate novelty, innovation, and utility. Each of these stages are supported with a specific FOA.

I. Novelty: Evaluating new, unrevealed concepts for feasibility or proof of concept (www.nigms.nih.gov/grants/R21-R01/Pages/Funding-Announcements-for-Three-Technology-Development-Stages.aspx#stage1) (**R21**) (grants.nih.gov/grants/guide/pa-files/PAR-19-254.html)

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II. Innovation: Inventive research and development for proving value of a Prototype (www.nigms.nih.gov/grants/R21-R01/Pages/Funding-Announcements-for-Three-Technology-Development-Stages.aspx#stage2) (R01) (grants.nih.gov/grants/guide/pa-files/PAR-19-253.html)

III. Utility: First biological applications of validated tools to solve unknown **biomedical hypotheses** (www.nigms.nih.gov/grants/R21-R01/Pages/Funding-Announcements-for-Three-Technology-Development-Stages.aspx#stage3) (**NIH parent R01**) (grants.nih.gov/grants/guide/pa-files/PA-20-185.html) ■

	FOA number*
Maximizing Investigators' Research Award (R35 - Clinical Trial Optional)	PAR-19-367
Maximizing Investigators' Research Award (MIRA) for Early Stage Investigators (R35 - Clinical Trial Optional)	PAR-20-117
Exploratory Research for Technology Development (R21 - Clinical Trial Not Allowed)	PAR-19-254
Focused Technology Research and Development (R01 - Clinical Trial Not Allowed)	PAR-19-253

*All due dates are subject to NIH policies. The applicant is responsible for confirming funding opportunity due date and associated submission policies within the funding opportunity announcement.

The National Institute of General Medical Sciences (NIGMS) supports basic research that increases our understanding of biological processes and lays the foundation for advances in disease diagnosis, treatment, and prevention. NIGMS welcomes applications that fall within its mission.

From the Archives: Celebrating 30 Years of the ASP Foundation

The American Society of Pharmacognosy Foundation turned thirty years old this year! Special thanks go to long time treasurer of the Foundation, Dr. Robert Krueger, for his assistance with this article and the integral role he played in the Foundation.

By Christine Jankowski, MA

While scouring the Lloyd Library archives, I happened upon three boxes from the American Society of Pharmacognosy Foundation. Out of curiosity, I opened one, and on the very top I found an inter-department delivery envelope marked "Lloyd Library archives - ASPF." A slew of name tags, a couple of letters and programs, and a folder were inside as I emptied the contents on the table. The name printed on all the tags was "Robert 'Bob' Krueger." Peering into the other boxes, his name kept coming up throughout the subject folders. While reading some of the contents, I also realized that the Foundation was now thirty years old! After confirming that he was the donor of these materials, I decided to give him a call, in hope to learn more about the Foundation and its history.

Dr. Bob Krueger, who had been the treasurer for the American Society of Pharmacognosy Foundation since its creation in 1991, described its beginnings. Dr. Matthew Suffness worked on the Foundation for two years prior to its inception. Suffness wanted to create a foundation for the ASP to address needs of members and soon-to-be members, including financial support for research and internship opportunities and starter grants for incoming ASP members. Suffness conducted an informal meeting attended by Drs. Bill Keller, Krueger, David J. Slatkin, and A.D. Kinghorn, all on the ASP's Executive Committee for that year, at the Bonn-BOCANS conference in 1990. They established plans for funding opportunities, an introductory piece for the 1990 fall newsletter, and a brochure design for the Foundation. After more months of planning and preparations, the team presented the newly recognized non-profit's proposed by-laws at the ASP 1991 Annual Meeting in Chicago. The by-laws were installed with Suffness serving as ASPF chair, A.D. Kinghorn as ASPF vice-chair, Krueger as ASPF treasurer, and Bill Keller as ASPF secretary. Slatkin and Alice Clark were the first Foundation board members.

Dr. Krueger's nametag from the 1990 conference that pushed the creation of ASPF.

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Left: Dr. Matthew Suffness (right) standing next to Charles Hufford in Halifax, Nova Scotia for the ASP Annual Meeting in 1994. Right: : Dr. Krueger standing in front of the Matt Suffness Memorial Yew Garden while attending the ASP Annual Meeting in Seattle, 2000.

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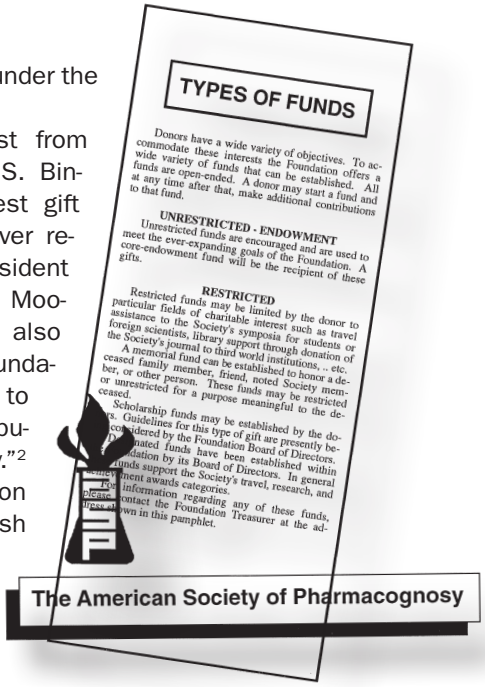
Initial supporters of the Foundation formation included longtime ASP member Lynn Brady who would go on to be an early Foundation Board of Directors member. He humorously commented: "Being a recent appointee to the Foundation Board of Directors, I have no responsibility for the actions by the group of radicals who met in Chicago; note that radical pertains to radix or root, and the designation of a 'group of radicals' is tantamount to a bunch of turnips."[1] To be on the Board, an ASP member had to be nominated to serve. Board members included past ASP presidents, the secretary of the ASP, and past ASP researchers. The Foundation Board would meet once a year during the annual ASP meeting to conduct any necessary business including financial status, yearly activities, and memberships.

After Suffness' death in 1995, Slatkin picked up the role as Foundation chair. Through the savviness of Krueger and Slatkin – both former ASP treasurers - they were able grow the Foundations' endowments and bring in additional funds to create various awards and grants. These include: the Matt Suffness Young Investigator Award, the Schwarting Fund and Beal Fund for the *Journal of Natural Products*, and seven travel funds. When Slatkin passed away in 2015, the David Slatkin Memorial Fund was created under the Foundation.

In 2018, a bequest from ASP member Audrey S. Bingel became the largest gift the Foundation had ever received. The ASP's president at the time, Dr. Susan Mooberry, said, "This gift also provides the ASP Foundation the opportunity to recognize her contributions and generosity."[2] Funds from this donation were used to establish the Audrey S. Bingel Fellowship for Female Scientists, a grant


TYPES OF FUNDS

Donors have a wide variety of objectives. To accommodate these interests the Foundation offers a wide variety of funds that can be established. All funds are open-ended. A donor may start a fund and at any time after that, make additional contributions to that fund.

UNRESTRICTED - ENDOWMENT

Unrestricted funds are encouraged and are used to meet the ever-expanding goals of the Foundation. A core-endowment fund will be the recipient of these gifts.

RESTRICTED

Restricted funds may be limited by the donor to particular fields of charitable interest such as travel assistance to the Society's symposia for students or foreign scientists, library support through donation of the Society's journal to third world institutions, ... etc.

A memorial fund can be established to honor a deceased family member, friend, noted Society member, or other person. These funds may be restricted or unrestricted for a purpose meaningful to the deceased.

Scholarship funds may be established by the do-
rs. Guidelines for this type of gift are presently be-
considered by the Foundation Board of Directors.
ated funds have been established within
dation by its Board of Directors. In general
funds support the Society's travel, research, and
ment awards categories.
information regarding any of these funds,
contact the Foundation Treasurer at the ad-
own in this pamphlet.

The American Society of Pharmacognosy

Above: A photocopy of the original brochure elements for the ASPF designed by Bob Krueger.

Left: Audrey Bingel, donor of the largest gift ever received by the ASPF funding the Fellowship for Female Scientists.

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The ASP Foundation was also instrumental in preserving the legacy and archival materials of the ASP and its members. In 2018, the Foundation matched a grant from the Society to provide funding to the Lloyd Library & Museum for the purchase and installation of compact shelving, significantly expanding the library's capacity to preserve and provide access to collections from the organization and its members.

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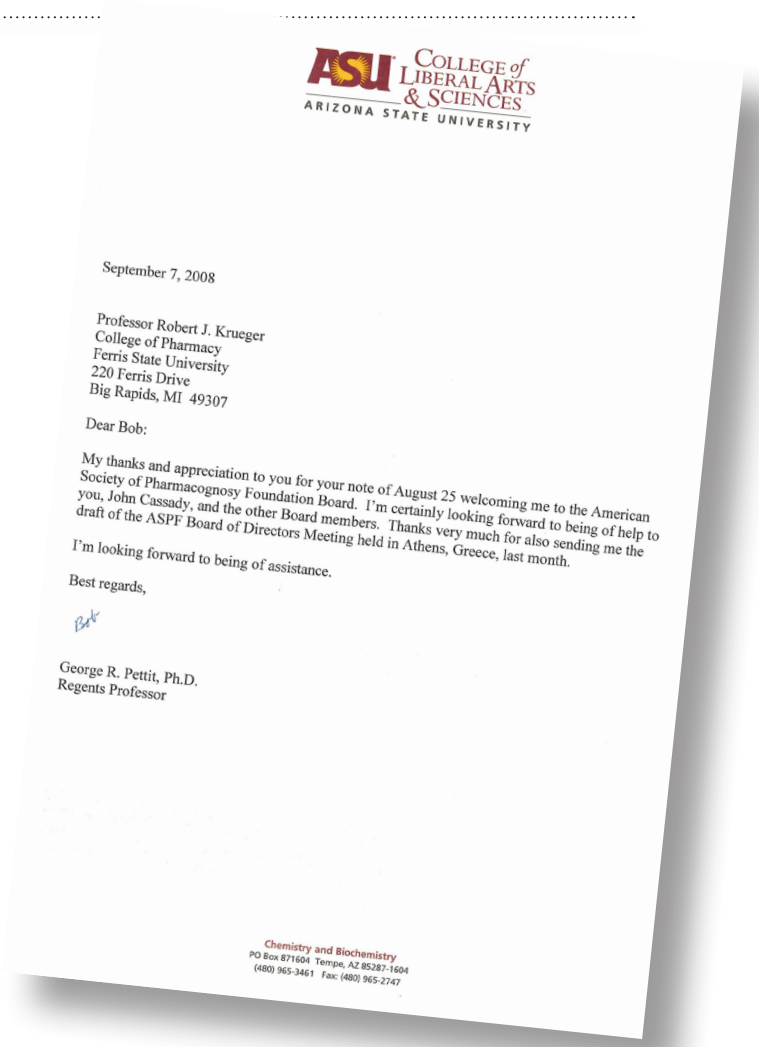
that supports women in science for their careers, research, assistance with childcare, and new career paths. Dr. Bingel's gift also provided a complete endowment for the Norman R. Farnsworth Research Achievement Award.[2]

The ASP Foundation was also instrumental in preserving the legacy and archival materials of the ASP and its members. In 2018, the Foundation matched a grant from the Society to provide funding to the Lloyd Library & Museum for the purchase and installation of compact shelving, significantly expanding the library's capacity to preserve and provide access to collections from the organization and its members.

Krueger has stepped down as Foundation treasurer and Dr. Kirk Manfredi has assumed the role. The Foundation's mission to promote, support, and further the interests and purposes of the ASP still permeates, as the Foundation continues to provide awards to ASP members for research and education of natural products, and Society membership.

A parting message from Bob Krueger? "Pay it forward. At its heart, the Foundation benefits from the support of ASP members." ■



ASU College of Liberal Arts & Sciences
Arizona State University

September 7, 2008

Professor Robert J. Krueger
College of Pharmacy
Ferris State University
220 Ferris Drive
Big Rapids, MI 49307

Dear Bob:

My thanks and appreciation to you for your note of August 25 welcoming me to the American Society of Pharmacognosy Foundation Board. I'm certainly looking forward to being of help to you, John Cassady, and the other Board members. Thanks very much for also sending me the draft of the ASPF Board of Directors Meeting held in Athens, Greece, last month.

I'm looking forward to being of assistance.

Best regards,

George R. Pettit, Ph.D.
Regents Professor

Chemistry and Biochemistry
PO Box 871604 Tempe, AZ 85287-1604
(480) 965-3461 Fax: (480) 965-2747

Above: : A letter from 2008 written by Bob Pettit to Bob Krueger accepting his role as an ASPF Board Member, mentioning "I'm certainly looking forward to being of help to you, John Cassady, and the other Board members."

LITERATURE CITED

1 Cassady, J.M. and Krueger, R. American Society of Pharmacognosy Foundation. *The American Society of Pharmacognosy: 50 Years of Progress in Natural Products Research 1959-2009*. Eds. Gordon M. Cragg, et al. Madison, WI: Omnipress, **2009**, 46.

2 Krueger, R., Manfredi, K.P., Cardellina, J.H. and Carver, P. Longtime ASP member Audrey Bingel generously bequeaths largest endowment ever to ASP Foundation. The *ASP Newsletter,* **2018**, *54* (3): 1, 4.

**A parting message from Bob Krueger?
"Pay it forward. At its heart, the Foundation benefits
from the support of ASP members."**

Jimmy Orjala, PhD, Treasurer
The American Society of Pharmacognosy
3149 Dundee Road, #260,
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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**.

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

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Dr. Barbara Timmermann, University of Kansas

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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