The American Society of Pharmacognosy

Discovering Nature's Molecular Potential

The ASP Newsletter: Volume 52, Issue 3

ASP Incoming Presidential Address

ASP President Cindy Angerhofer

MR. TOM O'LEARY

By Dr. Cindy Angerhofer

I am honored and excited to assume my duties as the new President of the American Society of Pharmacognosy for the coming year. That may sound worn and trite, but it is heartfelt! I have first and foremost to thank outgoing President Edward Kennelly for his strong leadership and guidance this year. He and the executive team have done an excellent job of moving the Society forward. Even as Vice President, I have been grateful for the support received from our Business manager, Ms. Laura Stoll, and know she will be a valuable partner again this year!

My goals for the year are to advance the Society by focusing on a revamp of the ASP website and by promoting diversity of our Society and of our planet.

Updating our website will create a more powerful resource for members and a potential draw for others interested in pharmacognosy. This was one of the recommendations from a study conducted by the Virginia Commonwealth University Brandcenter two years ago. This was a stated goal of President Kennelly, but unfortunately the existing website was hacked during his term and prevented him from making any progress. This hack was certainly an unintended learning experience for all of us, but I believe the site is now on a more secure platform and we will be able to make a number of improvements this year. We are still seeking formal proposals for website redesign, so please let me or our webmaster, Dr. John Porter, know if you have any leads.

We have a diverse membership, in terms of age, experience, gender, ethnicity, geography and more. Just this year, 158 members of the Brazilian Society of Pharmacognosy joined the ASP, and we welcome their active participation and will look for articles in the *Newsletter* to help introduce them to us. At the annual business meeting in Copenhagen, Denmark, ASP members have just approved an initiative to offer free associate membership to qualified pharmacognosists in Least Developed Countries (according to the United Nations (UN)). We know that this will be a benefit to the new members and will also enrich our Society with scientists who are under-represented.

Another aspect of diversity critical to our Society is that of the natural world. The UN published the Convention on Biological Diversity (CBD) in 1992, a treaty with

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IN THIS ISSUE: FALL 2016

EDITOR'S CORNER

In this issue of the *ASP Newsletter,* we welcome the newly installed ASP President, Dr. Cindy Angerhofer. As the past ASP President, I was very happy indeed to hand over the storied ASP *Rhamnus* gavel to Cindy at the ASP Business meeting in Copenhagen, Denmark. Cindy's lead article discusses her visions for the Society, and I wish her good luck as the outgoing president. She comes with considerable ASP expertise, including several decades of membership and service on the ASP Executive Board and ASP Foundation Board. I feel we are in good hands. Already as Vice President and Chair of the ASP Membership Committee, Cindy was extremely active and successfully brought forward a motion to offer reduced membership costs to members from certain economically limited areas of the world. Good luck with your presidency, Cindy!

In this issue, the *Newsletter* looks back at the Joint Meeting in Copenhagen, and provides in-depth articles on the two major award winners, Drs. Bill Gerwick (Farnsworth Award) and De-an Guo (Tyler Prize). Each of these scientists has done seminal work in their respective fields of marine natural products and traditional Chinese medicine, and their award lectures were highlights of the meeting. The Society also awarded the Matt Suffness Early Investigator Award to Dr. Harald Gross. I was heartened to learn that the country with the most representatives in Copenhagen was the United States, with about 200 ASP members in attendance.

Dr. Gordon Cragg seems to be more active than ever in his retirement, and as *ASP Newsletter* Editor, I am especially grateful for his continued efforts to write major pieces for us. In this edition, Dr. Cragg writes about the long and distinguished career of ASP Fellow, Dr. George Pettit. Dr. Pettit's research in drugs to treat cancer has been one of the most successful research programs of its kind in the world. For members who are not as familiar with Dr. Pettit's work, I urge you to take time to read about his accomplishments in developing new drugs for cancer. As a tie-in to this article, "From the Archives" writer, Ms. Devhra BennettJones, dug through the Lloyd Library's holdings and was able to locate Dr. Pettit's original application for membership to ASP.

At the 2016 Executive Committee Meeting of the ASP, a motion passed to grant *ASP Newsletter* columnist Dr. Georgia Perdue lifelong emeritus membership to the Society. Prior to joining the *Newsletter*, Dr. Perdue was known to many of you for her publication "Washington Insight." She continues to provide valuable information to ASP members through her volunteer work as a reporter to this publication. Incredibly, since volume 43, issue 3 (Fall 2007), she has never missed an issue. In fact her submissions are always timely, even when I am behind with my editing. The success of the ASP relies on dedicated volunteers like Dr. Perdue. Thank you Georgia!

I wish all of you a fantastic and productive autumn season, and look forward to seeing you in Portland, Oregon, next summer.

Dr. Edward J. Kennelly

Cindy's lead article discusses her visions for the Society, and I wish her good luck as the outgoing president. She comes with considerable ASP expertise, including several decades of membership and service on the ASP Executive Board and ASP Foundation Board.

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The Society offers a placement service to aid our members in seeking positions or employees. This service is available only to ASP members and is free to both the applicant and the employer.

For more information see the services website.
www.pharmacognosy.us/jobs/

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the goal of assuring conservation and sustainable use of biodiversity, as well as fair benefit-sharing with those providing genetic resources. Shortly thereafter, the first Interim Meeting of the ASP focused on the subject of Biodiversity and Intellectual Property Rights, bringing together people and institutions from around the globe to discuss the CBD and how it might be implemented. Almost exactly 20 years later, the Nagoya Protocol was brought into force, providing the legal framework for implementing the CBD. Because of the impact this has on ethical research and development of natural products, ASP should again lead the discussion of this crucial topic.

My relationship with ASP began almost 30 years ago when I was a graduate student and has afforded me countless opportunities to further my career in pharmacognosy. Relationships I have developed through ASP have provided me with mentors, sponsors, research colleagues and many close friends, such that the annual meeting is as much a family reunion as it is a stimulating scientific conference! This year has been no exception, with the added benefit of having the Joint Natural Products Congress recently convened in Copenhagen, Denmark, with five sister societies of natural products research AND an interim meeting at the University of Mississippi, Oxford, Mississippi, that also drew many attendees from ASP. Many thanks go to Dr. Barbara Timmermann for acting as the point person on behalf of ASP for the Joint Natural Products Conference, and to Dr. Ikhlas Khan and team for organizing and ramping up the Oxford International Conference on the Science of Botanicals for the largest attendance in its history.

Our meetings showcase natural products research through oral and poster presentations to be sure, but more than that, they start conversations and build relationships that can diffuse the sharp lines between all the many disciplines that are represented there as natural products research. It is working and playing at these interfaces that creates synergy and advances the field of pharmacognosy, and that was, in fact, what drew me to a postdoctoral position at the University of Illinois Chicago, Chicago, Illinois, in the Program for Collaborative Research in the Pharmaceutical Sciences many years ago. With continued explosion of technological developments that help fuel progress in all aspects of science, that kind of collaboration is as relevant and necessary and exciting as ever, and I believe our Society plays a key role in fostering collaboration, particularly through the annual meeting. Now that the Copenhagen meeting is past, ASP will be responsible for organizing the next seven meetings, and I am asking everyone to offer ideas for sessions, workshops, speakers, logistics, and other feedback to the future meeting organizers and the ASP conference committee (contacts are posted on the Officers and Committees page of the website).

Another pillar of the Society that extends the opportunity for association of natural products scientists is the *Journal of Natural Products*, co-published with the ACS. The *Journal* was a vision of our founders, and has been led into its present state as a premier publication by Editor-in-Chief Doug Kinghorn and his dedicated team of editors, all members of the ASP. Sincere thanks go to this team for continued excellence in bringing the best of our field to publication for global outreach! The success of *J. Nat. Prod.* also helps fund the ASP Foundation to provide a range of grants and awards to our members. We plan to provide more guidance this year to publicize these opportunities and strengthen applications.

With continued explosion of technological developments that help fuel progress in all aspects of science, ...collaboration is as relevant and necessary and exciting as ever, and I believe our Society plays a key role in fostering collaboration, particularly through the annual meeting.

I will close with a couple of comments on the name, American Society of Pharmacognosy, which was determined by a vote of members this year to remain our name going forward. I have just written about the diversity of our Society and the tangible benefits that can result from it. That said, it is unlikely that we could have come up with a name that is more inclusive of all participating disciplines than pharmacognosy, defined as the study of medicinal agents from natural products. While I admit that the average person is not familiar with the word pharmacognosy, introducing myself as a pharmacognosist almost always invites an engaging conversation. President Kennelly, in consultation with the ASP Executive Committee, directed that the tagline "Discovering nature's molecular potential" will accompany our name as a further descriptor, and I believe this will further open the conversation.

Finally it is our members, our actions and our science that define who we are as a Society, so I request your ideas and your involvement in continuing to evolve our ASP. Please feel free to contact me at cangerhofer@aveda.com. ■

Gerwick Receives ASP Research Achievement Award

By Dr. Kevin Tidgewell

Dr. William Gerwick, Distinguished Professor and Director of the Center for Marine Biotechnology and Biomedicine (CMBB) at Scripps Institute of Oceanography (SIO), La Jolla, California, was presented the Norman R. Farnsworth ASP Research Achievement Award on July 27, 2016, with an introduction by former Gerwick postdoctoral fellow Dr. Kerry McPhail. Dr. McPhail led attendees along Dr. Gerwick's full circle journey, from getting his PhD at SIO in the late 1970s, to now being a distinguished professor and director there.

Dr. Gerwick took the stage in a black shirt under a blazer that was a bit reminiscent of Steve Jobs, fitting for a man who has pushed the field and made a reputation of incorporating innovation into his search for drugs from the ocean. Dr. Gerwick recalled his very first ASP meeting in 1985, in Chapel Hill, North Carolina, which coincidentally was also a joint meeting with the Society for Medicinal Plant and Natural Product Research (GA), Association Francophone pour l'Enseignement et la Recherche en Pharmacognosie (AFERP) and Phytochemical Society of Europe (PSE), where he met Dr. David Kingston and became inspired by, not only the science, but the nurturing and open atmosphere of the Society. Dr. Gerwick has mentored several hundred graduate students, postdoctoral researchers, and visiting scientists over his career; he is quick to give credit to them for being the hands in the laboratory and also for enriching his own life both scientifically and personally.

Dr. Gerwick delivers his award presentation in Copenhagen, Denmark.

DR. AMY KELLER

ASP President Cindy Angerhofer told the *Newsletter,* "Hearty congratulations to Bill Gerwick for his well-deserved win of the Farnsworth Research Achievement Award this year! He has made strong and novel advancements in natural products, especially in the fascinating area of marine algae and cyanobacteria. Bill is also a master collaborator and has mentored and co-authored with many, many fellow ASP members (including this year's Suffness Young Investigator) – yet another contribution to the field and to the Society."

Through his positions at the University of Puerto Rico, San Juan, Puerto Rico (1982-1984, adjunct until 1995), Oregon State University, Corvallis, Oregon (1984-2005), the Karolinska Institutet, Solna, Sweden (visiting scientist 1990-1991) and the SIO (2005-present), his research focus has been on five major themes: 1) discovery of anticancer and neuromodulators from marine cyanobacteria, 2) exploring the biosynthetic pathways of these secondary metabolites, 3) oxylipin biosynthesis from macroalgae, 4) development of new methods for small molecule analysis (NMR and MS), and 5) biofuels research from marine microalgae. Dr. Gerwick went on to describe three tools for natural products research in detail and some specific examples of how these techniques can be used to discover new compounds and bioactive molecules.

The first project utilized MALDI-MS and feeding ^{15}N-labeled $NaNO_3$ precursor to cultured cyanobacteria in order to discover previously unknown nitrogen-containing metabolites. By analyzing the MS of small extracts, filaments, and cells, researchers were able to discover the small molecule cryptomaldamide. Combining labeled feeding studies with MALDI-MS and molecular networks formation resulted in a rapid discovery and identification of a novel compound. This type of an approach allows researchers to already know something about the molecules they are isolating, namely the number of nitrogens incorporated based on mass defect over time. By combining this feeding study with the rapid dereplication afforded by MALDI-MS molecular networks, the time from isolation to elucidation can be drastically reduced. Then, utilizing QUAST sequencing, the gene cluster for crytpomaldamide could be easily found because of the predicted unique amidotransferase.

The second was a bottom up genomic mining approach using MALDI-MS/MS and molecular networks. The informatics of MS/MS molecular networking and similarity scores have been widely employed in recent years by a number of laboratories after being pioneered by the Gerwick and (Dr. Pieter)

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Dorrestein teams in collaboration. While it can be utilized for dereplication and discovery of analogues of known compounds, it can also be used for the discovery of unrelated compounds. Based on a putative SHK gene found in a cyanobacteria, they were able to comb through the MS/MS data and find a cluster which seemed promising; this resulted in the discovery of columbamide, which was found to have affinity for the CB1 receptor, an uncommon screening target, but not unknown in cyanobacteria.

The third was an informatics analysis of HSQC spectra using AI, which his lab has most recently been working on. This new project looks at utilizing AI face recognition software to identify compounds or structural features from analysis of 2D NMR, specifically HSQC, experiments. They have initially trained their program using the HSQC spectra reported in the supporting information of papers from the *Journal of Natural Products* and are now in the testing phase to use it for dereplication and novel structural determination. This type of automated structure elucidation dereplication effort is something that can take natural products drug discovery into the 21st century and beyond.

Dr. Gerwick ended his speech on a philosophical note about the bright future ahead for natural products. He loves to create graphics and images showing interconnectedness, and so he ended with one of his famous geometric designs showing the interplay of disciplines that is involved in natural products chemistry. He discussed how this integrative approach of bringing in and using other fields will be the future of natural products. Dr. Gerwick's laboratory, much like the three stories he chose to talk about, is a blending of fields, expertise, and experience to find the common ground and use the skills and strengths of each to create a whole greater than the sum of its parts. His final slide was a picture of Dr. Lena Gerwick, his wife and collaborator, enjoying a bike ride in Germany before the conference.

On Monday night, two days before giving his award lecture, Dr. Gerwick and a group of about 20 former students, postdoctoral researchers, visiting scientists, and their families gathered at Karla's Restaurant, Copenhagen, Denmark, a few blocks from the conference venue, for a celebratory dinner. These dinners are not just for awards and celebrations but are a common occurrence for members of the Gerwick laboratory, and oftentimes this group seems more like extended family than co-workers. Dr. Gerwick said a few words and talked about how the interactions with former students and seeing the successes of everyone that has come through his laboratory invigorates him and lets him know that he has truly achieved something with his career. As the night wore on, it became clear that while the Gerwicks are overjoyed to have recently become grandparents for the first time, their scientific family has made them grandparents many times over. Dr. Gerwick's legacy and ripple effect has and will continue to advance the science of natural products chemistry. ■

Drs. Cardellina, Gerwick, and Kennelly, following Dr. Gerwick's award acceptance.

DR. AMY KELLER

Dr. Gerwick's laboratory, much like the three stories he chose to talk about, is a blending of fields, expertise, and experience to find the common ground and use the skills and strengths of each to create a whole greater than the sum of its parts.

Guo Awarded 2016 Tyler Prize

By Dr. Edward Kennelly

At the Joint Natural Products Conference held in Copenhagen, Denmark, this July, Dr. De-an Guo was the recipient of the 2016 Varro Tyler Prize, one of the top two scientific awards given by the ASP. Dr. Guo serves as Director of the Shanghai Research Center for Modernization of Traditional Chinese Medicine (TCM) at the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, China. Much of his career has been dedicated to the modernization of TCM and serving in leadership roles on the Chinese, United States and European Pharmacopoeias.

ASP President Cindy Angerhofer mentioned, "De-an Guo has been a force in so many aspects of the study, practical application, and quality control of botanicals, chiefly in Traditional Chinese Medicine. He has spearheaded the development of high quality monographs for herbal medicines in TCM, and has also played a key role for the U.S. and European Pharmacopoeial herbal monographs, helping develop and harmonize them. De-an is an excellent choice for the Tyler Prize, and I offer my sincere congratulations!"

Dr. Guo's research on TCM has left an indelible mark on at least three major pharmacopeias around the globe: the Chinese, U.S., and European, and he serves as chair or on expert committees on each. Dr. Guo's research is centered on the phytochemical analysis and elaboration of high-quality monographs of TCM herbal medicines. Together with his team, he has developed a novel phytochemical analytical approach for TCM herbal medicines coined the "trinity analysis," which was awarded the first National Natural Science Prize in the TCM field.

Dr. Guo told the *ASP Newsletter*, "I was astonished when I received the notification from American Society of Pharmacognosy that I would be awarded the 2016 Varro Tyler Prize. Professor Varro Tyler is a legendary figure in pharmacognosy, and I recall reading his pharmacognosy textbook early in my career, and later I excerpted some chapters from his book to teach my students professional English. I am deeply grateful to ASP for awarding me such a prestigious prize, which greatly encouraged me in my future career development. I also consider this award as the recognition of my past 30 years of efforts devoted to the modernization and globalization of traditional Chinese medicine, a cultural and historical heritage of China."

In his award lecture, Dr. Guo emphasized that one of his main scientific missions was to make TCM evidence-based. While the government of the People's Republic of China officially recognizes TCM as a Chinese Cultural Heritage, Dr. Guo feels especially compelled to bring the most modern phytochemical methods to bear on the scientific understanding of TCM.

Some of the major challenges facing TCM research, according to Dr. Guo, include quality, safety, efficacy, and mechanism of action. His Tyler Prize talk drew upon some of these issues to discuss his research. For TCM quality control, selecting a single marker to act as a stand-in for the verification of a given plant is not a good idea, due to the prevalence of misidentification. Dr. Guo discussed the case of ginkgo, if when it used as a single marker, can be adulterated. Dr. Guo prefers to use a pool of active markers to ensure TCM quality control, as he described in his 2015 *Science* paper.[1]

Dr. Guo's research has fully em-

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Together with his team, he has developed a novel phytochemical analytical approach for TCM herbal medicines coined the "trinity analysis," which was awarded the first National Natural Science Prize in the TCM field.

Dr. Guo's research has fully embraced modern analytical chemical techniques to better understand the complex chemistry of TCM formulations.

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braced modern analytical chemical techniques to better understand the complex chemistry of TCM formulations. Incredibly, in a 2016 paper of turmeric, Dr. Guo's group report 846 terpecurcumins by using neutral loss and precursor ion scanning together with statical analytical methods, like principle component analysis.[2] The scientific strength and rigor that Dr. Guo and his team bring to TCM analysis is outstanding.

Dr. Guo closed his Tyler Prize lecture by invoking the Nobel-Prize winning discovery by Ms. Youyou Tu of artemisinin from TCM decades ago. Artemisinin is now one of the principle drugs used to combat malaria worldwide. While TCM has indeed proven to be a valuable part of China's cultural heritage, more work is still needed to ensure it is used in a manner that is evidence-based and science-based. To that end, Dr. Guo invites all those interested in the modernization of TCM to attend the 9th Shanghai International Conference on TCM and Natural Medicines (S-TCM) from October 19-21, 2016, Shanghai, China, and the 66th GA Meeting jointly with S-TCM (500th anniversary of the birth of Li Shizhen), August 26-29, 2018, Shanghai, China.

At the end of the talk, Dr. Guo was presented the Tyler award, including a check and a commemorative clock, by ASP President Dr. Edward Kennelly and ASP Foundation President, Dr. John Cardellina. ■

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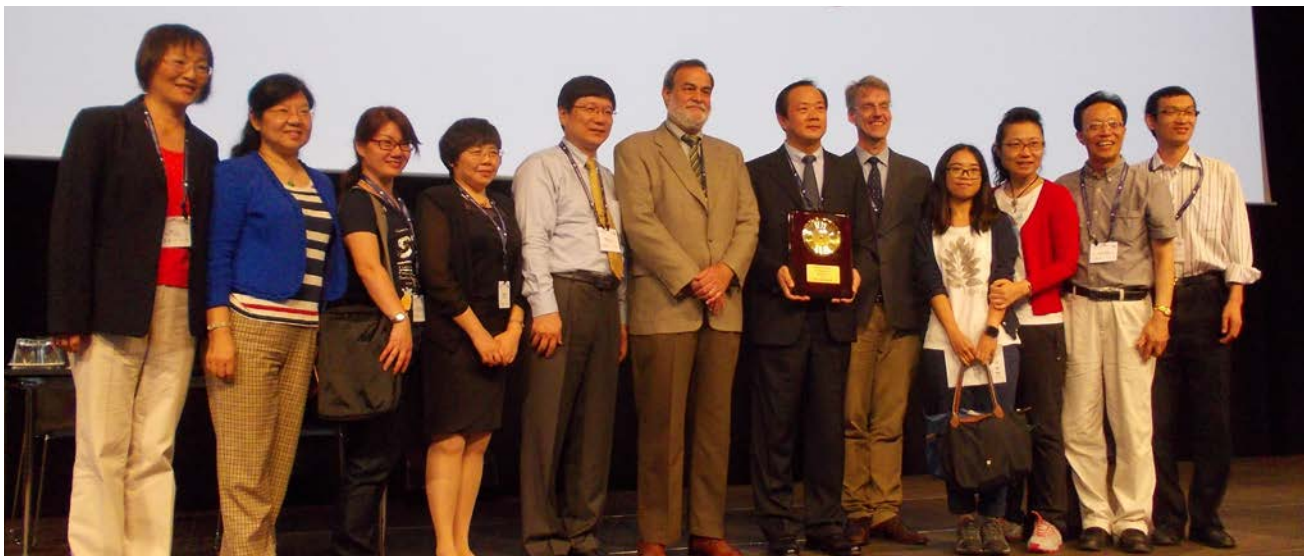

Drs. Cardellina and Kennelly present Dr. Guo with the Tyler Prize, with his colleagues looking on.

DR. AMY KELLER

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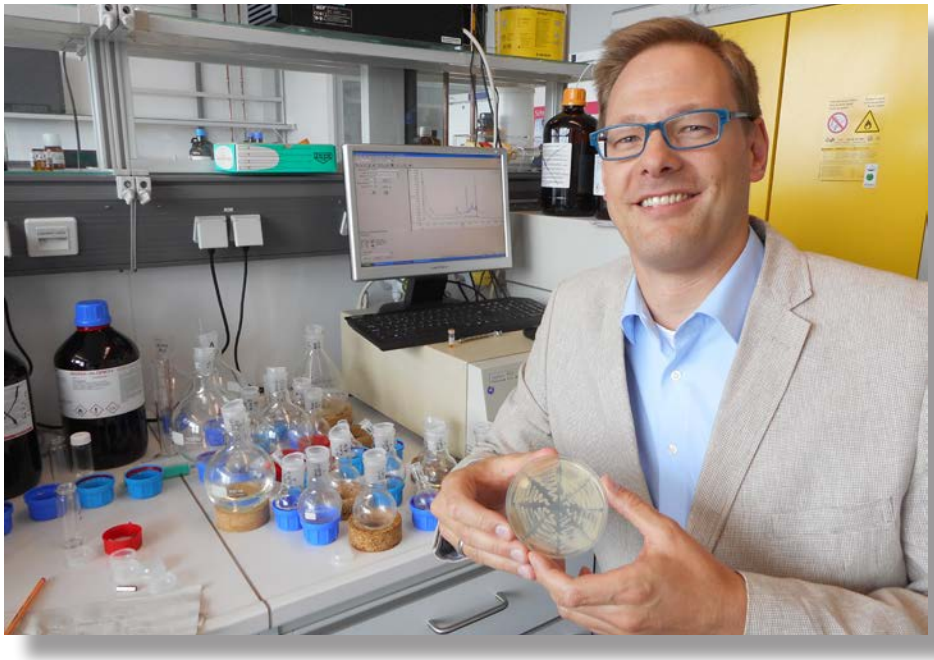
Gross Presented Suffness Award



Dr. Gross in his laboratory with an agar plate containing Pseudomonads.

By Dr. Amy Keller

ASP member Dr. Harald Gross, Pharmacist at the Pharmaceutical Institute, Department of Pharmaceutical Biology, University of Tübingen, Tübingen, Germany, was awarded the 2017 Matt Suffness Young Investigator Award at the Joint Natural Products Conference in Copenhagen, Denmark. His award lecture was entitled "Genome Mining in Pseudomonads – a Journey from Their Genomes to Secondary Metabolites and Back."

When asked about his reaction to winning the award, Dr. Gross responded, "Winning the Matt Suffness Award is a tremendous honor for me. I am truly humbled and looking at the list of the previous awardees makes me feel proud to be among this group of distinguished researchers."

Dr. Gross' laboratory focuses on genome mining of microbes for secondary metabolites, with the aim of finding and/or designing novel, bioactive natural products. This approach consists of using bioinformatics to identify genes upstream of natural product synthesis in an organism. This technique can present hurdles, however, as many genes associated with biosynthesis do not actually correlate to a compound. The bacteria in the *Pseudomonas* genus have been the major focus of Dr. Gross' laboratory. The discovery and development of new antibiotics are of paramount importance, and the Gross laboratory investigates natural products that may potentially be useful in treating infectious diseases, in addition to compounds that are cytotoxic and immunosuppressive.

ASP President Cindy Angerhofer relates, "Our Suffness Award winner, Dr. Harald Gross, presented a compelling lecture on his work elucidating how organisms like Pseudomonads synthesize bioactive compounds. His research approach of mining the genome of microorganisms for natural products will be certain to yield additional novel compounds and unprecedented discoveries well into the future. Kudos and congratulations to Harry!"

The Suffness award, named for former ASP President Matthew Suffness, is one of three major ASP yearly awards. In the early 1990's, Dr. Suffness was prominent in developing what was then called the Young Investigator Award, conceived as a mechanism to highlight the achievements of some of our younger members as they established independent careers.

Dr. Gross told the *Newsletter,* "I never had the pleasure of meeting Dr. Suffness, but learned that he made great contributions to field of anticancer natural products and that he was particularly committed in promoting young scientists. Of course, the award gives my research and I visibility. Even more important to me is that it shows that I am on the right track and provides recognition of my personal and my team's research efforts." ■

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ASP Award Winners

The *Newsletter* wishes to recognize and congratulate all ASP award winners. Best wishes and congratulations to all.

Norman R. Farnsworth Research Achievement Award

Dr. William Gerwick
University of San Diego/Scripps Institute of Oceanography, La Jolla, California

Varro Tyler Prize for Botanical Research

Dr. De-an Guo
Shanghai Institute of Materia Medica, Shanghai, China

Matt Suffness Young Investigator's Award

Dr. Harald Gross
University of Tübingen, Tübingen, Germany

2015 Arthur E. Schwarting Award

"LC-MS and ^{1}H NMR-based metabolomics analysis and in vitro toxicological assessment of 43 *Aristolochia* species"

Authors: Johanna Michl, Geoffrey C. Kite, Stefan Wanke, Oliver Zierau, Gunter Vollmer, Christoph Neinhuis, Monique S.J. Simmons, and Michael Heinrich

2015 Jack L. Beal Award

"Total synthesis of clavatadine A"

Authors: Stephanie J. Conn, Shannon M. Vreeland, Alexandra N. Wexler, Rebecca H. Pouwer, Ronald J. Quinn, and Stephen Chamberland

D. John Faulkner Travel Award

Ms. Emma Barnes
Macquarie University, Sydney, Australia

ASP Research Starter Grant

Dr. Daniel Dias
RMIT University, Melbourne, Australia

Dr. Christine M. Theodore
University of Tampa, Tampa, Florida

Dr. Suthananda Sunassee
University of Cape Town, South Africa

Dr. Tyler Johnson
Dominican University of California, San Rafael, California

ASP Undergraduate Research Grants

Mr. Javier Alejandro Ruiz Vargas
University of Biotechnology, Yucatan, Mexico

ASP Travel Award for Active Members

Dr. Amy Keller
University of Colorado Denver, Aurora, Colorado

Lynn Brady Student Travel Award

Mr. Ross Overacker
Oregon State University

Mr. Ram P. Neupane
University of Hawai'i, Manoa, Hawai'i

Mr. Stephen Parrish
University of Hawai'i, Manoa, Hawai'i

ASP David Carew Student Travel Award

Joohee Lee
Seoul National University, Seoul, Republic of Korea

ASP Waqar H. Bhatti Student Travel Award

Roshamur C. Forestrania
Ohio State University, Columbus, Ohio

ASP Jerry McLaughlin Student Travel Award

Munhyung-Bae
Seoul National University, Seoul, Republic of Korea

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JNPC in Copenhagen a Huge Success




By Drs. Anna Jäger and Amy Keller

The recent Joint Natural Products Conference in Copenhagen, Denmark was a fantastic meeting, by all accounts! There were approximately 1,100 attendees. Most attendees were from the U.S., followed by South Korea and France, with more than 100 delegates from each country represented. During the conference, six plenary lectures, 18 keynote lectures and 51 short lectures were delivered on various subjects of natural products research. During the three poster sessions, 1,115 posters were presented, showing the broad spectrum of attendees' research. On the day before the conference, the Young Researcher Workshop was held with 12 short lectures given by young scientists. There was also a well-attended workshop on Regulatory Affairs, as well as a pre-conference symposium on Advances in (Bio)-Analytical Techniques applied to natural products research.







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JNPC in Copenhagen a Huge Success

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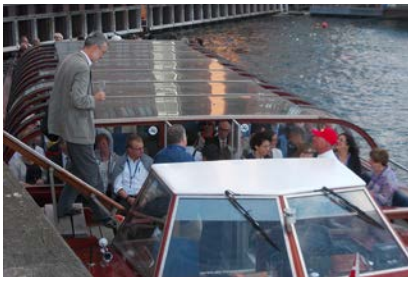
The social program of the meeting was especially lovely, including an excellent evening spent at the Copenhagen Botanical Gardens, with dinner selections from several food trucks. Conference attendees also enjoyed a traditional Danish meal, served at communal wooden tables at a beautiful restaurant on the canal. After the meeting's conclusion, attendees were offered an optional botanical excursion to Stevns Klint, a beech tree forest (originally a tree farm), and a few hours at the Viking Ship Museum. This trip offered visitors a chance to enjoy Denmark's stunning natural beauty and fascinating history. ■



The Search for Natural Substances with Therapeutic Activity: Summary of a Tribute to ASP Member Pettit

By Dr. Charles Chapuis and Dr. Gordon M. Cragg

In 2014, the eminent French natural products chemist and pharmacologist, Dr. Laurent Meijer, together with two of his colleagues, dedicated a review in *Médecine Sciences* to ASP Fellow Dr. George R. Pettit.[1] The French journal has published a series of reviews covering the "life and work" of famous researchers who have discovered major chemotherapeutics from natural products.

Dr. Pettit was awarded the Norman R. Farnsworth Research Achievement Award by the ASP in 1995 and the Ernest Guenther Award in the Chemistry of Natural Products by the American Chemical Society in 1998. From 1989 to 2001, his significant contributions to anticancer drug discovery were recognized; the National Cancer Institute (NCI) designated him an Outstanding Investigator, and in March 2008, a special issue of the *Journal of Natural Products (J. Nat. Prod.)* was published in his honor. In addition, he has served as a member of the *J. Nat. Prod.* Editorial Board. As noted by Editor-In-Chief Dr. Douglas Kinghorn, "In my opinion, the work of Dr. Pettit and his colleagues in natural product drug discovery is unparalleled, and it would behoove ASP and *J. Nat. Prod.* to disseminate information on his many contributions as widely as possible."

The authors briefly note Dr. Pettit's early life studying marine invertebrates on the beaches near his home in New Jersey and the development of a passion for chemistry at the age of ten. His observation of the ravages of cancer while assisting a pathologist in postmortem examinations at the age of 15 led him to speculate that the chemical defenses used by marine invertebrates to deter attacks by predators may well be useful in the fight against cancer. This set the stage for a lifelong career devoted to the "worldwide exploration of natural products, especially of 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."

A timeline illustrating key events and discoveries in Dr. Pettit's life to date is given in Figure 2 of the review,[1] dating from his birth in 1929 and proceeding through the award of Bachelors, Masters and Doctorate (1956) degrees, to faculty appointments at the University of Maine, Orono, Maine (1957-65), and Arizona State University, Tempe, Arizona (ASU, 1965-present). A highlight was the establishment of the ASU Cancer Research Institute (ASU/CRI) in 1975, and the authors note that, "against all odds and common sense," the ASU authorities closed the ASU/CRI in 2005. However, Dr. Pettit continues to pursue cutting edge research with a reduced research team. Discussed further are some of the most important molecules emanating from Dr. Pettit's productive program, research which has resulted in "more than 800 publications and 67 patents, covering all aspects of the chemistry of natural products extraction, purification, structure determination, biosynthesis, total chemical synthesis, biological and clinical evaluations." A comprehensive list of novel antitumor compounds isolated from arthropods, plants, marine and microbial sources by the Pettit team is reported in Chapter 4 of the *The American Society of Pharmacognosy. 50 Years of Progress in Natural Products Research*.[2]

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Most prominent among the detailed discoveries are the dolastatins, originally isolated in minute yields from the marine mollusk, *Dolabella auricularia*, (Aplysiidae), collected off the coast of Mauritius in the early 1970s. The synthesis of the most promising lead, dolastatin 10 (D-10; Fig. 1), provided sufficient material for preclinical and clinical studies. While clinical trials of D-10 have not shown significant

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promise, a synthetic derivative, soblidotin (auristatin PE; TZT-1027; Fig. 1), is currently in Phase II clinical trials in Japan, the U.S., and Europe. Another derivative, monomethyl auristatin E, conjugated to a monoclonal antibody directed against the CD30 epitope (SGN- 35 or brentuximab vedotin; Fig.1) has completed clinical trials against refractory lymphomas and large cell lymphomas and has been marketed worldwide since the end of 2011 under the trade name Adcetris® . Combinations of the same derivative with other antibodies targeting broad cancer epitopes are in early clinical trials.[3]

Halichondrin B (HB; Fig. 5, ref. 1), first reported by Uemura and Hirata from the marine sponge *Halichondria okadai* in 1986, was also isolated in 1987 by Blunt and Munro and colleagues from two species of New Zealand sponges, *Raspalia agminata* and *Lissodendoryx* spp. and by Dr. Pettit and colleagues in 1991 from an *Axinella* spp. collected from the Republic of Palau. Obtaining sufficient supplies of HB for further development proved to be challenging, but completion of the total synthesis of HB by Kishi et al. in 1992 led to a collaboration between the Kishi group and scientists at the then Eisai Research Institute (currently Eisai Co., Ltd., Tokyo, Japan). They identified the ring-portion of the molecule as being mainly responsible for the biological activity, and close to 200 derivatives of the truncated natural product were prepared and evaluated, paving the way for the selection of E7389 (eribulin; Fig. 5, ref. 1) as the candidate for preclinical and clinical development. Following advanced preclinical development and extensive clinical studies, eribulin mesylate (proprietary name, Halaven®) was approved by the Food and Drug Administration (FDA) in 2010 for the treatment of metastatic breast cancer in patients who had already been subjected to two chemotherapy treatments. In 2011, it received European marketing authorization (AMM) for the same indication.

Another important marine-derived discovery was bryostatin 1 (Fig. 3, ref. 1). This compound was isolated from the bryozoan, *Bugula neritina*, first collected in the Gulf of Mexico and subsequently from the Gulf of California and the California coast. A large scale recollection yielded sufficient bryostatin 1 to initiate clinical trials, and while monotherapy does not appear to be efficacious, it has been shown to increase the effectiveness of vincristine in the treatment of large cell lymphomas. However, extensive studies aimed at the reduction of the main side effect, myalgia, will be needed before the therapeutic potential of bryostatin 1 can be fully exploited. Bryostatin 1 also has antidepressant effects and is currently in Phase II clinical trials for the treatment of Alzheimer disease; early results indicate that it blocks the progression of cognitive decline and reduces depression associated with this neurodegenerative disease. Simpler synthetic analogs, the so-called "bryologs," are currently being tested against HIV infections. They have been shown to flush out the latent virus, making it sensitive to highly active antiretroviral therapy (HAART), which would permanently eliminate the virus from the patients.

Other marine-derived compounds discovered by the Pettit group are the cephalostatins (isolated from *Cephalodiscus gilchristi* collected in 1972 off the east coast of South Africa) and the spongistatins (isolated from a sponge of the family Spongiidae, collected in the Maldives in 1988). Cephalostatin 1 and spongistatin 1 (Fig. 6, ref. 1) both showed potent *in vitro* activity against various cancer cell lines, as well as promising 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.

Finally, the discovery of two classes of plant-derived

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The Search for Natural Substances with Therapeutic Activity: Summary of a Tribute to ASP Member Pettit

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compounds is discussed. The most significant of these is the combretastatins isolated from the bark and wood of *Combretum caffrum*, collected in southern Africa in 1979. Being members of the stilbene family, these are more readily amenable to chemical synthesis. The most promising of these is combretastatin A4, which was converted to the water-soluble phosphate prodrug, combretastatin A4 phosphate (CA4P; Fosbretabulin; Zybrestat®; Fig.1). Following several clinical trials, it 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 analog combretastatin A1, as its diphosphate prodrug CA1P (OXI4503; Fig.1), 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 assigned by the FDA for the treatment of acute myelogenous leukemia.

The second plant-derived compound is pancratistatin (Fig. 7, ref. 1), isolated from *Hymenocallis littoralis* (*Pancratium littorale*), which was collected in 1980 in Hawaii. Early testing demonstrated good in vivo activity in the P388 murine lymphocytic leukemia and M-5076 ovarian sarcoma models, and more recently it has been shown to completely inhibit tumor vascularization after only 2 hours of treatment. Several syntheses have been developed, holding out the prospect for further preclinical and possible clinical studies.

As the authors remark, it has been "an extraordinary scientific career which has led Dr. Pettit from exploration of nature to state-of-the-art organic and synthetic chemistry and from clinical trials to therapeutic successes."

In closing, they observe that "Dr. Pettit has combined research funding and optimization of results to allow the continuation of many promising projects in an academic setting sometimes not conducive to the development of candidate drugs. Tenacious and passionate, Dr. Pettit is only beginning his work at over 84 years old!" We might now add, at over 87 years old!

To sum up in the words of the late Dr. Carl Djerassi, "Pettit is one of the great heroes in the chemistry of marine natural products out of which he created a battery of anti-cancer agents not equaled anywhere."[4] ■

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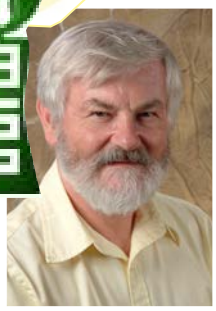
Hot Topics in Pharmacognosy: Some Rambles Through Recent Literature On Bacterial and Fungal Secondary Metabolites

By Dr. David Newman



Fungi are extremely prolific producers of secondary metabolites but are often overlooked as sources, perhaps due to the "strange" (at least to people used to growing bacteria) methods of growing them and increasing yields. Although static cultures of actinomycetes are sometimes used in studies on secondary metabolite production, the majority of such microbes are grown in shaking cultures or stir tank reactors. In contrast, fungi, particularly the filamentous fungi, are "happy and productive" when allowed to grow on static surfaces, from agar plates to corn cobs (or individual corn "grains") and at times, on grain-based human cereals such as "Cheerios" or their equivalents from other cereal manufacturers.

The genomic information on fungi and hence being able to identify potential secondary metabolites, is quite sparse when compared to the now thousands of actinomycetes that have had their genomes sequenced and their "innermost" secrets (biosynthetic gene clusters, BGCs) revealed. Most of the BGCs identified have not been characterized as to their exact function but have been catalogued, with recent published examples being those discussed by actinomycete taxonomists such as Dr. David Labeda at the United States Department of Agriculture (USDA) and his colleagues.[1, 2] In the first paper in 2014, they analyzed 830 genome sequences which included 344 specifically obtained for this particular study, deriving a mass spectroscopic technique to identify secondary metabolites from microbial metabolomes (178 strains), and linking back to specific gene clusters. In the second paper, interrogation of over 10,000 actinomycete genomes enabled the identification of natural products containing phosphonic acids, an unusual secondary metabolite series.

Though somewhat similar in concept to the systems derived by Dorrestein and coworkers using different methodologies and bacterial sources[3] and those described by Trautman and Crawford,[4] the scale is materially different and approaches that of interrogations of the human microbiome. Recently, Medema and Fischbach extended the area covering a variety of computational techniques for interrogating genomic data.[5] This paper contains an excellent coverage of the current methodologies plus the databases available (all URLs are given). We can add the paper on IMG-ABC to these examples, which aptly demonstrates the differences between current knowledge of the bacterial genomes versus those of fungi.[6]

However, and this is a very big "however," the eubacterial world (particularly the actinobacteria and some cyanophyta) is well covered, with data from over 10,000 genomic sequences available just for the streptomycetes; but in the case of the eukaryotic fungi, very little comparable information is available, though many of the most important therapeutic agents were isolated from fungi. Examples are the ß lactams (though there have been reports from some Streptomyces over the years) and the basic "statins" and cyclosporins, just to name a few of the blockbuster drug types. Fungi are frequently labeled as only producing "toxins" due to agents such the fumosins, the aflatoxins, or insecticidal agents such as the beauvericins, which are members of the ionophore class known as the enniatin antibiotics.[7]

One of the "perceived problems," until work in the early 2000s by the Keller group at the University of Madison, Madison, Wisconsin, was that the fungi, being eukaryotes, would have all of their biosynthetic clusters spread across their chromosomes, and/or they have a multiplicity of different organelles from the nucleus out-

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wards that could be involved in the production of secondary metabolites. However, the paper by Bok et al in 2006 demonstrated that, contrary to the current dogma, at least in the *Aspergillus* strain used, the biosynthetic clusters were not spread across all the chromosomes but were "nested" on proximal chromosomes.[8] This paper should be read in conjunction with a review the previous year by Keller et al.[9] In 2012, Keller demonstrated that in multiple strains of *A. nidulans* there were at least 33 to a then maximum of >70 identifiable biosynthetic clusters, ignoring terpene synthases, which could be a significant additional number.[10]

In the years since the 2006 paper, workers in groups other than those associated with Keller, have proceeded to investigate the complex control mechanisms involved in fungal secondary metabolite control and expression. Topics include the transport amongst organelles and whether or not these metabolites can be the equivalent of quorum sensing agents for both the fungus and, if an endophyte, the host organism as well. Some papers relevant to such discussions are the following from the Brakhage group,[11, 12] plus the methods described from the Larsen group in University of Denmark, Lyngby, Denmark covering predictions from fungal sequence data,[13] and Inglis et al.[14] In addition to these, two very recent papers have added to the methodologies for computational analyses of fungal genome data to search for secondary metabolites, namely those of Li et al,[15] and van der Lee and Medema.[16]

Techniques for rapid growth and subsequent interrogation of fungal secondary metabolites (for microbes that can be fermented) have recently been described by Barkal et al,[17] and should be read in conjunction with the recent paper from the Keller group.[18] Addressed are uses of fungal secondary metabolites as "fungal protective agents", similar to the comments earlier on quorum sensing agents.

There are two very intriguing papers that have recently been published that are relevant to the comment above; these discuss the use of nitric oxide (NO) as a signaling agent at various times on the growth cycle of *Aspergillus*[19] and the use of the same "messenger" in the establishment of fungal infection in plants.[20] As is well known, NO is a secondary messenger in animals but is also used in plants to close stomata against microbial invasion.[21] This brings up a very interesting question as to "is the fungus circumventing the plant's defenses by producing NO?"

Finally, the number of endophytic fungi now known to be functional in plants that produce "interesting drug compounds" (camptothecin, taxol, podophyllotoxin, etc.), that also produce them when fermented outside of the plant, has been recently covered in an excellent review in *Natural Product Reports* by the Kaltenpoth group at the Max Planck Institute for Chemical Ecology, Jena, Germany.[22] This paper should be read, in particular the data in the supplementary information, in conjunction with the examples given above of the multiplicity of fungal secondary metabolite clusters. Also, the very recent paper from Baccile et al on the production of isoquinoline alkaloids by a plant-like biosynthetic pathway in *A. fumigatus* should be read.[23] It raises all sorts of questions as to the role of a host plant. ■

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Behind the Scenes in Pharmacognosy: How New Techniques Help Preserve Endangered Species

By Dr. Amy Keller

In June of this year, the *Journal of Natural Products* published an article authored by ASP member Dr. Ping Li and others (co-last authored by Drs. Edward Kennelly and Chunlin Long) entitled, "UPLC-QTOFMS^E-guided dereplication of the endangered Chinese species *Garcinia paucinervis* to identify additional benzophenone derivatives." This publication stems from a 9-year collaboration known as the 111 Project (funded by the Chinese Ministry of Education), involving Dr. Long at the Ethnobotanical Laboratory at Minzu University of China in Beijing, China and Dr. Kennelly at the City University of New York, (CUNY) New York, among others. This initiative targets traditional medicinal plant use by minority peoples, among the 56 officially recognized ethnic groups, in China and has involved field and laboratory work in both China and the United States by visiting scientists and students. We thank Dr. Long for sharing some of the fruits of this labor.

Minzu University student, Ping Li working in the laboratory of Dr. Edward Kennelly at Lehman College as part of a China Scholarship Council Fellowship (2014-2015).

How did you become interested in *Garcinia* species and benzophenone derivatives?

Our group, the Ethnobotanical Laboratory at Minzu University of China in Beijing, China, has had an interest in the Clusiaceae family for a long time. According to our ethnobotanical investigations, many species in this family have been used for different purposes among the ethnic minority communities in southern China. Plants in the genus *Garcinia* are traditionally important for food and medicine. Fruits of most *Garcinia* species are edible, while the other parts are used for ethnomedicine. However, studies on the chemical metabolites of *Garcinia* species in China are limited. Some of bioactive compounds in *Garcinia* might explain why those species have medicinal uses. Benzophenone derivatives are rich in *Garcinia* species, and have demonstrated anticancer, antitumor, and antioxidant. For these reasons, we are interested in *Garcinia* species and benzophenone derivatives.

Who in your laboratory carried out the research?

Dr. Ping Li, my former PhD student, spent three years carrying out the research and focused on Chinese *Garcinia* species. He has just received his PhD in July, 2016, and is now a lecturer at South China Agricultural University in Guangzhou, China. Other people in my lab have studied and will continue to study different genera in the family Clusiaceae such as *Hypericum* and *Calophyllum,* covering chemical components and their pharmacological activities, molecular phylogeny, taxonomy and ethnobotany.

This was truly a collaborative effort between researchers in my laboratory, and in my collaborator's lab, Dr. Kennelly, at CUNY. Drs. Li, Kennelly, and others from my group did fieldwork in southern China in the summer of 2013 to collect a number of Clusiaceae species, including the rare plant *Garcinia paucinervis*. The field work was supported by a Chinese Ministry of Education grant, Program 111, to investigate the ethnobiology of plants used by the 56 minority groups in China.

The team spent several weeks going to remote areas of Hainan, Guangxi, Guangdong, and Yunnan Provinces to collect many different species. Some areas were so remote that Dr. Kennelly was the first Caucasian some locals had ever met. The next year, Dr. Li spent a year in the laboratory of Dr. Kennelly, supported by a grant from the Chinese Research Council, conducting LC-MS-QTOF analysis of the *Garcinia* species he had collected the year before.

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Could you provide a brief explanation of the work and results in your own words?

Garcinia paucinervis has high value due to its wood quality and has been used as ethnomedicine in southern China. We developed a strategy of analyzing benzophenone derivatives using UPLC-QTOF-MSE. As a result, we identified 31 peaks which might contain benzophenones. Five novel benzophenone derivatives were isolated and identified with MSE fragments, NMR, and ECD spectrum. We also tested five novel compounds and examined their cytotoxic effects on three breast cancer cell lines.

Your work reports a new methodology of discovering novel benzophenones with potential cytotoxicity towards breast cancer. What are the advantages for using this technique with an endangered species?

This technique has several advantages. I believe at least two benefits pertain to studying an endangered species. a) Only a small amount of sample is needed for analysis. This allowed us to analyze the main metabolites with limited samples. We only used 1 kg of seeds, a renewable resource, in this project. That was sufficient for all the analytical work, and we isolated more than five compounds. b) Powerful identification. MSE functions analysis can provide the accurate molecular weight and the fragment ions and their potential ions pathway used to deduce their structures. Thus, we could determine the structure-activity relationship of interesting metabolites to further the isolation work and bioactive study.

What is a favorite nonscientific activity of your lab?

We love spending time in outdoor activities, such as hiking in remote areas. We enjoy the beauty of nature when we are in the mountains, forests, grasslands, and agricultural ecosystems. Each summer, I organize field work for my students to collect plants, and while we work hard during this time, we also enjoy the beautiful and often remote areas of China that are home to many interesting plants used by the local minority peoples. My students and I very much like to see different plants and landscapes far from urban areas.

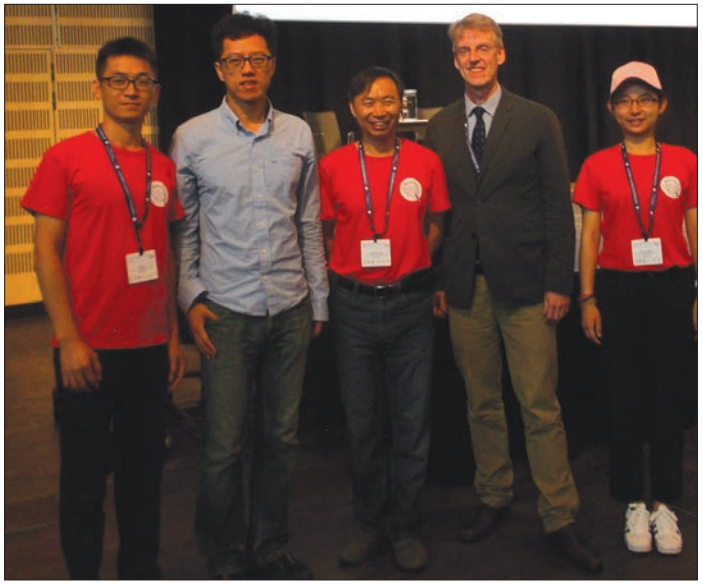
What is your lab's motto or slogan?

We are cooperative, innovative, rigorous, and optimistic. When we go to conferences, I often like to make a tee-shirt for everyone in the group to wear with our lab's name and insignia on it to show our teamwork.

What is your greatest extravagance in the lab?

Our laboratory enjoys the fine cuisine of many areas of China. Fortunately, tasty and fresh food is not so expensive in China, and I am often able to take my laboratory out to eat. When we are in remote field sites, I try to find restaurants that serve locally sourced ingredients, and I am especially pleased with finding local dishes using plants that are not commonly used in foods. They often taste delicious, and help to inspire our research! When we are in Beijing, we are fortunate that Minzu University is in an area of Haidian that is famous for having restaurants that specialize in famous and rare cuisines of China. Within a few kilometers of my university, we have reasonably priced restaurants serving foods from all around China. Dr. Kennelly has been collaborating with us for 8 years now, and has probably tried more Chinese dishes than many native Chinese.

My students work hard, and I wish they would have a meaningful life in our lab and obtain some interesting findings in their future scientific researches, and when they achieve success, we often celebrate with good food. ■



ASP Clusiaceae researchers at JCNP, Copenhagen, Denmark. From left: Ping Li, Bo Liu, Chunlin Long, Edward Kennelly, and Yizhou Wang.

DR. CLARA LAU

Meet a New ASP Member

Dr. Michael Tims, Academic Director for Herbal Medicine, Maryland University of Integrative Health, Laurel, Maryland, is our featured new ASP member. Dr. Tims, former ASP member and student poster award winner, is rejoining the ASP after a hiatus and shares with us his vision for his director position, his scientific passions and background, and his double life as an author, soccer fan, and oenophile.

By Dr. Dan Kulakowski

How did you hear about the ASP?
ASP member Dr. Joe Betz was my co-advisor on my doctoral work while he was at the Food and Drug Administration (FDA), Silver Spring, Maryland. (Dr. Betz is currently at the Office of Dietary Supplements at the National Institutes of Health, Bethesda, Maryland.) I was previously a member of the ASP; I won a student award for my poster on developing an analytical method for detecting goldenseal (*Hydrastis canadensis)* adulteration back around 2000!

Why did you join ASP?
I come from an herbalist tradition and, in the science realm, am an interdisciplinary chemical ecologist. At one point, the society had grown too much towards the grind and find side of the equation, and I no longer saw a place for my ideas. Outgoing ASP President Edward Kennelly recently talked me into rejoining. I met him when he was a postdoctoral fellow in the same FDA laboratories where I was a doctoral student.

Do you belong to any other scientific societies?
I am a member of the American Herbalist Guild and International Society for Chemical Ecology.

What are your current research interests in pharmacognosy?
I am Academic Director for the herbal programs at Maryland University of Integrative Health. I am focused on my role in institutional leadership and growing the herbal program, so I have less time for research. I still remain interested in exploring ecological influences in secondary metabolite formation in medicinal plants. I also use botanical pharmacognosy approaches with our students to develop good manufacturing practice methods suitable for smaller herbal product companies.

What is your scientific background?
As part of my doctoral work, I initially explored the role of lectins as signaling molecules in American mistletoe (*Phoradendron leucarpum*) to initiate the intercalation of mistletoe and host plant vascular structures. My final project focused on understanding the chemical ecology of goldenseal rhizosphere and its effect on soil fungi. During this time I collaborated with the Center for Food Safety and Applied Nutrition (CFSAN/FDA) to develop thin-layer chromatography methods for isolating pyrrolizidine alkaloids in comfrey (*Symphytum officinale)* and to provide assessment of heavy metals present in imported Chinese herbal products. I also co-developed HerbMed, a web-based herbal database providing access to scientific data on the use and safety of herbal medicine.

I then did a National Institutes of Health/National Institute of Standards and Technology postdoctoral fellowship, where I developed enzymatic extraction methods and performed certification measurements of green tea (*Camellia sinensis*) Standard Reference Materials (SRMs) in leaf powder, leaf powder extract, and finished product forms. I also worked on the development of analytical methods for the simultaneously separation and detection of a full spectrum of secondary metabolites found in kudzu (*Pueraria lobata*), soy (*Glycine max*), red clover (*Trifolium pratense*) and black cohosh (*Actaea racemosa*).


Dr. Michael TIms
JOHN WILSON

What would you like to achieve through your membership?
I wish to develop collaborations with other programs to benefit my program and to continue to learn about medicinal plants in a multi-disciplinary environment.

What do you like doing in your spare time?
I enjoy my family, including two Labrador retrievers, exercise, hiking, and gardening. I am a voracious reader with a passion for contemporary poetry and noir detective fiction. I am a published poet, and my book, *The Acoustic Properties of Ancient People,* has recently been accepted by Finishing Line Press. As a futbol (soccer) fanatic, I follow the exploits of the US Men's National Team, DC United and FC Barcelona. I am also on a lifelong quest to taste great Cabernet Sauvignons, Bordeaux, Rhone wines and Pinot Noirs.

What are you currently reading?
I am reading *An Obvious Fact* (Craig Johnson), *Fatal Pursuit* (Martin Walker), *The Other Side of Silence* (Philip Kerr), *Braiding Sweetgrass: Indigenous Wisdom, Scientific Knowledge and the Teachings of Plants* (Robin Wall Kimmerer), and *Herbal Drugs and Phytopharmaceuticals* (Ed. Max Wichtl).

What is your favorite organism (to study, or for general interest)?
I am fascinated by plant symbionts that have medicinal value, among them *Pedicularis canadensis*, *Phoradendron leucarpum*, and *Monotropa uniflora*. ■

New Members of ASP 2016

ASP would like to welcome 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 2 domestic full members, 3 international members, and 5 associate members. We look forward to meeting you and learning more about you and your work.

ACTIVE MEMBERS

Dr. Edith Antunes
Cape Town, South Africa

Professor Denzil Beukes
Cape Town, South Africa

Dr. Robert Bussey III
Winston Salem, North Carolina

Dr. Jeff Gautschi
Bend, Oregon

Dr. Simon Jackson
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Saint John, New Brunswick, Canada

Sofia Kokkaliari
Tampa, Florida

Mr. Andrew Shilling
Tampa, Florida

Santana Thomas
Tampa, Florida

Ms. Nassifatou Tittikpina
Saarbruecken, Germany

Welcome to ASP!

Keeping it Weird: 2017 ASP Annual Meeting

By Dr. Kerry McPhail

The 2017 ASP Annual Meeting will be held in Portland, Oregon, from July 29 to August 2, at the Hilton Portland & Executive Tower. The Lewis and Clark Expedition-inspired theme, "Natural product corps of discovery: venturing into the unknown," will be explored in three adventurous symposia. After opening with the welcome reception on Saturday evening, Sunday morning will march on with the *Natural Products Biosynthesis and Synthetic Biology* symposium. *Molecular Pharmacology of Natural Products and Complementary Medicine* will be the topic for Monday morning, and Tuesday morning will follow with the third symposium delving into *Natural Products from Unique Ecosystems*.

There will be an awards symposium on Wednesday morning. Afternoon sessions with invited and contributed oral presentations will encompass natural products biosynthesis, herbal and plant natural products, synthetic biology, synthesis of natural products, epigenetic activity of natural products, microbial natural products, molecular pharmacology of natural products, advanced technologies in natural products research, and plants and neurology. Poster sessions will be on Sunday and Monday.

We hope you will all join us for an outing on Monday evening to the Oregon Museum of Science and Industry (http://www.omsi.edu). The younger members event on Tuesday evening will include a taste of Oregon microbrews.

The conference venue, Hilton Portland & Executive Tower, is located at 921 SW Sixth Avenue, in downtown Portland, 44 minutes from Portland International Airport (PDX) by the MAX light rail train or a 20 minute drive by car. Portland, officially known as the City of Roses, is located in the Willamette Valley region of the Pacific Northwest, at the confluence of the Willamette and Columbia Rivers, and is generally warm and dry in summer. There are over 500 food carts available at any given time; locate the food cart "pods" at http://www.foodcartsportland.com/. For anyone interested in arriving a little early, the 30th Annual Oregon Brewers Festival will be held along the riverfront a few blocks away from the hotel from July 26-30, 2017.

You will have plenty of opportunity to discover that a less official slogan of the city is "Keep Portland Weird!" ■

Brief News From Washington

By Dr. Georgia Perdue

- **At the June 9 meeting of the Advisory Committee to the National Institutes of Health (NIH) Director (ACD), Dr. Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID), provided a few highlights about the Zika virus, which he said is "evolving even now."** Zika is related to Flavivirus, which includes dengue, yellow fever and West Nile Fever. Vaccines now exist for yellow fever, dengue and Japanese encephalitis. **In 1947, the Zika virus was identified in Nigeria, and the virus was first isolated from a monkey found in the Zika forest in Uganda. In 1952, the first human cases were reported scattered in Nigeria. Subsequently, vaccines were developed. In 2007, the first outbreaks occurred in South America, Central America, and the Caribbean; currently, 48 countries and territories have active Zika transmission.** The symptoms include a rash, fever, and congenital abnormalities like microencephaly. Dr. Fauci noted that 216 million passengers journey annually by air, land, and sea, from areas with local Zika transmission. **"It is unlikely that it will have an impact on the Olympics." Six hundred people in the United States have Zika …a result of traveling to the areas mentioned.** There have been dengue outbreaks in Texas and Florida and some outbreaks of **chikungunya** cases. **"We went ahead with our research with $47 million from USAID, using our knowledge from dengue etc. We can determine the difference between Zika, dengue,** and chikungunya, w**ith specific tests and mutagenesis studies. We are also testing compounds."** In September 2016, there will be a Phase I clinical trial with a West Nile DNA vaccine and a trial with Zika DNA. The trials should end by January 2017. A large Phase II trial will be done in specific countries– details to follow. **At the June 6 NIAID Advisory Council meeting, Dr. Fauci noted that "many scientists have turned around on a dime and are going into Zika research. [That is] "very impressive; it says a lot about our researchers."** The ultimate goal is to develop therapeutics, vaccines, and diagnostics.
- **On August 3, NIAID announced it has launched a Phase I clinical trial of a vaccine which would prevent Zika virus infection.**
- At his Advisory Council meeting, Dr. Fauci stated, **"Ebola is not done. We still need to do things to keep it in check."** He noted that under the new undertaking PREVAIL, (partnership for research on Ebola virus in Liberia), the clinical trials that were conducted with two vaccines showed they were well tolerated in Phases I, II, III, and there was no sign of Ebola.
- **At the ACD meeting, Dr. Douglas Lowy, acting director of the National Cancer Institute (NCI), gave a brief summary of the Cancer Moonshot goals. They include, "encouraging greater cooperation and breaking down silos within and between academia, government and the private sector." "We in cancer research feel the substantive changes in the attitudes toward discovery and are encouraged that there is interest in data sharing. We are poised to make progress," he noted.**
- Dr. Lowy gave a brief description of the **goals of the Blue Ribbon Panel that has been formed for the Moonshot effort. The final report of this panel will be presented to the National Cancer Advisory Board meeting the end of August and to the ACD in early December. Goals:**
  - identify major scientific opportunities poised to be accelerated by additional emphasis and funding
  - identify major scientific and regulatory hurdles that can be overcome with additional emphasis and funding
  - suggest mechanisms to address research gaps in knowledge, development, key technologies, and aid to overcome these impediments to progress
  - develop 5 to 10 recommendations of opportunities to be pursued.

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At the June 6 NIAID Advisory Council meeting, Dr. Fauci noted that "many scientists have turned around on a dime and are going into Zika research…"

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At his own National Cancer Advisory Board/Board of Scientific Advisers meeting, Dr. Lowy noted that Moonshot is an opportunity for focused research, taking advantage of current research and understanding and improving outcomes of treatments.

- **At his own National Cancer Advisory Board/Board of Scientific Advisers meeting, Dr. Lowy noted that Moonshot is an opportunity for focused research, taking advantage of current research and understanding and improving outcomes of treatments. NCI will continue to support all of its other research. Developing a formulary is also very important and will help with combination therapy. The formulary idea was propelled by the opportunity to get access to trials and some drugs and to get companies and others involved in combination trials with NCI as the broker. NCI met with representatives from 20 companies in late May and early June and all the reviews were positive. The hope is that by the end of the year several drugs will be made available.** At the end of June, there was a Moonshot summit at Howard University in Washington, DC. Thirty new initiatives were announced. Public-private partnerships with many pharmaceutical and biotechnology companies will be expediting access to investigational agents for cancer researchers. The American Cancer Society will provide $200 million over the next five years for this effort. The NCI will put together 25 to 30 public / private partnerships with pharmaceutical and biotechnology companies.
- **As part of the Moonshot effort, Food and Drug Administration (FDA) Commissioner, Dr. Robert Califf, announced the end of June, the appointment of Dr. Richard Pazdur as acting director of FDA's Oncology Center of Excellence (OCE).** The OCE will "expedite the development of novel combination products and support an integrated approach to tackle this devastating disease…."
- A June 22 statement from the NIH National Center for Complementary and Integrity of Health **(NCCIH) Director Dr. Josephine Briggs notes that Americans spent $30.2 billion ($28.3 for adults and $1.9 billion for children), out of pocket for complementary health approaches and herbal supplements.** "With so many Americans using and spending money on complementary health approaches, it is extremely important for us to provide the public with evidence-based information to help inform decisions. This underscores the importance of conducting rigorous research to know whether the products and practices being used are safe and effective."
- The **European Medicines Agency** committee for medicinal products for human use **gave the green light for the Shire's ONIVYDE® (an irinotecan combination) to treat metastatic adenocarcinoma.**
- **NCI's late July Physician Data Query (PDQ) notes the use of laetrile to treat cancer. Laetrile's main compound is cyanide, amygdalin,* found in the pits of many fruits and plants. It was isolated in 1835 by French chemists and first used as a cancer treatment in Russia in 1845 and in the U.S. in the 1920s. Laetrile is not approved for use in the U.S .** *(The Greek word for almond is *amygdalo; plural = amygdala, hence amygdalin*).
- **Halichondrin keeps on giving even to the far reaches of the world. The China FDA will review a new drug application (NDA) for HALAVEN® (eribulin mesylate) for the treatment of metastatic breast cancer. *Halichondrin* was isolated from the marine sponges Halichondria and was worked on by ASP Fellow Dr. George Pettit.**
- **Prostate cancer patients in the United Kingdom won access to the drug Jevtana®, (Sanofi Genzyme). Jevtana is cabazitaxel, a paclitaxel derivative, 10-deacetylbaccatin III. Paclitaxel keeps on giving!**
- An August 3 article in *Nature* has caused a flood in lay press. **German scientists, led by Dr. Andréas Peschel at the University of Tüebingen, Tüebingen, Germany, have discovered that the human nose contains bacteria that could produce antibiotics to kill many bugs including methicillin-resistant *Staphylococcus aureus* (MRSA).** The researchers highlighted one important fact: **the human microbiome is a potential new source of antibiotics.** Stay tuned. ■

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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.phcog.org. If you have a conference or event you would like mentioned, please send us relevant information, including any graphics or appropriate fliers, at asp.newsletter@lehman.cuny.edu.

The 9th Shanghai International Conference on Traditional Chinese Medicine and Natural Medicine

October 19-21, 2016

Shanghai, China

www.s-tcm.com

ASP Annual Meeting

July 29-August 2, 2017

Hilton Portland & Executive Tower

Portland, Oregon

http://www.pharmacognosy.us/wp-content/uploads/ASP-2017-Portland.pdf

3rd Natural Products Conference: Interface of Science and Technology as Applied to Natural Product Research

March 20-23, 2017

Fiesta Americana Condesa

Cancun, Mexico

www.fusion-conferences.com/conference55.php

From the Archives: George Robert Pettit, PhD

By Devhra BennettJones

Dr. Pettit

Among chemists world-wide it is an understatement to refer to Dr. Pettit as a super-star chemist. He has always adhered to the highest standards of scientific excellence in his leadership, research, and publications. In 1995, Dr. Pettit was selected as the recipient of the ASP Research Achievement Award honoring his outstanding contributions to research on natural products.[1]

In 2008, the ASP and the American Chemical Society honored Dr. Pettit with a special issue of the *Journal of Natural Products* dedicated to his prolific work, with guest editors Drs. Gordon Cragg, Richard Powell, and Sheo Singh. As an introduction to that special issue, they described his extensive research endeavors as, "Bob Pettit's career has been devoted to the discovery and development of novel and more effective anticancer agents from natural sources, and those of us who have collaborated with Bob know him as an outstanding and resourceful scientist totally committed to improving the treatment and quality of life of cancer patients worldwide....[2]

The esteem in which Dr. Pettit is held is well expressed by his ASP peers. Dr. Richard Powell described his respect for Pettit's work: "I first met Bob and became aware of his exceptional work in the area of anticancer natural products while attending various meetings at the National Cancer Institute in the late 1960s. This was during the time when Dr. Cecil Smith and I were attempting to isolate and determine the structures of the antileukemic alkaloids from *Cephalotaxus* plants. Bob was always interested in and encouraged our work. By 1970, the cephalotaxine esters homoharringtonine, harringtonine, and isoharringtonine were identified as the major active principles. As a member of the National Academy of Sciences Delegation to the People's Republic of China, Dr. Pettit reported that homoharringtonine was being prepared there for clinical trials in June 1974 (Pettit, G. R. China Q. 1976, 68, 789–796). Since then, we have met at many of the annual meetings of the ASP. Bob usually had a camera handy, and I have had the pleasure of assisting publication of a number of papers authored by the group of Dr. Pettit during my tenure as an Associate Editor of the *Journal of Natural Products.*"[3]

ASP Fellow, Dr. Dave Newman, characterized Dr. Pettit and his commitment to chemistry:

> "Bob was one of the earliest academic investigators to work with the National Cancer Institute to investigate the potential of natural products as a source of novel agents against cancer.... In those early days, Bob chose to look at marine-sourced collections whereas his contemporary in the program, Monroe Wall, elected to study plant-sourced materials (taxol and camptothecin came from those studies by Wall). Bob did a superb job that required great perseverance in studying very active extracts from the nudibranch *Dolabella auricularia* culminating in the dolastatins and from the fouling bryozoan *Bugula neritina* culminating in the bryostatins.... Derivatives of the dolastatins, which would never have been made without the initial studies from his laboratories, have reached approval as a warhead on monoclonal antibodies as a treatment for cancer under the trade name of Adcetris®. Bob set up the Cancer Research Institute at Arizona State University [ASU] (where he has been since 1965). He then proceeded to gather his own collections of plants and marine organisms world-wide and over the years has published a large number of papers (over 500 if my memory is correct) on very complex but very potent structures with antitumor activity, including the combretastatins where semi-synthetic variations are now in Phase II clinical trials under license to small companies.[4]

Dr. Pettit's regard for scientific excellence is well-known. He has dedicated his life to the advancement of cancer knowledge. His journey was chronicled by Richard Byar in *Waging War on Cancer: Dr. Pettit's Lifelong Quest to Find Cures* (2015). It is an exceptional account of his exemplary career and tenacity in the face of extreme adversity. Dr. Pettit's MS and PhD Professor, the late Dr. Carl Djerassi, wrote, "Pettit is one of the great heroes in the chemistry of marine natural products out of which he created a battery of anti-cancer agents not equaled anywhere."[5]

Numerous ASP colleagues have praised Byar's account of Pettit's career. Dr. John H. Cardellina wrote, "Most readers of this review are likely familiar with Professor Pettit's significant contributions to the discovery of antitumor compounds from nature... Perhaps less known to readers is the grand plan that Bob conceived early in his career for a multifaceted cancer research center, where discovery, medicinal chemistry, pharmacology, toxicology, and mechanism of action studies would all be conducted under one roof. That vision was fulfilled at ASU and, for a time, succeeded admirably. The book winds to its end by dealing frankly with the untimely demise of that very successful institute and the ongoing legal battle that now distracts Bob from his real, continued focus: finding and providing successful treatments for cancer."[6]

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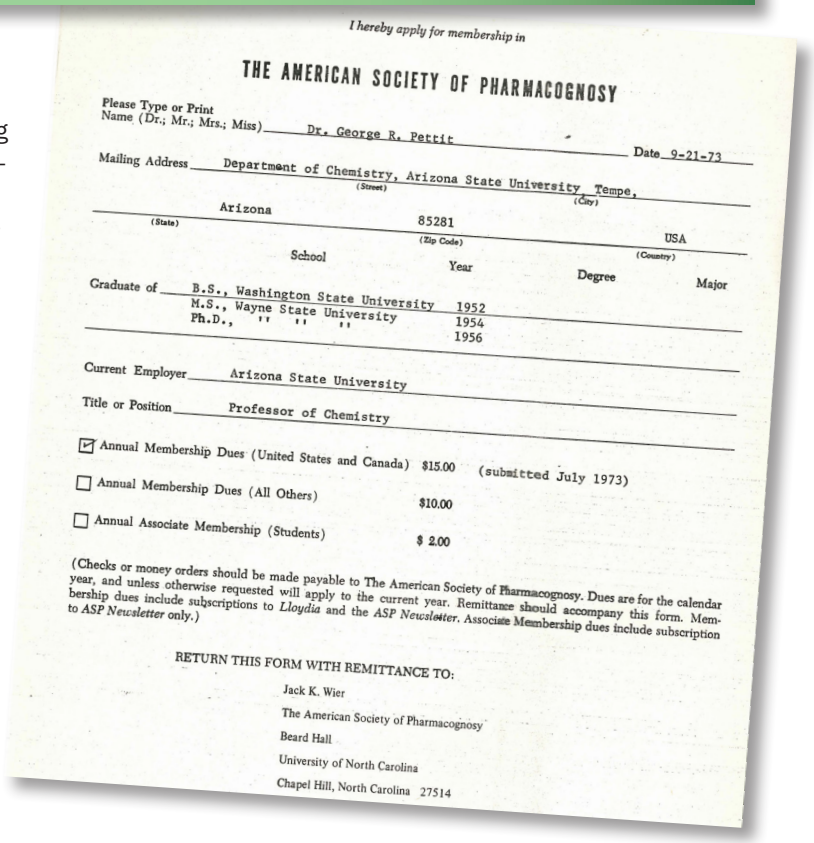
Dr. Pettit's long-time friend and colleague, Dr. Gordon M. Cragg lauded his research achievements and astutely gauged his scientific conscientiousness in lieu of the circumstances at ASU,

"…conflicts in opinions and confrontations with university authorities lead to the demise of his frontline Cancer Research Institute at ASU in January, 2006. The events leading to this catastrophe are outlined in a final chapter comprising an article by Megan Irwin entitled "A Cancer on ASU" which appeared in the Phoenix New Times on January 18, 2007, with the intriguing subtitle 'Could Bob Pettit Have Cured Cancer in His Lifetime? We Might Never Know, Thanks to Nasty University Politics'. But undaunted by an apparently crushing setback, this remarkable and indomitable scientist continues in 2015…, and with only a handful of researchers, to pursue his lifelong quest 'to find new cancer cures and treatments.' This tenacity and commitment clearly reflect his philosophy for leading a worthwhile and productive life…"[7]

The ASU controversy remains unresolved. The university administration incorporated Pettit's research initiatives into the Biodesign Institute. Dr. Pettit responded with a lawsuit that is still pending against ASU.[8] Meanwhile, he marches on immersed in the lengthy process of scientific research and the accumulation of evidence in his search for a cancer cure. ■



I hereby apply for membership in

THE AMERICAN SOCIETY OF PHARMACOGNOSY

Please Type or Print
Name (Dr.; Mr.; Mrs.; Miss) Dr. George R. Pettit Date 9-21-73

Mailing Address Department of Chemistry, Arizona State University Tempe,
(Street) (City)
Arizona 85281 USA
(State) (Zip Code) (Country)

	School	Year	Degree	Major
Graduate of	B.S., Washington State University	1952		
	M.S., Wayne State University	1954		
	Ph.D., " " "	1956		

Current Employer Arizona State University

Title or Position Professor of Chemistry

☑ Annual Membership Dues (United States and Canada) $15.00 (submitted July 1973)

☐ Annual Membership Dues (All Others) $10.00

☐ Annual Associate Membership (Students) $ 2.00

(Checks or money orders should be made payable to The American Society of Pharmacognosy. Dues are for the calendar year, and unless otherwise requested will apply to the current year. Remittance should accompany this form. Membership dues include subscriptions to *Lloydia* and the *ASP Newsletter*. Associate Membership dues include subscription to *ASP Newsletter* only.)

RETURN THIS FORM WITH REMITTANCE TO:

Jack K. Wier
The American Society of Pharmacognosy
Beard Hall
University of North Carolina
Chapel Hill, North Carolina 27514

Dr. Pettit's ASP membership form from 1973.

Bob was one of the earliest academic investigators to work with the National Cancer Institute to investigate the potential of natural products as a source of novel agents against cancer….

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1 *American Society of Pharmacognosy Newsletter*, Vol. 30, No. 3, Winter **1995**, and Vol. 31, No. 3, Fall 1995.

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4 Newman, Dave. August 18, 2016, email to Devhra BennettJones.

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8 Wilson, Elizabeth. Cancer Drug Research Group Dismantled: Move is latest in a conflict between chemistry professor and Arizona State University, Chemical & Engineering News, American Chemical Society, February 6, **2006**, p. 10.

Jim McAlpine, Ph.D, Treasurer
The American Society of Pharmacognosy
3149 Dundee Road, #260,
Northbrook, Illinois 60062

ASP Membership

Full Membership

Full membership is open to any scientist interested in the study of natural products.
Current membership dues and Journal of Natural Products subscription rates can be found at **www.pharmacognosy.us**.

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Associate membership is open to students of pharmacognosy and allied fields only. These members are not accorded voting privileges.
Current membership dues and Journal of Natural Products subscription rates can be found at **www.pharmacognosy.us**.

Emeritus Membership

Emeritus membership is open to retired members of the Society who maintained membership in the Society for at least five years.
Current membership dues and Journal of Natural Products subscription rates can be found at **www.pharmacognosy.us**.

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