



Homoharringtonine: A Pharmacognosy Success Story

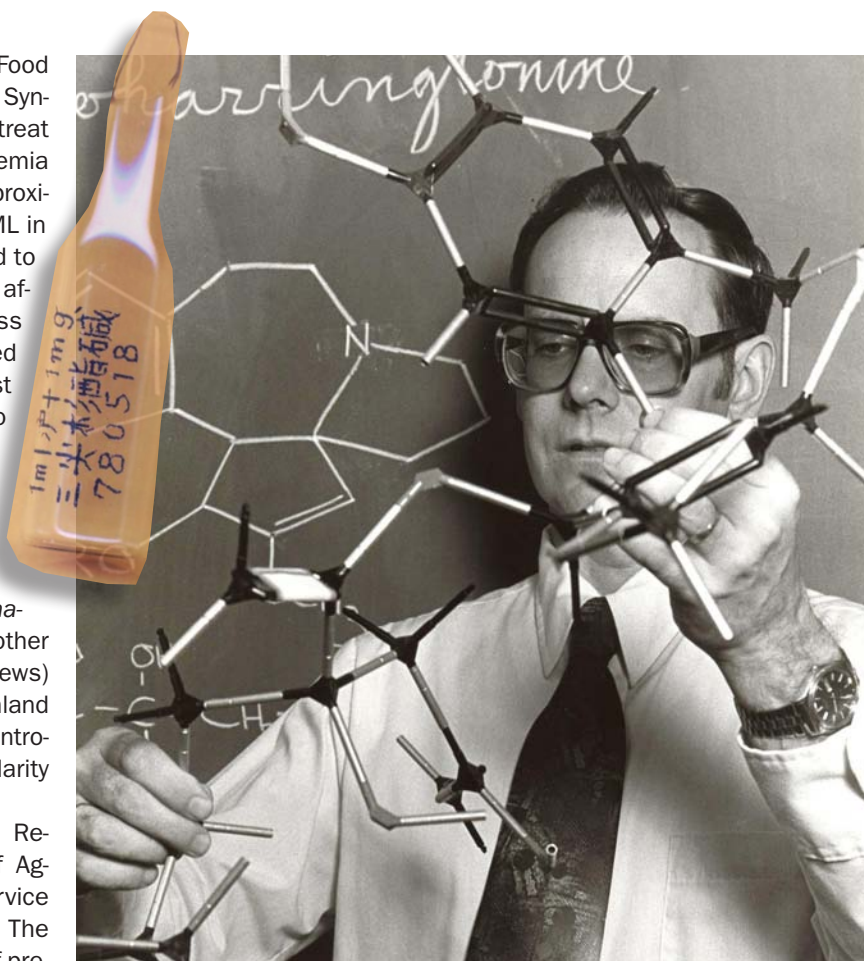
By Dr. Richard Powell

On October 26, 2012, the United States Food and Drug Administration (FDA) approved Synribo® (omacetaxine mepesuccinate) to treat adults with chronic myelogenous leukemia (CML), a blood and bone marrow disease. Approximately 5,430 people will be diagnosed with CML in 2012, according to the NIH. Synribo is intended to be used in patients whose cancer progressed after treatment with at least two drugs from a class called tyrosine kinase inhibitors (TKIs), also used to treat CML. My work on this drug began almost five decades ago, and I originally gave Synribo the common name homoharringtonine in 1970.

The road to approval of Synribo for treatment of leukemia in the United States has been a long and torturous one, but in the beginning it ran closely parallel to that of the discovery of the well-known antitumor drug Taxol®. *Cephalotaxus harringtonia* (Cephalotaxaceae) and other *Cephalotaxus* species (commonly called plum yews) are mostly small trees native to Japan and mainland China. *Cephalotaxus harringtonia* had been introduced as an ornamental but gained little popularity in the United States prior to 1960.

I began working at The Northern Regional Research Center, United States Department of Agriculture (USDA), Agricultural Research Service (ARS), Peoria, Illinois, in the summer of 1963. The position involved chemical analysis of seeds of previously uninvestigated plants, determining struc-

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Above left: Homoharringtonine from China, 1mg/ml.

Dr. Richard Powell working out the structure of homoharringtonine, 1980.

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EDITOR'S CORNER



As 2013 arrives, this issue of the *ASP Newsletter* marks several new beginnings.

At the 2011 ASP Meeting Annual Meeting in San Diego, there was some excellent brain storming about potential changes to the *Newsletter* that could be implemented in the future. I am glad to report that the future is upon us, and two new series that were suggested at that time make their debut in this issue: "Pharmacognosy Field Notes" and the first installment of a series from the ASP Fellows.

"Pharmacognosy Field Notes" is meant to provide some perspective on the work that first inspired many of us to enter pharmacognosy. I hope that the information provided in this article will especially inspire younger members to work in pharmacognosy. From what I have heard, the

late ASP member Dr. John Daly was not only a great chemist but also an inspired and fearless field researcher. We hope that hearing about experiences from the field will provide motivation and insight to our members. I thank Dr. Doug Kinghorn for helping to develop the concept for this article, and to his former doctoral student, Dr. Alison Pawlus, for taking on the first in this new series.

Dr. Bill Gerwick is the Chair of the ASP Fellows. As part of our discussions in the San Diego meeting, there was interest in having the Fellows contribute in a significant way to the *Newsletter*. In his article, Dr. Gerwick describes a meeting with the Fellows at the recent 2012 New York meeting, and one of the recommendations he reports is, "Providing a regular contribution to the *ASP Newsletter* on Perspectives on Natural Products Research." I am thrilled to have the Fellows on board with this project, and I look forward to regular contributions from them in future *Newsletters*.

Another good idea for a new *Newsletter* series can be traced back to a recent ASP Foundation meeting. Dr. John Cardellina describes the Foundation's hope to inform ASP members more broadly about the history and impact of various ASP Foundation awards. The Foundation and Society agreed that it would be good to begin with the Matt Suffness Award. You can read more about the award itself and see remembrances from the first awardee and the most recent. We plan to continue to profile former Suffness awardees in future *Newsletters*.

The 2013 Annual Meeting organizers provide information on the upcoming meeting in St. Louis, Missouri, from July 13-18. The science program is almost complete, and it should be a stimulating meeting at relatively low costs. Please look at the website when it goes live at: www.asp2013.org

Our regular series includes two new columnists. We bid farewell to Lloyd Library archivist Ms. Anna Heran, author of "From the Archives" for several years, and welcome Ms. Devhra BennettJones, also of the Lloyd Library, who has provided us with a fascinating history of Dr. Dick Powell's work on a newly approved cancer drug. We thank Dr. Diane Swaffar for her tremendous work profiling new members, and welcome on board Younger Member, and my own doctoral student, Mr. Daniel Kulakowski for this column. The *Newsletter* would not be possible without committed volunteer writers, and we are especially indebted to these regular columnists, including Dr. Georgia Perdue.

I hope you have a happy, healthy, and productive 2013!

Dr. Edward J. Kennelly

EMPLOYMENT SERVICE

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/?page_id=163

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tures of new and unusual lipids and fatty acids. The seed collections were largely from USDA botanists from many countries that had received aid from the Food for Peace program under Public Law-480. During this same time, extracts of plant materials were being solicited for testing in the anticancer screening program at National Cancer Institute (NCI), National Institutes of Health (NIH). Our purpose was to identify and introduce new crops with previously unknown components with commercial potential.

Early in 1966, I was offered a fellowship to study with Dr. Frank Gunstone at the University of St. Andrews, Scotland. Dr. Gunstone was the acknowledged expert in the study of fatty acids and lipids. Having just completed a project, and before leaving for a year, Dr. Ivan Wolff, our Laboratory Chief, asked me to look through a large stack of correspondence that had accumulated in his office. The correspondence dealt with antitumor tests of 200 seed extracts that he and Dr. Cecil Smith had sent to the NCI screening program around 1961. If there was anything that looked interesting, I was instructed to prepare fresh extracts for confirmation testing.

It was immediately apparent that 20 of the original extracts were positive in initial tests, and that an extract of *C. harringtonia* was of particular interest as it showed activity against L-1210 leukemia in mice. I prepared extracts for confirmation testing and left for Scotland.

Initial tests took months in those days due in part to the backlog of samples to be tested and to the relatively long periods required for in vivo tests. However, test results of the extract were encouraging as it showed significant in vivo activity against L-1210 and P-388 leukemia in mice.

When I returned to Peoria in late 1967, there was another stack of correspondence and test results waiting for me. Dr. Jonathan Hartwell (NCI) was strongly urging our group to fractionate the *C. harringtonia* extract and determine the structure of the active compound(s). This was not a priority at ARS since the plant had low crop potential. Dr. Hartwell soon placed it on the high priority list for fractionation and identification of the active component(s), and the group at Research Triangle Institute (Drs. Monroe Wall and Mansukh Wani) was requesting that they be given priority for work on this plant if ARS was not going to pursue the matter.



Dr. Richard Powell.

MS. ROSEMARY POWELL.

Dr. Smith and I were selected to carry out the fractionation, isolation, and structure determinations. The process involved periods of intensive lab work followed by months of waiting for test results on the various fractions and pure compounds. Periodically there were conferences to report fractionation progress with others involved in similar studies convened by Drs. Hartwell, Matt Suffness, John Douros, and others at NCI. Those usually attending the meetings were prominent natural products chemists including Drs. S. Morris Kupchan, Robert Pettit, and Monroe Wall.

By 1970, the cephalotaxine esters harringtonine, homoharringtonine, and isoharringtonine were identified as the major active principles. The results were published in 1972 (*J. Pharm. Sci.* 61(8): 1227-1230).

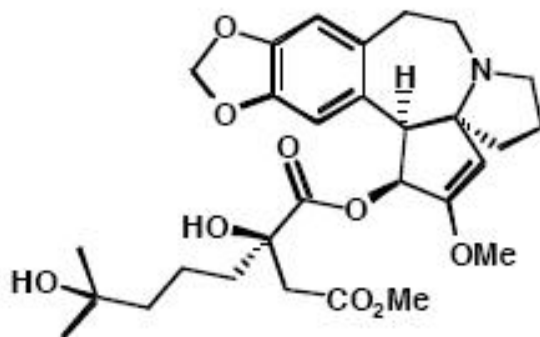
Homoharringtonine was active in the conventional murine leukemia assays, L-1210 lymphoid leukemia (T/C 123-142 at 0.25-1.0 mg/kg) and P-388 lymphocytic leukemia (T/C 244-338 at 0.25-1.0 mg/kg). NCI requested quantities of these alkaloids sufficient for preclinical trials; however, there was no known source of *Cephalotaxus* plants in the United States. Dr.

Robert Perdue, then of the USDA, Beltsville, Maryland, in cooperation with NCI, was eventually able to obtain 1,000 lbs. of *C. harringtonia* var. *harringtonia* cv. *fastigiata*, representing 17 entire trees including roots, from a nursery in Oregon. Extraction of this collection at National Center for Agricultural Utilization Research (NCAUR) yielded 330 g of mixed alkaloids and, ultimately, 16.6 g of homoharringtonine which was selected for preclinical studies.

Additional plant material needed to provide quantities of homoharringtonine for clinical trials was unavailable to us at that time.

However, availability of plant material was less of a problem in mainland China. Dr. Pettit, a member of the National Academy of Sciences Delegation to the People's Republic of China, reported that homoharringtonine was being prepared there for clinical trials in June of 1974. The People's Republic of China has continued to be the major supplier of *C. harringtonia* alkaloids. Difficulties in obtaining these alkaloids in desired quantities and the novel and relatively complex structures led many to attempt

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ASP Announces New Treasurers

By Dr. Amy Keller

The ASP Executive Committee has approved the appointment of Dr. Guido Pauli as the new ASP Treasurer, and Dr. Nam-Cheol Kim as the Assistant Treasurer.

Dr. Pauli is an Associate Professor of Medicinal Chemistry and Pharmacognosy at the College of Pharmacy, University of Illinois, Chicago, and has been an ASP member for 16 years. Dr. Kim, an ASP member of 20 years, is a Scientist IV at the United States Pharmacopeia, Rockville, Maryland.

These appointments come after the retirement in July, 2012, of long-time ASP Treasurer Dr. David Slatkin, after 31 years of dedicated service to the Society. (Dr. Pauli has served as Assistant Treasurer since 2006.)

The Treasurer manages the finances of ASP and the *Journal of Natural Products (JNP)*, financial reporting, and the planning and related management of Annual Meetings. The Treasurer also serves on the *JNP* management board, is involved with ASP awards and funds management, and oversees dues collection.

When asked about his general thoughts of the Treasure position, Dr. Pauli told the *Newsletter* via e-mail, "The dedication with which David [Slatkin] has served as ASP treasurer for over 30 years is unsurpassed and has undoubtedly set the gold standard in this office."

Dr. Pauli continued, "ASP is the world's prime network of natural products researchers and can greatly benefit from the electronic age. I encourage all, and particularly the younger members, to get involved and take an active role in creative new developments." ■



Drs. Pauli and Kim at the Slatkin Symposium in October.

DR. EDWARD J. KENNELLY

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synthetic approaches to cephalotaxine and its esters. Dr. Tomas Hudlicky and his group described a stereospecific total synthesis of homoharringtonine in 1983 and reviewed synthetic work on these alkaloids in 2007.

Early studies in mainland China reported high response rates in patients with leukemia, and recent studies in the United States and the United Kingdom have shown promising results in patients with CML. FDA approval to treat CML is encouraging, and the drug Synribo is currently marketed by the Israeli drug maker Teva Pharmaceuticals, with United States headquarters

in Frazer, Pennsylvania.

Ideally, this compound will provide an avenue of effective treatment to those for whom the first lines of treatment have failed. As this story of discovery illustrates, the importance of pharmacognosy cannot be underestimated. The natural world holds many treasures, not the least of which may be novel therapeutics for tomorrow's cures. As we continue to study new compounds and their bioactivity against chronic and other diseases, the approval of another phytochemical for cancer treatment holds great promise for others in both pharmacognosy and cancer research. ■

ASP Annual Meeting 2013: Meet Us in St. Louis!

By Drs. Ray Cooper and Mark O'Neil-Johnson

The Organizing Committee for the 2013 Annual Meeting of the American Society of Pharmacognosy is pleased to host "Natural Products at a Crossroad: Current and Future Directions," from July 13 to July 18, 2013, in Saint Louis, Missouri.

Plans are moving well ahead for the 2013 Annual Meeting. We have a marvelous meeting planned to be held in the heart of downtown St. Louis by the mighty Mississippi River at the Hyatt Regency St. Louis at the Arch. The hotel and venue for the Annual Meeting is situated next to the famous St. Louis Gateway Arch and within walking distance of many downtown attractions and restaurants.

In consideration of making the Annual Meeting cost effective for doctoral and postdoctoral students and hopefully entire laboratories, we have obtained very reasonable rates of \$135 per night with free wifi at the Hyatt Regency while keeping the quality of the venue at its highest.

At the Hyatt, we have secured one entire floor allocated to the meeting with lecture halls and a large adjacent area for the posters and breakout gatherings.

SCIENTIFIC PROGRAM: We are reaching out to a broad and diverse natural products community involved in industry, academia and education. We hope to attract new "voices" to our meeting. Our theme embraces the fact that natural products touches on many scientific disciplines. The scientific program includes advanced analytical technologies emphasizing their importance to the long-term success of natural products and the traditional topics of natural products in drug discovery, marine and microbial natural products, botanicals, and ethnobotany.

This year's plenary lectures will highlight remarkable successes involved in natural product synthesis, recently commercialized drugs inspired from natural products, and a one-of-a-kind perspective of the evolution of NMR over the last 50 years.

Several noteworthy sessions include new anticancer therapeutics derived from natural products and natural products enhancing the experience of pet foods. Covered scientific foci include Natural Products: Drug Research and Current Drugs on the Market, Application of Natural Products for Pet Foods, Chemistry, Biology and Ecology of Marine Natural Products, Botanicals: The Road to the Clinic, Natural Products as Anti-Cancer Agents, Ethnobotany and Botanical Discovery, Spectroscopic Technique in Natural Products Chemistry, Frontiers of Discovery Through Spectroscopy, Botanicals and Foods, and New Innovations in Agrochemical/Biotechnology. Also,



The central location and affordable meeting venue, in St. Louis, should make this an outstanding opportunity for students and postdoctoral investigators.

the conference will kick off with three workshops on Saturday which focus on NMR, botanicals, and microbiology.

GETTING THERE: The city of St. Louis is served by St. Louis Lambert International Airport. A host of major airlines offer daily service; there is also both excellent taxi service and the Metro link light-rail service running to the downtown area, making the arrival transfer to the conference venue very convenient.

SOCIAL ACTIVITIES: For the conference, we have planned several exciting social activities. The traditional Saturday opening mixer will be at the Hyatt, followed by an "Evening at the Gardens" at the fabulous Missouri

Botanical Gardens on Monday. On Tuesday afternoon, we are planning a free afternoon with the option of an Anheuser Busch Brewery tour and hope to make this a Young Investigator Event.

For those wishing to venture further, there are other major attractions in St. Louis that include the famous Arch (you can go to the top), the St. Louis Zoo (free admission), and many local museums (mostly free admissions). There are Mississippi River access and attractions, downtown jazz clubs, microbreweries and a wonderful vodka bar in the hip Central West End.

Please consult the web page in January for registration and hotel (www.asp2013.org). On behalf of the Scientific Organizing Committee, we are delighted to have the opportunity to create a wonderful ASP program and we do hope you will "Meet Me in St. Louis." ■

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The ASP Matt Suffness Award: A Brief History

By Dr. John Cardellina

At the most recent meeting of the Board of Directors of the ASP Foundation, we discussed how we might promote some of our less well known awards. The Suffness Young Investigator Award seemed a logical place to start.

In the early 1990's, ASP President Matt Suffness was a pivotal player 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. Following his untimely death in 1995, the ASP renamed the award in Matt's honor. Longtime ASP members had the privilege of knowing Matt; most of us benefitted from his wisdom, help, and advice in developing and focusing research programs in our early careers.

Recognizing that our younger members were not so fortunate to know Matt, we thought a series of reflections by previous winners of the Suffness Young Investigator Award would help provide them with a sense of the man, his vision, and his contributions. We also realized that a series of articles in the *ASP Newsletter*, based on those reflections, would achieve that goal, but also draw broader attention to the award itself and, hopefully, induce members to nominate deserving individuals for the award in the years to come.

Response to our request to previous winners for their thoughts on the award was quite good. So, in the next several issues of the *Newsletter*, readers will enjoy the thoughts of our colleagues on winning this award and the impact it has had on them and their careers. The series begins with comments from our very first awardee, Dr. Tadeusz "Ted" Molinski, and our most recent honoree, Dr. Philip Williams.

Dr. Ted Molinski: The late ASP member Dr. Matt Suffness was an early inspiration to all young natural products investigators. In the summer of 1992, I was an Assistant Professor at University of California, Davis, and onstage in Williamsburg, Virginia, at the ASP Annual Meeting as one of two recipients of the inaugural Young Investigator Award (the other was

Dr. Kevin Reynolds, now at Oregon Health and Science University, Portland, Oregon).

Dr. Suffness was off-stage, smiling beatifically, as I presented my award address with a mixture of pride and humility – and nervousness. Later, I learned how Matt worked behind the scenes encouraging young scientists and with the help of others, bringing his now eponymous award to maturation. Current recipients of the Matt Suffness Award, as it is now known – who never knew Matt – should conjure an image of a great man, not only a champion of natural products (think of his tireless efforts to promote Taxol®), but a kind, generous spirit at the National Institutes of Health (NIH) who nurtured fledgling scientific careers.

Over the years, I met Matt several times, the last being at an NIH study section where I was impaneled to evaluate natural products proposals. Matt was a program officer at the back of the room and, again, I could see his smile but this time it was from behind a surgical mask (he was recovering from immuno-compromising cancer therapy). He could not shake my hand, but we nodded in recognition and exchanged pleasantries. Since that day, I wished I had said more by way of gratitude. Better still, I aspire to be more like Matt and 'pay it forward.'

Dr. Philip Williams: I never had the pleasure of meeting Dr. Matt Suffness, but his influence is evident throughout the Society. The sense of community and service that permeate the organization and its commitment to actively nurturing the next generation of natural product researchers reflect the values and principles attributed to Matt by those that did know him. Being connected directly to Dr. Suffness' legacy as this year's awardee is a tremendous honor. It is an honor as recognition of my scientific accomplishment, but also as a reminder that my career has matured to the point where there is a duty to promote the careers of my younger colleagues, be they students, postdocs, or assistant professors. ■



Dr. Molinski in Western Australia desert coast in 1992 after a successful day's collection of marine organisms.

DR. DENISE MANKER



Dr. Williams in the laboratory.

DR. JINGQIU DAI

Behind the Scenes in Pharmacognosy: Jiminy Cricket!

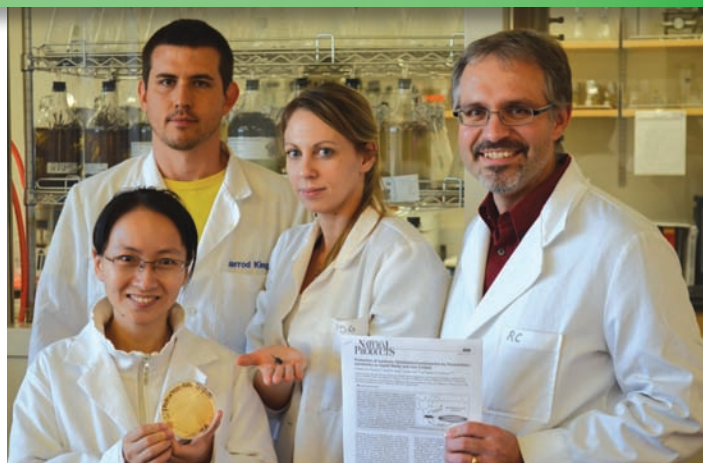
By Dr. Amy Keller

This past October, the *Journal of Natural Products* published an article from ASP member Dr. Robert Cichewicz and his colleagues at the University of Oklahoma's Institute for Natural Products Applications and Research Technologies (INPART) in Norman, Oklahoma, entitled, "Production of Cytotoxic Glidobactins/Luminmycins by *Photorhabdus asymbiotica* in Liquid Media and Live Crickets". Please read the full article in the *Journal of Natural Products*, 2012, 75(11), 2007-2011. DOI: 10.1021/np300623x.

1. How did you become interested in working with bacterial compounds, and how did you come to focus on their expression in live crickets?

Since 2005, our laboratory has focused on investigating secondary metabolites from microorganisms. While most of our work has been concerned with the drug development applications of fungal natural products, opportunities to work with bacteria have emerged from time to time. For example, we have worked with Dr. Felicia Qi at the University of Oklahoma Health Science Center to study hybrid polyketide-nonribosomal peptide metabolites produced by a bacterium that occupies the human oral cavity. More recently, we have engaged in new collaborative project with Dr. Brad Stevenson from the University of Oklahoma Department of Plant Biology and Microbiology to investigate bacteria from the microbiomes of mammals native to the southeastern United States as a source of new bioactive substances. During this time, a paper caught our attention describing *Photorhabdus asymbiotica* as an emerging bacterial pathogen that may infect humans via a nematode host (J. G. Gerrard, et al. Nematode symbiont for *Photorhabdus asymbiotica*. *Emerg Infect Dis*. doi.org/10.3201/eid1210.060464). Further supporting our interests in this bacterium was the tremendous insights provided in the work by Dr. Helge Bode about the natural product chemistry of *Photorhabdus* and *Xenorhabdus* species. In addition, these bacteria engage in a variety of curious symbiotic relationships with entomopathogenic nematodes. Despite reports of natural products from other taxonomically related isolates, *P. asymbiotica* had not been subjected to an investigation of its secondary metabolites.

Our initial results were disappointing. We knew the bacterium's genome contained nearly two dozen biosynthetic gene clusters (based on analysis with antiSMASH), yet culture extracts were devoid of detectable metabolites. Doctoral student, Ms. Christine Theodore, showed tremendous resolve testing a large number of media until she finally discovered conditions supporting the production of an assortment of the organism's cryptic metabolites. This led to a new question, "Why is the production of these metabolites under such strict control and how can we overcome this limitation in the lab?" Considering many possibilities, we arrived at the hypothesis that the production of these compounds may require very specific environmental cues such as those experienced when *P. asymbiotica* is released from its nematode host



The University of Oklahoma Natural Products Applications and Research Technologies team members who carried out the cricket studies. From the left: Dr. Jianlan You (holding a plate containing *P. asymbiotica*), Mr. Jarrod King, Ms. Christine Theodore (holding a cricket), and Dr. Robert Cichewicz (holding a copy of the published cricket manuscript).

MS. ASTRUD REED.

into an animal or insect. At the same time these events were unfolding, postdoctoral fellow Dr. Jianlan You, had been developing insect-based assay models of infectious disease for our group. It seemed reasonable that we could adapt those experiences to test whether an invertebrate host could provide an appropriate environment for the growth and production of *P. asymbiotica* metabolites. Both Jianlan and Christine worked together to establish a test system using crickets. We were very excited to see that the controlled inoculation of crickets with *P. asymbiotica* resulted in the accumulation of many of the bacterium's metabolites within the insects. Performing LC-MS on the crickets, we found that glidobactins/luminmycins metabolites were among the most prevalent of the microbial-derived compounds recovered from the organic extracts. Mr. Jarrod King, who operates our team's bioassay screening unit, was able to test these metabolites in cytotoxicity and proteasome-inhibition assays demonstrating that our compounds exhibited potent inhibitory effects similar to those for other members of the glidobactins/luminmycins family.

2. Who in your laboratory carried out the research?

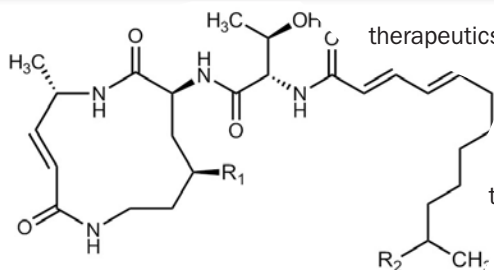
Similar to all projects in our lab, this work was a collaborative effort among several individuals within our research group. Although we are affiliated with the Department of Chemistry and Biochemistry, we pride ourselves on maintaining a diverse group of students, postdoctoral fellows, and research associates with formal academic training in chemistry, biochemistry, molecular biology, microbiology, and pharmaceuticals. Christine is a biochemistry Ph.D. candidate who is training in the area of natural products chemistry. Both Christine and I worked together to design the experiments. She also performed all of the metabolite purification, structure determination analysis, and analytical chemical studies. Dr. Jianlan You is a microbiologist who has been develop-

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Behind the Scenes in Pharmacognosy: Jiminy Cricket!

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ing new assays for our research program as well as providing a wealth of expertise concerning the molecular biology of both bacteria and fungi. She collaborated with Christine to establish the cricket-based experiments. Mr. Jarrod King is the lead biologist responsible for all of the antibacterial, antifungal, and cancer cell cytotoxicity screening operations in our group. He is also a key player in our fungal and bacterial isolate procurement efforts. This bottom-up integration of scientists with diverse backgrounds is one of our fundamental strengths and it was certainly an important factor in this project.



glidobactin A $R_1 = \text{OH}$, $R_2 = \text{H}$

luminmycin A $R_1 = \text{H}$, $R_2 = \text{H}$

luminmycin D $R_1 = \text{H}$, $R_2 = \text{CH}_3$

Structures of the glidobactins/
luminmycins obtained from crickets
infected with *P. asymbiotica*.

therapeutics to treat a myriad of human diseases. This is our group's primary research focus. We are also rapidly expanding our efforts in this area with the establishment of the new Institute for Natural Products Applications and Research Technologies at the University of Oklahoma. We are in the process of hiring and sustaining six natural products research groups who will work on a collaborative basis toward the development of new lead molecules for several disease indications. We are using the same ecological principals utilized in this study to further enhance the bioactive compound discovery process and help provide an efficient path toward preclinical drug development.

3. Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

One of the important themes contained in this paper is the incredible level of acute sensitivity that many microorganisms exhibit when it comes to biochemical responses to the environment. While this is by no means a new observation, it is certainly one that has created an enormous range of challenges and possibilities for the field of microbial natural products. Although molecular-based approaches to controlling secondary metabolite production have provided important opportunities for uncovering the products of silent biosynthetic pathways, they also inadvertently perpetuate a fundamental scientific dilemma: How do the microorganisms interpret their local environments and why are they capable of making such an amazing array of secondary metabolites? The combination of modern genomics technologies and systems biology have helped reveal many new insights concerning these problems, but they alone are insufficient to understand how microbial systems (populations of cells) function as the basic operational units within an ecological context. When one considers the extent to which many bacteria and fungi exhibit a profound mutual reliance on other microbes, plants, and animals, it becomes apparent that understanding the role of natural products within an ecological context is an immense challenge. This is why theory from the field of ecology coupled with classic descriptive biological sciences will continue to play important roles in addressing the "big" questions about natural products (e.g., Why are natural products made at all?). Our paper represents a very modest, but potentially useful contribution to moving us incrementally closer to understanding why secondary metabolites have evolved into one of nature's most fascinating forms of organic chemistry.

4. What impact does this research have on natural product science and health research in general?

Using ecological insights to manipulate microorganism into revealing their secondary metabolites is the best approach to effectively mining nature for new bioactive compounds. Although the multitude of roles that natural products play in our world is fascinating, a more pressing problem is the need for new small-molecule

5. What is a favorite nonscientific activity of your lab?

Outside of weekly group research meetings, we do not have any compulsorily nonscientific lab activities. The group is highly diverse and our members work incredibly hard based on their passion for their research. Individuals or small groups of lab members engage in a variety of activities including sports (e.g., soccer, olympic weightlifting, running, etc.), reading, drawing, coin collecting, and life with family. Our group's greatest strength, its diversity of individual backgrounds and ideas, is optimally maintained by having each member engage in their own unique pastimes.

6. What is your lab's motto?

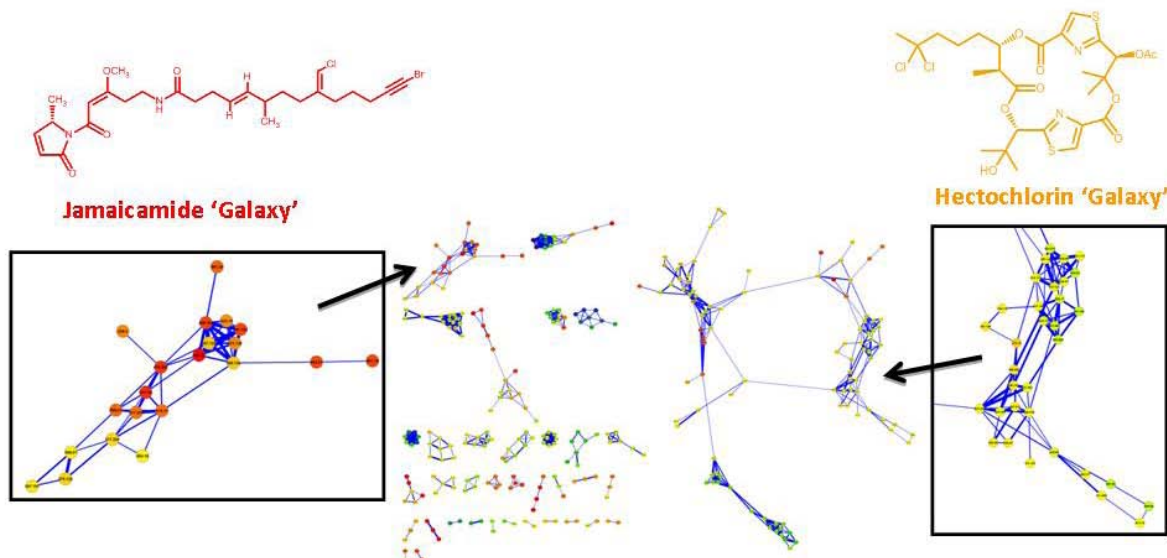
Our lab's motto, "Transforming the chemistry of nature into products that improve lives," has evolved into the guiding principal for the Institute for Natural Products Applications and Research Technologies. This motto is a constant reminder of why we are here and what our goals are. Everything we do is focused on the development of new therapeutic agents ranging from direct natural products discovery to efforts aimed at enhancing the hunt for new bioactive compounds. Our recent paper highlights the latter as a means for improving the approaches we use to find new hit molecules.

7. What is your greatest extravagance in the lab?

We really do not have any "extravagances" in our lab. Every tool, instrument, and machine was purchased with state or federal funds and we have a responsibility to the taxpayers of the United States and state of Oklahoma to ensure their money is put to the best responsible use. With that said, our group and institute are appropriately outfitted to take on a range of research challenges including analytical studies (LC-MS), compound purification and structure determination (HPLCs, various evaporators, and spectroscopy tools), and biological testing (BSL2 facilities with hoods, incubators, plate readers, and other molecular biology equipment). Having this equipment is also a key component of student training with individuals who have worked in our group having hands on exposure with all of our instruments. ■

ASP Fellows Series: Perspectives on the Natural Products Sciences

The 'Molecular Universe' of *Moorea producens* JHB



The 'molecular universe' of the marine cyanobacterium *Moorea producens* JHB, plotted in Cytoscape. Circles (= nodes) represent individual compounds as determined by their molecular ion (MS1) peaks whereas lines connect to other nodes possessing related MS/MS (MS2) spectra. The thickness of lines between nodes reflects the degree of correlation between their MS2 spectra. Colors of nodes are chosen here to reflect mass on a continuous gradient of color where 400 amu = red, 600 amu = yellow, 900 amu = green, 1200 amu = blue and 1300 = violet (appreciative thanks to Paul Boudreau, UCSD Ph.D. student, for preparation of this figure!). For literature on this technique, see: Watrous J, Roach P, Alexandrov T, Heath BS, Yang JY, Kersten RD, van der Voort M, Pogliano K, Gross H, Raaijmakers JM, Moore BS, Laskin J, Bandeira N, Dorrestein PC "Mass spectral molecular networking of living microbial colonies." *Proc. Natl. Acad. Sci. U. S. A.* 2012, 109, E1743-52.

By Dr. Bill Gerwick

This is the first in a series of articles that will appear in the ASP Newsletter, hopefully on a regular and continuing basis, that are intended to give the ASP Fellows an opportunity to address key issues, challenges, and opportunities in the discipline of natural products science, as well as provide some perspectives on topics of specific scientific interest to each of them. As the current chair of the ASP Fellows, I am providing this lead-off article to describe some of the background to this new feature and then will give a short personal perspective on an aspect of the natural products sciences that has long been of fascination and interest to me.

First, however, who are the ASP Fellows? This was another of the progressive ideas of the late Dr. Norman Farnsworth, co-founder of the ASP. In this case, he envi-

sioned another mechanism by which to acknowledge members of the ASP that have provided "continuing, high level contributions in the field of natural products and records of sustained achievement within their sub-disciplines." [see ASP website] Moreover, the charge to the ASP Fellows is to serve an "active role in the ASP by furthering natural products sciences," thus forming an advisory body to the ASP in scientific and professional matters. The Fellows also serve as general advocates for the ASP and the field of natural products. Norm served as the chair of the Fellows until shortly before his passing, at which time I took over these duties.

The ASP Fellows was created relatively recently in 2006, and includes all former Norman Farnsworth Research Achievement Award winners as well as new mem-

bers elected by the Fellows in an Annual Meeting, but cannot exceed more than 5% of the membership in total. The current Fellows are familiar names to the ASP membership, and include Drs. John Blunt, John Cardellina, Jon Clardy, Geoff Cordell, Gordon M. Cragg, Phil Crews, William Fenical, Heinz G. Floss, Jim Gloer, Sidney M. Hecht, Susan Band Horwitz, Chris Ireland, A. Douglas Kinghorn, David G. I. Kingston, K.H. Lee, Tom Mabry, Les Mitscher, Murray Munro, Koji Nakanishi, George R. Pettit, Jack Rosazza, Yuzuru Shimizu, Otto Stichler, Mansukh Wani, and myself.

This past summer at the spectacular 2012 Annual Meeting in New York City (thanks again Drs. Guy Carter, Ed Kennelly and Mark O'Neil-Johnson and the rest of the conference organizers!), the Fellows as-

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sembled for a no-host lunch and discussion of plans for how this group can best serve the Society and its membership. There was a considerable wealth of years of experience around the table, and the ideas were extensive and fun to consider, including:

- Creating a mentoring panel or service for younger members
- Writing a white paper in support of natural products research and advocating for increased research funding and newer contemporary models of funding
- Providing a regular contribution to the *ASP Newsletter* on Perspectives on Natural Products Research
- Organizing a scientific meeting specifically designed for “Young Scientists” with the goals of creating a different level of contact, networking and collaboration among those entering this discipline
- Helping the Society to embrace new disciplines which enrich the field of natural products science and invigorate the society
- Documenting the activities of the Fellows for the future of the Society

With 2012 drawing to a close, I would like to provide my perspective on where we stand in the field of natural products. I am very excited! This is an era of great innovation and powerful new tools by which to study the chemistry, biochemistry, biology, ecology and pharmacology of natural products. Looking around, I see the field populated in academia as well as in industry by a dynamic and highly energized group of young scientists. It is the ‘charge’ to each new independent investigator, and in a sense, to each new generation of investigators, to think outside of the established paradigms, conceptualize new ideas and methodologies by which to take the field to deeper levels of understanding, and to create a distinctive niche within the field. And with the relatively recent focus on translational science, it is also important to envision how this new knowledge can aid society in terms of useful biotechnology, sustainability and thoughtful conservation. This cadre of new young scientists has taken

up this challenge to be innovative in their pursuits, and is moving our field in novel interdisciplinary directions of high relevance to society’s needs.

But where do we turn to for the inspiration of new ideas? One approach to innovation is to draw on new methodologies or techniques from one discipline, and apply these in novel, sometimes revolutionary ways to another field of study. It should be noted that such innovation, termed ‘disruptive innovation’ in contrast to ‘evolutionary innovation,’ inherently involves risk and risk-taking behaviors. Examples of disruptive innovations commonly encountered in everyday experience include solar cells, transistor radios, digital control mechanisms, the iPhone, and electric cars, just to name a few.

As an example from the marine natural products world (my advance apologies to my many colleagues who are innovatively studying terrestrial natural products, but I have chosen my examples from the programs I know best), at the time Drs. Bill Fenical and Paul Jensen at Scripps Institution of Oceanography, University of California, San Diego (UCSD), made the decision to really commit to an examination of marine microbes as sources of novel secondary metabolites, the dogma in the field was that everything that was in the sea was also on the land and that there were no antinobacteria in the oceans. Their innovation in this respect was to apply thinking from other branches of microbiology to create media and culture conditions that fostered the growth of an increasing percentage of the bacteria unique to the marine environment, previously uncultured because of their slow growth and requirement for different nutrients in generally lower concentrations. As a result of their pioneering discoveries, a substantial proportion of the researchers in the field of marine natural products compound discovery have shifted their focus to studying the rich microbiota of the sea.

Dr. Raymond Andersen at the University of British Columbia, Vancouver, British Columbia, is another such innovator; in his case, he looked to the tools and ap-

proaches being used by his synthetic and medicinal chemistry colleagues and riskily developed these methodologies in his own laboratory. It has been hugely successful to combine a discovery program with a medicinal chemistry effort, thereby advancing lead compound series to a level more attractive for industrial pursuit. Recently, my UCSD colleagues Drs. Pieter Dorrestein and Nuno Bandeira have been applying a number of advances from the world of mass spectrometry and computational science, including MALDI imaging and molecular networks, to approach various facets of natural products in fundamentally new ways (**Figure 1**). The innovative integration of genomics, molecular biology, and organic chemistry by my colleague Dr. Bradley Moore represents another outstanding program that has benefited from its interdisciplinary approaches.

The adoption of new methods and technologies from other areas of science, and their application to studies in the natural products sciences, is something my laboratory has consciously and purposefully attempted to do as well, mixing our compound discovery efforts with biosynthetic investigations, new methods in NMR and mass spectroscopy, and a phylogenetic understanding of the producing organisms. Sometimes this takes us out of our ‘comfort zone’ of knowledge and techniques; however, this is part of the journey of exploring our natural world and should be welcomed as both the challenge and opportunity it represents.

If we, individually and as a discipline, can continue to be innovative and continuously push the boundaries of our field, in both evolutionary and revolutionary ways; if we can continue to attract, foster and support creative young scientists from the broad range of natural products disciplines; if we can be true to our ideals of scientific exploration and welcome the risk inherent to trying new approaches; then yes, I think our field and our society of the natural products sciences will be highly successful, relevant and impactful, well into the foreseeable future.

It is a great time to be a natural products scientist! ■

Pharmacognosy Field Notes: Enjoying the “Fruits” of Our Labors

By Dr. Alison Pawlus

Editor's Note: Pharmacognosy Field Notes is a new series for the ASP Newsletter. This idea originated at the 2011 ASP Executive Committee, when Journal of Natural Products Editor, Dr. A. Douglas Kinghorn, suggested that the Newsletter include a series of articles about field collections in pharmacognosy. He and members of the ASP Executive Committee thought this may be especially interesting for younger members who are considering careers in the discipline. This series also ties into an ongoing effort to support student fieldwork by the creation of an ASP travel award, named in honor of the late ASP member, Dr. John Daly. We are pleased that Dr. Pawlus agreed to describe her work in the debut of this series. If you are interested in contributing to this series in the future, please contact the Newsletter (asp.newsletter@lehman.cuny.edu).

I recently finished a three-year phytochemical investigation into wine in Bordeaux, France, as a Fulbright Aquitaine Research Scholar. I specifically studied which compounds contribute to wine's health promoting properties and their mechanisms of action to ultimately answer which wines are healthiest and for whom. My goal was to equip myself with biological, chemical, and epidemiology data to fully delve into the French Paradox. While I do not necessarily consider my fieldwork “work”, in the traditional sense, I did have the opportunity to travel extensively and learn a tremendous amount about my subject outside of the lab.

During my three years in France, I visited the many different wine regions within Bordeaux and elsewhere around France and neighboring countries. A favorite activity of mine was to bike to wineries during *portes ouvertes* – open doors - weekends where up to 100 chateaux from an individual region would welcome visitors, give tours, tastings, and answer questions.

Every year, approximately 10 different regions within Bordeaux host this event, including famous regions such as Médoc, St.



Dr. Pawlus in the Pessac-Leognan wine region of Bordeaux, France, taking part in a grape harvest, “vendange”, collecting Cabernet-Sauvignon grapes for wine.

Emillion, Pessac Leognan, Graves, and Sauternes. France has no dearth of people willing to talk about wine. Since there were so many wineries to choose from, I often had the full attention of the winemaker and/or owner. The subject of wine includes a remarkable and tumultuous history (dating back to Roman times), in addition to chemistry, microbiology, agriculture, geography, and sensory analysis, thus the questions and answers were unlimited.

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First of all, the majority of wines are blended, a traditional characteristic of Bordeaux.

Secondly, the labels focus on the origin of the wine rather than cultivars used.

What finally demystified French wines for me was learning that if I knew where the wine was from, then I knew what kind of wine to expect!

Pharmacognosy Field Notes: Enjoying the “Fruits” of Our Labors

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Many of my trips were centered around visits to chateaux, wine museums, and well-regarded wine boutiques. Bicycling to and around the different wine regions was an excellent way to experience firsthand the different climates, altitudes, and soil type, *le terroir*. I helped with the grape harvest, picking Cabernet-Sauvignon grapes in the Graves region of Bordeaux to see how a traditional harvest is done and become familiar with the initial steps in the wine making process. The “vendange”, as it is called in France, is a long-standing tradition of great importance.

One of the most confusing traits of French wines is their lack of specific cultivar name on the label. Americans, in particular, typically buy wine based on cultivar, i.e. Pinot noir, Cabernet-Sauvignon, Malbec, or Syrah. Wine labels touting a single vari-

d'origine contrôlée (AOC), which controls the kind of cultivars, and at what percentages, allowed within each specific region. Therefore, knowledge of geography and grape temperament can be incredibly useful when deciding on a French wine. Even small changes in temperature and geography can influence which grapes grow best. A good example is the case of Cabernet-Sauvignon and Merlot, the dominant cultivars in Bordeaux.

A few degree differences in the average temperature, influenced by proximity to the ocean, soil type, and sun exposure, make certain areas better suited for one cultivar over the other as the predominant grape in their blend, or assemblage. The diversity of climate and their respective wines became more tangible once I was able to compare the hot Mediterranean climate of southeastern France that support Grenache, Mourvèdre and



Many chateaux throughout France still do traditional grape harvests. It takes many people to harvest the grapes by hand, while the grapes are at optimal ripeness. The sorting of grapes, upper right, (“triage”), done immediately prior to destemming, crushing, and placing into stainless steel tanks for the initial fermentation step.

ety is rare in France for several reasons. First of all, the majority of wines are blended, a traditional characteristic of Bordeaux. Secondly, the labels focus on the origin of the wine rather than cultivars used. What finally demystified French wines for me was learning that if I knew where the wine was from, then I knew what kind of wine to expect!

The majority of French wines are certified under the *appellation*

Syrah grapes to the cooler northern regions where Pinot noir and Riesling can be found.

From the specific cultivar grown to the type and extent of aging, wine has many variables that can influence the chemistry. My field work helped me understand these variables, allowing me to steer my research towards more pertinent and interesting questions. ■

From the specific cultivar grown to the type and extent of aging, wine has many variables that can influence the chemistry.

Meet a New ASP Member

ASP is pleased to welcome a new international member to the society this year. One of our new members for 2012 is Dr. Celso Guerreiro Almeida, a post-doctoral researcher at the University of Lisbon, Lisbon, Portugal, and Fundacion Medina, Granada, Spain. We thank Dr. Almeida for the opportunity to learn more.

By Mr. Dan Kulakowski



Dr. Celso Guerreiro Almeida.



Fungal specimens in Dr. Almeida's work.

Bonn, Germany, where I conducted Ph.D. research in novel fungal marine secondary metabolites with my mentor ASP member Dr. Gabriele Koenig (thesis online). After a postdoctoral position at the International Cooperative Biodiversity Groups (ICBG)-Smithsonian Tropical Research Institute in Panama studying secondary metabolites from plant-derived endophytic fungi, I am currently in another postdoctoral position at the University of Lisbon/Fundación Medina in a self-built project concerning the biology and chemistry of intracellular mutualistic symbiosis from a fungus and probable endobacteria-produced novel bioactive natural products.

1. How did you hear about the ASP?

I heard about the Society from fellow colleagues in 2007. In 2009, I attended the 50th ASP Annual Meeting in Hilo, Hawaii, and saw the importance and organization of the society.

2. Why did you join ASP?

I wanted to join a collective group with the same research interests, networking with researchers with common interests in the field, and get better fees for conferences!

3. Do you belong to any other scientific societies?

No

4. What are your current research interests in pharmacognosy?

I am interested in fungal (marine and endophytic) bioactive metabolites, Actinomycetes-derived bioactive natural products, intracellular mutualistic symbiosis between fungi and endobacteria, and management of research networks.

5. What is your scientific background?

I graduated with a biology degree in Portugal and followed that with research in Belgium and Brazil (proteomics, genetics, and plant metabolites). I then earned a Masters degree in Pharmacognosy at Leiden University, Leiden, Holland, under my mentor ASP member Dr. Robert Verpoorte. After undertaking a postgraduate position in natural products chemistry in Portugal, I went to the University of Bonn,

6. What would you like to achieve through your membership?

I am interested in research opportunities, research synergies, and acknowledgment of work achievements.

7. What do you like doing in your spare time?

I read books, play sports (especially soccer), find good movies and music, and find time to enjoy social life!

8. What are you currently reading?

A Portuguese book, *A Vida Num Sopro*, by author José Rodrigues dos Santos.

I am interested in fungal (marine and endophytic) bioactive metabolites, Actinomycetes-derived bioactive natural products, intracellular mutualistic symbiosis between fungi and endobacteria, and management of research networks.

New Members of ASP 2012

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 9 domestic full members and 7 associate members. We look forward to meeting you and learning more about you and your work.

ACTIVE MEMBERS

Naohito Abe
University, Mississippi

Dr. John Bowling
Oxford, Mississippi

Dr. Qiao-Hong Chen
Fresno, California

Amar G. Chittiboyina
University, Mississippi

Dr. Stephen Deyrup
Loudonville, New York

Edgar Grigorian
Salt Lake City, Utah

Mr. Paul Ocanas
Spring, Texas

Dr. Vijayasankar Raman
University, Mississippi

Dr. Rashmi Tiwari
Hawthorne, New York

ASSOCIATE MEMBERS

Haroon Iqbal
London, United Kingdom

Dr. Anila Kethe
Plainsboro, New Jersey

Mr. Christopher Kitalong
Koror, Palau

Wei-Ting Lui
La Jolla, California

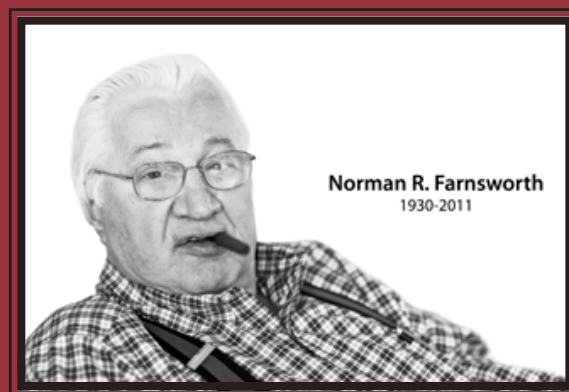
Ms. Julia E. Sears
Chicago, Illinois

Ms. Mackenzie M. Stinehart
Watertown, Massachusetts

Mr. Chinni Yalamanchili
University, Mississippi



College establishes lectureship in honor of venerated pharmacognosy pioneer



The UIC College of Pharmacy is proud to announce the establishment of the Norman R. Farnsworth Lectureship in Pharmacognosy in memory of one of its most dedicated pharmacy educators and internationally renowned, transformational pharmacognosy researchers on the chemistry, biology and therapeutic properties of medicinal plants and natural products.

Norman R. Farnsworth, Distinguished University Professor, served on the UIC College of Pharmacy faculty for more than 41 years (1970-2011). During his tenure, he served as head of the department of pharmacognosy and pharmacology for 12 years, followed by 30 years as director of the Program for Collaborative Research in the Pharmaceutical Sciences. This multi-disciplinary research unit is dedicated to all aspects of collaborative studies on medicinal plants, including chemistry, biology, clinical effects, biodiversity inventory and conservation, informatics and intellectual property rights.

Farnsworth also served as director of the World Health Organization Collaborating Centre on Traditional Medicine at UIC, and was the inventor and editor of the NAPRALERT database, a relational database on medicinal plants and natural products.

"Farnsworth brought to UIC a culture of sophisticated research that has persisted. It is a legacy that we cherish. We are consistently rated one of the top five research colleges of pharmacy in the United States, and that can be traced back to Norm," says Dean Jerry Bauman, "[His arrival] transformed us from being predominantly a teaching-oriented institution to one making major scientific contributions that complement our educational programs. Norm had the ability to recruit extremely talented colleagues and get them to work collaboratively toward common research and scientific goals."

Born in Lynn, Mass., Farnsworth received his bachelor's and master's degrees from the Massachusetts College of Pharmacy and a Ph.D. from the University of Pittsburgh, where he also served as a faculty member for 15 years.

Under Farnsworth's direction, the UIC/NIH Center for Botanical Dietary Supplements Research was established in 1999 as one of six such research centers funded by the National Institutes of Health to study botanical dietary supplements. UIC's Center, the only continuously funded unit, focuses on studying botanicals that may improve women's health and quality of life, specifically in the areas of menopause, premenstrual syndrome and persistent urinary tract infections.

Throughout his distinguished career, Farnsworth was the recipient of numerous national and international awards, too numerous to cite. A sampling includes three honorary doctorates and three honorary professorships; appointments as special delegate and commission member by former Presidents Richard Nixon and Bill Clinton, respectively. A reflection of the esteem held by his peers is exemplified by the American Society of Pharmacognosy's designating its Research Achievement Award as the "Norman R. Farnsworth Research Achievement Award". In recognition of his contribution to pharmacognostical education and research, special symposium programs honoring Farnsworth were held by the 12th Annual Oxford International Conference on the Science of Botanicals and by the American Society of Pharmacognosy at the International Congress of Natural Products Research in 2012.

To ensure the preservation of his enduring academic legacy as an educator, innovator and pioneering researcher whose contributions have impacted not only UIC, but have also changed the face of pharmacognosy and medicinal plant research, **the UIC College of Pharmacy seeks your assistance in establishing the Norman R. Farnsworth Lectureship in Pharmacognosy** with an annual public lecture on topics encompassing all aspects of pharmacognosy research and education by internationally recognized researchers/educators.

Make your gift today at pharmgiving.uic.edu

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.

Plant Lipids: Structure, Metabolism & Function (Gordon Research Conference)

Galveston, Texas

January 26-27, 2013

www.grc.org/programs.aspx?year=2013&program=grs_plntli

ASP 54th Annual Meeting

St. Louis, Missouri

July 13-18, 2013

www.pharmacognosy.us/calendar-of-events/future-asp-meetings/

ACS National Exposition & Exposition: Chemistry of Energy & Food

New Orleans, Louisiana

April 7-11, 2013

www.acs.org

Society of Ethnobiology 36th Annual Meeting

Denton, Texas,

May 15-18, 2013

http://ethnobiology.org/conference/upcoming/registration.aspx?year=2013&program=grs_plntli

61st International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA)

Muenster, Germany

September 1-5, 2013

www.ga2013.org/



Brief News From Washington

By Dr. Georgia Perdue

➤ It seems that **Taxol®** just keeps on giving. In October of 2012 the Food and Drug Administration (FDA) approved an injectable suspension of **paclitaxel** (Abraxane®) for the treatment of “**local advanced or metastatic ... non-small cell lung cancer (NSCLC)**.” In many cases it will be given in combination with carboplatin. Abraxane has been developed by Abraxis Biosciences, a subsidiary of Celgene Corporation.

➤ Another **natural product-derived anticancer drug, omacetaxine mepesuccinate**, (Synribo®), a derivative of the **alkaloid homoharringtonine** from *Cephalotaxus harringtonia* was approved by the FDA on “fast track” the end of October. It is for the treatment of **chronic myelogenous leukemia (CML)**, a blood and bone marrow disease. Synribo is marketed by Teva Pharmaceuticals. The FDA's Dr. Richard Pazdur, Director of the Office of Hematology and Oncology Products, said, “...[this] provides a new treatment option for patients who are resistant to or cannot tolerate other ... drugs [for chronic myelogenous leukemia (CML)]....” The alkaloid languished for many, many years!

➤ Dr. Anthony Fauci, Director National Institute of Allergy and Infectious Diseases (NIAID), told his Advisory Council meeting that the **West Nile virus** outbreak in the United States was the worst since the first “explosion” of the disease in 2003. He noted that four criteria were needed: a virus, mosquitoes, humans and lots of birds. “...We project this will be... at best, the second, and at worst, the worst year we have had.” He also noted that “companies don't really want to make vaccines [for it]. ...They have the scientific basis for a good West Nile virus vaccine, but we don't have [it] for the simple reason ... who are you going to vaccinate?.... The problem we face is that there are not a lot of infections each year....”



➤ Highlights from National Cancer Instituted (NCI) Director Dr. Harold Varmus' presentation at the November meeting of the Board of Scientific Advisors:

- Congress has only approved a Continuing Resolution for funding the government until March, 2013. New grants and renewals will continue to be paid. **The success rate will remain at 14% for all Research Project Grants (RPGs), “the lowest rate in years.”**
- Grants that receive a percentile of seven or better “will almost certainly be funded.” The aim is to fund “close to 1,100 grants.”
- Investigators who have received **grants of more than one million dollars in direct costs** are being looked at more carefully. “Some are not spending all that they get. We are looking into **capping such grants**. Merit should be the primary consideration,” noted Dr. Varmus.
- **Congress has a great interest in pancreatic cancer and introduced a bill, Pancreatic Cancer Research and Education Act, (S.362)**, which Dr. Varmus said, “tells us what we can and cannot do in this area. We tolerate that ...[but] it is not useful. We would be required to do pancreatic studies.” The bill has been held up in the Senate. Congress is unhappy that only 272 grants have been awarded in this area. A very brief sketch of the bill: it calls for a “cadre” of new investigators in this area, the formation of an Interdisciplinary Cancer Coordinating Committee to give instructions about research, deal with grant awards, and develop a strategic plan for pancreatic cancer research. There is a lot more!! In a letter to NCI, Senator Tom Coburn (R-OK) asked if it is appropriate [for Congress] to focus on specific cancers. Answer is pending.
- Dr. Varmus likes workshops. Not too long ago

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It seems that Taxol® just keeps on giving.

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one was held on **pancreatic cancer**. Some results: Patients with type 2 diabetes have a higher risk of getting pancreatic cancer. Screening for this disease will be looked into. Pancreatic cysts pose a higher risk of becoming cancerous. Familial pancreatic cancer is also being looked into. Work is continuing on immunotherapy and targeted drug therapy.

- Another recent workshop focused on **researchers compelled to publish in prestigious journals**. In many cases this results in “sloppy, substandard work with results which cannot be duplicated by industry,” said Dr. Varmus, adding, “there should be scientific rigor [associated with] publishing in these journals to prevent punitive and remedial effects.” NCI wants to help improve this situation and perhaps prevent it.

- **An old antimalarial drug, quinacrine, is the basis for the development of the anticancer drugs known as curaxins.** One of them, CBLC10, went through Phase II studies as a monotherapy for “hormone- refractory taxane-resistant prostate cancer. According to the company developing these drugs (Cleveland BioLabs, Inc.), this one was “well tolerated and there were no serious adverse events.” Stay tuned for the results of the other curaxins.
- It seems that some **dietary supplements continue to plague the FDA**. One company, Alternative Health & Herbs Remedies, Albany, Oregon, was selling products claiming they were herbs and supplements to treat diseases such as cataracts, viral and bacterial infections, and cancer. FDA has, for now, stopped the production of these products. ■

(**A personal note:** Many ASP members are young and do not know who the world renowned botanist, Dr. Robert E. Perdue, Jr. was. His agency, United States Department of Agriculture (USDA), and the NCI had an interagency agreement for plant collections as a source of anticancer agents. Even though he oversaw both the U.S. and world-wide collections by his hand-picked contractors, he personally collected many, many of the plants. *C. harringtonia* was one of his “babies.” The news about homoharringtonine is bittersweet for me because he is not with us to share the good news!)

Editor's Note: Dr. Robert E. Perdue, Jr., the husband of long-time Newsletter contributor Dr. Georgia Perdue, passed away on July 20, 2011. Our thoughts have been with her and her family during this difficult time, but we are pleased to see the work of both Dr. Perdue and Dr. Robert Powell come to fruition. Please see our articles on the homoharringtonine discovery in this issue.

Even though Dr. Robert E. Perdue, Jr. oversaw both the United States and world-wide collections by his hand-picked contractors, he personally collected many, many of the plants. *C. harringtonia* was one of his “babies.”

From the Archives: Homoharringtonine and Powell



Dr. Powell receives the Distinguished Alumnus Award from Western Illinois University, Macomb, Illinois, in 1981.

By Ms. Devhra Bennett Jones

One of the great joys of science is the achievement of sharing it and making an impact on people's lives. ASP member Dr. Richard "Dick" Powell and his fellow research colleagues have the satisfaction of contributing to the betterment of humanity in their ground-breaking work on the alkaloid isolated from *Cephalotaxus harringtonia*, homoharringtonine. With the FDA's recent approval, it will now be used in the treatment of adults with chronic myelogenous leukemia.

When homoharringtonine was isolated at the then named Northern Regional Research Center (now called the National Center for Agricultural Utilization Research), the news was widely covered by the local press in Peoria, Illinois, and national correspondents. In 1981, Dr. Powell's achievement was also honored by his alma mater, Western Illinois University, Macomb, Illinois, with a "Distinguished Alumnus Award." The Peoria, Illinois, *Journal Star* newspaper covered the event. Dr. Powell stated, "We have no idea what is out there in nature that has not been discovered yet." These are wise words that inspire medical research chemists in the present and will continue to do so in the future.

Quoted in the *Journal Star* in 1981 about the research on *Cephalotaxus harringtonia*, Dr. Powell said, "We felt the seeds would be a good place to look in plants because they represent the plant as a whole." The compounds "appear less toxic to normal cells and just as active against leukemia." The breakthrough was also covered by *The Washington Post*. Dr. Powell discussed how their initial seeds research to determine the viability of

new cash crops led to the discovery of homoharringtonine. He said, "...we had the seeds, so we thought we would test them out." At that time relatively few drugs had been developed from plants to combat tumors.

Dr. Mansukh Wani is of the same opinion, "In the 1940's and 1950's there were very, very few anti-cancer agents. Scientists in general were not really enthusiastic about finding drugs from plants to treat diseases. In the 1950's there was public pressure to explore this, as in the other parts of the world; India, China, and Latin America were using herbal medicines. That is how it got started, looking at plants in the field of medicinal chemistry."

Dr. Powell's work is highly respected among his peers. Dr. Wani stated, "He is a very good chemist, and because of his procedures, homoharringtonine was discovered, and he still contributes to the field of chemistry through the *Journal of Natural*



Distinguished Alumnus Award

Products." Editor-in-Chief Dr. Douglas Kinghorn praised Dr. Powell, "Dick Powell, ably assisted by his wife, Rosemary, has served as a highly capable Associate Editor of the *Journal of Natural Products* for some 22 years. Authors can be assured that when he deals with a submitted manuscript, it will be treated fairly and efficiently in a very timely manner."

Dr. Powell continued to serve as a chemist and leader at the National Center for Agricultural Utilization Research in Peoria, Illinois, from 1963-1994. In a lead research position, he directed four vital United States Department of Agriculture research projects during 1990-1994. He is also an accomplished author and holder of patents.

ASP member Dr. Robert Pettit remembers, "In 1965, I was appointed as a special government employee of the National Cancer Institute. I had known about Dr. Dick Powell's work, and Dr. Cecil Smith was a classmate of mine, they systematically were working on *Cephalotaxus harringtonia*. Dick Powell was the group leader at that point, and with Cecil, they discovered homoharringtonine, and a whole set of compounds. We knew at that time we had very good experimental anti-cancer activity. We knew that homoharringtonine needed to go to clinical trials. I did everything that I could to advance homoharringtonine and so did my superiors at the NCI. Dick is a splendid guy, and an excellent chemist." ■

David J. Slatkin, 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.

Associate Membership

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

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