



The American Society of Pharmacognosy

The ASP Newsletter: Volume 54, Issue 1

Discovering Nature's Molecular Potential

Reflections on Gender Bias in Science

By Dr. Susan Mooberry

The future of the American Society of Pharmacognosy is bright, but we must be vigilant to attract new members and retain current members while expanding our diversity. Our goal must be to keep attracting the best and brightest scientists in our field. The vibrant future of our Society depends upon increasing our inclusiveness, and efforts are underway to do this for women, minorities, and for international outreach. Limiting the inclusion of any group, based on gender, race, religion or sexual orientation, does not serve our ability to advance the best science.

The article in the winter ASP Newsletter, "The (In)convenience of Gender Blindness" by Dr. Brian Murphy¹ demonstrated that we have much to do to increase representation of women in several important aspects of our Society. This is clearly not the only challenge we face; the horrifying stories of sexual harassment in *Chemical & Engineering News*² last fall have no doubt had parallels among our members. To begin addressing the host of challenges in this area, I would like to highlight the topic of *continued on page 3*



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EDITOR'S CORNER



In the current issue of the *Newsletter*, we continue to explore the role of women in the ASP by the current ASP Vice President, Dr. Susan Mooberry. An initial examination of the issue of the number of invited speakers at annual meetings was discussed at the 2017 Annual Meeting in Portland. Some ASP members, including Dr. Tawnya McKee, expressed concerns that women were not well represented as invited speakers. This led to a deeper examination that was published in two separate front-page articles in the Winter 2017 *ASP Newsletter* looking at the participation of women in ASP meetings in the past, as well as their representation in the *ASP Newsletter*. In one of these articles entitled "The (In)convenience of Gender Blindness," ASP member Dr. Brian Murphy called for specific changes to occur with regards to how to consider the representation of women at invited conferences, including being vigilant about examining the issue, and speaking out when an inequity is noticed. In this issue of the *Newsletter*, Vice President Mooberry reviews the literature about gender bias in science, and suggests ways that ASP as a society, and ASP members individually, can begin to address this important issue. I hope everyone will take time to read this article, and I hope this can be a starting point for even deeper discussions for the ASP as a whole.

In a related article, ASP President, Dr. Cedric Pearce, discusses the progress of the ASP Constitution and By-Laws Committee on adding an ASP inclusion clause into the ASP Constitution. A working draft of a new clause has been prepared by the committee members, and they are looking for feedback from the ASP membership. Please review the clause, and give your feedback directly to members of the committee who are listed in the article.

The Organizing Committee for the 2018 Annual Meeting have worked hard to get more female speakers involved. Dr. Sylvie Garneau-Tsodikova updates ASP members on many changes to the Lexington scientific program to respond to concerns about gender bias. This includes a new workshop that will take on this issue of gender inequity squarely.

Dr. Tatsuo Higa, a long-time member of the ASP, passed away almost two years ago. As Editor of the *ASP Newsletter*, I feel an important role of this publication is to honor those members who have died. I was sorry that I had missed compiling a comprehensive obituary in 2016, but when ASP member Dr. Phil Crews told me he was preparing a tribute to Dr. Higa at a Gordon Research Conference in March of this year, I thought it was a good time to revisit a tribute to this deceased ASP member. My sincere thanks to Drs. Junichi Tanaka and Roy Okuda for writing the article in this issue.

The final installment of ASP Fellow Bob Pettit's amazing early trip to the People's Republic of China concludes with descriptions of his travels to biomedical research facilities in Guangzhou. Dr. Pettit has had a long and distinguished research career in natural products for cancer, and it is great to see his impressions of China from about 40 years ago. With China's considerable investments in science and healthcare, I wonder how much he would recognize if he went back today.

Spring is arriving late in New York City this year, with temperatures in mid-April still below freezing. I hope you are having a good spring where ever you may be, and please plan to join us at the ASP Annual Meeting this July in Lexington.

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.

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Reflections on Gender Bias in Science

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unconscious bias, which has been well documented in controlled studies, and to offer solutions to overcome this often subtle but significant obstacle.

Does gender bias remain a problem in science? The answer is yes. The late neuroscientist and Stanford Medical School professor, Dr. Ben Barres, had a unique opportunity to experience and write about gender bias because of his perspective as a scientist who transitioned genders, from female to male. If you have not read his outstanding commentary in *Nature*,³ I strongly urge you to do so. It helps us understand the depth of the challenges we face

The vibrant future of our Society depends upon increasing our inclusiveness, and efforts are underway to do this for women, minorities, and for international outreach.

in eliminating gender biases that continue to undermine the advancement of women at all levels of science. It is a provocative and well-referenced article. While this commentary is fact-based, notable quotes from Dr. Barres after his transition include: “I can even complete a whole sentence without being interrupted by a man.” Another incident, highlighted in the *Wall Street Journal*,⁴ described a comment following a seminar Dr. Barres gave at MIT, where a scientist commented that Barres’ work was so much better than his sister’s, not realizing that they were, in fact, the same person.

A double-blind scientific study published in *PNAS* demonstrated gender bias against females by science faculty at research intensive universities.⁵ In the study, faculty members in chemistry, physics, and biology ($n = 127$) of both genders, judged and rated identical applications from an undergraduate student who had ostensibly applied for a laboratory manager position. The applications differed only in the gender of the applicant. The results showed a statistically significant bias against the female applicant for competence, hireability, and career mentoring which the faculty respondent would offer.⁵ The salaries recommended were also less for the female than the identical male applicant, although the female applicant rated higher for likeability. Interestingly, both male and female faculty exhibited the

early, at a gateway point for the prospective doctoral student, demonstrating the need to intervene very early to avoid limiting the progress of female and minority scientists.

As more women move into careers in natural sciences, medicine and pharmacy, bias remains. The extreme bias against women faculty at MIT in the 1990’s was a rallying point,⁷ and progress was made, but recent studies show that inequities remain. Female early career scientists overall earn 31% less than men.⁸ After controlling for field of study, the discrepancy went down to 11%. Lower earnings among female scientists were

linked to having a family, a discrepancy not seen with males. In academic medicine, women are paid lower salaries than their male counterparts.⁹ Even with adjustments across multiple metrics, including experience and specialty, an almost \$20,000 yearly salary discrepancy remained. Disturbingly, adjusted salaries for female full professors were equal to the salaries of male associate professors.⁹ Pharmacy is now a majority female profession in the US and Canada, yet females still lag in obtaining leadership positions in US pharmacy schools and recognition with awards.¹⁰ Thus by a number of measures, some of which are described here, gender equality has not yet been achieved. Continued, subtle bias likely plays a large role.

Using the designation of “Dr.” when introducing male colleagues versus the use of a first name when introducing female colleagues subtly undermines women’s credibility. A study by Dr. Files and colleagues demonstrated that women were less likely to be introduced by their professional titles in medical grand rounds.¹¹ The results are fascinating, but alarming. All participants in the study, introducers and speakers, were professionals with doctoral degrees. Female introducers used the professional title 98% of the time for a female speaker and 95% of the time for a male speaker. Male introducers used the professional title 72% for males and

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bias against the female student applicant. This controlled study demonstrates that subtle gender bias exists, and the authors suggest that “chronic subtle bias harms women in academic science and that it begins early in an academic career.”⁵

A more recent study involved a fictional prospective doctoral student seeking a 10 minute meeting with professors to discuss future research opportunities.⁶ The applications were identical with the exception of gender and ethnicity. The faculty members responded at a higher rate for white males than females or minorities, and the discrimination gap was wider at private institutions than public ones.⁶ These studies indicate that bias occurs

49% of the time for female professionals.¹¹ Many have criticized this report as whining, but consider how it would feel to have your colleagues or administrative assistant call you by your first name in front of students and fellows while referring to male colleagues by their title, which is another common occurrence for women faculty. This is a subtle, but real bias against women that can be easily fixed. I urge all of us to be consistent in the use of professional designations in professional settings for all of our colleagues.

So what can we do to overcome this documented gender bias that occurs among scientists of both genders? First we

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acknowledge it exists and then implement strategies to help us overcome this bias. If you are interested in seeing if you have unrecognized bias, check out the Project Implicit website: <https://implicit.harvard.edu/implicit/aboutus.html>. This site has various tests for evaluating unconscious thoughts and feelings. A few questions we can ask ourselves:

- Do you use the professional title when addressing women peers?
- How many of the seminar speakers invited for your departmental seminars are women, and does the percentage match the gender balance in the field, in your faculty and in your trainees?

Considering that the majority of graduate students in many disciplines of pharmacognosy are women means that they need to have role models of accomplished women scientists throughout their training. Many men are excellent mentors for women and are committed to their advancement, but also having female role models provides another validation of their chosen path. A list of female speakers with expertise in the wide areas of interest to pharmacognosists is being curated by Dr. Murphy. As mentors, we can evaluate if subtle bias is affecting the mentoring of students. To those in leadership positions, conscious evaluations of equality between women and men for space assignments, salary, start-up packages,

and service assignments are needed. I also propose that a session be scheduled during an upcoming ASP meeting for a presentation on how to overcome unconscious bias that limits scientific diversity. Some of these presentations have validated, documented success in reducing gender bias. The evidence-based workshop entitled “Scientific Diversity” has been presented to more than 1,400 scientists over the past decade.¹² The presentations, given by trained instructors, result in reduced unintentional gender bias immediately following the presentation as well as two weeks later, suggesting that these biases can be mitigated.¹² However, recognition and elimination of bias is only the first step that then must be followed by adaptation of actions and behaviors that reduce inequality, a much tougher task. An experimental intervention found that male faculty in STEM fields were less likely to accept evidence of gender bias in these fields.¹³ It will not be easy, but, after first recognizing the role each of us must play to ensure gender equity, we together can ultimately reduce the loss of talented women in the sciences.

This is a unique time with a societal focus on sexual harassment and discrimination that allows us all to consider our biases and work to eliminate them for optimal inclusion and diversity in the ASP. While not the focus of this article, we also need to understand that other minority groups based on race, religion and sexual orientation are also significantly burdened and hindered by biases. It behooves us all to make an effort to overcome overt and subtle bias so that our Society will be stronger going forward. ■

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ASP: An Inclusive Society with a Single Purpose

By Dr. Cedric Pearce

The American Society of Pharmacognosy is, and always has been, an inclusive organization, based on members' shared interest in scientific aspects of biologically-active natural products and natural medicines, regardless of gender, race, religious beliefs, sexual orientation, or anything else other than a legitimate interest in natural products. Not only should the ASP be inclusive, we should also actively encourage the involvement of all scientists, especially women, and certain minority groups, who remain underrepresented in STEM fields. This inclusiveness covers all aspects of the Society and our activities. Although the current constitution makes this clear, our Constitution and By-Laws Committee has been charged with defining this more explicitly. A working draft of the new clause was made available by Dr. Gil Belofsky, who has been working with committee members Drs. Steve Swanson and Maged Sharaf; the current working statement is as follows: ***"The American Society of Pharmacognosy is a community committed to shared values of diversity and inclusion that help us to achieve and sustain excellence."*** However, I suspect this will be embellished by the committee over the next couple of months leading up to the meeting in Lexington. Dr. Belofsky welcomes input if anyone has comments.

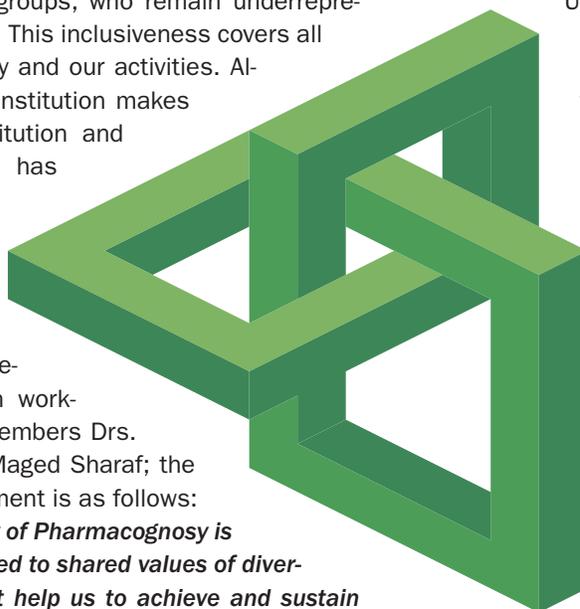
Furthermore, after discussions with Vice President Dr. Susan Mooberry and other members of the EC, we have established the Diversity and Inclusion Committee; current membership includes Drs. Laura Sanchez, Melany Puglisi-Weening, Brian Murphy, and Glenroy Dean Martin. The goal of the committee is to establish

guidelines to ensure that every member of the Society has an equal opportunity to be part of the ASP's activities, especially those associated with the annual conference, and we look forward to discussing these proposals at the business meeting in Lexington.

Finally, and as disclosed in the last *Newsletter*, we have also established the International Relationships Committee, primarily to develop and maintain strong ties with ASP members from countries other than the US. This latter group, under the leadership of Dr. Nam-Cheol Kim, is active, and we look forward to discussing their recommendations in July.

Regarding the ban on the use of Californian state funds to travel to states with discriminatory legislation or laws, I have written to Governor Jerry Brown to let him know personally of our actions to be sure that we are an inclusive and transparent society, and that the travel ban will potentially harm the ASP and California by making it difficult for their scientists who are ASP members to attend the meeting in Lexington. In part the letter states: ***"...the Society has gone to some lengths to ensure that we are a transparent organization that welcomes all those***

interested in our science without any restrictions to gender, race, religion, sexual orientation or any other distinction, natural or preferred." Currently this is a lose-lose situation, wherein Californian scientists desiring to attend a beneficial conference, and other ASP members who do attend, may both have decreased opportunity to share the newest results and trends in pharmacognosy. I am certain that this was not the goal of the restrictions drafted by California's politicians. ■



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2018 Annual Meeting Confronts Gender Inequality

By Dr. Sylvie Garneau-Tsodikova

There are many extremely talented and successful women working in the field of natural products; there is no question about that.¹ However, not confined to the natural product research arena, an important global issue in most fields of research is that of gender inequality and a lack of inclusion of women at scientific meetings. As clearly pointed out by Dr. Brian Murphy in a recently published *ASP Newsletter*,² there is still an overwhelming imbalance in gender representation as invited speakers at conferences, with men being heavily favored.³

Many wonderful suggestions were provided by Dr. Murphy to help remediate that problem. At the ASP 2018 meeting, which will be held in Lexington, Kentucky from July 21-25, we have decided to create a platform to address this issue in two ways: (1) by offering a workshop, *Towards Overcoming Gender Inequality: Challenges and Opportunities for Women in Science* and (2) by having our Young Members Event led, in major part, by early career women natural product scientists.

WORKSHOP: Through panel and subgroup discussions/activities led by female role models working on different aspects of natural product research in diverse work places, a goal of the workshop is to provide a safe environment to learn about and discuss gender inequality in science and share/come up with ideas about opportunities and action items that the participants will be able to work on (alone or in a team) after the meeting. It is our expectation that men who wish to provide ideas on this gender gap will also participate, as the battle can only be won if both women and men unite

and work as a team to overcome the gender imbalance in science. The workshop is designed to foster camaraderie among natural product scientists and networking with like-minded individuals. The workshop is also aimed at inspiring participants to take action and arm them with the necessary tools to do so. It is our hope that this workshop will launch a new trend of bringing the issue of gender inequality in science to the forefront of discussions at national and international meetings.

YOUNG MEMBERS EVENT: This year, the ASP Young Members Event will take place at the historical and picturesque Buffalo Trace Distillery in Frankfort, Kentucky, the oldest continuously-operating distillery in the USA. Early career women alumni from various natural product research groups at the University of Kentucky will lead most of the discussions. These women are now leaders in diverse work environments, such as academia, governmental agencies like the US Food and Drug Administration, and industry. It is our hope that future ASP and other national meetings will follow in our footsteps and have young member events led by alumni from universities from the state where the meeting is being held.

Finally, as a woman representative on the 2018 ASP meeting organizing committee, I am very proud to say that attendees will also have the privilege to hear from and learn about the latest discoveries of 11 distinguished female scientist plenary speakers from Brazil, Nigeria, the United Kingdom, and the USA. I cannot wait to see you all in the stunningly beautiful Bluegrass State this summer! ■

“...there is still an overwhelming imbalance in gender representation as invited speakers at conferences, with men being heavily favored.”

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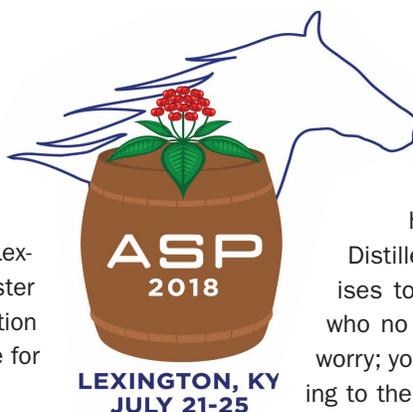
ASP Annual Meeting 2018: Natural Products Riding High in Kentucky



By Dr. Sylvie Garneau-Tsodikova

The ASP's Annual Meeting will be held this year at the Lexington Hilton Downtown located in the heart of the vibrant city of Lexington, Kentucky from July 21-25. Register by May 15 to receive the early registration discount (goo.gl/Z63FpT). The deadline for the submission of abstracts is May 1.

This year the meeting boasts an amazing lineup of plenary speakers¹ from Brazil, Canada, China, Germany, the United Kingdom, and the US. Also, there will be a variety of educational and engaging workshops.² There are workshops to learn about molecular networking and 3D visualization, new separation techniques, and novel computational approaches to structure elucidation of natural products, or to discover new ways to biologically evaluate natural products with anticancer potential. A workshop on grant writing strategies is available for those interested in career development. The workshop, "Towards Overcoming Gender Inequality: Challenges and Solutions for Women in Science" with ASP Vice President Dr. Susan Mooberry as one of our diverse panel members, will be comprised of women, including graduate students and faculty from academia, industry, and other disciplines. This will be an opportunity to expand your network and work towards changing the culture in the scientific community.



The Young Members Event, to be held at the historical Buffalo Trace Distillery in Frankfort, Kentucky, also promises to be very exciting. For those of you who no longer qualify for this event, do not worry; you can also enjoy the distilleries by going to the Bourbon Distillery Tour. Wine lovers, please note that there are several wineries in the Lexington area. There are also plenty of other beautiful places to see and fun things to do in Lexington and its surroundings.

The meeting's theme, "Natural Products Riding High," should give you a hint about one of my favorite places to visit in Lexington, the Kentucky Horse Park! Located only a few minutes away from the city, the Kentucky Horse Park is the place to go to see and interact with majestic horses from different parts of the world. There are always exciting competitions to watch and enjoy. If you love horses (if not yet, you will), I would also suggest you take advantage of the organized excursion of the Blue Grass Horse Farm Tour or go to Keeneland, an internationally renowned racecourse, or to the Red Mile, the second oldest harness track in the world.

If you like the outdoors, there are multiple beautiful locations to explore. The University of Kentucky Arbo-

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return, located on campus, is a great place to go for a walk and have a picnic. Raven Run is a stunning 734-acre nature sanctuary where you can spend your day hiking. If in addition to hiking you like other outdoor adventures, the Red River Gorge is the place you want to be.³ With its Natural Bridge, numerous trails, a zipline, and rock climbing activities, a fun day is guaranteed. People actually come from all over to rock climb at the Red River Gorge. (Note: If you do not have equipment

in Lexington is the childhood home of first lady Mary Todd Lincoln, wife of the 16th President Abraham Lincoln, which is often a nice surprise to many visitors. For history lovers, there is also the Henry Clay estate, a beautiful park with the home of the former senator, secretary of state, and speaker of the house, also known as the great compromiser in the pre-civil war period. Last, but not least, you also can visit the Hunt-Morgan house, home of the famous evolutionary biologist and

There are workshops to learn about molecular networking and 3D visualization, new separation techniques, and novel computational approaches to structure elucidation of natural products, or to discover new ways to biologically evaluate natural products with anticancer potential.

and you want to try it, all you need will be provided!) If you are ready to drive a little longer, the Mammoth Cave National Park is simply breathtaking and will provide you with a very unique experience. It is worth adding a few days to your trip just to visit all these interesting places.

For those who prefer more educational activities, I would suggest the optional excursion to Cincinnati Scientific Research Libraries. However, if you prefer to stay in town, another treasure



noble laureate Thomas Hunt Morgan, who pioneered using fruit flies (*Drosophila*).

No matter which activities you select to enjoy during your time in the Bluegrass State, one thing is for sure, you probably want to go to Thursday Night Live and, at least once, go for some delicious

ice cream at Crank & Boom Ice Cream Lounge! I cannot wait to see you all this summer and hope you will love Kentucky as much as I do! ■

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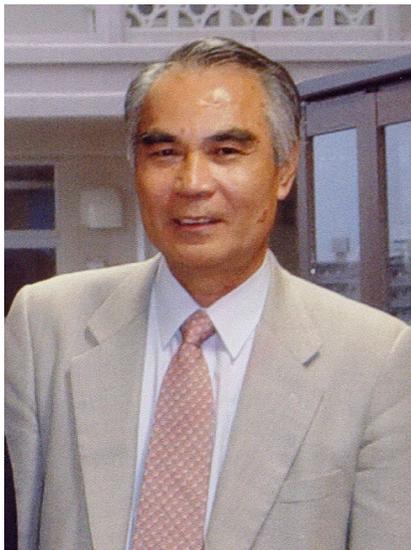
- ¹ Confirmed symposium speakers include Drs. Sean Brady, Michael Burkart, Rebecca Butcher, Robert Cichewicz, Jon Clardy, Jeroen Dickschat, Catherine Drennan, Taiwo Elufioye, Sylvie Garneau-Tsodikova, Chirlei Glienke, Rebecca Goss, Andrew Gulick, Paul Hergenrother, Christian Hertweck, Hazel Holden, Jianhua Ju, Amy Lane, Roger Linington, Hung-Wen (Ben) Liu, Nathan Magarvey, Cathie Martin, Kerry McPhail, Shahriar Mobashery, Rolf Müller, Sarah O'Connor, George O'Doherty, George Phillips, Eric Schmidt, Chris Schofield, Ben Shen, Yi Tang, and Peter Wipf.
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In Memoriam: Tatsuo Higa

By Drs. Junichi Tanaka and Roy Okuda

ASP Member Dr. Tatsuo Higa passed away on May 24, 2016. Dr. Higa was born in 1939 in Nago, Okinawa, Japan. He received his Bachelor's degree in Engineering from the Yokohama National University in 1963. After returning to Okinawa, he worked for a sugar factory for one year, then became a high school teacher for four years. He obtained a Government Aid and Relief in Occupied Areas (GAR-IOA) scholarship from the US government to continue his studies at Ohio State University, where he received MS (1968) and PhD (1971) degrees in Chemistry.

Following his graduation from Ohio State, Dr. Higa travelled westward to Hawai'i, where he worked as a postdoctoral fellow under the late Dr. Paul J. Scheuer (also a well-known figure in the ASP) at the University of Hawai'i at Manoa from 1971 to 1975. Dr. Higa re-



Dr. Tatsuo Higa

turned to Okinawa in 1975 and initially worked as an English-speaking guide at the Okinawa World Expo. In 1976, he was appointed as an Associate Professor at University of the Ryukyus in Okinawa; in 1982 he was promoted to Professor of Marine Sciences. He held this position until his retirement in 2005. He then became Vice President of University of the Ryukyus for two years, then served as a director of the Okinawa study center of the Open University of Japan for three years. As he was eager to continuously learn, he became a student of the Open University afterwards.

the southernmost part of Japan, and the waters of the island chain range from subtropical to tropical. As such, a rich marine biota are found around the islands of Okinawa, which Dr. Higa and his group investigated and which led to the discoveries of many important and unique natural products. In addition to his research in Okinawa, Dr. Higa and three of his students were involved in research projects at the Harbor Branch Oceanographic Institution, where he was a consultant from 1985 - 1986. He also assisted other research groups with their collections in the Okinawa Islands.

Dr. Higa published over 140 research articles in marine natural products, which primarily dealt with organisms collected in Okinawan waters. His representative molecules include thelepin, bromophenols from hemichordates, hippuristanol, manzamines, misakinolide A, onnamide A, hennoxazoles, miyakolide, agelasphins, echinoclathrines, pachastrissamine, and floresolides.

Dr. Higa was a significant contributor to the field of marine natural products. At University of the Ryukyus, he founded a long-standing research program in marine natural products.

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Dr. Higa was a significant contributor to the field of marine natural products. At University of the Ryukyus, he founded a long-standing research program in marine natural products. The Ryukyu Islands are

For most of his tenure at University of the Ryukyus, the highest academic degree offered by Dr. Higa's department was a Masters of Science. Therefore, his research group consisted primarily of undergraduates and MS students, although he supervised three PhD students in his group during 1998 - 2003. He was supportive of international students working in his laboratory. He mentored graduate students from many countries including Bangladesh, India, Indonesia, New Zealand, Philippines, Singapore, Tanzania, Thailand, and Turkey, and hosted short term visiting students from China, Denmark, Korea, Pakistan, Taiwan, Thailand, and USA. Among the many students who worked with Dr. Higa are Prof. Ryuichi Sakai (Hokkaido University), Prof. Junsei Taira (National Institute

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In Memoriam: Tatsuo Higa



A joint meeting of the Higa-Tanaka lab and the Kuniyoshi lab at University of the Ryukyus, Okinawa, Japan, circa December 1999.

JUNICHI TANAKA

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of Technology, Okinawa College), Assoc. Prof. Tomoyuki Koyama (Tokyo University of Marine Science and Technology), Dr. Tan Lik Tong (Nanyang Technological University), Prof. Ilkay Erdogan Orhan (Gazi University), Prof. Musri Musman (Syiah Kuala University), Dr. Agus Trianto (Diponegoro University), Dr. Sirirath Sodngam (Khon

nawa, including the VII Pacific Science Inter-Congress in 1993, the 42nd Symposium on the Chemistry of Natural Products in 2000, the 10th International Symposium in Marine Natural Products in 2001, and the International Symposium on Toxins and Natural Products in Honor of Professor Anthony T. Tu in 2002. As a result, a large per-

Dr. Higa published over 140 research articles in marine natural products, which primarily dealt with organisms collected in Okinawan waters. His representative molecules include thelepin, bromophenols from hemichodates, hippuristanol, manzamines, misakinolide A, onnamide A, hennoxazoles, miyakolide, agelasphins, echinoclathrines, pachastrissamine, and floresolides.

Kaen University), and Prof. Junichi Tanaka, who succeeded Dr. Higa at University of the Ryukyus.

Dr. Higa was a consummate promoter of his island home and took every opportunity to encourage colleagues to visit Okinawa. Indeed, to facilitate this, Dr. Higa organized numerous scientific conferences in Okinawa,

including the VII Pacific Science Inter-Congress in 1993, the 42nd Symposium on the Chemistry of Natural Products in 2000, the 10th International Symposium in Marine Natural Products in 2001, and the International Symposium on Toxins and Natural Products in Honor of Professor Anthony T. Tu in 2002. As a result, a large percentage of researchers in the marine natural products field have visited Okinawa and enjoyed the outstanding hospitality provided by Dr. Higa, his group members, and the local citizens.

Dr. Higa is survived by his wife, Tomiko, a daughter and two sons. ■

Epic Rot: Cichewicz Curates an Incredible Exhibit of Fungal Decay

By Dr. Nicholas Oberlies

ASP member Dr. Robert Cichewicz and his colleagues from the University of Oklahoma, who skillfully organized the 2015 ASP Annual Meeting, have now used their talents to create a fascinating special exhibit running through August 12, 2018 at Science Museum Oklahoma entitled, *Decomposition: Discovering the Beauty and Magnificence of Fungi* (www.sciencemuseumok.org/science-museum-oklahoma-university-of-oklahoma-researchers-explore-the-magnificence-of-fungi-in-new-exhibition).

This exhibit explains how fungi decompose matter. Dr. Cichewicz's Natural Products Discovery Group has created a wonderfully graphic YouTube video (www.youtube.com/watch?v=d6UWRpUNxxs), but think twice about watching it over lunch. Dr. Cichewicz, in his typically understated way, sent the video around to a few ASP members who also love fungi. The following is an interview with him that provides more details about the exhibit. If you find yourself in Oklahoma City, I hope you will stop and check it out. We congratulate Dr. Cichewicz for bringing the chemistry and biology of fungi to the general public in such an engaging and vibrant manner.

Science Museum Oklahoma's recently established smART Space (a newly renovated gallery space with the purpose of making science more accessible to everyone by merging the fields of science and visual art), it immediately sounded like a perfect fit for our Citizen Science Soil Collection Program (www.whatsinyourbackyard.org). Though the exhibit first began as a discussion of how to promote our citizen science program, it quickly escalated into much more – an interactive exhibit highlighting both the scientific and artistic elements of the world of fungi. With those parameters in play, we set about designing how to bring these disparate elements together into one cohesive presentation.

How did you decide on the various things you let rot?

Three of the displays in the exhibit focus on fungi as decomposers. We do this through time-lapse video (www.youtube.com/watch?v=d6UWRpUNxxs), a display of how decomposition shapes the natural world, and decomposition rot boxes. The rot boxes explore some of the foods fungi consume and how they use the decomposition process to convert biomass into fungal struc-



Two of the displays at Science Museum Oklahoma which highlight the fascinating research of Dr. Robert Cichewicz and his Natural Products Discovery Group. The exhibit explores decomposition and the hidden beauty of the fungal kingdom.

CANDACE COKER

Please give me a little background on the origin of this unique idea.

The exhibit is entitled, *Decomposition: Discovering the Beauty and Magnificence of Fungi*. It is designed to expose people to the value of fungi in our world. The exhibit covers their ecological roles, uses as food and medicine, and diversity. When we heard about Sci-

ences. We have done this by setting up five boxes that contain the same tray of food (i.e., sandwich, orange, vegetable slices, cupcake, pasta salad, and orange juice), but temporally spaced apart by two weeks each. In this way, we show what happened during the decomposition process to the foods over a ten-week period. Deciding on which foods to use led us to create a re-
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Epic Rot: Cichewicz Curates an Incredible Exhibit of Fungal Decay

“All things that have form eventually decay.”

—Masashi Kishimoto, artist

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alistic lunch setting; however, fungi are the only diners invited to this meal. The time lapse video foods were selected based on sampling a range of different colors and textures. As a result, it has been fun to see how different people respond to seeing the rot boxes and video. What one person may find disgusting, another person finds beautiful.

How did you set up studies? What were the parameters, the lighting, the frequency, etc.? Did you run this in your lab?

The time-lapse video, which we entitled “Epic Rot,” was carried out in our lab. Project Manager, Ms. Candace Coker, has a background in the arts with photography experience and that played a huge role in getting this part of the exhibit to work. The time-lapse video was produced through high-resolution photography, set up in a controlled, secure lab environment with consistent lighting and temperature. Minor editing was also completed in-house. After experimenting with these parameters, which took roughly four months, another four and a half months was invested in shooting this portion of the project. It was a challenge, but extremely fun to see the video slowly come together. Seeing each clip for the first time was exciting for everyone involved. We are now producing some new time-lapse videos that will continue this series, as well as serve as materials for grade school and middle school curriculum guides that we plan to release in 2018.

Did you seed the microorganisms onto the specimens, or did they just pick it up from the air?

We opted to seed the food items in the first video series since we had a tight schedule and wanted to make sure we could showcase many type of fungi rather than having the same ones show up again and again. However, some of the fungi came from the foods that were used. For example, the fungus used in the strawberry video was a fungus found growing on a strawberry in the super market. In other cases, we simply left food to “spoil” for

several weeks before a video shoot took place so that we could obtain the cultures that were used in the video. However, some of the fungi starring in the videos were not introduced by us. They were present in the food, and they really made the video even more spectacular.

What else can someone see if they visit the museum display? Did you work with an artist at all, or were you and your team the artists?

In addition to the decomposition elements and video, there is a display of 100 fungi that were preserved in resin with a story about each fungus. The fungi selected for this part of the exhibit cover a broad range of intriguing concepts from fungi that make medicines to commercial applications, to even a few new and yet undescribed organisms from the bottom of Lake Superior. The resin process makes many of the fungi look jewel-like and created a stunning display. There is also a fungal apothecary filled with medicinal and edible mushrooms along with their uses. There are interactive question/answer flip panel sections that invite participants to learn more about fungi. Additionally, the exhibit features artwork created from fungi. Two pieces were designed for the exhibit. One is a multicomponent abstract piece showcasing the beauty of the colors and textures of fungi.

The other is a conceptual piece making a statement about how fungi fit into our world. With both “paintings,” the fungi act as the “paint.” This was quite a challenge and involved a lot of preparation time working out how fungi grow on canvas and making them create the pallet of colors that we needed. The exhibit also features several high-resolution photographs of fungi on Petri plates, which are suspended from the ceiling. (They are three-foot diameter, so you feel like you enter into the plate.) The walls in between pieces have different quotes about fungi from scientists and literary figures. Finally, there is a component that talks about citizen science and invites people to get involved in the process by

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A rot box featuring a live decomposition display.
CANDACE COKER

— an interactive exhibit highlighting
both the scientific and artistic elements of the world of fungi.

Epic Rot: Cichewicz Curates an Incredible Exhibit of Fungal Decay

“An adult is just a child who started to rot.”

—Rene Barjavel, writer

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contributing soil samples to our lab’s discovery efforts.

We did not work with a practicing artist to create the artwork featured in the exhibit. However, Candace’s expertise and background working in the arts greatly assisted in guiding the team to create a cohesive exhibit, bridging the gap between science and art. The team was excited to try and work through the challenges together to see what we could create. In the end, this was a good decision because it pushed us to think about fungi in novel ways and build new methods and tools that will probably feed into our research program and future outreach efforts.

Can you think of any unique challenges you overcame to make this all work?

The whole exhibit was a series of new challenges that tested the entire team. Since we had nothing to go on in terms of preexisting exhibits, we had to find new ways to highlight fungal chemistry, ecology, and drug discovery in ways that made fungi not only interesting, but also beautiful and engaging. Since this exhibit space is aimed at merging both science and art into one cohesive display, it meant having to find novel ways to bring these worlds together. Many of the elements involved were entirely new to us. We had no prior experience with time-lapse photography and had never even seen actual artwork made with real fungi. Because of this, we were venturing into areas and overcoming many challenges along the way. As with most worthwhile challenges, it was often both painful and exhilarating. Overall, it was a once in a lifetime opportunity that we were all happy to



Above and below: Stills from Dr. Cichewicz’s Natural Products Discovery Group’s YouTube video exhibiting how fungi decompose matter

have experienced.

What has the response been, both from scientists, non-scientists, school children, etc.?

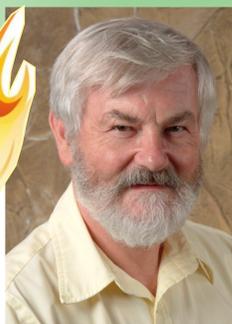
The exhibit has just opened, but we have already had several people express their pleasure with the exhibit. When we go there to drop off materials and check on the displays, I have had fun listening to the comments from families as they explore the exhibit. The rot boxes have been a standout component as people tend to react with kneejerk repulsion, but then stop covering their eyes and really look at the fungi, which is when you start to hear “that’s cool,” “awesome,” and “I never knew fungi were so beautiful.” That is when you feel like things have been a success as another person learns to see fungi in a new way.

What is the potential impact of this exhibit on the public?

We are thrilled to have had the opportunity to partner with Science Museum Oklahoma on this exhibit. Based on projected visitor attendance over the exhibit’s eight-month run, we anticipate upwards of 750,000 people will view the exhibit. If we can help many of these people view fungi, chemistry, and natural products in new ways and increase their appreciation for these organisms, then we have accomplished our mission. ■

“We are scarcely born ere decay begins for us, in such a way that the whole of life is but one long combat with it.”

—Gustave Flaubert, writer



Hot Topics in Pharmacognosy: Production of “Nominal” Medicinal Plant Compounds by Endophytes and Epiphytes

By Dr. David Newman

If one goes back into issues of the *Journal of Natural Products*, there is a well-cited 2006 review¹ (463 citations in Scopus as of 21FEB18) by Leslie Gunatilaka, on the discovery of microbes from plants that produce the same metabolites when fermented independently of the plant “host.”

This phenomenon has been covered in a variety of reviews/papers by multiple authors since the early reports by Stierle et al. on taxol production by microbes isolated from *Taxus* species, and the many discussions since that 1993 paper as to whether it was carry-over of the compound(s), horizontal gene transfer or genuine fungal production. Some of the furor over taxol production by fungi was clarified by the reports by Soliman et al.² in 2013 and Yang et al.³ in 2014, on differences in the biosynthetic genes in two different fungi isolated from taxol-producing plants.

Very recently, a paper published by Naik et al.⁴ may well have added “fuel to the fire” as they reported the isolation of endophytic fungi from the well-known plant *Datura metel* L., that produced tropane alkaloids when fermented independently of the plant. By using a PCR-based search for fungi containing genes encoding for putrescine N-methyltransferase (*pmt*), tropinone reductase 1 (*tr1*) and hyoscyamine 6 β -hydroxylase (*h6h*), they were able to isolate and identify endophytic fungi that contained those genes from the plant’s tissues. Scopolamine (**1**) and hyoscyamine (**2**) were definitively identified by MSⁿ techniques following fermentation of the isolates. Yields were in the 4 mg.l⁻¹ level in each case.

One may well claim that these are very low levels, but they are in fact comparable if not slightly higher than transformed hairy root cultures of the “producing plant,” and thus are potentially viable sources. What is significant is that in their fermentation conditions, no aeration was used (static cultures) nor were there any comments as to the addition of sterilized plant extracts (see comments in next paragraph). Currently, extraction of the roots of whole plants is the method used for production of these tropane alkaloids.

As alluded to above, addition of extracts from the “nominal producing plant” that had been sterilized and did not contain any of the compound/precursor(s), “rejuvenated” a subculture of an endophyte so that it produced the original material (and could be repeated). This is the work from the Oberlies group at the University of North Carolina, Greensboro⁵ on the

production of silybins A and B and demonstrates that methods used in the past in antibiotic discovery, but never formally published academically, are still valid. They were not published because everyone in “that trade” in the 1950s-1970s was aware of the method.

Another recent report, but without specifying the level(s) obtained, was that by Li et al.⁶ reporting the production of salvianolic acid C (**3**) by the fungus *Phoma glomerata* D14 isolated from the medicinal plant *Salvia miltiorrhiza*, a plant that is also the source of the tashinones. This particular fungus was obtained from a wash of the leaves of the plant, followed by the usual route of surface sterilization and then “grow-out” of leaf tissue samples on suitable media.

That unexpected metabolites can be found from endophytic fungi from Chinese medicinal plants, was demonstrated by Yan et al.⁷ in 2014. They found that the fungal endophyte *Gibberella fujikuroi* isolated from the medicinal plant *Curcuma wenyujin* produced not only gibberellic acid, but also kaempferol and curcumin (**4**). All are considered to be plant metabolites, and this is the first report of curcumin from an endophytic fungus.

Finally, in 2017, the very well-known “plant structure” betulinic acid (**5**) and other closely related structures were discovered from use of an anti-dengue virus assay, using as the source of the assay “candidates,” an extract of the host plant *Diospyros carbonaria* Benoist, together with assays of 38 fungi covering five different orders.⁸ Of these, nine demonstrated activity in an anti-DENV-2 NSS assay, and from these, a *Phomopsis* sp. was the most active. Chemical investigation of the fungal fermentation products after use of a solid-state fermentation protocol led to the identification of betulinic acid in the extract following preparative HPLC.

This is the first report of a lupane-type triterpenoid from a plant and an endophytic fungus. Whether the genes were transferred by horizontal gene transfer or the fungus occupies a specific niche in the plant microbiome is not yet known.

In the last few years, the plant microbiome is now beginning to be appreciated for what it probably is, a reservoir of bioactive source materials that may act as elicitors, sources of protective agents (such as maytansine, which was covered a few columns ago), or even be the actual source of what were thought to be solely plant-produced products.

If any of the comments above are even close to “reality,” then
continued on page 15

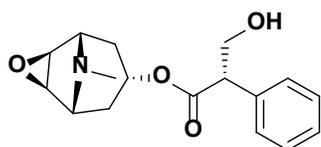
Hot Topics in Pharmacognosy: Production of “Nominal” Medicinal Plant Compounds by Endophytes and Epiphytes

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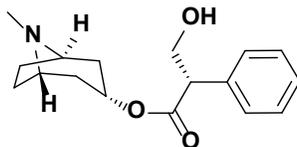
it lends credence to what was always described in the early days of Traditional Chinese Medicine, in that the collection timing, altitude and meteorological conditions needed to be considered before any harvesting. If one thinks about it for a moment, then what may be being described are the optimal conditions for an endophyte/plant relationship. Thus, simply collecting a “medicinal plant” because it has the “correct taxonomy” is probably not optimal in any way, particularly if grown far away from where

the original sample in TCM was collected and processed. These caveats apply equally to any other “medicinal plant” collection and/or use program.

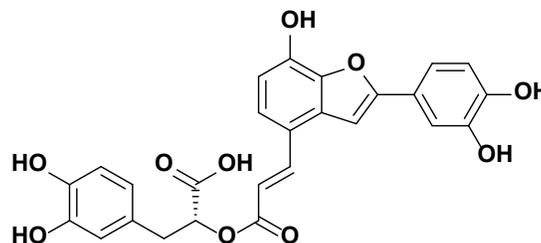
I can speak from knowledge from the early NCI plant collection program, where we frequently went back to the same site to collect, but at a different time or climate from the original collection, and often did not recover the same metabolites, possibly due to one or more of the caveats above. ■



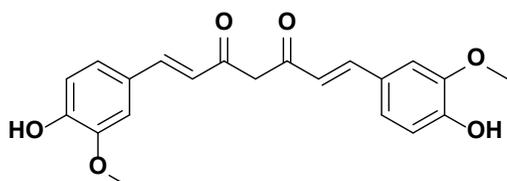
1. Scopolamine



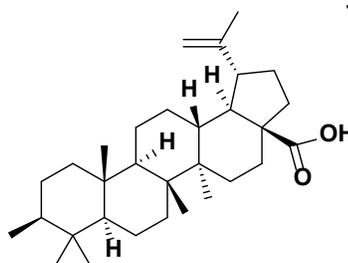
2. Hyoscyamine



3. Salvianolic acid C



4. Curcumin



5. Betulinic Acid

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Behind the Scenes in Pharmacognosy: Multidimensional Phenotypic Screening of Natural Products

By Ms. Andrea Rague

In July of 2016, the *Journal of Natural Products* published an article entitled, “A Grand Challenge. 2. Phenotypic Profiling of a Natural Product Library on Parkinson’s Patient-Derived Cells,” authored by ASP member Dr. Ronald J. Quinn and others. Dr. Quinn is a professor at the Griffith Institute for Drug Discovery in Brisbane, Australia. We thank Dr. Quinn for taking some time to share his work and insights with ASP members. Please read the full article in the *Journal of Natural Products*, 2016, 79, 1982–1989.

How did you become interested in multidimensional phenotypic screening of natural products?

This came about because of my work around molecular recognition. Natural products are made by biosynthetic enzymes and have a level of biological validation in the sense that they have already bound to proteins during their synthesis. This embedded biological imprint can then be used by natural products to interact with other

proteins, including therapeutic targets. Multidimensional phenotypic screening seemed to offer the greatest possibility to experimentally show that most natural products have biological function associated with binding to and modulating the function of proteins.

Who in your lab was involved with this research?

The theoretical work on molecular recognition was mainly the work of two PhD students, Bernadette McArdle and Noé Sturm. I was also fortunate to collaborate with Esther Kellenberger in Strasbourg.

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

It is an impossible task to test all natural products against all protein or cellular targets to determine biological function. We thought that an unbiased method that examined cellular machinery could be more successful.

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Dr. Ronald J. Quinn and his group at Griffith University, Brisbane, Australia

RONALD QUINN

Behind the Scenes in Pharmacognosy: Multidimensional Phenotypic Screening of Natural Products

Multidimensional phenotypic screening seemed to offer the greatest possibility to experimentally show that most natural products have biological function associated with binding to and modulating the function of proteins.

Were there any new techniques or instrumentation that you learned to use specifically for this research?

Yes, we used confocal microscopy and high content biology. This was new to my laboratory and was the project mainly of a PhD student, Marie-Laure Vial. We aimed to target several cell components simultaneously to increase the likelihood of finding phenotypes.

Your work reports that all natural products in your dataset showed at least one phenotypic response in the multidimensional phenotypic screen. What relevance does this have to the future of natural products chemistry?

Every natural product has the potential to have biological function. I think one lesson is that if your natural product is inactive in a screen then consider a phenotypic screen.

Have you continued with this research since the article was published?

Yes, we are using the phenotypic assay to help to identify the molecular targets. We have included natural products with known mechanisms of action, and this may provide a clue to the mechanism of action of other compounds in the same cluster. We are using the assay for both isolated natural products and synthetic libraries based on scaffolds that occur in natural products. A further interesting application has been looking at Traditional Chinese Medicine to use the phenotype to investigate the effect of mixtures.

What is a favorite nonscientific activity of your lab?

Bush walking, movies, and lab parties at Christmas and Chinese New Year.

What is your lab's motto or slogan?

Our motto is: as simple as possible—we strive to achieve simplicity. Two examples are to examine active fractions using NMR fingerprints in order to develop a method that avoids bioassay-guided fractionation. A second example is to use mass spectrometry to develop assays that involve mixing unmodified natural products with unmodified proteins.

Our slogan is "Why not?" This is related to the scientific questions that we ask. The question is "Why not?"—why can we not do it, why can we not try it, how can we get it to work? Everyone can do anything.

Lastly, we believe in perseverance.

What is your greatest extravagance in the lab?

Probably equipment, such as a CryoProbe™ 800MHz NMR and a 12 Tesla FTMS.

How do you celebrate accomplishments in your lab?

Group parties. We sample food from the countries of our group members, currently Australia, China, Italy, Algeria, Libya, and Iran.

What advice would you give to scientists starting their careers in natural products?

Try to expand your skills into a new area. Practice presenting your work, go to conferences, and be more visible. Try to speak up. ■

Our slogan is "Why not?"

This is related to the scientific questions that we ask.

The question is "Why not?"—why can we not do it, why can we not try it, how can we get it to work? Everyone can do anything.

Meet a New ASP Member

Dr. Aaron Kirkland is our featured new member in this spring issue of the Newsletter. He is a Senior Research Scientist with Alltech, leading the Analytical and Bioanalytical Chemistry Group as part of the Division of Chemistry and Toxicology. They are located within the Alltech Center for Nutrigenomics and Applied Animal Nutrition at Alltech HQ in Nicholasville, KY. We are grateful for a chance to officially welcome Dr. Kirkland to ASP.

By Dr. Dan Kulakowski

How did you hear about the ASP?

I first learned of ASP from speaking with someone at last year's ASMS conference in Indianapolis.

Why did you join ASP?

I was searching for an organization to join that emphasized natural product chemistry and especially plant-derived bioactives. The ACS meetings were very large and very diverse but just didn't have enough of what I was looking for. ASP seemed to be a much better fit.

What would you like to achieve through your membership?

I am new to this discipline but would really like to make contacts and to become part of a network that I can learn from, bounce ideas off of and potentially develop future collaborations or working relationships with. I'm also hoping that I will have something meaningful from my background that I can share that would benefit members of the organization.

Do you belong to any other scientific societies?

I am a member of several professional scientific organizations. The largest are the American Chemical Society, the American Society for Mass Spectrometry, the American Society for Microbiology, and the Institute of Food Technologists.

What are your current research interests in pharmacognosy?

I am interested in the nutritive and antimicrobial properties of carotenoids and non-canonical polyunsaturated fatty acids from the archaea. I am also interested in the chemistry of mycotoxins and their bioremediation as well as plant-derived sesquiterpenes, flavones and stilbenes with antiparasitic properties or bioactivities that support digestive or reproductive health in food animal species.

What is your scientific background?

I earned my PhD from the University of Florida where I worked on ubiquitin-independent protein degradation in the halophilic archaea. From there, I spent three years as an IRTA fellow at the NIH/NIDDK where I transitioned to the yeast model investigating naturally occurring prion structures and their structural/functional determinants for propagation and curing. I then moved to strain engineering and analytical chemistry roles with a small startup called Allylix (now Evolva) in Lexington where we specialized in genetically engineering yeast as a biocatalytic platform for producing valencene, nootkatone and other sesquiterpene products for the flavor and fragrance industry. I joined Alltech in June of 2016 where I continue my work with natural



Alltech's Dr. Aaron Kirkland in his lab in Nicholasville, Kentucky.

REBEKAH BUCHANAN

products from plant and microbial sources as well as fungal toxins and their impact on the beef, dairy and poultry industries.

What inspires you in your work?

I consider protecting our food sources and helping to make farming economically sustainable for future farmers to be an incredibly noble cause, and I like to think that I am helping to advance this cause, even in the smallest of ways.

What is your favorite organism (to study or for general interest)?

Haloferax volcanii, my first (microbial) love, and *Saccharomyces cerevisiae* because we go way back.

What do you like doing in your spare time?

I like playing music, hiking, woodworking and taking road trips with the family.

What are you currently reading?

I am slowly working my way through *House of Leaves* by Mark Z. Danielewski and also reading *A Tree or a Person or a Wall*, which is a series of short stories by Matt Bell. ■

New Members of ASP 2018



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 10 full members and 4 associate members. We look forward to meeting you and learning more about you and your work.

FULL MEMBERS

Ms. Adeyoyin Adeniji
Phytocare Health Services
Operations Manager
Lagos, Nigeria

Dr. Vinayak Agarwal
Georgia Institute of Technology
Assistant Professor
Atlanta, Georgia

Dr. Asmaa Boufridi
Griffith Institute for Drug Discovery
Postdoctoral Research Fellow
Brisbane, Australia

Dr. Lukasz Ciesla
University of Alabama
Assistant Professor
Tuscaloosa, Alabama

Dr. Sherif Elshahawi
Chapman University
Assistant Professor
Irvine, California

Dr. Phillip Kirkland
Alltech, Inc.
Senior Research Scientist
Nicholasville, Kentucky

Dr. Rkia Moutiq
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Dr. Markus Nett
Technical University - Dortmund
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Dortmund, Germany

Dr. Shyam Ramakrishnan
Amway Corp.
Fellow, Global Discovery
Buena Park, California

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Graduate Student
Storrs, Connecticut



Welcome to ASP!

Conference Calendar

The *Newsletter* is pleased to announce the following upcoming conferences and meetings. The events portrayed here reflect what listings and notices the *Newsletter* has specifically received. For a more extensive calendar, please visit the ASP website at www.pharmacognosy.us. If you have a conference or event you would like mentioned, please send us relevant information, including any graphics or appropriate fliers, at asp.newsletter@lehman.cuny.edu.

15th Annual NHPRS Conference & Tradeshow

May 14-18, 2018

Delta Guelph Conference Center

Guelph, ON, Canada

www.nhprs.ca/annual-conference/

Joint Conference of the Society of Ethnobiology & Society for Economic Botany

June 3-7, 2018

Memorial Union on the UW-Madison campus

Madison, Wisconsin

[www.ethnobiology.org/conference/
upcoming](http://www.ethnobiology.org/conference/upcoming)

Phytopharm 2018

June 25-27, 2018

**ZHAW Life Sciences and
Facility Management Wädenswil**

Wädenswil, Switzerland

[www.zhaw.ch/en/about-us/news/events/
events/event/detail/1731-20180625-phyto-
pharm-2018/](http://www.zhaw.ch/en/about-us/news/events/events/event/detail/1731-20180625-phytopharm-2018/)

ICP + TC 2018

**XXIXth International Conference on
Polyphenols, 9th Tannin Conference**

July 16-20, 2018

**Memorial Union and Shannon Hall on
Lake Mendota, Madison, Wisconsin**

www.conferences.union.wisc.edu/icp/

Gordon Research Conference on Natural Products and Bioactive Compounds

July 29 - August 3, 2018

Proctor Academy

Andover, New Hampshire

[www.grc.org/natural-products-and-bioactive-
compounds-conference/2018/](http://www.grc.org/natural-products-and-bioactive-compounds-conference/2018/)

66th International Congress and Annual Meeting of the Society for Medicinal Plant and Natural Product Research (GA) jointly with the 11th Shanghai TCM Conference

August 26 - 29, 2018

Parkyard Hotel Shanghai

Shanghai, China

www.ga2018.cn





Brief News from Washington

By Dr. Georgia Perdue

- As of the time the President's budget was unveiled in February, it appears that NIH's budget will be close to the one in 2017. Whether slight increases will be added remains to be seen.
- Last December the new National Cancer Institute Director, **Dr. Norman Sharpless**, held his first town hall meeting at NIH. **He noted it was a time "to get to know me ... and a chance to ask questions about me."** His first job as a scientist was at NCI between his second and third years of medical college. **"I loved the work, the other scholars and the lab dynamic. It was the best year of my life."** He trained as a medical oncologist and molecular biologist. **"As much as I liked clinical medicine... I had to go back to the lab."** "Bruce Chabner, one of my encouragers, told me to go back to the lab." Dr. Sharpless did his post-doc in molecular biology at Dana Farber Institute and the University of North Carolina. He was closely connected with NCI from which he received several grants. "I felt I really knew this place." And so, **he was nominated by President Trump for his new position. "... I had five months to go around and talk to people," as his nomination languished on the Hill. He noted that he believes the "Cancer Moonshot" is a good idea. "Good ideas are half the battle."** He plans to take more time to understand NCI before he announces his priorities. **"We still are not good at understanding cancer....We need better data, human capital and to develop novel therapeutics. We have an enormous natural product library that can be used for screening."** He also noted that "scientists can put forth ideas and bureaucrats [should] get out of the way. **I am here to lead great science, take risks and to do unimaginable things."** He hopes to have a lab of his own in a couple months. He proudly noted that his wife is an endocrinologist, currently unemployed, and his mother was a pediatrician.
- **At the December 14 Advisory Committee to the Director (ACD) of NIH, Dr. Francis Collins noted he was "quite gratified with the results of the Century Cures Act in just one year."** He noted, **"The Administration has developed an increased interest ...in the NIH research. It is coming to understand why NIH is important as an investment for the federal government."** Dr. Collins considers Dr. Sharpless a "visionary with enormous skill as a researcher." He also offered kudos to Dr. Douglas Lowy who "held NCI together as Acting Director. He has brilliantly and ably been acting in that capacity and is staying on." Collins also noted he is "still looking for a replacement for Dr. Josephine Briggs," former Director of NCCIH.
- Also at the ACD meeting, **Dr. Lawrence Tabak**, NIH Principle Deputy Director talked about the progress to date on the **Next Generation Researchers Policy. He described the policy working group as "unique because of their passion, energy and individual insights."** The policy will provide a pathway to the "brightest and best." This "team sport" and "tremendous effort" by advisors, is to have an **NIH-wide strategic plan "to enhance stewardship."** The plan's objectives are:
 - Set priorities
 - Foster scientific opportunity
 - Advance research opportunities presented by rare diseases
 - Consider the value of permanently eradicating a pandemic
 - Recruit and retain outstanding research workforce
 - Enhance workforce diversity
 - Encourage innovation
 - Enhance impact through partnerships

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Brief News From Washington

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- Reduce administrative burden
- Excel as a federal science agency by striving for results
- Develop a policy supporting the Next Generation Researchers Initiative

The data show the number of younger R01 grantees has dropped since 1990. It is difficult for junior investigators to obtain initial funding. “They get lost in the pipeline.” The committee realized it is necessary to provide recommendations how best to **prioritize funds to ensure support for investigators at risk of losing all funding support, e.g., the junior investigators. “There is very low morale and lack of trust in NIH among the next generation investigators,”** said Dr. Tabak. **“FY 18 may be a stronger year for implementation of the [new policy].” Final recommendations are expected in December 2018.**

- At last, on January 24 the Senate voted 55-43 to confirm Alex Azar as HHS Secretary (see December ASP Newsletter issue for details). At the National Institute of Allergy and Infectious Diseases (NIAID) Council meeting, Dr. Anthony Fauci noted **Eric Hargan was appointed as Deputy Secretary for HHS,** and remarked a **“positive outcome for HHS and the department.”** Dr. Fauci also noted that **Peter A. Sands was named Executive Director of Global Fund to fight AIDS, Tuberculosis and Malaria. He was Chief Executive of the Standard Charter Bank, the “world’s leader in international finance.”** In discussing the “unusually bad seasonal flu,” **Dr. Fauci said the “particularly bad influenza season” was the fault of the vaccine. “We need to do better; we need a universal influenza vaccine.”** He went on to explain that **“this year when the virus was put in eggs to grow they mutated. The molecule responsible for protection mutated by the time it got out of the eggs. That is why we are having a bad season.”** On another topic Dr. Fauci noted there are 216 million cases of malaria worldwide, five million more than 2015 and deaths due to malaria are the same as 2015. **“TB remains the top infectious disease killer; 600,000 new cases ...were drug resistant.”**
- **In December NIH reported that resiniferatoxin (RTX) isolated from *Euphorbia resinifera*, a cactus-like plant**

found in Morocco, “shows promise in controlling post-operative incision-site pain.” It also has shown high efficacy as a “blocker of pain in multiple other preclinical animal models” and in a Phase I NIH clinical trial in patients with “severe pain associated with advanced colon cancer.”

- In January scientists at NIAID reported in *Immunity* that the **white fat tissue under skin, muscles and organs “stores immune cells, or memory T cells that fight against infectious agents.”**
- **In December FDA reported it has a new policy to enforce homeopathic products.** Since 1988 homeopathic products “have been manufactured and distributed without agency approval.” It seems there has been a “spike in recent years in products labeled homeopathic, but marketed as treatments for diseases and conditions of varying degrees,” said FDA Commissioner Scott Gottlieb.
- In early January Teva Pharmaceuticals Industries, Inc. announced that **FDA had approved Trisenox (arsenic trioxide) injection “for first line treatment of acute promyelocytic leukemia.”**
- **Tamoxifen keeps on giving.** In the seemingly busy month of January, the **FDA granted “breakthrough therapy” designation for Kisqali (ribociclib) in combination with tamoxifen or an aromatase inhibitor produced by Novartis. One use is for metastatic breast cancer.**
- **Eat your one serving of green leafy vegetables every day because it will help slow down the cognitive decline as you age. One or two servings per day “was equivalent of being 11 years younger compared to those who never or rarely consumed [them].”** (see *Medscape* 1/8/18).
- NIH reported in January that an NIH-funded study suggests **“impaired blood flow and dementia can result from a high-salt diet.”**
- Also in the prolific month of January, **NIAID reported beneficial bacteria on the skin of lab mice “work with the animals’ immune system to defend against disease-causing microbes and accelerate wound healing.”** This could be translated to the human immune system!
- Check out an article in *Medscape Pharmacists, Pharmacognosy, a Classical Theme Tuned to a Contemporary Melody*, which quotes the *American Journal of Pharmaceutical Education!* ■

Eat your one serving of green leafy vegetables every day because it will help slow down the cognitive decline as you age. One or two servings per day “was equivalent of being 11 years younger compared to those who never or rarely consumed [them].”

—*Medscape* 1/8/18

From the Archives Part IV: Pettit's "Incredible Journey into the People's Republic of China"¹

By Ms. Devhra BennettJones

On January 4, 1971 President Richard Nixon articulated a toast to Chairman Mao Zedong, "If we succeed in working together where we can find common ground, if we can find common ground on which we can both stand, where we can build the bridge between us and build a new world, generations in the years ahead will look back and thank us for this meeting that we have held in this past week. Let the Chinese people and the great American people be worthy of the hopes and ideals of the world, for peace and justice and progress for all."² President Nixon's trip to China and the Shanghai Communiqué marked a turning point in Cold War-era US-China relations.³ The Communiqué endorsed both commitments to normalizing relations and provided a framework for realizing this goal through the exchange of scientists. Venerated scientists from both countries served as delegates in the mission of rapprochement.⁴ A key factor in the growth of the relationship was the people who served as bridges between the two societies.⁵ Esteemed ASP members Drs. Norman R. Farnsworth, S. Morris Kupchan, Thomas H. Maren, George R. Pettit, and Michael A. Schwartz were among the medicine and pharmacology emissaries that formed the 1974 National Academy of Sciences Delegation. The relationships established during this period led to subsequent research opportunities. The following is the final of four excerpts from Dr. George R. Pettit's travel journal.

NO. 1 TEACHING HOSPITAL OF CHUNG SHAN MEDICAL COLLEGE, TUESDAY, JUNE 25⁶

We left at 8:00 p.m. for the approximate 15-minute ride by car to the No. 1 Teaching Hospital. Over tea we were given a brief description by the responsible member of this medical college. This teaching facility was established in 1953 by consolidation of three separate medical colleges and college faculties. Presently the teaching hospital has 750 beds and another 200 beds are devoted to the tumor hospital section. The medical college specializes particularly in cancer, ophthalmology and microsurgery for joining severed limbs and fingers. The total staff numbers 3,500, of which 800 are teachers in the medical college. As a typical example, the pharmacology faculty numbers 30. Student enrollment totals 1,200 and another 120 students are enrolled in the nursing college.



With the advent of the cultural revolution,⁷ entrance exams were discontinued. Students are now accepted after three years of practical experience with a minimum of junior middle school education. They also must be about 20 years of age. The former six-year curriculum was dropped to three years. In effect, it is hoped that this will produce twice as many doctors in the six-year period. As part of this accommodation, 36 subjects previously taught were dropped to 15 by elimination and consolidation. Before the three-year curriculum is begun, the beginning students spend the first half year reviewing middle school subjects.

The first-year program entails courses in pharmacology (84 hr. total, 200+ western drugs and 70 medicinal plant drugs), physiology, pathology and diagnosis. In the second year, dermatology, obstetrics, regional anatomy and traditional medicine constitute the formal courses. Students are then sent to rural areas to study public health subjects. In this regard venereal diseases have been dropped from the curriculum as China has apparently wiped out this problem. The third year constitutes courses in clinical pharmacology, recent progress in medicine and a five to ten patient contact responsibility.

As part of the visit we were shown four groups of students doing a blood pressure experiment (using dogs) in the pharmacology department. A research project in this same department was concerned with an extract of *Ilex pubescens* Hook (Aquifoliaceae). In the dog, blood pressure begins to

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**President Nixon's trip to China and the Shanghai Communiqué
marked a turning point in Cold War-era US-China relations.**

From the Archives Part IV: Pettit's "Incredible Journey into the People's Republic of China"

**A key factor in the growth of the relationship was
the people who served as bridges between the two societies.**

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fall in 30 minutes and lasts several hours. The extract is also being studied chemically for its useful effects on angina pectoris and reduction (50%) of the plaques in the aorta.

The *Ilex* extract is under study in the chemistry department by Dr. Wang Mei-Hsiang. However, only the common triterpene mixture oleanolic-ursolic acids has so far been isolated. Interestingly, a small factory has been set up in the college with 30 staff to extract and formulate the product for clinical use.

The factory operation viewed was the last word in pragmatism. Two former bathtubs were converted to steam heated extractors and two more served as steam heated evaporators. The residue from the hot water extract was diluted with alcohol and this solution was filtered. The alcohol extract was either evaporated (alcohol still) with sugar to give an oral form of the drug or made up in ampule form as follows. The alcohol solution was concentrated, treated with hydrochloric acid and extracted with ethyl acetate. The latter extract was filtered and evaporated (fan, open air). Ampule production was conducted in a sterile room and pyrogens were evaluated using rabbits.

Another member of the pharmacology department was studying hydroxyurea, hexamethylmelamine, the dichlorodiammineplatinum complex, 5-fluorouracil (5-FU), cephalotaxine (active in their WA-256) and homoharringtonine. All of these compounds are well known in our National Cancer Institute program, but are apparently being obtained from Japan. They are readying for clinical trials of cephalotaxine and homoharringtonine. The screening program used in this department covers hepatoma 22, U-14 (a Chinese tumor, uterine carcinoma induced by carcinogens), S-180, WA-256 and Ehrlich ascites.

After lunch at the Guangzhou Guest House, we returned (2:30 p.m.) for a tour of the general hospital and tumor hospital. In the former we were told of their efforts since 1964 to perfect techniques of microsurgery for joining severed limbs and fingers by means of a Chinese language surgical film and discussions of their successes with joining severed limbs and fingers up to 33 hours after the accident. Successful transplantations of toes to replace missing thumbs are now made routinely. One of the more dramatic examples entailed a female farm worker who suffered a severed wrist. She bur-

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ied the hand, went for help and was told to retrieve the hand, which she did, and it was successfully joined. In each of the examples viewed, the damage due to laceration, etc. was severe and required very careful joining of arteries and nerves. The surgeons work in a magnified field and success averaged about 70% with both limbs and fingers. The *Ilex* extract reviewed above was employed to dilated blood vessels. Techniques for the fingers were worked out using monkeys, and artery joining is done where necessary by saphenous vein grafts.

On a subsequent ward tour, we saw a woman factory worker of perhaps 35 who had lost her right thumb about seven years ago. A week or two prior to our visit, a toe (3rd from left foot) had been transplanted to replace the thumb. Healing seemed to be progressing well. The same observation applied to a commune (an orphan) boy who had suffered loss of his left thumb (at the hand).

In the nearby tumor hospital, we first saw two male patients with squamous cell carcinoma of the nasopharynx. The first, of about 35 years, was admitted, unable to move his eyes (except to the left), ringing in the ears and headache. The second was of middle age and had a large swelling in the neck on admission. Both were treated with 5-FU and a series of plant extracts to improve their general condition and reduce nausea. The second patient described also was given courses of Cytoxan and bleomycin. At the time viewed, both were in remission. Eye movement had returned to the first patient, but the movement seen was not coordinated. After questioning it was learned that nasopharynx patients are generally given radiotherapy (5,000 to 7,000 rads) with cobalt-60, and survival (five years) is about 50%. This reviewer wonders whether the indoor fires, common in this part of China, are producing the carcinogens leading to the high incidence (in the 30 to 50 age groups) experienced. In this hospital, nasopharynx (first), liver (second), and stomach (third)

cancer are most commonly seen.

Two patients viewed with liver cancer had been treated as above. For example, a male of 36 years admitted on April 6 with a large abdominal mass diagnosed as a hematoma was given radiotherapy, 5-FU and medicinal plant extracts (to reduce nausea, improve general condition). When seen some jaundice was evident, but the mass had receded and his general condition was much improved.

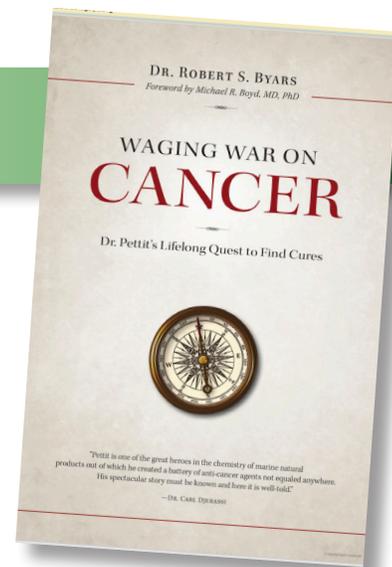
A stage 2+ cervical cancer patient was viewed and discussed. With advanced cancer of this type, localized infusion with nitrogen mustard is generally employed. This woman of about 40 years was obviously very uncomfortable, but did her best to remain calm. Another woman of about 40 with choriocarcinoma (who delivered a dead fetus three months prior to admission), metastasized to lung and vagina, was being given 5-FU (1 g/day) and actinomycin D (200 ug/day) simultaneously by IV drip. Each course is for ten days with a two-week rest period. Then three or four more such courses are given as required.

While making the ward rounds some general observations were made. Each room was equipped for six to eight beds and almost none were seen empty. Linens, bedding, patient clothing (shirt and pants units) and the hospital itself were exceptionally clean and odor free.

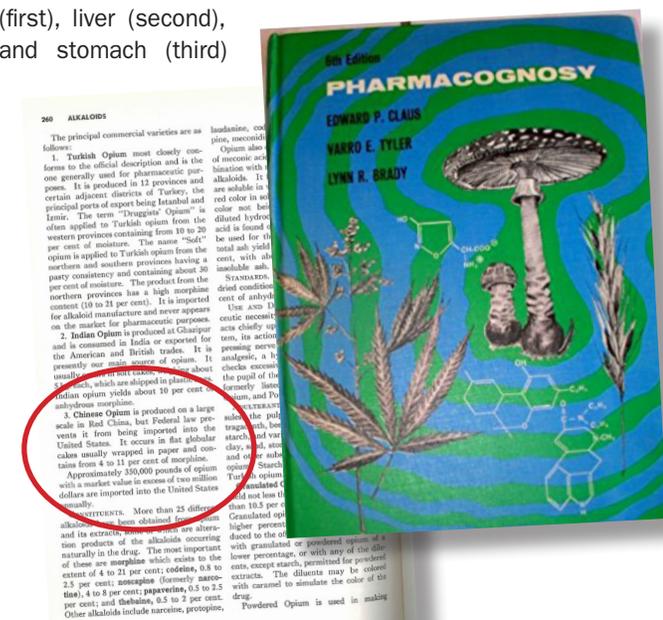
This visit followed the general pattern of two to three hours duration. Meanwhile, Dr. Maren visited the ophthalmology section and noted the use of pilocarpine with Diamox and one acupuncture needle in the left arm (below shoulder) as a useful treatment for open angle glaucoma. At 5:30 p.m. we returned to the guest house and made ready for the 7:00 p.m. going away banquet our hosts had arranged. Both parties made a series of friendship speeches and toasts. In customary form the banquet was brought to a close at 9:00 p.m. I sat with Dr. Hsu Hsiao-Li of the Chung Shan Medical College, Biochemistry Department, who spoke English and was very pleasant. Shortly thereafter, Mr. Chung of our Peking group contacted our chairman and with obvious embarrassment for him returned the six copies of *Pharmacognosy* which had been presented as gifts to the Institutes

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Multiple copies of the classic textbook *Pharmacognosy* were given as gifts during Pettit's 1974 journey, but all were returned due to a controversial passage about China and the opium trade.



Dr. Robert S. Byers 2015 book reporting the travels and insights of the Pettit team



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in Peking, Shanghai, Hanking, and Guangzhou. The book contained a statement that Red China was one of the main sources of illicit opium going to the US.⁸ This was considered a lie, which it probably was, and the books (contributed by Dr. Farnsworth and the publishers) could not be accepted. Although this was indeed an unfortunate incident, with a potential for deep repercussions, the matter was handled well and quickly dropped. Of some interest to this writer was how all the books found their way so quickly to Guangzhou.

Our Guangzhou hosts greeted us the next morning (June 26) at 7:30 a.m. for our departure.

We left about 8:00 a.m. for the railway station. After exchanging many warm wishes, we boarded (about 8:30 a.m.) an air-conditioned section of the train for the 1.5 hour trip to the border. As is the custom, our new friends remained on the platform and waved good-by until the train departed.

The preceding days in Guangzhou had been quite uncomfortable from the weather standpoint. Day and night temperatures were above 85°, the rain was almost continuous, and humidity was 90+%. Only the chairman's room was air-conditioned, but each bed was equipped with netting and a large bath towel. Several of the members competed with cockroaches for a place in bed, but otherwise our hotel was superb. In fact, the Guangzhou Guest House is used for visiting presidents, premiers, etc. The

tropical landscaping was attractive and the three large buildings inside the walled compound has an entry-way with a military armed guard. Because of the tropical location of this city and consequent high temperatures and humidity, it must be a constant battle to keep the guest house free of roaches, fungus, etc.

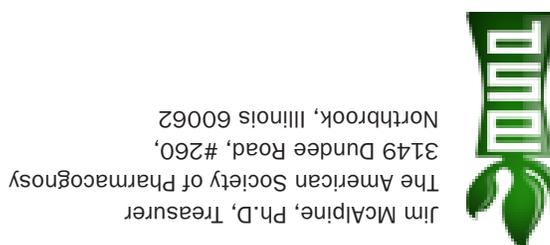
On the border trip Mr. Chung Leong (29 years, trained at the Peking foreign language school, for a rural area) and one assistant accompanied us and very expeditiously passed us through customs (no baggage check) and the army security guard. The rain was still coming down in force when we walked across the railroad bridge to Lo Wu Station. A representative of the China Travel Service met us when we emerged from Hong Kong Immigration. The about one-hour train trip to Kowloon Station was uneventful, and our incredible journey into the People's Republic of China ended.

4-1/2 hr. Hong Kong to Tokyo and 6-1/2 hr. Tokyo to Honolulu. ■

Local photos in this article were provided by Dr. George Robert Pettit during his 1974 tour of the People's Republic of China. Dr. Pettit could not provide any details about these photos, but most were apparently taken at the various scientific institutions he and the other American delegates visited during their 27 day visit.

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- ⁶ Today Chung Shan Medical College is Guangzhou Medical University formerly known as Guangzhou Medical College. The University has two campuses in Guangzhou City offering undergraduate and graduate degrees through sixteen schools of applied medical science. **2015**. <http://www.gzhmu.edu.cn/gyEnglish/index.html>
- ⁷ Lieberthal, K. *Cultural Revolution: Chinese Political Movement*. Encyclopædia Britannica, Inc. Mao Zedong adopted four goals for the Cultural Revolution (1966-1976). He sought to replace his designated successors with leaders he assessed as devoted to his ideology. Mao wanted to rectify the values of the Chinese Communist Party that he believed had gone astray with the economic advancements during the Great Leap Forward. He sought to involve China's youth in the revolutionary experience. Mao focused on policy changes in education, health care, and Chinese culture in the quest to reduce elitism. **2018**. <https://www.britannica.com/event/Cultural-Revolution>
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