



The American Society of Pharmacognosy

The ASP Newsletter: Volume 51, Issue 4

Discovering
Nature's
Molecular
Potential

ASP Fellow Ōmura Awarded Nobel Prize

By Drs. James B. McAlpine and David J. Newman

Dr. Satoshi Ōmura was one of three 2015 Nobel Prize winners in Physiology or Medicine. The ASP was "ahead of the game," as he was the Norman R. Farnsworth awardee at the 2013 ASP Annual Meeting for his superb work in antibiotics and related compounds; he also became an ASP Fellow as a result of this award by the Society. It is propitious that ASP recognized his stature before the award of the Nobel Prize for Medicine this year for his work on the avermectin/ivermectin class of microbial metabolites, sharing the award with Dr. William Campbell, originally from Merck Sharp and Dohme, (one half the award to these two gentlemen) and the other half to Dr. Tu Youyou for her work on artemisinin.



Drs. McAlpine and Ōmura.

Dr. Ōmura has the phenomenal number of 1,108 cited documents in Scopus, a total citation count of 25,420 (as of November) and an *h* factor of 68 (since 1996). These figures demonstrate the immense effect that he has had during his scientific career investigating molecules from terrestrial microbes.

Dr. Ōmura was born in July of 1935 and has the distinction of having
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In Memoriam David J. Slatkin

By Drs. Paul L. Schiff Jr., Melany Puglisi-Weening,
and John H. Cardellina II

On November 16, 2015, David Joseph Slatkin, PhD, former Treasurer and longtime Honorary Member of the ASP, passed away after a long battle with Parkinson's disease. Many ASP members are likely to think of David as the long time ASP Treasurer who was a driving force in growing the Society's financial holdings, but Professor Slatkin was also one of the country's most influential pharmacists, spending most of his career making tremendous contributions to pharmacognosy and pharmacy education.



Dr. David Slatkin

Born in Brooklyn, New York, David was the third of four children of Max and Bertha (Schwartz) Slatkin. He grew up in Scarsdale, New York, and graduated from Scarsdale High School. He earned baccalaureate degrees from Wayne State University, Detroit, Michigan, and Mercer University's Southern School of Pharmacy, Atlanta, before pursuing Masters and PhD degrees from the School of Pharmacy,
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See 'Snow on Red Plum Blossoms' p.7

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EDITOR'S CORNER



2015 was truly a momentous time in history for the discipline of pharmacognosy. The Nobel Prize in Physiology or Medicine was awarded to scientists who conducted pharmacognosy research that led to cures for parasitic diseases. As I traveled to China in late 2015, I was struck by the amount of press that one of these Nobel Laureates, Tu Youyou, received in her country. I saw newspapers and magazines with major front page articles on her accomplishments in discovering a new cure for malaria from the wormwood plant. I was most impressed that a small gift shop in the Drum Tower Hutong area of Beijing had a specimen of *Artemisia* on display with a note congratulating

Youyou Tu on her Nobel work in phytochemistry. Pharmacognosy is certainly being appreciated by people more widely thanks to this recognition from the Swedish Academy.

This Nobel announcement also marked the first time in which a member of the American Society of Pharmacognosy was recognized with a Nobel Prize. ASP Fellow, Dr. Satachi Ōmura, was presented with this honor in Stockholm, Sweden in December 2015, and ASP Treasurer, Dr. James McAlpine, was on hand to witness this historic event for the Society and for the pharmacognosy world at large. Our lead article, written by ASP Fellow Dave Newman, along with Dr. McAlpine, goes into detail about Dr. Ōmura's research in natural products that produced a drug that has ultimately almost eradicated river blindness. Drug discovery with such significant impact on human health is a goal many ASP members dream of, but only a few have been able to achieve.

In addition to celebrating this Nobel achievement, we also mark the death of Dr. David Slatkin. David served the Society for decades as our Treasurer. In the old days when we mailed in checks for ASP dues, David was the first person many of us interacted with in the Society. I attended the memorial service for David in November in suburban Chicago, and I was struck by his commitment to his lovely family, his work as founding dean of three colleges of pharmacy, his synagogue, and the American Society of Pharmacognosy. ASP was an integral part of David's life professionally, but also personally. Speaking with his wife, she recalled family vacations that revolved around ASP meetings, and the Slatkin diningroom table filled with ASP newsletters that would be labeled and mailed out from their home in the days before email. I am very grateful to David and the entire Slatkin family for their devotion to the ASP, and I am honored that the Slatkin family asked that contributions be made in his honor to the ASP Foundation. I have already done so, and I hope that other members who knew David well will also consider doing this. <http://www.pharmacognosy.us/what-is-pharmacognosy/the-asp-foundation/> David's legacy in ASP will live on in many ways, including the hard work of his daughter, Laura Stoll, as ASP Business Manager.

We honor another long-time ASP member, former ASP Secretary Dr. Bill Keller, for his decades of work for the Society. Bill has stepped down as Secretary in 2015, and his work for the Society is considered in a piece by Dr. Douglas Kinghorn. As you plan your conference attendance for 2016, I hope you will consider going to 9th Joint Natural Products Conference, to be held in Copenhagen, Denmark, from July 24-27. ASP will be one of the hosts of this joint meeting, and it is a great way to make contacts with our European colleagues in pharmacognosy. If you are not able to make it to Europe this summer, please consider coming to the the joint 16th International Conference on the Science of Botanicals with the ASP Interim Meeting, to be held in Oxford, Mississippi, April 11-14. I hope 2016 is a wonderful and productive year for you, and I hope to see you in Copenhagen or Oxford.

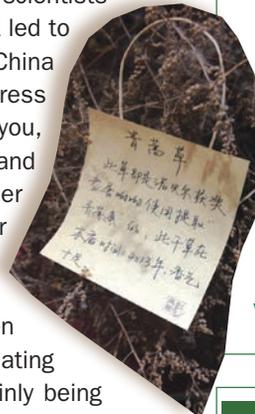
Dr. Edward J. Kennelly

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

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Above: Beijing gift shop display of *Artemisia annua* with hand written note about 2015 Nobel Prize awarded to Tu Youyou for her work on this species.

Ōmura: 2015 Nobel Laureate in Medicine

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ing not one, but two PhDs, the first in Pharmaceutical Sciences from the University of Tokyo, Tokyo, Japan, in 1968 and the second in Chemistry from the Tokyo University of Science, Tokyo, Japan, his alma mater, in 1970. Aside from two years as a research associate at the Yamanashi University, Kofu, Japan, he has spent the whole of his scientific career at the Kitasato Institute, Tokyo, Japan, first as a researcher, then rising through the ranks until his appointment as President in 1990, followed by appointment as President Emeritus from 2008 to 2012, and is currently a “Distinguished Emeritus Professor and Special Coordinator of the Research Project for Drug Discovery from Natural Products in the Kitasato Institute for Life Sciences, Kitasato University.” He also spent a year’s sabbatical leave at Wesleyan University, Middletown, Connecticut, and has held the position of the “Max Tischler Professor of Chemistry” at Wesleyan University since 2005. He continues to hold this position at the time of writing. In addition to these academic pursuits outside of the Kitasato Institute, he was Editor-in-Chief of the *Journal of Antibiotics* for several years until earlier this year, when he became Editor-in-Chief Emeritus.

Since 1965, the Ōmura group at the Kitasato Institute have been instrumental in the discovery of very important bioactive agents principally from soil microbes, not only in the *Actinobacteria* and true fungi, but also plant-based agents.

Using novel fermentation and isolation/assay techniques, his group has reported more than 480 novel structures to date, including many widely used antibiotics and inhibitors of specific enzymes. Examples include: pyrimycin; staurosporine; herquiline A, avermectins B1a and B1b; vineomycins A1 and B2; herbimycin A; virantomycin and virustomycin A (both antivirals and antibiotics); cervinomycin A1; luminamicin; the four metabolites with herbicid-

He is an accomplished calligrapher and artist and has established art museums in Japan... a genuine “Renaissance Man,” talented in both the sciences and the arts.

al activity, phosalacine, oxetin, phthoramycin and phthoxazolin A; diazaquinomycins A and B, the nematocide, jietacin A. In addition, the Ōmura group also reported the very important proteasome inhibitor lactacystin. Adding to this list are the acyl-coenzyme A: cholesterol acyltransferase 2-selective inhibitor, pyripropene A, the farnesyl-transferase inhibitors pepticinnamin E and andrastins A - D and the five inhibitors of type III secretion systems guadinomines A , B and D, 28 β -OH-factumycin and aurodox.

Although the Nobel Prize was awarded for the work around the avermectins, there are at least two other extremely important metabolites first reported by Dr. Ōmura’s group that demonstrated very significant advances in the production of metabolites. In chronological order these were cerulenin, produced by the true fungus *Acremonium caeruleum* and staurosporine, which

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Memoriam: David J. Slatkin

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University of Mississippi (Ole Miss), Oxford, Mississippi. It was there at Ole Miss that a young assistant professor, Dr. Paul Schiff, first met David and worked with him on several projects that eventually became an important part of David’s doctoral dissertation research; these projects involved a study of the constituents of *Cocculus carolinus* roots and *Cannabis sativa* roots. Dr. Schiff recalls his first impressions of David as “... intelligent; focused; energetic; ambitious; likeable; and possessing an unmistakable kinesis in his actions and manner.” Wherever “Slats” was, things were happening!

He joined the faculty at Northeast Louisiana University School of Pharmacy, Monroe, Louisiana, in 1971. By 1972, Dr. Schiff had taken a position at the University of Pittsburgh, Pittsburgh, Pennsylvania. When another faculty position opened there, Drs. Schiff and Joseph Knapp recruited David vigorously, luring him to serve on the faculty of University of Pittsburgh School of Pharmacy for almost 20 years, rising to Assistant Dean for Student Affairs and Director of Graduate Programs. The three professors worked so closely together in teaching, curriculum

In 1999, David was selected by *American Pharmacist* magazine as one of the 50 Most Influential Pharmacists in the U.S.

development, and research that students referred to them as “The Terrible Trio, The Unholy Three, The Gruesome Threesome and The Three Stooges.” The trio of professors developed the concept of a “patient-oriented” curriculum, linking the traditional “science–drug–disease” approach in traditional pharmacy education to the patients’ medical needs. This enhanced both the course and curricular viability and credibility and ultimately formed the basis for the development of many modular courses in PharmD curricula in the 1990s. Even as he developed a strong focus on pharmacy administration, his pharmacognosy research resulted in over 80 scientific publications.

Dr. Schiff offered this insight into David’s evolution as an administrator that he recalls “...with both fondness and amusement. One day, sometime around 1986, I walked into his office just to hear him speaking to himself as he said: “I’m not going to do THIS the rest of my life.” In a nanosecond I glimpsed on his desk to see an “organized clutter” of: first, partially constructed undergraduate course test questions; second, a random stack of proton and carbon NMR spectra; and third, a pile of correspondence dealing with his responsibilities as an officer in the Section of Teachers of Biological Sciences in the AACR. I knew of his love for administration and I sensed right then that his focus in the immediate future would be in that direction. It was not long afterwards that David became an Assistant Dean in our School and, just a few years later, the Founding Dean at Midwestern. We often recalled that instant in time when I entered his office with great fondness and mirth.

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Ōmura: 2015 Nobel Laureate in Medicine

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materially aided in the exploration of the protein kinases (PKs). Cerulenin was the first inhibitor of lipid biosynthesis ever found and it can be considered the initial compound for development of cholesterol (lipid) biosynthesis inhibitors. It is still used as an important inhibitor of lipid biosynthesis in microbes and was often utilized for what could be considered the enzymatic equivalent of epigenetic metabolic manipulation, particularly in fungi.^{1,2}

In 2009, Dr. Ōmura authored an excellent review³ of the work

Since 1965, the Ōmura group at the Kitasato Institute have been instrumental in the discovery of very important bioactive agents principally from soil microbes, not only in the Actinobacteria and true fungi, but also plant-based agents.

on staurosporine covering the thirty years since the first report⁴ and demonstrating just how important this indolocarbazole was in opening up inhibition of protein kinases, in this case, protein kinase C (PKC). Today, there are still variants of the basic structure in clinical trials with K-252a-PEG(2K) in Phase II trials for atopic dermatitis directed against the high affinity nerve growth factor receptor (TrKA) and midostaurin in Phase II trials against leukemia. More than 30 years after the initial report, this base molecule is still providing potential drug molecules. It is also extremely heavily used as a probe for mechanisms with 12,911 citations to staurosporin(e) in Scopus as of November, probably the most highly cited microbial-derived probe compound ever.

However, these compounds are really the initial “players” in the materials isolated and characterized by the Ōmura group. The Nobel Prize was awarded for the work on the *S. avermitilis* compounds, the avermectins and the subsequent modifications by Merck scientists, leading to the slightly modified ivermectin class. These have been very well described in the initial article by Dr. David Kroll in the previous *ASP Newsletter* 2015;51(3) and should be read in conjunction with this essay for information on the reason for the award and how the ivermectins came about. Dr. Ōmura has done an enormous amount of work over the years.

One area that has often been overlooked is that the Ōmura group actually published⁵ the first almost complete genome of a streptomycete in 2001 when they published 99% of the sequence of *S. avermitilis* almost a year before the Hopwood group in the UK published⁶ the complete genomic sequence of the considerably smaller DNA of *Streptomyces coelicolor* in 2002. The Ōmura group then published⁷ their complete sequence of *S. avermitilis* in 2003. Both groups demonstrated that there were several silent (i.e.; hitherto unexpressed) clusters in their respective genomic data sets and thus pointing out the continuing potential of even heavily examined actinomycetes to produce novel secondary metabolites.

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Memoriam: David J. Slatkin

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He possessed a great loyalty and a strong sense of fairness. I shall never forget one time when I was not doing a very good job of being a department chair and David had a closed-door discussion with me. His comments were truthful and incisive, helping me see where I was failing others. I was so thankful that he took the time to speak so directly but lovingly to an old friend.”



Drs. Barry O'Keefe and David Slatkin playing poker with the 50th ASP Anniversary playing cards where David is featured as one of the joker cards.

ASP PHOTO ARCHIVE

David became a widely respected leader in the field of pharmacy education, providing the energy and leadership required to establish three new colleges of pharmacy. He was Founding Dean and Professor of Pharmaceutical Sciences at the Midwestern University (MWU) College of Pharmacy-Glendale, Glendale, Arizona, Founding Dean of the Chicago College of Pharmacy at MWU, and Founding Dean and Dean Emeritus

David is widely recognized as someone who demonstrated “fierce loyalty to family, friends and colleagues.”

of the Chicago State University (CSU) College of Pharmacy, Chicago, Illinois.

He served as a reviewer for the *Journal of Natural Products* (*J. Nat. Prod.*) and *Journal of Pharmaceutical Sciences* and was the advisor for many graduate students. He was very active in professional and scientific organizations, including serving as Treasurer of the ASP for 30 years. Dr. Doug Kinghorn, *J. Nat. Prod.* Editor in Chief and former ASP President, noted one of the very important roles David played in the history of the ASP, “David Slatkin was a leader of the team representing ASP when discussions were ongoing leading to co-publishing the *J. Nat. Prod.* with the American Chemical Society in 1996. There was considerable trepidation among some ASP members about the possible ramifications of this action, but throughout the negotiations, David provided a calming influence. For about 15 years after this, David represented ASP as an *ex officio* member of the Management Board of the

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Ōmura: 2015 Nobel Laureate in Medicine

Both here and in the avermectin story, one sees the willingness of Dr. Ōmura to collaborate with other groups at the forefront of science. Here he worked with the Hopwood group to produce the first genetically engineered, novel antibiotics, mederrhodins A and B.⁸

Though we have demonstrated Dr. Ōmura's scientific talents, there is an "Arts" side to the "Scientific" side of this man. He may be prouder of his Master's Degree in Fine Arts than his scientific exploits. He is an accomplished calligrapher and artist and has established art museums in Japan, so one can certainly not be incorrect in labeling him not only a Nobel Laureate in Medicine but a genuine "Renaissance Man," talented in both the sciences and the arts.

Ivermectin is donated to the World Health Organization by Merck for medicinal uses, and is sold commercially for veterinary and agricultural uses. Dr. Ōmura used the royalties he obtained from these sales to build a large teaching hospital and led a donation of paintings such that the hospital is also one of the art museums that he has sponsored. He has commented that the aim is to improve both the physical and spiritual health of the patients. An example of the culture and the character of this remarkable man is the included essay he wrote after the 9.0 underwater earthquake triggered the devastating tsunami which hit northeastern Japan on March 11, 2011. (Dr. Ōmura had kindly allowed us to reproduce this essay, please see page 7.) He sees beauty in the world around him, in science, art, nature, and humanity, and he works tirelessly to enhance that beauty. ■

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Memoriam: David J. Slatkin

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journal, and came to Columbus for an Annual Meeting. During these meetings, he was particularly concerned with fulfillment aspects of the journal operation, and all in attendance were greatly impressed with both David's ever-present charm and his mastery of the relevant details."

Dr. John Cardellina reflected on meeting David, "At my first ASP meeting, hosted by David Slatkin, Paul Schiff and Joe Knapp in Pittsburgh in the early 1980s, David handled the financial aspects of that meeting with the same calm, focused demeanor that he did 30 years later. Over the next three decades, I came



Dr. David Slatkin and other members at an ASP banquet.

ASP PHOTO ARCHIVE

to know David better and my respect and appreciation for all he did for the Society grew exponentially. I always found it amusing that a man who was so good a steward of the ASP money was also a guy who enjoyed gambling; I like to think the ASP deck of cards from our 50th Anniversary was inspired by David."

ASP Foundation Treasurer Dr. Bob Krueger remembers expressing an interest in serving as an Assistant Treasurer under David many years ago. He approached David and in typical 'Slats' fashion, was told that he (Bob) would make a fine recruit..." 'Just follow my lead' was Dave's reply. A few years later, when the ASP Foundation was proposed and started by President Matt Suffness, Dave suggested that I would make 'a good Treasurer' for it. He gradually sent money the Foundation's way as the Society prospered, as well as helping me with solicitation requests, etc. He was always just a phone call away if I needed him! He will be sorely missed, but his legacy will long extend into the future of the ASP as our Foundation has done marvelously well employing the critical principles he taught me."

In 1999, David was selected by *American Pharmacist* magazine as one of the 50 Most Influential Pharmacists in the U.S. Most important to him among his academic accomplishments was the education and mentoring of pharmacy students. Dr. Chris Ireland, former ASP President and himself a pharmacy school Dean, noted, "Working with David while I was President of ASP and throughout our many years together

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Mitscher Honorary Issue of *Journal of Antibiotics*

By Dr. James McAlpine

As an ASP member, those of you who knew our past president, Norman R. Farnsworth Research Award winner and ASP Fellow, Dr. Les Mitscher, will have already felt the loss of this great scientist and teacher. One of the things that Les and I had in common was that we were both members of the Editorial Board of the *Journal of Antibiotics* for more than 30 years. The *Journal* plans to produce a memorial issue in Les's honor in 2016. I have been asked to be the Guest Editor of this issue and request that those of you who do any work with microbes consider submitting a manuscript in his memory. The *Journal* publishes on antibiotics or other bioactive microbial metabolites, and publications may be in the form of reviews, original articles, notes or communications. Author instructions can be accessed via www.nature.com/ja. We would like commitments to contribute an article by January 2016, with a deadline of submission of March 15, 2016. Please e-mail me directly (mcalpine@uic.edu) or Ms. Yoko Takagi at the editorial office (takagi@antibiotics.or.jp).

Thank you for your consideration.

Memoriam: David J. Slatkin

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in the ASP was a true joy. David was the consummate professional when it came to managing the financial portfolio of the Society. He was a cautious but wise manager of investments and the society benefited greatly from his stewardship of our finances. These same skills served him well as the Founding Dean of multiple Colleges of Pharmacy. Having served as a Dean of Pharmacy myself, I greatly admire the scope of David's understanding and commitment to professional pharmacy education. He will be greatly missed."

In 2012, Chicago State University, Chicago, Illinois, established a symposium honoring his career. This event, attended by David and his family, celebrated his contributions to science and pharmacy education featuring speakers from all facets of his life. The respect and admiration of the attendees for David was unmistakable during the two days family, friends, and colleagues gathered with him to celebrate his accomplishments.

David is widely recognized as someone who demonstrated "fierce loyalty to family, friends and colleagues." That sentiment was shared by his brother-in-law during his eulogy, as well as by colleagues at CSU. ASP Executive Committee member, Dr. Melany Puglisi-Weening noted that "as a founding faculty member of the Chicago State University College of Pharmacy, I have been deeply touched by the support and encouragement of Professor Slatkin. He recruited me in 2008, also helping to secure a position for my husband at Chicago State University. He cared about the whole person and wanted people to be happy at work and at home, encouraging us to spend time with our families and include them in college events. He found ev-

ery opportunity to promote my career and those of the people around me."

Dr. Elmer Gentry, Associate Dean of Academic Affairs, CSU College of Pharmacy, reflected that "David was an amazing mentor and had a tremendous impact on my career choices. He saw something in me as a new assistant professor and took time to work with me to develop skills—he had a gift to find and bring out that potential in others. He was consistently able to bring groups of people together to work with him and accomplish tremendous things. Many people doubted that Chicago State University could successfully begin a College of Pharmacy, but under his leadership it was proven possible."

David is survived by his beloved Judy (née Norris), his wife of 49 years. He was the very proud and devoted father of daughter Laura and the late Scott Stoll of Buffalo Grove, and daughter Stephanie and her husband Martin (Irgang) of Long Grove. David was the adored Papa of Molly, Matthew, Danielle, Becca, Shayna and the late Rebecca. He was predeceased by his sisters Sondra and Claire and his brother Edgar. He will be missed by many nieces, nephews, cousins and friends. He will be remembered for his devotion to his family and for his generous and kind nature. He will also be remembered by the community and Jewish organizations he was always willing to help whenever and wherever he was needed.

It speaks volumes that his family requested that, in lieu of flowers, memorials may be made to the ASP Foundation. It is personally heartwarming to the authors of this article, and the Society as a whole, that David's daughter Laura now fills his very substantial shoes as Business Manager of the ASP. ■

Snow on Red Plum Blossoms

By Satoshi Omura, Ph.D.
April 5, 2011

Early in the morning, late in March (2011), I opened my shutters to the sight of red plum flowers, blooming unusually late in the season and garbed in a light coating of snow. However, my contentment and appreciation of this scene of red and white elegance, emerging for the first time this year, as fleeting at most. Uppermost in my mind was the plight of the victims of the Great East Japan Earthquake and Tsunami, which struck on March 11, so many of whom were enduring severe cold and other dire conditions. Mindful of the paradox of the beauty and cruelty of Nature, my own mood plummeted. Adding to the misery following the massive earthquake and tsunami that followed, along with the damage done to the Fukushima Daiichi Nuclear Power Station by the disaster, it was also reported that the stricken area was going to be struggling through a severe cold spell – to a degree far worse than usual.

Taking on various different work projects of late, I have been left with little time to devote to my writing. However, with close to three weeks having passed since the disaster as I write these words, and rattled by a steady stream of large aftershocks continuing to violently and frighteningly jolt an extensive area of northeast Japan, I determined to at least record my current thoughts on the triple disaster that has struck at the hearts and lives of so many.

Torahiko Terada, a renowned physicist and writer of the 19th century, once stated: “Disasters come when they are least expected.” Nothing could be truer. In the areas devastated by the recent catastrophic events, while there was obviously no reliable knowledge of when a major earthquake or tsunami might occur, levees had been constructed and evacuation drills conducted regularly. These measures had been introduced based on past tragic experiences with such natural disasters. A particular case in



point is the Taro district of Miyako City in Iwate Prefecture, an area particularly hard hit by this current catastrophe which resulted in 70% of its community being destroyed. In 1933, a tsunami striking this same region resulted in 900 persons being killed or lost. Based on that grim experience, dual seawalls 10 meters in height were constructed, with emergency evacuation maps strategically placed throughout the community. These and other disaster preparations in Taro were considered so scrupulous and effective that the area even attracted inspection tours from officials from various countries in Southeast Asia, with the local people reported to be totally at ease with the state of extensive preventive measures installed. The confidence ran so high that, in some places, homes had actually been constructed between the two separate seawalls.

Any such peace of mind, however, was mercilessly crushed by the sheer power of nature on March 11, as 20-meter tsunami waves assaulted the coast.

In the face of such utter and irresistible power, the man-made precautions proved totally inadequate and over 4,000 townspeople were swept away in minutes. The height of the tsunami that advanced on the city of Miyako is estimated to have reached some 38 meters. At the graduation ceremony of a junior high school in that area, one of the graduating students later reported: “We had prepared for the possibility of disasters. However, we found ourselves totally powerless against the fury of nature, with the tsunami carrying away everything that we had readied for such a situation.” Another survivor explained how tsunami alarms were sounded in the community every time an earthquake occurred, but that nothing serious had happened for so many years. That was an admission, in other words, that not taking this particular warning to heart may have added to the losses.

During a past visit to Kamaishi City, I noticed that seawalls had

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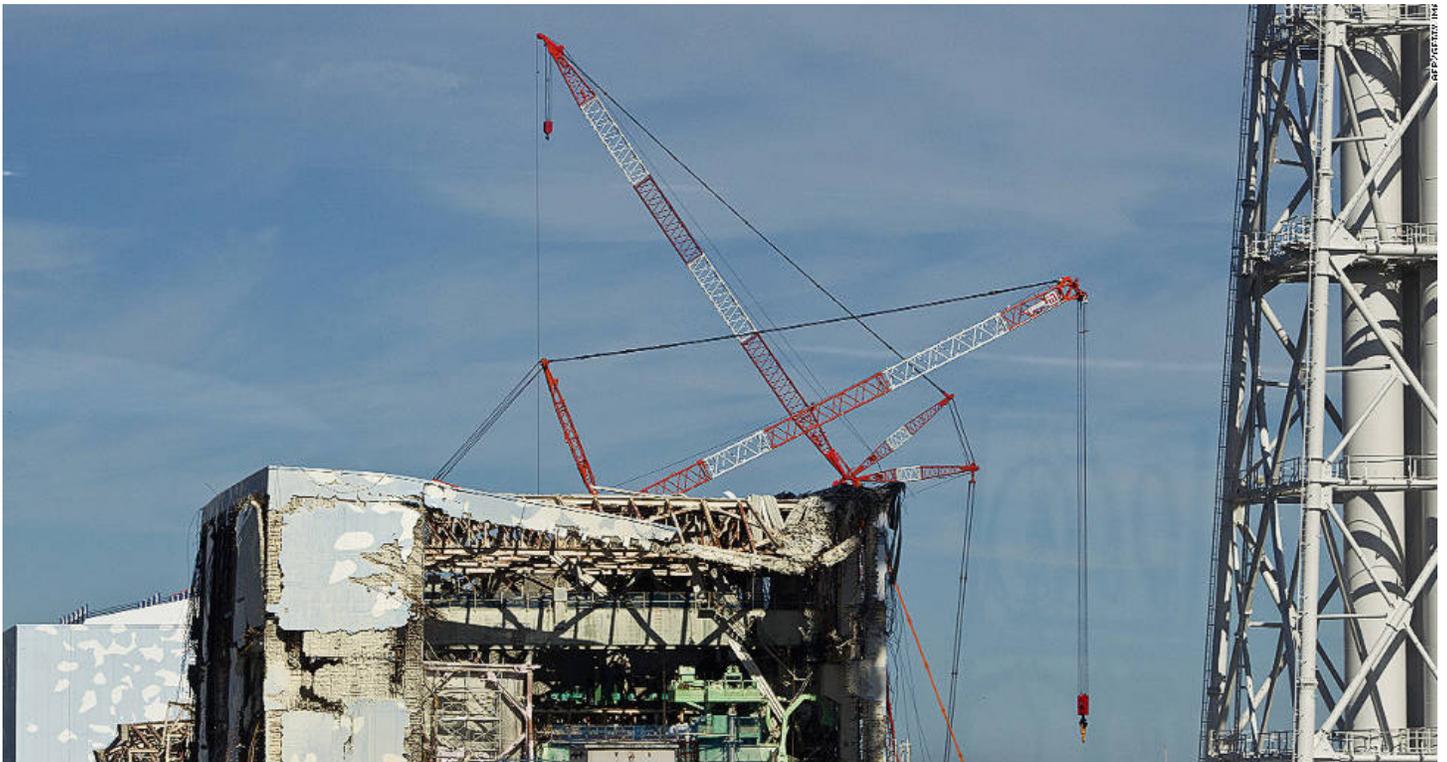
Snow on Red Plum Blossoms

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been erected along the coastal stretches of almost all of inlets there. I was fairly startled, however, to see that private homes had been built directly alongside the seaward sides of these embankments. My surprise was linked to the fact that these residences stood well below the levels of the signs posted to mark the height of past tsunami that had struck here. I suppose the residents believed they would be safe as long as they fled to the areas at or above the flood-level signs at the issuing of tsunami warnings following a major quake. As I write, some 20 days after the Great East Japan Earthquake, it has been announced that 11,362 persons have died in the disaster, with another 16,290 people missing. The fact that the number of those unaccounted

uled to pay a visit to Kamaishi, the older brother of “Y,” hearing that I enjoyed golf, took time from his own busy schedule to spend the entire day out on the links with me. Furthermore, just recently, I learned that upon request from “Y,” the brother had visited the “Shibasaburo Kitasato Exhibition” held at the Kitasato University School of Marine Biosciences – located in the Sanriku Town area of Ofunato City, Iwate Prefecture. He had gone to check out the event since “Y” couldn’t make it. After the earthquake on March 11, the brother was fleeing with his wife when the tsunami hit and swept him away. His wife narrowly survived the waves by running up toward a restaurant on higher ground.

Another acquaintance of mine, a student from Kitasato University, remains missing. I can only sadly assume that another



for far outnumbers the confirmed deaths is testimony to the truly savage devastation that this tsunami wreaked.

The incredible and wide-ranging damage from this event has also extended to touch my own personal relationships.

My research colleague “Y,” with whom I shared the joys and sorrows of research work in my younger days, is a native of a neighborhood close to the seaside in Kamaishi City. His older brother lost his life in the huge tsunami that hit the Kamaishi community. In the traditional Japanese family structure, as the eldest son, he was responsible for and devoted to looking after the needs of “Y,” who was the younger sibling. Many years ago, when I was sched-

young, promising and unfulfilled life has been tragically lost. While having first evacuated from the area with friends, the student decided to return to his lodgings to retrieve something left behind. That was when the tsunami hit and dragged him away. I have talked to some survivors, who provide grim reports of how they just narrowly escaped the same fate as that student. From their sorrowful and dreadful words, I realized anew how the difference between life and death in such circumstances is often little more than a few fateful inches or a split second in time.

In addition to the immeasurable human toll, this disaster, as

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**The crippled Fukushima Daiichi nuclear power station
after the epic 9.0 earthquake and the subsequent tsunami March 11.**

WWW.CNN.COM

Snow on Red Plum Blossoms

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with many others, brings horrors to our eyes while, at the same time, ripping joy and beauty from our sight. This tragedy swept away a cultural asset built and sustained over the years as a key fountainhead of the Japanese heart and mind. Vanishing into the raging waters was a hexagonal shaped building erected along the Izura coastal area in Ibaraki Prefecture. This was the brainchild of Tenshin Okakura, a figure who spearheaded much artistic endeavor during the Meiji Period (1868-1912) of Japanese history. As the second-generation headmaster of Tokyo Arts School (the current-day Tokyo University of the Arts), Okakura played a key role in the early stages of that institution's history. While in more recent times it had served as a key part of the Izura Institute of Arts and Culture at Ibaraki University, during the Meiji years the facility excelled as a mecca for all

compassing the personal histories of individuals and their ancestors in its rampage.

Then again, according to analysis conducted by the Earthquake Research Institute of the University of Tokyo, the largest movements in the earth's crust during this quake occurred on the ocean floor about 200 kilometers offshore of Oshika Peninsula in Miyagi Prefecture. The institute reported that a landmass about 55 km wide and 160 km long moved some 55 meters toward the southeast. At the time of the quake, meanwhile, this stretch apparently was thrust up about five meters (this information from the April 8, 2011 issue of the *Asahi Shimbun* newspaper). Here we have yet another monumental lesson that the actions of human beings, when viewed in comparison to the mighty powers of nature, are extremely tiny in scale.

Clearly, this earthquake and tsunami, events of unprecedented



types of artists devoted to utilizing the powers of friendly rivalry to advance the arts in wide-ranging shapes and forms.

Likewise, I will also never be able to again lay my eyes upon a certain work of art that left a profound impression in my mind. I am referring to a magnificent hanging scroll, the work of renowned artist Shohin Noguchi, which had been displayed in the alcove of "Y's" family home when I lodged there.

Thus, I can hold only bitter memories in my heart towards the tsunami, which so viciously stole away people's lives, cultural treasures, and precious, priceless artifacts and heirlooms en-

ed scale and force in Japan, provide a sobering reminder of the severity and devastating power of natural phenomena. But then we come to the damage at the Fukushima Daiichi Nuclear Power Station, which now poses a major obstacle in the efforts to emerge from the debris of the tsunami and rebuild the devastated regions. This, by anyone's definition, is a man-made disaster. It has been reported that, due to the power station damage, this summer we will experience power shortages of close to 30%. Viewed in such terms, this can definitely be viewed as a human *continued on page 10*

Journalists view a newly built sea wall next to the crippled power station.

WWW.CNN.COM

Snow on Red Plum Blossoms

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disaster resulting from the combination of overconfidence in our own science and the loss of humility.

It is being said that the Japanese government will issue a policy calling for mandatory power savings of 25 % at companies and 15% in general homes. This may indeed provide an opportunity to once again review our own sphere of endeavor and personal action. I am referring to the fact that the many shapes and forms of social problems, global warming, contaminated medicines, traffic accidents and other occurrences, although occurring at various different scales, can all be viewed as disasters caused by human beings. I have stated and written often over the years about my belief that we regularly encounter difficulties, accidents and catastrophes of our own making, all stemming from overconfidence in science and technology.

Albert Einstein once remarked that an eternal secret is the ability of mankind to understand nature. I would like to state my view, however, that human beings are only able to grasp a tiny bit of nature, with that understanding falling far short of the realm of true profundity. Though dictionaries contain the word 'perfection', when dealing with the almighty natural world, I feel it is vital to take to heart the fact that there is no state of so-called 'perfection', and to base our thoughts and action in the foundation of that wisdom.

In today's world, the outbreak of war triggers fluctuations in foreign exchange markets aimed at taking advantage of such global upheaval to generate profit. The recent global recession, traceable to the pressure-based selling of products that eventually resulted in someone suffering losses (home mortgages in this case) and similar developments, are evidence of a deplorable trend that finds the world economy manipulated by persons largely devoid of standards or morals. The Great East Japan Earthquake and Tsunami struck against this backdrop, and we were soon reading reports of how projections that yen would be needed for the rebuilding efforts had pushed the Japanese currency to a 16-year high against the dollar (¥76.25/\$) on the New York foreign exchange market. Rather than heaving a heavy sigh of relief over this development, however, I felt a rush of anger. It is obvious that any such appreciation in the yen will become a serious hindrance for Japan for the immediate and foreseeable future. Here in Japan, meanwhile, numerous reports have been issued of thieves running off with earthquake disaster donation boxes, charlatans mounting fraudulent appeals for financial contributions for that cause, and other troubling events. The occurrence of natural disasters can prompt disgraceful and totally unacceptable human action that further undermines the caliber of the world in which we live.

Yet, even in these dark and dismal times, there is also much light emerging that can lead the way to hope for the human cause.

In the wake of this earthquake and tsunami disaster, it only required a few days for people in the private sector to launch rapid responses to the dire situation. This included people contributing clothes and food, collecting financial donations, indi-



Taro District of Miyako City, hard hit in 1933 and again in 2011.

BLOGS.REUTERS.COM



Tenshin Okakuru's legendary hexagonal structure along coastal Izura.

JAPANTRAVEL.COM

viduals and groups throwing their support behind relief activities organized by national and local government offices and others. With this outpouring of aid coming right on the heels of a recent flood of laments about how today's Japanese have become excessively self serving, there was a sense that the virtues of the Japanese as a comforting and dependable people had been resurrected. Moreover, people in other nations were startled and inspired by television coverage of large numbers of victims waiting orderly in lines to receive food, water and other relief supplies. Reports have been received of a steady stream of such supplies from other countries, with overseas teams and others also arriving in Japan to engage in support activities at the disaster sites.

Relief activities are likewise getting off the ground among researchers as well. According to the latest issue of the international scientific magazine *Nature* (volume 471, published March 24), the National Institutes of Health (NIH) of the United States

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is preparing to establish an interim research institute in support of Japanese researchers suffering displacement and/or damage in the disaster. Backed by a network supported by the *Nature* Group, meanwhile, a request has been received from Germany to host 18 researchers. In addition, from the German National Academy of Sciences Leopoldina (Harley), of which I am a member, and the German Academy of Science and Engineering (Berlin), a proposal has been tendered to promptly supply US\$7.1 million in research assistance. I have also heard reports that the National Center for Nanoscience and Technology of China is prepared to accept researchers who fell victim to the disaster. I believe this may be the very first time in the history of the world that a disaster has prompted such offers of support from the international community in the field of science. This is not only an indication of regret over the possible recent stagnation of Japan's science and technology, but likewise an expression of the strong bonds that have been forged between scientists across national borders.

areas prone to be targeted in bombing raids during World War II. At the same time, however, current-day Japan is far more prosperous than back in those days. Along with this affluence, if the DNA of the virtues and spirit of mutual aid remaining in the Japanese people can be mobilized, it should be possible to transform the hardship of the evacuees into strength and unwavering commitment for rebuilding.

Japan has a long history of rising up to recover from major adversity. More recent examples include the Great Kanto Earthquake (1923), the previously mentioned Great Sanriku Earthquake and Tsunami (1933), the defeat in World War II (1945), the Great Hanshin and Awaji Earthquake (1995) and other challenges. I extend my most heartfelt support and encouragement to the gallant people now standing up in the midst of rubble from the massive tsunami waves and pledging their resolve to rebuild their lives – externally and from within. I am likewise determined to do whatever I can to lend a hand.

In the aftermath, as always, there is time to reflect, analyze

We have an opportunity to set our sights on the work of building up a new foundation for the individual hearts and minds of the people, and as a society as a whole, and progressing equitably on that basis.

Speaking for myself, I have already received e-mail messages from over 20 persons overseas with whom I have nurtured personal ties, extending words of concern and sympathy on this occasion. They include President J. Hacker of the German National Academy of Sciences Leopoldina, Professor D. Hopwood of the United Kingdom, Professor H. Kagan of France Academy of Sciences, Professor Emeritus H. Kleinkauf of the Berlin Institute of Technology and other illustrious individuals. Among their ranks are also several friends with whom I had been out of contact for some time. This came at a time when I was personally quite disheartened by the situation here in Japan, despite suffering no any direct physical damage from the disaster myself. I was filled with gratitude for the warmth and compassion expressed by these good friends.

Television news programs reported that the residents of Minami-Sanriku Town in Miyagi Prefecture, where 69% of the community suffered destruction, were evacuated as a group to Kurihara Town in the same prefecture. An elementary school serving as one of the shelters hung out a banner emblazoned with the word "Welcome," while the classroom floors were covered in tatami mats in preparation for the evacuees. Although not always at a scale as large as this, such group evacuations organized at the individual administrative district unit are occurring throughout the stricken regions.

For me, stories and scenes of such responses conjure up memories of the evacuation of schoolchildren out of urban

and reconsider – and to regret so many things that, for whatever reason, we did or did not do or didn't have a chance to say. For example, the harmful effects of the process that has served to concentrate the nation's people, culture and politics in Tokyo, along with the social tendencies that have built up such a structure, are manifest. We must also consider the scenario of being hit by another such huge disaster like this in the future. We have to learn from the experience, move forward and apply the lessons learned to better protect future generations. Japan needs to seize this renewal as an opportunity for a comprehensive review of what we have done and what we are doing in all manner of human actions and endeavors. We have an opportunity to set our sights on the work of building up a new foundation for the individual hearts and minds of the people, and as a society as a whole, and progressing equitably on that basis. In particular, with regard to moving away from the over concentration of power and influence in Tokyo, I look forward to the positive role to be played by our politicians.

In closing, I extend my most profound sympathy and regards to everyone who has suffered loss and damage in this monumental disaster, together with my sincere and profound hopes for their recovery at the earliest possible point in time.

Finally, I fervently pray for all those who lost their lives in the calamity. In memory of the myriad aspirations and accomplishments cut short by this terrible tragedy. I hope that their souls will rest in eternal peace. ■

JNPC2016 in Copenhagen!

By Dr. Anna Jäger, Conference Chair

Welcome to the 9th Joint Natural Products Conference (JNPC), to be held in Copenhagen, Denmark, from July 24-27, 2016! It is a privilege and a great honor to welcome you to this joint conference organized by University of Copenhagen, Copenhagen, Denmark, on behalf of the Society for Medicinal Plant and Natural Product Research (GA), the American Society of Pharmacognosy (ASP), the Phytochemical Society of Europe (PSE), Società Italiana di Fitochimica (SIF), Association Francophone pour l'Enseignement et la Recherche en Pharmacognosie (AFERP), and the Japanese Society of Pharmacognosy (JSP).

The conference takes place at the Tivoli Congress Centre in central Copenhagen, Denmark. The conference covers a broad range of scientific disciplines within natural products research. We have put together a tantalizing program of high scientific standard, with interesting talks and time for networking. The scientific program includes plenary lectures by invited speakers, and both keynote and short talks on recent topics of natural product research. The poster sessions will also provide opportunities for scientific discussions.

A Young Researcher Workshop takes place the day before the conference. There will also be a pre-conference workshop on Regulatory Affairs and a pre-symposium entitled, Advances in (Bio)Analytical Techniques Applied to Natural Products Research. We hope you will enjoy the various social events, such as an Evening in the Botanical Gardens, and make the most of the light Nordic summer nights. The day following the meeting, we have organized a Botanical Excursion to three unique habitats on Zealand, the island where Copenhagen is situated.

More information can be found on the conference homepage: www.jnpc2016.dk. We hope to see you in Copenhagen this summer. ■

9th Joint Natural Products Conference 2016

July 24-27, 2016, Copenhagen, Denmark

www.jnpc2016.dk



Abstract submission: March 1, 2016

Notification of acceptance or rejection: May 1, 2016

End of early registration: May 15, 2016

ASP Interim Meeting: Oxford, Mississippi

By Dr. Ikhlas Khan and the International Conference on the Science of Botanicals

We would like to invite everyone to attend the joint 16th International Conference on the Science of Botanicals (ICSB) with the American Society of Pharmacognosy Interim Meeting, to be held in Oxford, Mississippi, April 11-14, 2016. The organizing committee is working to prepare not only an informative scientific program, but also a diverse and entertaining agenda of social events to make sure your visit to Oxford really does provide you the “South’s warmest welcome!”

The theme of the meeting is “The Synergy Between Natural Products and Human Health.” Our scientific programs will include general symposia and a poster session from participants’ submitted abstracts, as well as invited oral presentations. The symposia will focus on the areas of contributions of natural products, biosynthesis/biotechnology, marine natural products, frontiers of discovery through instrumentation, natural product synthesis, botanicals, traditional medicine, and regulatory aspects.

Oxford has been named one of “America’s 100 best small towns” by *USA Today*, and is a place with deep roots of culture, history and a strong tradition in the arts and literature. There will be plenty of opportunity to experience the richness of our town with the opening reception and other events. On Tuesday, April 12, we will have an ICSB favorite, a delicious dinner of Indian cuisine, as well as traditional music following the poster session. Wednesday will be a busy day, with tours of the National Center for Natural Products Research on the University of Mississippi campus, our traditional ICSB outdoor games, BBQ, and a live band. The final day of the conference will conclude with a delightful dinner banquet, featuring the perennial hit: a closing speech and presentation from Dr. Ikhlas Khan.

Memphis International is the main airport for travel to Oxford, and you can book our shuttle services to and from the conference through the on-line registration portal (<http://oxfordicsb.org>). The meeting will be housed at the Oxford Conference Center, a venue with over 25,000 square feet of space. We have reserved blocks of rooms at four area hotels with special conference rates of \$139 - \$159 per night. Two of these, the Hampton Inn Oxford and newly completed Marriott Towne Place Suites are located on-site, just a short walk from the Conference Center itself. These rooms are limited in number and will be reserved on a first-come first-served basis, so be sure to book your accommodations early. You should also be sure to register for the meeting as soon as possible, as we are offering special lowered rates for early registration. The deadline to register at these special rates is January 15, 2016. For more information on booking your trip, visit our web site at <http://oxfordicsb.org>.

Please be sure to visit our site at www.oxfordicsb.org for detailed information on registration, abstract submission, hotel and all other



Above: Oxford Conference Center

OXFORD CONFERENCE CENTER

relevant information as well as updates about the upcoming meeting. If you have any additional questions, contact us through our webpage or by emailing icsb@olemiss.edu. We are excited to be presenting this meeting for all of you. We look forward to your participation and providing you with true Southern hospitality. ■

The theme of the meeting is “The Synergy Between Natural Products and Human Health.”

ASP Past Secretary Keller: 30 Years of Loyal Service

By Dr. A. Douglas Kinghorn

Honorary ASP member Dr. Bill Keller, ASP Secretary since 1985, has recently stepped down from this position, as well as his full-time industrial position, due to health reasons. The ASP has been incredibly fortunate to have found someone as dedicated as Bill in performing the Secretary's job, since he also served a very great stabilizing influence over the years, and had a prodigious memory on past events and former members. Bill worked very diligently as Secretary at the same time as he was having a distinguished career in both academic pharmacy and later in the botanicals industry.

For the last two years, the American Society of Pharmacognosy has been "green" and thus eschewed the use of hard copies of committee reports. However, for the remaining 28 years when Bill Keller was ASP Secretary, he would ship a big box to his hotel room at each Annual Meeting containing about 100 copies of the minutes for the previous Business Meeting. In addition, there would about 30 copies of an even more detailed report dealing with the minutes of the Executive Committee meeting from the year before, as well as copies of the Teller's Report. If a copy of each of these reports were to be piled on top of one another from 1985 when Bill took over the Secretary's job, the stack would probably almost reach the ceiling of an average room! Each report required many hours to compile, and, as a former President and a present long-term member of the Executive Committee myself, I have found these always to be presented in a meticulous manner, and to accurately document the important affairs of the Society from the previous year.

Bill, or more formally, William J. Keller, received a BS in Pharmacy (1966) and an MS in Pharmacognosy (1969) from Idaho State University, Pocatello, Idaho. He then received a PhD degree in Pharmacognosy in 1972 from the University of Washington, Seattle, Washington, where he trained with Drs. Jerry L. McLaughlin and Lynn Brady on cactus alkaloids. Later in 1972, Bill was then appointed to the faculty at Northeast Louisiana University (now the University of Louisiana at Monroe), Monroe, Louisiana. He worked there for over 20 years, became Head of the Division of Pharmaceutics and Medicinal Chemistry in 1978, and was named Clarke Williams Distinguished Professor in 1989.

In 1995, Bill then moved to Samford University in Birmingham, Alabama, to take up the position of Professor and Chair of the Department of Pharmaceutical Sciences. In 2001, he moved

from academia to the botanicals industry, when he became Vice President of Health Sciences and Educational Services and Chief Scientific Resource Officer at Nature's Sunshine Products, Inc., Spanish Fork, Utah, where he remained until retiring earlier in 2015. For the first few years Bill was at Nature's Sunshine, he worked with his PhD mentor, Dr. McLaughlin, after he retired as a Professor of Pharmacognosy at Purdue University, West Lafayette, Indiana. Bill has served on several advisory boards in both industry and colleges of pharmacy and has presented about 200 scientific addresses in the U.S. and worldwide. He has published over 100 scientific papers and abstracts and became an Honorary Member of ASP in 2010.

About his time as Secretary of ASP, Bill relates, "I remember that hot summer day during July or August 1985 on the University of North Carolina campus when Larry Robertson informed me that I would be taking over his duties as ASP Secretary. He seemed to be relieved and joyful at the same time. I was thrilled and honored but a little bit intimidated that the voting membership had placed their confidence in me to complete the duties as Society Secretary for the three-year elected term. As it turned out, I continued as Secretary for 10 consecutive elected terms."

Bill described starting the process of the ASP Secretary, "I started to prepare the various minutes in the Fall of 1985, and it was at the meeting at the University of Michigan where I brought an audio

tape recorder. Everyone thought that I was crazy! Another point that I would like to mention is that back in the late 1980s or early 1990s, the EC thought that a review of the Constitution and Bylaws was needed. I remember going over that document with a fine toothed comb and revising it. I remember that the process of minute preparation was completed in the days before computers and word processors. We did not have e-mail or all of the sophisticated mechanisms of tracking revisions back in the late 1980s."

Three former ASP Presidents (Drs. David Kingston, Gordon Cragg, and Barbara Timmermann) who worked with Bill in different decades were asked to provide comments on their impressions of him. (Please see sidebar, page 15.) Not surprisingly, due to Bill's outstanding professional and personal attributes, he has created a uniformly positive impression.

For my part, I first recall meeting Bill in 1979 at the ASP Annual Meeting at Purdue University in 1979, since, at that time, we had

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DR. BILL KELLER

DR. MANSOOR KHAN

ASP Past Secretary Keller: 30 Years of Loyal Service

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a mutual interest in quinolizidine alkaloids from plants. Later, in the early 1990s, we both were fortunate enough to be able to go on sabbatical at different times to the Department of Pharmacy, Swiss Federal Institute of Technology (ETH Zurich), Zurich, Switzerland, where we worked with Dr. Otto Sticher, gained new scientific insights and made numerous new shared acquaintances. For many years, I shared a room with Bill at ASP meetings.

I remember driving back with him from the ASP meeting at New Brunswick, New Jersey, in 2002 to Newark Airport, and he asked me the question “Doug, have you ever heard of xeronine?” I had to admit my complete ignorance of the matter, so Bill informed me that this is a purported biologically active alkaloidal constituent of noni (*Morinda citrifolia*). He offered to send me a sample of authentic noni fruit powder from his company, so we could try and isolate and characterize this “will-o’-the-wisp” alkaloid in the lab. Despite purifying and identifying about 25 compounds, including some previously known substances containing nitrogen, and a number of bioactive lignans and anthraquinones, we were never able to find xeronine in the sample provided. Following our preliminary investigations on noni, over the last decade I have had the great pleasure of collaborating with Bill on about a dozen papers we published together, describing biologically active constituents of several botanical dietary supplements such as those of açai, black chokeberry, licorice, and mangosteen, among others.

Bill relates, “I could mention many other memorable experiences involving events such as International travel to joint meetings, interacting with icons of the Society, and the close association that was built with colleagues who served with me as officers. The Presidents and Society members were great personalities with a résumé that reflected their outstanding scientific contributions to the field of Pharmacognosy. Resigning as Secretary of the ASP was not my choice. My health did not cooperate and surgery was an option that I had put off for too long. I just hope that after 30 years (1985 through 2015) of what I considered dedicated service as the Society Secretary, those associated with/connected to the ASP will consider Bill Keller as an individual who always did a good job, and was a conscientious fellow who always had the best interest of the Society at heart. I wish the very best to all ASP members.”

All of us in the ASP wish him well as he recovers from his recent back surgery. Bill can look back on an outstanding professional career as a pharmacognosist and as one of the leaders of the Society for 30 years through his past role as Secretary. Bill and his wife Tram are to be given our very best regards for the future! ■

‘SPEAKING OF’ BILL KELLER...



MR. JACK SILVER

DR. DAVID KINGSTON

ASP President in 1988-1989: “The ASP has been fortunate to have been served by Bill Keller as Secretary for 30 years. Presidents come and go, and elected Executive Committee members come and go, but Bill has faithfully served for a longer time than some of our younger members have lived. He has been a large part of the “institutional memory” of the ASP, and the Society would be much poorer without his selfless service.”



DR. GORDON CRAGG

“When I served as President of the ASP in 1999-2000, Bill Keller had already been serving as secretary for 15 years, and his knowledge of Society history, protocols and procedures was legendary. His advice and wisdom greatly helped me cope with the issues confronting the Society, especially as we approached the new millennium, which was celebrated at the joint meeting with our sister European societies in Amsterdam in July, 1999. John Beutler, William Jones and I also tapped into Bill’s incredible “corporate” knowledge when co-editing the volume on “50 Years of Progress in Natural Products Research” published in honor of the 50th Anniversary of the founding of the ASP celebrated at the meeting in Honolulu in 2009. Bill, I salute your dedicated service to our Society, and I thank you for your gracious and ever-helpful manner - it has been a pleasure and privilege to be associated with you these past 30 years.”



CHUCK FRANCE
UNIVERSITY OF KANSAS

DR. BARBARA TIMMERMANN

President of ASP from 2011-2012: “Working with Bill during the time I was ASP President was a sheer delight. This was not the first time I had professional interactions with him but this special occasion reinforced what I always knew about this very good colleague and friend of mine. Bill is a man of great integrity, very respectable, dedicated to his work, loyal to our Society, and with an institutional memory that somebody should record for future generations. We shared many conversations that occasionally started in frustration but ended up on a light and funny note. I especially remember his hard work during the time when ASP decided to switch from paper to electronic ballots. During meetings, he produced very detailed and organized notes in a legible and elegant handwriting, something I liked to peek at during the process. In summary, Bill’s sense of duty and loyalty are very strong and he has a genuine love for our Society. I am sure my feelings are shared by many other colleagues who have the fortune to know and interact with Bill.”

Fun With Pharmacognosy: 3D Printing for the Natural Products Laboratory

By Dr. Nicholas Oberlies

Have you embraced 3D printing for your lab? I purchased a printer for my lab about a year ago, and my students and I find new uses for it almost daily. While some of the print jobs were more for fun, there are many examples where we printed objects that help make our research easier, faster, or more efficient. All of the examples were produced via a printer we purchased from Fusion. Although there are many other printers out there, what we like about the Fusion printer is the ease of use and the quality of the printed products; it is also produced in Greensboro, North Carolina, so it was easy for us to demo, order, and pickup. The only problem we have ever encountered was when we had a mass spectrometer (MS) plugged into the same circuit; the MS would draw too much power, causing the print job to fail. This was easily solved by plugging the printer into a UPS battery backup, and since then, we have had no other issues.

One of my favorite designs was created to solve a pragmatic issue with our NMR facility. We have access to a 700 MHz instrument with a cryoprobe, a valued tool for any structure elucidation jock. However, the facility is a 10 minute drive from our labs, and students were driving samples there. Quite literally, the world's supply of a new compound could be accidentally spilled all over a car if someone had to slam on the brakes suddenly. Thus, after a few trial and errors, my students designed an NMR holder that was shaped like a coffee mug, so that it could fit in the cup holder of the car. It is even deep enough to



Above: Coffee mug NMR tube holder.

Below: Solvent drying splitter.

DR. NICHOLAS OBERLIES



protect the tubes from being broken by an errant arm while putting a car into park, and the holes are numbered so that the samples stay organized (i.e. so that you do not mistake which tube had the R- vs S-Mosher's ester analogue). While the 3D printer cost a little over \$3,000, the plastic needed to print the mug, and many other designs, costs only a few cents to few dollars per print job. The amount of time and effort it would take to regrow the fungus and then re-isolate the hypothetically spilled compound would be much greater than all of that.

Besides the pragmatic uses for a 3D printer, I think they also hark back to an earlier age of scientific research, when scientists made their own supplies. When I started my doctoral studies at Purdue University, West Lafayette, Indiana, I was among one of the first classes of chemistry students that did not have the opportunity to take a course on glass blowing. What I observed in the late 1980s and early 1990s, both at my undergraduate institution (Miami University, Oxford, Ohio) and Purdue, was that the glassblowers on campuses were reaching retirement age and not being replaced. Glassware was being mass produced, and it was much less expensive to order supplies through a catalog as opposed to blowing it yourself.

While previous generations may have made some of their own supplies, my generation, and those that followed, did not need to trouble themselves with such endeavors. To be honest, I always felt a little disappointed, as I thought it

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Besides the pragmatic uses for a 3D printer, I think they also hark back to an earlier age of scientific research, when scientists made their own supplies.

Fun With Pharmacognosy: 3D Printing for the Natural Products Laboratory

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would have been fun to learn some of those techniques. All those great paintings in Sigma Aldrich catalogs had 18th Century scientists making great discoveries in front of their hand made glassware. Have we lost some of those artisan qualities to our research?

While my students and I do not blow glassware for the lab with a 3D printer, we do use it to help fuel our creativity. When working on a new idea, my students may print little implements that will make it easier to hold or analyze a sample, or print a piece that can be glued to repair something. While some of the designs may seem like novelty, many of them can be quite useful. Does the creative use of computer aided design tools and a 3D printer put a little artisan spin on the 21st Century laboratory? I hope so.

How does one get started? The trick to 3D printing is not really in the printing. It is in the design file. Thankfully, Google has developed (or at least championed) SketchUp (originally called 'Google SketchUp,' <http://www.sketchup.com/>), which can be downloaded and used to create 'stl' files (the link is here: Google Sketchup). Like many software programs today, it may be easiest to simply use it via trial and error. There are also many helpful websites where one can download an 'stl' file (for example, Thingiverse), and then use that as a starting point for

any design you want to create. There are also many YouTube videos that will walk you through the process of creating an original design. To get started, I suggest trying the above resources and perhaps reaching out to someone who has made some designs previously. In fact, when I was drafting this piece, I noticed an article in my local newspaper about the public library in Greensboro installing a 3D printer and having staff on hand that will help educate the public in their effective use; certainly, similar resources are likely available in your own neighborhood.

I hope you will consider trying out 3D printing. Just as you cannot function without your inkjet or laser printer, I predict that not too far in the future, we may all have 3D printers in our labs. Their costs are going to continue to go down and their usability will continue to increase. You are welcome to download and augment any of the designs on my website. For scientists, the National Institutes of Health has a great site where you can download and share models of compounds, proteins and other 'biomedical resources' (NIH 3D Print Exchange). There are also loads of other resources on the internet, even designs for printing guitars, car parts, and pieces for prosthetic limbs. You can download some of the designs and see photographs of a few of the projects on my website: Oberlies 3D Printing, https://www.uncg.edu/che/Group_Research_Page/NicholasOberlies/3d-printing.html. Good luck! ■

**All those great paintings in Sigma Aldrich catalogs
had 18th Century scientists making great discoveries
in front of their hand made glassware.
Have we lost some of those artisan qualities to our research?**

ASP Travel Award and Named Award Nomination Deadlines

The deadline for submission of a nomination package for Norman Farnsworth Research Achievement Award, Varro Tyler Prize for Botanical Research, and the Matt Suffness Young Investigator Award is February, 15, 2016. Please note that nominations for the Norman Farnsworth Research Achievement Award and Varro Tyler Prize will be awarded in 2017, while the Matt Suffness Young Investigator Award will be given in 2016 at the joint international meeting in Copenhagen, Denmark.

The deadline for travel awards for the international meeting is also February, 15, 2016. ■

Please send the travel and Suffness award applications and nominations to Dr. Anthony Wright at adwhawaii@gmail.com.

Details and information can be found on the ASP website www.pharmacognosy.us/grants-and-awards/ and in the By-laws.

Pharmacognosy Field Notes: Chatham Fellowship

By Dr. Ryan Case

Graduate school can be a tough time for many students. Friends are working and making money, while we are all stuck working a many hours and barely scraping by on whatever fellowship or assistantship we were lucky enough to receive. For those of us pursuing fieldwork, this is especially difficult. The hard work, we can do. The studying for countless hours, no problem. The sleeping on dirt floors or bumbling through a foreign language we do not understand, we have accepted. But there is one thing, one mighty hurdle, which we cannot simply push through on our simple strength of will and determination: funding.

This is how the Chatham Fellowship saved my dissertation. Receiving this award gave my project legitimacy and kicked off subsequent funding opportunities that led to my being able to carry out my proposal of doing fieldwork in Papua New Guinea (PNG). For example, the Chatham Fellowship paid for my flights to this far-flung region of the world. Since I was going to be there studying and collecting plants, I leveraged a collaborative opportunity with another professor to collect plants for their anti-cancer program. More funding meant more time in PNG, more research experience, more learning, and more adventures.

PNG did not disappoint. My field work was done on Manus Province, the smallest and most remote province. With a host of endemic species, I was able to collect nearly 200 interesting and different speci-



Bundrahi Village.

DR. CASE



Dr. Case taking notes in the field and climbing to those hard-to-reach places.

PAKOP BUNA



Drying plant specimens.

DR. CASE

mens. I spoke with dozens of people across the islands that make up the province and learned about countless uses of plants. Sure, I got malaria a half dozen times. And, of course, there were moments pondering, “What the ^&#% have I gotten myself into?” But those are the memories that I cherish and share the most.

To me, fieldwork is one of the deepest and most profound learning experiences one can have. To be done right, it requires the highest balance of patience, planning, adaptability, optimism and work ethic. No one does fieldwork just for the science. Even if you tried, you would still come home with much more than specimens and data. It changes you in a way that few other experiences in life can.

The Chatham Fellowship ignited my hopes of doing fieldwork. It was the spark that let everyone else know that my project was really happening. In a lot of ways, it set the path for the rest of my graduate school experience, which, in turn, set the pace for the rest of my career.

To all those out there pursuing the dream of fieldwork: Do not give up, it is completely worth it! Hopefully, the Chatham can help you get there. And to all those that helped fund the fellowship, I cannot thank you enough. My career may not still bring me back to PNG regularly, but what you helped to provide goes way beyond the South Pacific. ■

<http://www.missouribotanical-garden.org/plant-science/plant-science/william-l-brown-center/wlbc-resources/wlbc-awards/annes.-chatham-fellowship.aspx>

ASP Fellows: What Are We Missing?

By Dr. Jon Clardy

To increase the probability that bombers survived their missions over enemy territory during World War II, the U.S. military examined returning planes for the areas damaged by enemy fire. Researchers from the Center for Naval Analyses identified the most frequently damaged areas, and recommended that more armor be added there. Dr. Abraham Wald, a brilliant mathematician working in the Center, pointed out that considering only the returning planes and ignoring the missing planes ignored a crucial part of the available data. When he took the missing planes into account, he reached the opposite recommendation: add armor to the areas on the returning planes that were *undamaged*. Damaged areas on the surviving bombers represented places where damage could be survived; undamaged areas represented places where damage was likely to be fatal to the aircraft.

This simple and graphic example, which is regarded as one of the foundational studies in operations research, illustrates *survivor bias*, the logical errors that can be

argued that survivor bias, among other factors, contributed to the declining efficiency observed in pharmaceutical research and development.¹ They noted that focusing only on drugs that enter the market “makes drug discovery and development sound more prospectively rational than it really is.” They go on to describe how a typical story, such as “... drug x works by binding receptor a, which influences pathway b, which adjusts physiological process c, which alleviates disease d,” makes the discovery process sound rational because none of the many failures, which had equally powerful qualifications before they unexpectedly failed, are considered. The 90-95% failure rates in clinical trials mentioned earlier are ignored, and what the authors describe as the “basic research – brute force” approach (high throughput screening of large molecular libraries against a biological target) is supported more by survivor bias than actual efficiency.

The natural products field is especially susceptible to survivor bias. Most of our papers begin by recounting the

Eliminating survivor bias is an important analytical process in many fields, especially investment and statistics, but it probably plays little or no role for most ASP members. It should.

introduced by looking only at things that survived some selection and ignoring those that did not. Eliminating survivor bias is an important analytical process in many fields, especially investment and statistics, but it probably plays little or no role for most ASP members. It should. The path to discovering useful naturally occurring molecules, the process that directly or indirectly pays the bills in most of the labs and offices we occupy, conceptually resembles the survival of bombers on their missions but with a drastically lower survival rate. Many are tested but few survive.

In a typical primary screen used in modern drug discovery, the survival rate is around one out of a thousand, and the survivors are subjected to numerous additional screens. Even molecules that survive all these screens and advance to clinical trials only have a 5-10% chance, depending on the therapeutic area, of becoming a Food and Drug Administration (FDA)-approved drug. In our training, in our writing, and most importantly, in our thinking, we focus on these few survivors. This is a pronounced form of survivor bias. What are some of the potential consequences of this behavior?

In a 2012 paper, Dr. Jack Scannell and his colleagues

important contributions of natural products to biological and medical science, and the same handful of molecules (you know the ones I am thinking of) tend to be featured. It is uplifting to look at the successes in our field, and the reviews authored by Drs. Gordon Cragg, Dave Newman, and colleagues on the success of natural products as the sources of new drugs have inspired us all.² But while we admire these past successes and strive to make our own contributions to this legacy, it is important both to remember that the odds are not good and to think about strategic ways they can be improved.

Recently several articles have appeared that begin to address some of the more systematic liabilities of natural product screening strategies. ASP member Dr. Guido Pauli and his colleagues have just published an important addendum to the growing literature on members of large screening libraries that frequently appear as actives in early screens, only to lead to disappointment further down the development pathway. Researchers using these screening libraries have recognized that some structural classes hit in suspiciously large numbers of primary screens, but can

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ASP Fellows: What Are We Missing?

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never be developed into useful drugs. Examples include redox active molecules, ene-rhodanines, and isothiazolones, and the general class is called pan-assay interference compounds or PAINS.³

Some natural products, curcumin for one, are also included in the PAINS. In a parallel effort, Dr. Pauli and his colleagues sought to identify natural products that hit in suspiciously large numbers of screens but had not led to useful drug candidates. These compounds had a promiscuity similar to the PAINS but were structurally and functionally distinct, so they were called invalid metabolic panaceas or IMPS.⁴ The report by Dr. Pauli is lengthy but well worth reading carefully, especially if you are involved with plant-based natural products. For this essay, the most important feature is in the concluding paragraph: "... [this research] has the potential to spark further thoughts that may eventually lead to a paradigmatic shift in natural product-based drug discovery and related fields."

While PAINS and IMPS represent efforts to spot molecules that make it through initial screens too readily, other researchers are working on what can be learned from molecules that make it through rarely or never. In one report, Dr. Kim Lewis and his colleagues wanted to identify members of a bacterial extract library that would be selectively toxic to *Mycobacterium tuberculosis*.⁵ As their extract library had been screened repeatedly for antibiotic and other activities, they elected to screen only those extracts that had never hit in an assay. It was an unusual strategy, as a likely outcome was no screening positives, but it was a completely appropriate strategy to achieve specificity. The screen did uncover a molecule, which they

named lassomycin that not only had extraordinary specificity for *M. tuberculosis*, it also had an unusual mechanism of action. Lassomycin may *never* be developed as a drug, but the strategy that led to it is noteworthy.

Dr. Meir Glick and his colleagues used a similar strategy with libraries of synthetic molecules from both their Novartis library and the National Institutes of Health (NIH) Molecular Libraries program.⁶ As they knew the structures of the library members, they were able to screen molecules that had never hit in an exhaustive set of high-throughput assays both computationally and experimentally. They called these library members "dark chemical matter" or DCM. Computationally screening DCM would identify what features or combination of features distinguished DCM molecules from their more active mates. The answer from the computational screen was clear: there were no easily identifiable molecular features that differentiated the DCM molecules. The experimental screen, an antifungal assay for activity against the pathogen *Cryptococcus neoformans*, uncovered a DCM member with strong antifungal activity but little activity against human targets – precisely what they were looking for. They concluded that DCM represented promising starting points for drug lead discovery.

In ending this brief consideration of the effects of survivor (and other) biases on natural products research, I must note the irony of having it appear as a contribution in the ASP Fellows series. I was born the year Dr. Wald carried out his seminal analysis on survivor bias, and I am not the oldest ASP Fellow. We have all been involved with natural products research for multiple decades. So, having an ASP Fellows series in the ASP Newsletter is yet another example of survivor bias. ■

In a 2012 paper, Dr. Jack Scannell and his colleagues argued that survivor bias, among other factors, contributed to the declining efficiency observed in pharmaceutical research and development.

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Meet a New ASP Member

New ASP Member Dr. Emily Whitson is a scientist at Bayer CropScience Biologics in West Sacramento, California. Dr. Whitson got her doctoral degree in Medicinal Chemistry under Dr. Chris Ireland at the University of Utah, Salt Lake City, Utah. We were excited to hear about her work on pesticides from natural products at this year's Annual Meeting in Copper Mountain, Colorado, and are glad to hear more about her favorite organism and recent enthusiasm for non-fiction science history.

By Dr. Dan Kulakowski

How did you hear about the ASP?

I believe the first time would have been my first year of graduate school in Dr. Ireland's laboratory.

Why did you join ASP?

I joined ASP to reconnect with the natural products community.

Do you belong to any other scientific societies?

I belong to the American Chemical Society.

What are your current research interests in pharmacognosy?

I am currently interested in microbial natural products chemistry and its application in agriculture. Our laboratory is working on innovative ways to approach natural products chemistry, and various "omics" technologies are certainly on our radar. I still have a soft spot for natural products discovery and get excited at the possibilities of finding something truly new.

What is your scientific background?

I have an undergraduate degree in Chemistry and Marine Biology from Roger Williams University in Rhode Island, Bristol, Rhode Island. I did some environmental toxicology research as an undergraduate. I received my PhD from the University of Utah in Medicinal Chemistry with Dr. Chris M. Ireland and a focus on marine natural products chemistry. I also did a postdoctoral fellowship at the National Cancer Institute with Drs. Tawnya McKee and Kirk Gustafson in natural products chemistry, with application against various cancer targets.

What would you like to achieve through your membership?

I would like to stay connected to the natural products community and continue to attend meetings to gain insight into recent developments in natural products research.

What do you like doing in your spare time?

I enjoy spending time with my family and playing with our two-year-old son. I also play on a couple of slow-pitch softball teams. When time permits, I like traveling and exploring new places.



Dr. Emily Whitson

MR. RAY JOHNSTON

What are you currently reading?

I am currently reading *Radioactive: Marie & Pierre Curie: A Tale of Love and Fallout* by Lauren Redniss. I received it as a gift, and I do not normally read non-fiction, but this book sparked my interest.

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

I really like ascidians; they are great sources of chemical diversity. The first project I worked on in Dr. Ireland's laboratory was identifying a new compound from an ascidian. The project presented a lot of challenges, but in the end of my graduate work it was great to see it all come together and see how much I had learned along the way. ■

Our laboratory is working on innovative ways to approach natural products chemistry, and various "omics" technologies are certainly on our radar.

New Members of ASP 2015



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 1 domestic full member, 1 international member, and 2 associate members. We look forward to meeting you and learning more about you and your work.

ACTIVE MEMBERS

Mr. Michael Spittler
Dortmund, Germany

Yudi Rusman
Minneapolis, Minnesota

ASSOCIATE MEMBERS

Mr. Chaudhry Khan
Baldwin, New York

Ms. Nausheeen Siddiqui
Karachi, Pakistan



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.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.

251st American Chemical Society National Meeting & Exposition

March 13-17, 2016

San Diego, California

www.acs.org/content/acs/en/meetings/san-diego-spring-2016.html

Society of Economic Botany 57th Annual Meeting

June 3-9, 2016

Pine Mountain Settlement School

Harlan County, Kentucky

www.econbot.org/index.php?module=content&type=user&func=view&pid=103

Interim Meeting of the American Society of Pharmacognosy and

16th Annual Oxford International Conference on the Science of Botanicals

Oxford, Mississippi

April 11-14, 2016

oxfordicsb.org

9th Joint Natural Products Conference 2016

July 24-27, 2016

Tivoli Congress Centre

Copenhagen, Denmark

www.jnpc2016.dk

Leiden Symposium

April 14-15, 2016

Learning From Nature, Learning from our Ancestors; From Tradition to Evidence Based Medicines

Naturalis Biodiversity Center

Leiden, The Netherlands

<http://science.leidenuniv.nl/index.php/events/learning-form-nature-learning-from-ancestors/>

The 9th International Countercurrent Chromatography Conference (CCC 2016)

July 30-August 3, 2016

Dominican University

Chicago, Illinois

www.ccc2016.com

International Symposium on Advances in Lamiaceae Science

Wow Topkapi Palace Hotel

Antalya, Turkey

April 22-25, 2016

www.lamiaceae2016.org

Gordon Research Conference: Natural Products

July 31- August 5, 2016

Proctor Academy

Andover, New Hampshire

www.grc.org/programs.aspx?id=11733





Brief News From Washington Natural Products in the Spotlight

By Dr. Georgia Perdue

- **“NIH AWARDS NEARLY \$35 MILLION TO RESEARCH NATURAL PRODUCTS,”** was the September 9, 2015, press release headline. Five year funding will support **three Botanical Dietary Supplements Research Centers at \$2 million per year**, and two new Centers for Advancing Natural Products Innovation and Technology at \$1.25 million each per year. The money will be provided by the Office of Dietary Supplements (ODS) and the National Center for Complementary and Integrative Health (NCCIH). Some of the “botanical supplements” to be studied include black cohosh, chasteberry, fenugreek, hops, milk thistle, resveratrol, licorice and valerian. **The two new centers “... will develop pioneering methods and techniques to catalyze research on these products,”** stated Dr. Paul Coates, ODS Director. **NCCIH director Dr. Josephine Briggs noted “Natural products have a long and impressive history as sources of medicine and as important biological research tools.”**

CENTERS FUNDED

- **Dietary Botanicals in the Preservation of Cognitive and Psychological Resilience**, Icahn School of Medicine, Mt. Sinai, New York City. Dr. Giulio Pasinetti and Dr. Richard Dixon, Principal Investigators. Partners: Purdue University, West Lafayette, Indiana, Rutgers, The State University of New Jersey, New Brunswick, New Jersey, and University of North Texas, Denton, Texas.
- **Botanicals and Metabolic Resiliency**, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, Louisiana. Dr. William Cefalu, Principal Investigator. Partners: North Carolina State University, Raleigh, North Carolina, Rutgers, The State University of New Jersey, New Brunswick, New Jersey, and University of Illinois Chicago, Chicago, Illinois.
- **Center for High-Throughput Functional Annotation of Natural Products**, University of Texas Southwestern Medical Center, Dallas, Texas, ASP member Dr. John MacMillan, ASP

member Dr. Roger Linington and Dr. Michael White, Principal Investigators. Partners: Simon Fraser University, Burnaby, British Columbia, Canada, and University of California Santa Cruz, Santa Cruz, California.

- **The University of Illinois Chicago Natural Products Technology Center**, ASP member Dr. Guido Pauli, Principal Investigator. In a sense, this center will be working in tandem with the one above. It will “[mine] bioanalytical knowledge of natural products ... [to] produce documentation of good research practices for natural products and promote ... coherence of [the outcomes ... with the above named center].” It will “develop and share cutting edge bioanalytical methodologies [to] address important biomedical questions and advance a more holistic research approach [re:] natural products and their metabolomic complexity.”
 - **Botanical Dietary Supplements for Women’s Health**, University of Illinois Chicago, Chicago, Illinois. Dr. Richard van Breemen, Principal Investigator. This center was established in 1999.
- Five days after the lead headline above, there was news from NCCIH Program Director and ASP member Dr. Craig Hopp: **“NEW CENTER TO PROVIDE LEADERSHIP ON NATURAL PRODUCT-DRUG INTERACTIONS.”** A multidisciplinary team of “leading scientists in the fields of pharmacology, natural products chemistry, bioinformatics, drug interactions and health communications will lead the Center.” The studies will include three priorities: 1. Preclinical and clinical trials on “four to six priority natural products that potentially have risks for clinically relevant interactions with drugs.” 2. “Creating an open-access repository for the data and methodology resources developed....” 3. “Developing and sharing best practices recommended for ...natural product drug interaction studies....” The Center’s team leaders will be Dr. Danny Shen and Dr. Mary

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Brief News From Washington

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Paine, both at the University of Washington College of Pharmacy, Seattle, Washington. Collaborators will include scientists at the University of North Carolina-Greensboro, Greensboro, North Carolina.

- In September, the President nominated **Dr. Robert Califf to be the next Food and Drug Administration (FDA) Commissioner.** Since January, Dr. Califf has been Deputy Commissioner of FDA's Medical Products and Tobacco. A prominent cardiologist, his stellar career includes professor of cardiology at Duke University, Durham, North Carolina, and a long-time researcher and founding director of Duke's very large Clinical Research Institute. On November 17, 2015, the Senate Committee on Health, Education, Labor & Pensions, chaired by Senator Lamar Alexander (R- TN) held a hearing on his nomination. Most senators were laudatory; Senator Bernie Sanders (D-VT), with flailing arms, was in campaign mode over the high price of drugs, boldly telling Dr. Califf he would not vote for him. Senator Alexander noted that Dr. Califf had submitted 3,200 pages of his lectures and published papers as requested, which the committee reviewed over two months. "My committee tells me they found nothing [to prevent you] from being FDA Commissioner.... The way you conducted clinical trials was very impressive to me." Ranking member Patty Murray (D-WA) said "Dr. Califf would provide leadership...he is a strong nominee for the position...with a history of being a leader. Our review reveals no conflicts.... I urge the committee to confirm him." She also asked Dr. Califf about his being influenced by industry in clinical trials. He replied: when we publish papers... industry has no say in what we write...." He assured Senator Elizabeth Warren (D-MA) that the clinical trials he conducted "were not influenced by industry even though they financed some of the research." "FDA and academia etc... had a say in the public process." "All contracts have databases and if not we walked away.... industry cannot influence publications. We stay independent." "NIH," he continued, "now says without transparency we can't publish." As to his consulting fees, he told Senator Warren that he donates all such monies. Senator Richard Burr (R-NC) called him "an outstanding nominee...I urge my colleagues to expeditiously vote...." Senator Bill Cassidy (R-Louisiana), also a medical doctor, had a good exchange with the nominee. Some issues in the two hour hearing covered high cost of drugs, generics, dietary guidelines, sickle cell anemia, compounding drugs, importing drugs from India and China, dietary supplements, a subject about which Dr. Califf noted, "...we know our authority [in this area] and plan to implement [it]." The committee had until November 24 to submit any more questions. Confirmation is expected before the end of the year.
- The FDA approved, in late October, Onivyde™, (irinotecan liposome), Merrimack Pharmaceuticals MM-398, in capsule form to treat metastatic pancreatic cancer. (See the *ASP Newsletter* 2015;51(3)).
- At the end of October the World Health Organization (WHO) recommended that GlaxoSmithKline start pilot tests with Mosquirix™ (RTS,S) vaccine to determine how best to use the vaccine "in a real world setting." WHO will make its final recommendations by the end of the year. (See the *ASP Newsletter* 2015;51(3)).
- A study at the National Institute of Allergy and Infectious Diseases (NIAID) revealed in late October that "...[artemisinin-resistant] *Plasmodium falciparum*... has been rapidly spreading in parts of Southeast Asia making it difficult to treat and control [malaria] there." Of great concern is that this drug-resistant parasite could spread to Africa.
- The FDA amended its regulations the end of September pertaining to colors used in coating tablets etc., to include the blue color from extract of the cyanobacterium *Spirulina*. The petition was originally filed by Colorcon Inc. The colors produced also include green or purple.
- It has been reported that resveratrol, in a Phase II study, has shown to be safe and well tolerated. It acts by "[stabilizing] levels of amyloid beta in cerebrovascular fluid (CSF) and in plasma in patients with mild to moderate Alzheimer disease." Resveratrol is found in red wine, red grapes and dark chocolate. Researchers at the University of Illinois isolated the compound a few years back and had suggested it might aid in preventing cancer. (Some information from *Medscape Medical News*, September 17, 2015.)
- At the September meeting of NIAID Advisory Council meeting, NIAID Director Dr. Anthony Fauci reported that there are **more than 300 Chikungunya virus cases in the U.S.** Prior to 2013 outbreaks were only in China and Europe. **Since 2013, 1.7 million cases have been reported in the Americas, including 300 cases in the U.S. since July.** ■

NIH AWARDS NEARLY \$35 MILLION TO RESEARCH NATURAL PRODUCTS

The Nobel Prize and the American Society of Pharmacognosy

By Ms. Devhra Bennett-Jones

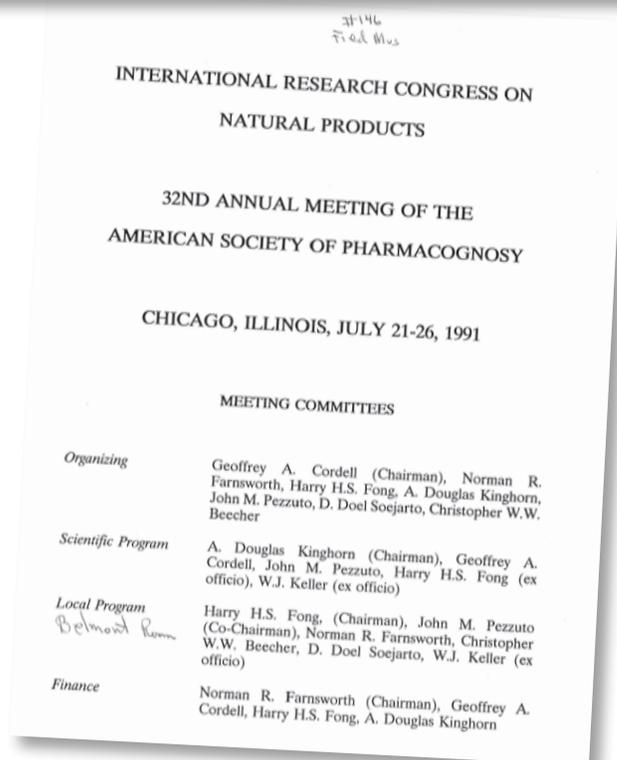
The ASP membership congratulates ASP Fellow Dr. Satoshi Ōmura, along with Drs. William C. Campbell and Youyou Tu, as they are honored by the 2015 Nobel Prize in Physiology or Medicine. As an ASP member, Dr. Ōmura received the ASP Norman R. Farnsworth research Achievement Award in 2013. To state that the Society is bursting with joy over these pharmacognosists contribution to the field of study and medical science is an understatement. Their research in bacterial strains and their bioactive constituents impacts millions of lives across the globe where patients suffer from infections by roundworm parasites and malaria.

While Dr. Ōmura is the first ASP member to be honored with the Nobel Prize, the ASP has appreciated prior associations with Nobel scientists. In 1976, Dr. Baruch Samuel Blumberg (July 28, 1925 – April 5, 2011) and Dr. Daniel Carleton Gajdusek (September 9, 1923 – December 12, 2008) were co-recipients of the Nobel Prize in Physiology or Medicine for their work on the Hepatitis B virus. At the 1991 ASP Annual Meeting in Chicago, Illinois, Nobel Laureate Dr. Blumberg delivered the keynote address, “An Exercise In Systematic Plant-Derived Medication Discovery: *PHYLLANTHUS AMARUS* And Hepatitis B Virus.”¹ He collaborated with researchers Drs. P.S. Venkateswaran, I. Millman, and D.W. Unander. The abstract of the address outlined their research and results.

Ethnobotanical selection system was used to identify plants from which medications for the treatment of carriers chronically infected with hepatitis B virus (HBV) AND OTHER VIRUSES COULD BE DERIVED. More than 1,000 plants used for the treatment of jaundice and other symptoms of liver disease in indigenous medical systems were identified and listed alphabetically. From these, species which had been used in three or more continents or other major geographical areas were identified. Less than 100 species were included in this short list.

Plants from the short list were collected in various parts of the world and screened in two tests: (1) inhibition of the reaction between the surface antigen of HBV and the antibody against it (anti-HBs) and (2) inhibition of the DNA polymerase (DNAP) of HBV. We then selected a plant on the list *Phyllanthus amarus* (first identified as *P. niruri*) that had already been used by one of us (PSV) in earlier experiments. Methods for cultivating the plant were successfully developed.

A series of studies in woodchucks infected with woodchuck hepatitis virus (WHV) showed that whole extracts of



First page of the 1991 program from the ASP Annual Meeting in Chicago, Illinois.

P. amarus decreased or eliminated WHV surface antigen in animals acutely or chronically infected with WHV. We helped in the design and analysis of a clinical trial conducted in Madras, India by Thyagarajan et. al. which showed a striking effect on the removal of HBsAg from the blood of human carriers. Following these studies, we recommended their repetition to determine if our original findings could be replicated.

A published clinical study from Thailand failed to confirm our original findings in Madras. (Other clinical studies are in progress but are as yet unpublished.) Plant extracts were not effective in ducks infected with duck hepatitis B virus. Additional woodchuck studies are now in progress as well as trials on tissue cultures infected or transfected with HBV or WHV.

We are currently identifying fractions (separated by chromatography) with activity against DNAP and isolating compounds with this activity. One or more of these will in the future be evaluated for clinical effectiveness if pre-clinical studies are sufficiently encouraging.²

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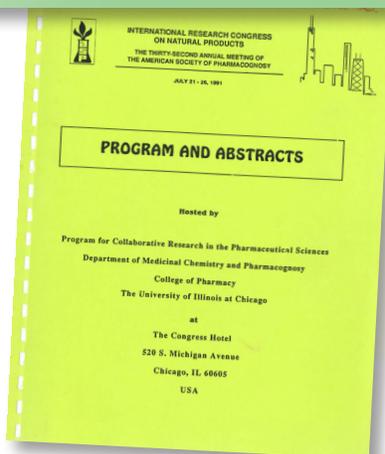
¹ American Society of Pharmacognosy Archives, Conference Materials, ASP Annual Meeting, 1991, Box 12, Folder 3, Lloyd Library and Museum, Cincinnati, Ohio.

² ibid

The Nobel Prize and the American Society of Pharmacognosy

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Dr. E. John Staba's notes from the address highlighted that in 1991, 300 million people carried Hepatitis B with 20-40 million annual deaths from the disease. Dr. Blumberg's collaborative research was recognized by the Nobel Committee, "for their discoveries concerning new mechanisms for the origin and dissemination of infectious diseases in the field of disease transmission and epidemiology."³ ASP members can thank the excellence of Drs. A. Douglas Kinghorn, Geoffrey A. Cordell, John M. Pezzuto, Harry H.S. Fong, and W.J. Keller in their service on the 32nd ASP Annual Meeting Scientific Program Committee for inviting Dr. Blumberg to be the keynote speaker.



Meeting program showing
Keynote Address by Dr. Blumberg.

Whereas Dr. Ōmura is the first ASP member to become a Nobel Laureate the Society had a long term member that served on the Nobel Committee, Dr. Albert Hofmann (January 11, 1906 – April 29, 2008). In 1960, ASP President, Dr. Varro E. Tyler sent an ardent letter to the Society's members. He wrote, "One of the purposes of the newly organized American Society of Pharmacognosy, an organization designed to formalize and perpetuate the standards of the Plant Science Seminar which was founded in 1923, is to promote the publication of meritorious research."⁴ His letter went on encouraging charter members to recommend pharmacognosists in the U.S. and abroad for membership. Characteristic of his dedication to the ASP, Dr. Norman Farnsworth suggested Dr. Hofmann as a potential member.⁵ Dr. Hofmann was a dedicated and honorary member of the Society from 1961 until his death in 2008. Upon his retirement in the 1970s, Hofmann worked as a member of the Nobel Prize Committee in Physiology or Medicine.

Many ASP members may wonder how nominees came before the Nobel Prize Committee in Physiology or Medicine in which Hofmann served. The committee entertained nominations from individuals that fit the following criteria:

SWITZERLAND	
<u>Names</u>	<u>Addresses</u>
Albert Hofmann	Sandoz A. G. Basel Switzerland
Dr. Hans Hurlimann	Rennweg 102 Basle, Switzerland
Dr. E. Steinegger	Sudbahnhofstrasse 17 Pharmaceutical Institution University of Bern Bern, Switzerland

Dr. Hofmann's official ASP membership.

Members of the Nobel Assembly at Karolinska Institutet, Stockholm; Swedish and foreign members of the Medicine and Biology classes of the Royal Swedish Academy of Sciences; Nobel Laureates in Physiology or Medicine and Chemistry; Holders of established posts as full professors at the faculties of medicine in Sweden and holders of similar posts at the faculties of medicine or similar institutions in Denmark, Finland, Iceland and Norway; Holders of similar posts at no fewer than six other faculties of medicine at universities around the world, selected by the Nobel Assembly, with a view to ensuring the appropriate distribution of the task among various countries; and, Scientists whom the Nobel Assembly may otherwise see fit to approach.⁶

In 2015, Dr. Ōmura was among 327 scientists nominated for the Nobel Prize in Physiology or Medicine. The Nobel Committee evaluated the nominations during spring and summer of this year. The final selection was made by the Nobel Assembly at Karolinska Institutet in October. His admirable achievement is of great significance to the health of humanity across the globe. The ASP is honored to have an association with Dr. Ōmura and takes great pride that he utilizes the science of pharmacognosy in his medical research. ■

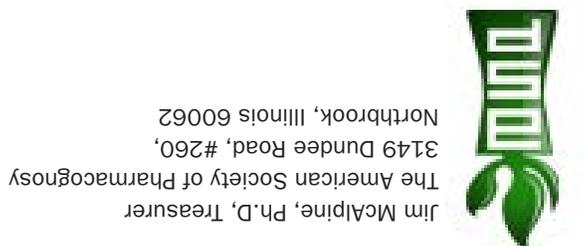
Author's Note: The connections with Drs. Blumberg, Hofmann, and Ōmura are the known ASP links with the Nobel Prize. Please contact the ASP President, Dr. Ed Kennelly, if Society members are aware of others.

³ The Official Web Site of the Nobel Prize, Nobelprize.org, *Baruch S. Blumberg – Facts*, http://www.nobelprize.org/nobel_prizes/medicinelaureates/1976/blumberg-facts.html

⁴ American Society of Pharmacognosy Archives, Membership Materials 1960-1969, Box 11, Folder 4, Lloyd Library and Museum, Cincinnati, Ohio.

⁵ American Society of Pharmacognosy Archives, "List of Pharmacognosists from Prof. Norman Farnsworth", Membership Materials-Membership Lists 1959-1960, Box 9, Folder 8 and 9, Lloyd Library and Museum, Cincinnati, Ohio.

⁶ The Official Web Site of the Nobel Prize, Nobelprize.org, *Nomination and Selection of Medicine Laureates*, <http://www.nobelprize.org/nomination/medicine/index.html>



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