The Portland Section meeting_notice_newsletter

Vol 57 number 2 February 2018

Next Portland Section Meeting

Thurs. Feb. 15

Overcoming Drug Resistance in Malaria—From the Lab to the Clinic

a talk presented by

Prof. David Peyton, PSU
and Dr. Sandra Shotwell, DesignMedix

7:45 pm Thurs. February 15

Reed College Vollum Lounge

3203 SE Woodstock Blvd, Portland, OR 97202

map

Dinner reservations

Dinner reservation FIRM deadline midnight Monday Feb. 12.
Prices increase after deadline!

NOTE: On 1/21/18 the Portland Section Executive Committee approved a late reservation fee of $15/$25. Prices will remain $10/$20 until midnight of the Monday before the meeting. Prices increase after the deadline (including at the door)!

Schedule: 6:00 pm social•6:45 pm buffet dinner•7:45 pm talk

Upcoming events: Science Expo Judges needed

Contact Scott Vanderwerf if you have questions

(go to next page)

ACS Chemistry for Life®

Portland Section ACS L620
PO Box 1741
Portland OR 97207-1741
503.912.4360
http://portland-or.sites.acs.org

BIO Sandra Shotwell

Dr. Shotwell is an experienced biotech entrepreneur, with a passion for global health. She is cofounder and CEO of DesignMedix Inc., and co-founder of Elex Biotech LLC, firms that develop small molecule therapeutics for infectious disease and heart disease, respectively. She previously cofounded Alta Biomedical Group LLC, a consulting firm focused on commercialization of life science technologies. A Certified Licensing Professional, she has done biotech and pharmaceutical licensing deals as a Licensing Associate for Stanford University, as founder and Chief of the Technology Licensing Branch for the National Institutes of Health/FDA/CDC, and as Director of Technology Transfer at Oregon Health & Science University. Dr. Shotwell has served on several for-profit and non-profit boards of directors and is an active angel investor.

More information about DesignMedix is available on the website **https://www.designmedix.com**.

Abstract

Malaria is one of many diseases that are rapidly losing useful treatments. Resistance has taken out drugs that were both safe and effective. David Peyton and Sandra Shotwell will share the trials and tribulations of bringing a novel antimalarial from concept to the clinic. DesignMedix drug DM1157 was invented by David and his team at Portland State University, and licensed to DesignMedix. The company has guided preclinical development, and recently submitted an investigational new drug (IND) application to the Food and Drug Administration to begin human safety trials at Duke Clinical Research Institute. Join us to learn the ups and downs of drug development in an entrepreneurial environment—a "Made in Oregon" story.

Bio David Peyton

"Parasite Prescription"

"Revising solutions, reviving hope"

By re-engineering the decades-old malaria drug Chloroquine, PSU chemistry professor David Peyton may save millions of lives. Teams at his startup firm DesignMedix and PSU have shown the new drug's effectiveness in mice, and human trials may be only a couple years away. Peyton's approach could have applications in curing other infectious diseases as well. (**https://www.pdx.edu/profile/david-peyton**)

The main research theme in the Peyton research group is the study of the relation of structure to function in biological molecules by application of nuclear magnetic resonance spectroscopy. However, other tools may be used, depending on the nature of a particular problem. These tools include organic synthesis, electronic spectroscopy, and computer modeling/dynamics. (**http://web.pdx.edu/~peytond/**)

This **link** is the most recent collaborative effort by Shotwell/DesignMedix and Peyton. *(more on page 5)*

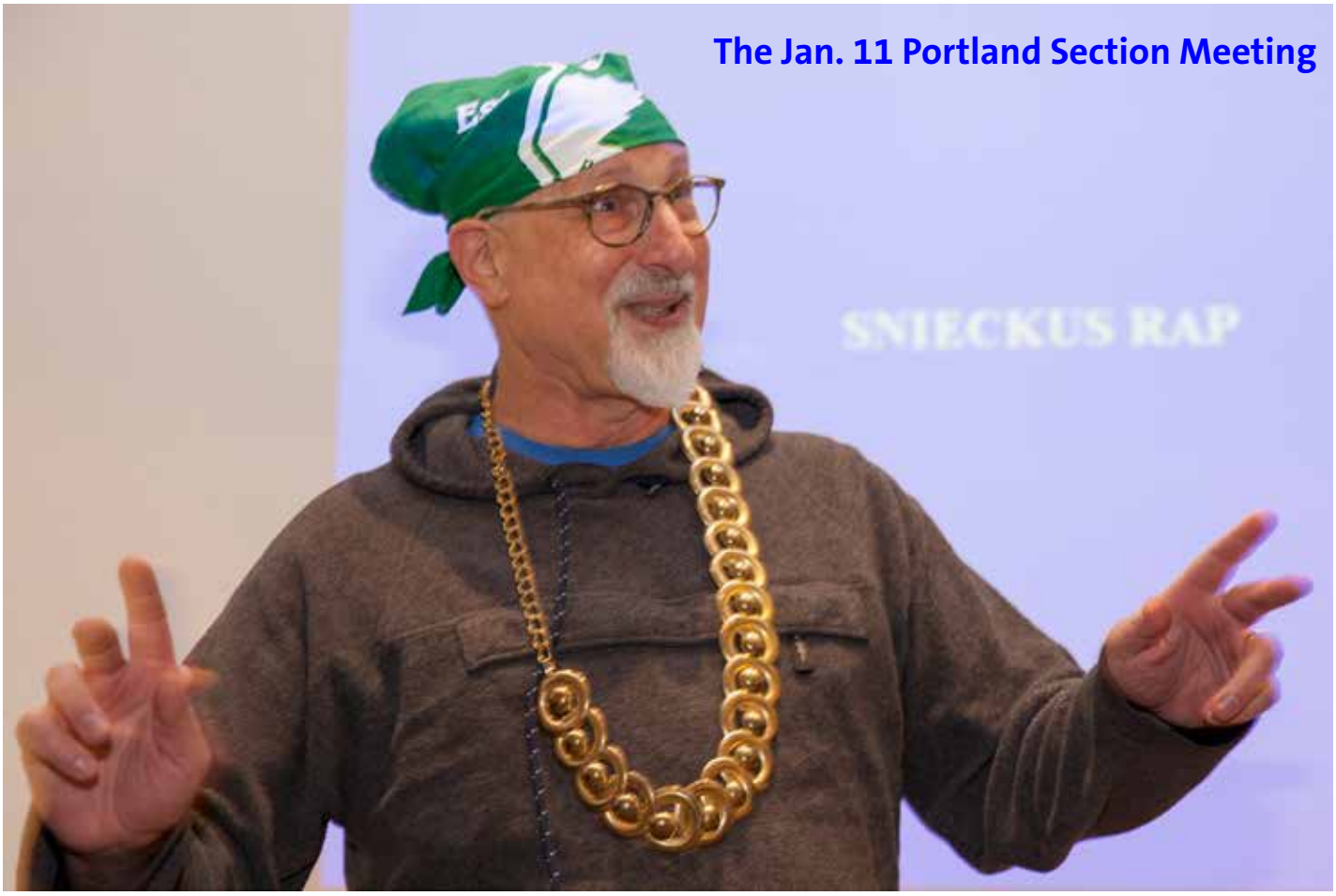
Upcoming Science Fairs

The Aardvark Science Expo will be held Friday, February 23, 2018 at the SPARC (OES Sports and Recreational Center located at 6699 SW Oleson Road). Go to **http://www.nwse.org/judges** to sign up to judge the Aardvark Science Expo. If you have questions, contact Tanja Horvatt **horvatt@oes.edu.**

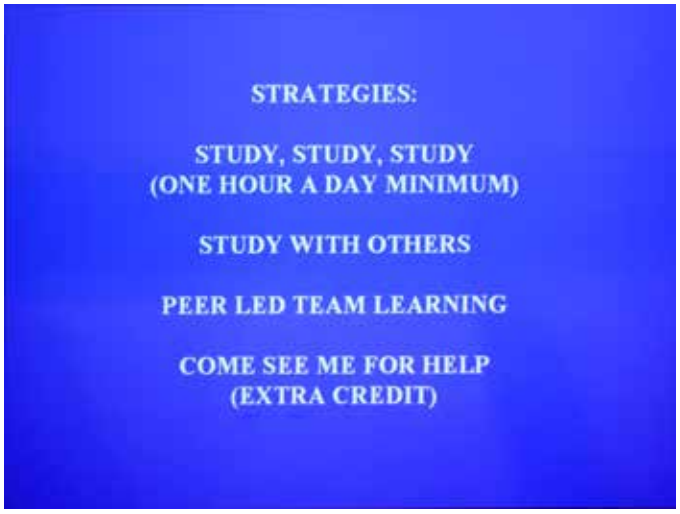
Intel Northwest Science Expo (NWSE) will be April 13th in the new Viking Pavilion at Portland State University. Both middle and high school fairs will be held at the same time. Please publicize this event to **recruit judges**. There will be half day judging options for middle school to try and get more college students.

go to next page

The Jan. 11 Portland Section Meeting



Dave Reingold at 2018 January 11 meeting "Singing Organic Chemistry". Past-Chair (2015) Reingold gave an inspiring and chemically accurate lesson in Organic Chemistry based on his textbook, which introduces Organic Chemistry students to Organic Chemistry without first requiring General Chemistry. Dave's songs and chemically accurate song lyrics entertained the Section for a full hour ending in this costume change!



2018 Portland Section Officers

Chair: Scott Vanderwerf
Chair-Elect: Keri Bishop
Past Chair: Jean Eames
Secretary: Elaine Nam
Treasurer: Dave Reingold

Councilor: Angela Hoffman
Councilor: Marcie Merritt
Alternate Councilor: Warren Ford
Alternate Councilor: Aida Melendez

to page 4

Left to right: Kevin Makinson, Abigail Thompson, Aliya Whitehill

Passing the Gavel

Each year the incoming Chair of the Portland Section takes possession of a special gavel made by a master scientific glassblower especially for the Portland Section. The Chair has use of the gavel during that one year. On January 4, 2018 Jean Eames, Immediate Past Chair, presented the glass gavel to incoming Chair Scott Vanderwerf. The glass gavel is safely stored in a custom padded wood box made by John Sherman in 2010.

Portland Section Radiochemistry Summer School Students present at Cascade Chapter Health Physics Society Meeting in Olympia WA

Students Abigail Thompson, PSU, and Aliya Mae Whitehill, George Fox University, presented an overview of their ACS summer school experience at San Jose State University (San Jose, CA) at the Fall Meeting of the Cascade Chapter of the Health Physics Society. The ACS Division of Nuclear Chemistry and Technology sponsors two INTENSIVE six-week Summer Schools in Nuclear and Radiochemistry for undergraduates. The Schools are held at Brookhaven National Laboratory (Eastern Site, Long Island, NY) and San Jose State University (Western Site, San Jose, CA). Funding is provided by the US Department of Energy. Aliya Whitehill was the Section's James G. Anderson Scholarship awardee.

to page 5

Continued from page 2

The following is taken from **http://researchfeatures.com/2016/10/31/hybrid-drugs/**, an article aboutDesignMedix and Dr David Peyton.

Researchers at DesignMedix, led by Dr David Peyton, have successfully combined two bioactive compounds to restore the effectiveness of an anti-malarial drug neutralised by the emergence of resistant strains. Their work is paving the way for a new approach to combatting the growing problem of drug resistance.

Malaria is a devastating disease which disproportionately affects emerging economies: it is estimated to cost African nations alone $12bn a year in healthcare costs and loss of economic output. This is compounded into the perfect storm when low-cost treatments are rendered ineffective due to the evolution of resistance in parasite populations. The search for novel therapies and other control methods is ongoing, but Dr David Peyton from Portland State University (PSU) is refusing to surrender in the battle against drug resistance.

With an academic career at PSU which focussed initially on heme proteins, antigen–antibody binding, and virus particle formation, Dr Peyton naturally became involved with public health. On moving to the study of medicinal chemistry, with a particular interest in malaria treatment, he came across the issue of drugs lost to evolved resistance and developed a unique approach to combat the phenomenon.

Determined that chloroquine, the safest and least expensive drug to be used against the malarial parasite, should not be lost, Dr Peyton set out to re-engineer the compound to overcome the parasite's evolved ability to eliminate the drug. Chloroquine diffuses into the acidic digestive vacuole of the parasite during the asexual stage of its life cycle, when it is within red blood cells degrading haemoglobin for nutrition. In the acidic environment of the digestive vacuole, chloroquine undergoes protonation: because acidity is effectively the number of free protons (H+) in a solution, some molecules will accept these free protons and be changed as a result. As well as the obvious changes in charge and mass from accepting another proton, many chemi-

to page 6

Letters from student attendees of Pauling Medal Award Symposium

The following are two letters from Molalla High School students who attended the Linus Pauling Medal Award Symposium Nov. 18, 2017 with their teacher, Emmely Briley. *(Published with permission*)

The first poster we went to was talking about plastic beads ("Molybdate") that could break down pesticides. In their research they found that they could do it but the problem they have to find and fix is a way to make it more reusable than just a couple times. The stated that their goal was to use the beads but find a way to make it last longer by coating it and possibly using a different polystyrene. They also talked about why they wanted to use beads to break down the pesticide rather than liquids because liquids would take longer to extract and take out of the broken down pesticides. If they found a plastic that could also be used a couple times it would also be economically better as well. I thought it was cool that we spent the first part of the trimester learning about polystyrene in our class at Molalla High School. In class we talked about how we use and could recycle plastics better. I would recommend other students next year to go because it lets you know what college students study and how much work goes into college work.

—Madison Fischer, Molalla High School Senior

It was great to be able to go and to see how much more there is to learn in college and how they actually get to go and do their projects. It is very interesting that they made these beads and made a liquid form of them to get rid of pesticides. I would tell other peers and the next years students to go if they ever get the chance to go.

—Megan Denardis, Molalla High School Senior

to page 6

cal attributes of the molecule may also be changed. In the case of chloroquine, these chemical changes mean that it can no longer diffuse back out of the digestive vacuole the way it came in and it builds up, preventing the parasite from eliminating the toxic by-products of haemoglobin metabolism.

The rise of resistance

Due, at least in part, to the use of mass drug administration as a method of controlling malaria in areas with high endemicity (high levels of the disease), selective pressures have resulted in the emergence and spread of drug-resistant strains. Mutations in a particular transmembrane protein effectively render chloroquine useless as a treatment. The transmembrane protein is responsible for exporting chloroquine out of the digestive vacuole and the key mutation results in a significant increase in efflux efficiency (how quickly chloroquine is removed). The P. falciparum chloroquine resistance transporter (PfCRT) has been found to be 40-50 times more effective at removing chloroquine from the digestive vacuole in mutated versus original strains. It is thought that this protein may be using the proton gradient across the vacuole membrane to drive the export of the protonated form of chloroquine. Dr Peyton and his team hypothesised that, by linking a known inhibitor of the transmembrane protein to the chemical skeleton of chloroquine, they could create a revitalised version of an established treatment. The parasite would once again be unable to eliminate the drug and it could form the basis of new mass administration and/or targeted programmes, this time using combination therapies to reduce the likelihood of evolved resistance.

DM1157 returns a tool with chloroquine's advantages to its previous status as a low-cost and effective weapon in the fight against malariaQuote_brain

The challenges involved in this are significant, however, as any new compound needs to tick all the boxes on the malarial treatment wish list. It must be stable at tropical temperatures to allow for cheap transport and storage in the countries where malaria is endemic. Similarly, with oral dosing as the preferred route of administration for public health programmes, aqueous solubility is of prime importance. But perhaps the most challenging of all, and one of the reasons investment in this area is lacking, it must still be of sufficiently low cost to make it economically viable for healthcare services in developing countries. Confident of their abilities to overcome these hurdles, the team spun out DesignMedix, Inc. a start-up focused on using this technique to resurrect previously effective treatments. With support from the National Institutes of Health and colleagues at PSU, an arsenal of new compounds was developed and each one tested against the malarial parasite.

There are a number of suitable candidates for inhibition of the transmembrane transport protein responsible for the efflux of chloroquine. Known as reversal agents (because they reverse resistance to a drug) they include verapamil, a drug used in the treatment of heart disease and hypertension, and the anti-depressant imipramine. These chemicals are among a large group known to have the right chemical structure to interact in this way with the mutated protein and imipramine was chosen by the team as being particularly suitable for attachment to the chloroquine molecule. Through a small number of simple reaction steps, chloroquine can be restructured to become essentially a hybrid with imipramine, prepared as a free base, or converted to a hydrochloride (or other) salt to promote water solubility.

A new weapon emerges

From more than two hundred similar compounds (termed 'reversed chloroquines') created in this way, one was selected. Given the title DM1157, this novel chemical has been put through its paces in in-vitro and ex-vivo studies, as well as having proven efficacy in mice. These impressive results mean it is now ready for its first in-human clinical trials, as it forges a new path to return a tool with chloroquine's advantages to its previous status as a low-cost and effective weapon in the fight against malaria. With the right support, the success of DM1157 could open the way for the same approach to be used across a range

to page 7

of treatments and pathogens, potentially returning many drugs to therapeutic use.

Malaria remains a devastating disease across much of the developing world, preventing many emerging economies from realising their full potential. In spite of intense research efforts and new control methods, the fight against this destructive protozoan will continue to need novel tools in the shape of drugs, insecticides and perhaps even vaccines. DM1157 will be one such weapon which, in combination therapies with other effective treatments and alongside public health programs, could give us the upper hand in the battle for eradication.

NEWS RELEASE - EMBARGOED UNTIL APRIL 10, 2017

CONTACT: Sandra Shotwell, CEO, shotwell@designmedix.com, 503-348-0855

DesignMedix's malaria drug to enter clinical trials with support from NIH

Portland OR: DesignMedix Inc., a drug development company targeting drug resistant infectious diseases, has entered into an agreement with the National Institutes of Health (NIH) that will pave the way for first-in-human clinical trials of DesignMedix's malaria drug DM1157. The agreement is with the National Institute of Allergy and Infectious Diseases (NIAID), part of the NIH, and builds on the strong package of preclinical data DesignMedix has developed to prepare its malaria drug for clinical trials.

Under the agreement, NIH will sponsor a Phase I clinical trial of DM1157. The trial will be conducted at Duke Clinical Research Institute, and is expected to commence in late 2017.

"Diseases like malaria are a significant hurdle to the health, productivity and prosperity of millions of people around the world," said DesignMedix CEO Sandra Shotwell, noting that malaria parasites have developed resistance to almost every malaria drug currently available. "Our malaria drug is designed to overcome drug resistance. We believe it will make a positive impact on global health, and appreciate the support provided by NIAID's services to achieve this key milestone: the first-in-human studies of our novel malaria treatment."

DesignMedix exclusively licensed the malaria drug technology from Portland State University, where drugs were designed to have two important functions: kill the malaria parasite, and block drug resistance. The World Health Organization has identified emergence of antimalarial drug resistance as one of the greatest challenges facing malaria control today. The U.S. Congress established a significant incentive program, Priority Review Vouchers, to encourage development of drugs for tropical diseases, including malaria. In addition to being eligible for a Priority Review Voucher upon FDA approval, DM1157 has received Orphan Drug designation from the FDA.

About DesignMedix, Inc.
DesignMedix, Inc. was founded in 2008 to develop small molecule drugs to overcome drug resistance in treating infectious diseases. In addition to the malaria drug program, DesignMedix has early-stage drug development programs for additional bacterial and parasitic diseases. DesignMedix is housed in the Portland State Business Accelerator, a leading technology incubator and home to more than 30 promising science and technology startups. For more information please visit: http://www.designmedix.com.

About Portland State University (PSU)
As Oregon's only urban public research university, Portland State offers tremendous opportunity to 27,000 students from all backgrounds. Our mission to "Let Knowledge Serve the City" reflects our dedication to finding creative, sustainable solutions to local and global problems. Our location in the heart of Portland, one of America's most dynamic cities, gives our students unmatched access to career connections and an internationally acclaimed culture scene. "U.S. News & World Report" ranks us among the nation's top 10 most innovative universities.

##########