THE Arubication by The American Society for Pharmacology and Experimental Therapeutics Pharmacology and Experimental Therapeutics Vol. 59 • Number 4 • December 2017

### **Enbrel:** A biotechnology breakthrough

Inside:

ASPET Year in Review 2018 Election 2018 Annual Meeting Program



The Pharmacologist is published and distributed by the American Society for Pharmacology and Experimental Therapeutics.

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The Pharmacologist (ISSN 0031-7004) is published quarterly in March, June, September, and December by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995. Annual subscription rates: \$25.00 for ASPET members; \$50.00 for U.S. nonmembers and institutions; \$75.00 for nonmembers and institutions outside the U.S. Single copy: \$25.00. Copyright © 2017 by the American Society for Pharmacology and Experimental Therapeutics Inc. All rights reserved. Periodicals postage paid at Bethesda, MD. GST number for Canadian subscribers: BN:13489 2330 RT.

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Postmaster: Send address changes to: *The Pharmacologist*, ASPET, 9650 Rockville Pike, Bethesda, MD 20814-3995.



# Message from The President

Dear ASPET Members,

Wow, how time flies! As the end of 2017 approaches, it is appropriate to reflect on this past year and take stock of the Society's many accomplishments.

Many of us have fond recollections of participating in ASPET-sponsored events early in our scientific careers. Although we have a growing number of undergraduate members and attendees at our annual meeting, there are still challenges in this area. Because pharmacology is not commonly taught at the undergraduate level in the US, and there are few undergraduate pharmacology programs, many young people are unaware of our discipline when selecting an area of the biomedical sciences for graduate studies. Pharmacology thus has a pipeline problem! Importantly, one of the goals in our new strategic plan is to "attract and develop the next generation of pharmacologists." As part of the strategic plan implementation, we will provide additional opportunities for undergraduate and graduate students to engage with representatives from pharmacology graduate programs during our annual meeting. Specifically, during several events, representatives from pharmacology programs will be present to provide information that describes pharmacology research programs of interest to both undergraduates seeking graduate programs and graduate students looking for postdoctoral fellowships. This proposal has been percolating for a while, and I would like to acknowledge Charles France, PhD, for taking nascent ideas and coalescing them into a proposal that Council passed at the October 2017 meeting. This new initiative stands with our successful Summer Undergraduate Research Fellowship (SURF) program (see testimonials from SURF alumni in previous 2017 issues of The Pharmacologist) and Council's recent approval of funding to sustain the BIG IDEAS initiative, "enhancing undergraduate engagement in ASPET at EB meetings" including the networking luncheon, travel awards, and poster awards available for undergraduates. In addition to our annual meeting events, this past November ASPET participated for the first time in Health Professions Week, a virtual outreach event for high school and college students interested in learning more about careers in health professions. We had over 300 high school and undergraduate students interested in learning more about pharmacology.

Hopefully, all of you have visited the new and improved ASPET website, which was launched at the end of August 2017. Suzie Thompson's marketing team spearheaded the effort, but its culmination was made possible through a team effort from all ASPET staff. Importantly, the website has incorporated several features suggested by a survey of our members including the ability to adjust to desktop, tablet, and smart phone screens, thereby providing easier navigation, plus it has a new clean and modern look. This project was completed in just a year and included choosing a new web vendor, researching designs, cleaning up webpages, designing new templates, importing content, integrating the site with all of our programs and software, creating new pages and importantly checking that all existing pages were compatible. Kudos to ASPET staff for this accomplishment.

Another goal in the strategic plan is to revitalize and re-imagine the annual meeting experience, in part by strengthening the interactions among our divisions and creating an environment for greater cross-pollination. We do not want to be shackled by the mindset: "because this is how we have always done it." As a step toward this goal, the annual meeting will feature a daily ASPET datablitz, an idea that was supported by all divisions. This will be a series of short rapid-fire oral presentations in the ASPET poster discussion lounge. These short talks will be like hors d'oeuvres to the full presentations that will take place at the poster boards afterward. To be eligible, you must be a graduate student, postdoc, or undergraduate ASPET member and submit your research to an ASPET topic category.

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In an effort to further strengthen our Society's publications, the Board of Publications Trustees and ASPET's journals director, Rich Dodenhoff, incorporated new features and services into the journals. Among them is TrendMD, which uses behavioral click data and semantic text analysis to personalize journal recommendations to augment your reading. This is similar to Amazon's "customers who bought this item also bought" feature. So, when someone opens an article in an ASPET journal, articles in other ASPET journals are recommended unobtrusively. *Molecular Pharmacology* recently began highlighting a trainee author each month (see bit. ly/2yX1YeH for the October through December highlighted trainee authors). Trainees may be nominated by either a corresponding author or may be self-nominated. The selection criteria were developed with the help of ASPET's director of education Catherine Fry, PhD, and this feature is managed by Adriano Marchese, PhD, a *Molecular Pharmacology* Editorial and Advisory Board member.

As I reflect on our recently approved strategic plan (the goals are outlined below), I am confident that ASPET will remain strong because of the commitment and dedication of its members. However, there is untapped social and intellectual capital in our membership. For instance, a short time ago, our young scientists asked for a more unified voice and Council approved the formation of the Young Scientists Committee (YSC). So far, the YSC contributions to ASPET have been exemplary. I believe there are other members with whom we need to connect, and such engagement would likely increase retention, participation and strengthen ASPET.

#### **Goal A: Promoting Pharmacology and ASPET**

This is something to which we all can contribute - affiliation with a specific committee is not necessary! This holiday season, teach your friends, colleagues, and relatives what pharmacology is and how it benefits society.

#### Goal B: Attracting and Developing the Next Generation of Pharmacologists

I believe we are proactive in our efforts to recruit and foster the next generation of pharmacologists. We must ensure, through recruitment and development, the pipeline for pharmacology. We cannot risk losing talent.

#### **Goal C: Reimagining the Annual Meeting Experience**

As mentioned above, we are implementing new approaches to showcase our science and especially improve the experience for our trainees.

#### **Goal D: Enhancing the ASPET Journals**

I encourage you to submit your best science to our journals to help raise their profile. In addition, cite ASPET journals as much as possible when publishing in other journals and consider suggesting a topical review to our editors.

#### **Goal E: Advocating for Critical Science Policies**

The efforts of the Science Policy Committee play a key role in bringing the message of the importance of research funding to Capitol Hill.

#### **Goal F: Strengthening ASPET**

As part of the strategic plan, we have, or are developing, policies to financially strengthen our Society and leverage our global partnerships to benefit all pharmacologists.

In conclusion, ASPET is many things to many people, and one's perspective is colored by their level of involvement. For over 100 years, our Society has had a strong impact on pharmacology and science. Some of the work that is achieved may be below the radar for most of our membership, although it might be felt indirectly. A vast network of committee members freely devote their time and efforts to make the Society better. This would not be achieved without volunteers, but importantly, none of this could be accomplished without a highly dedicated staff throughout ASPET, all under the watchful eye of our Executive Officer, Judy Siuciak, PhD.

Best wishes to all of you during the holiday season! I especially look forward to seeing you at EB 2018.

Warm regards,

John D. Schuetz, PhD President, ASPET

## **ASPET Year in Review**

Membership

4,913 total members in 69 countries

**425** new members in 2017



### Career Center

The ASPET Career Center averages **106** jobs available on the site daily

There have been **18,715** page views on the ASPET Career Center

On average, there are **87,468** searchable resumes on the ASPET Career Center

#### **Education & Awards**



**123** travel awards provided to young scientists to attend the Annual Meeting

58 poster awards provided to young scientists at the Annual Meeting

\$103,303

provided to ASPET scientific achievement award winners

215



#### **Publications**

ASPET's journals achieved notable statistics this year.



**51** Open Access articles were published

60% of all articles in the journals (back to 1908) were accessed

Published papers from **28** different countries

2,966 manuscript reviews were completed

Data supplements were accessed an average of **12,236** times

per month

Figures were downloaded to PowerPoint an average of

**36,531** times per month

*PR&P* was added to **3** major indices

Articles were accessed through RSS feeds an average of **56,378** times per month



*The Pharmacologist* continues to be an important publication with

12,458 total impressions in 2017

#### • Annual Meeting at EB 2017



**14,031** overall attendees at Experimental Biology 2017 – an **11%** increase over last year

ASPET attendees at EB 2017 traveled

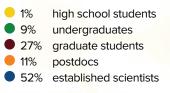


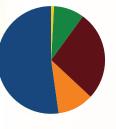
PHARMACOLOGY was the primary interest of **1,626** attendees at EB 2017 – an **18%** increase over last year

**888** abstracts submitted to pharmacology topics at EB 2017 – a **27%** increase over last year

**131** participants in the ASPET Student/Postdoc poster

The mixture of younger and established scientists at the ASPET Annual Meeting allowed for great networking:





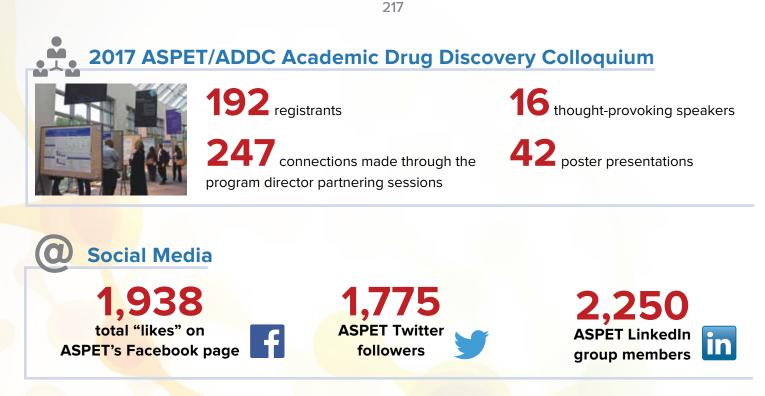
ASPET symposia at EB 2017 were rated an average of **4.7** out of **5** stars by session attendees

Over **95%** of EB 2017 attendees would recommend Experimental Biology to others

The number of members taking advantage of the ASPET Member Lounge at EB 2017 increased **42%** over last year

competition / 101 judges

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All of the statistics in the "ASPET Year in Review" were taken as of October 31, 2017.

### Submit Your Next Paper to an ASPET Journal



Visit us for more information: www.aspet.org/aspet/journals

# **2017 Contributions**

### ASPET gratefully acknowledges the following individuals who made contributions from November 2016 through October 2017:

Tagreed Altaei Bradley Andresen Leslie Benet Elaine Bush Michael Callahan Gary DeLander Robert French Kelvin Gee Susan Gonsalves Ingeborg Hanbauer Joseph Hanig Jorge Iniguez-Lluhi Kenneth Jacobson Kenneth Johnson Diana Krause Atul & Jayashree Laddu John Lazo Dennis Marshall Bettie Sue Masters Alejandro Mayer Joseph Moerschbaecher Rajesh Mohanraj Naveen Neradugomma Richard Okita Mark Osinski Walter Prozialeck Gary Rankin John Raymond Mitchell Steinberg Craig Stevens Roger Sunahara Palmer Taylor John Thomas Kenneth Thummel Pancras Wong

### Thank you to our Annual Meeting Sponsors:

Pfizer

University of Minnesota University of Michigan University of Florida, College of Medicine University of Wisconsin, Madison Monash University

### Thank you to our Colloquium Sponsors:

AbbVie Inc. ChemBridge Corporation Discovery | Charles River Eli Lilly & Co. Janssen Research & Development LLC Millipore Sigma Pfizer Waters Corporation Wilson Sonsini Goodrich & Rosati

### Consider Donating to ASPET as Part of Your Year-End Giving

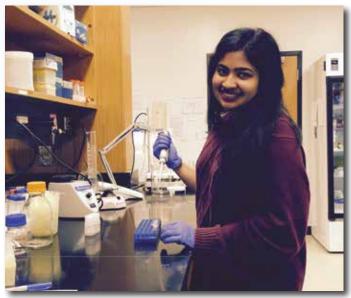
Thank you to all our members for your continued support of ASPET. By renewing your membership each year, publishing in our journals, and attending our annual meeting, you contribute to the growth and success of ASPET and the future of pharmacology.

We especially thank all our individual, institutional, and corporate contributors who have made donations to ASPET above and beyond their membership dues. These donations have helped ASPET support research, publications, travel awards, science advocacy, and career development for scientists. Contributions from members help increase ASPET's impact in the science community and beyond.

If you would like to help support ASPET's mission and strategies for a stronger pharmacology community, please consider donating to ASPET. There are many ways you can give and all donations are tax-deductible.

#### Contribute to ASPET's 2017 Featured Fund: Summer Undergraduate Research Fellowship Fund

Celebrating its 25th anniversary, the ASPET Summer Undergraduate Research Fellowship (SURF) program is designed to introduce pharmacology



research to undergraduates through a 10-week summer laboratory experience. Programs like SURF are not possible without continued support from our members. Funds are used solely for student support in the form of stipends and housing during the summer research period.

"The SURF program is one of the greatest highlights of my undergraduate career, as I spent a summer learning and growing in my research field. I left the program thinking like an investigator and eager to do more; I am a changed student because of my experience with SURF" - Surabhi Rao

Donate to the ASPET SURF Fund at www.aspet.org/ donate.

### Contribute to ASPET's Travel Award Funds

The ASPET Travel Awards program encourages the career development of young scientists through their participation in the ASPET Annual Meeting at Experimental Biology. ASPET believes that attendance at the ASPET Annual Meeting provides the opportunity for young scientists to learn about recent advances in pharmacology, network with peers and international experts in the field of pharmacology, and to contribute their own work to the scientific dialogue. Members may donate to our Young Scientist Travel Award fund, Memorial Travel Award fund, or one of our Commemorative Travel Award funds.

"The travel awards have provided me with amazing opportunities to travel to the meeting and present my research - I believe that they are a great way for young scientists to attend the meeting and be part of the ASPET community!" - 2016 Travel Award Winner

Donate to ASPET's Travel Award Funds at www.aspet.org/donate.

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Surabhi Rao, 2013 SURF participant

#### Contribute to ASPET's Awards Funds

ASPET and its divisions present several major awards to recognize accomplishments in the field of pharmacology. With the support of your generous donations, we will be able to sustain these awards and continue to honor individuals who have made great contributions to pharmacology.

Donate to ASPET's Awards Funds at www.aspet. ora/donate.

#### Contribute to the ASPET Sustaining Members Fund

ASPET member dues pay only a small fraction of the member services that we provide. The Sustaining Members Fund was created to allow our members, who recognize and appreciate the benefits of ASPET membership, to contribute to the many activities of the Society without specifying a single fund.

Donate to the ASPET Sustaining Members Fund at www.aspet.org/donate.

#### Support ASPET When You Shop at AmazonSmile

AmazonSmile is

a website operated

by Amazon that

lets customers

enjoy the same

wide selection

low prices, and

shopping features

of products,

convenient



the AmazonSmile Foundation will donate 0.5% of the price of eligible purchases to the charitable organizations selected by customers.

Shop on AmazonSmile and support ASPET at https://smile.amazon.com/ch/58-6032060.

#### Establish a Commemorative Travel Award Fund

Commemorative **Travel Award Funds** are established to recognize the contributions of members to the field of pharmacology and their service to ASPET. Funds are provided by family, friends,



and colleagues to help support young scientists travel to the ASPET Annual Meeting. Our two most recent commemorative travel awards, the Atul & Jayashree Laddu Travel Award was established in 2016 by Dr. and Mrs. Laddu and the Nancy Rutledge Zahniser Travel Award was established in 2017 by an anonymous donor. Find out more about these new commemorative travel awards in the March 2017 issue of The Pharmacologist. If you are interested in initiating a new ASPET commemorative travel award, please contact ASPET's Executive Officer, Dr. Judy Siuciak at jsiuciak@aspet.org.

#### **Qualified Charitable Distributions** from IRAs

Federal legislation has permanently extended the Qualified Charitable Distribution (QCD) allowing IRA owners over age 70½ to make direct Trustee transfers from a traditional or Roth IRA to a qualified charity, such as ASPET, of up to \$100,000, and exclude it from gross income for federal tax purposes. Since the withdrawal is excluded from income, the payment to the charity is not deductible as a charitable contribution deduction, but may be counted toward an individual's required minimum distribution. Please consult your tax advisor.

ASPET is committed to providing the best possible Society for our members who conduct research to save lives. The research of our members helps to develop new medicines and therapeutic agents to fight existing and emerging diseases. Your tax-deductible contribution, at any amount, will make a difference!



The ASPET election for president-elect, secretary/ treasurer-elect, and councilor will open on January 8, 2018. Eligible voting members will receive notification when the election opens.

All regular, postdoctoral, and retired members are eligible to vote. In addition, the following divisions are holding elections:

- Division for Cancer Pharmacology
- Division for Drug Discovery and Development
- Division for Drug Metabolism and Disposition

### Nominees for President-Elect



#### Wayne L. Backes, PhD

Associate Dean for Research, School of Medicine/Professor of Pharmacology, Louisiana State University Health Sciences Center, New Orleans



Charles P. France, PhD

Professor of Pharmacology and Psychiatry, Robert A Welch Distinguished Chair in Chemistry, University of Texas Health Science Center

- Division for Molecular Pharmacology
- Division for Neuropharmacology
- Division for Toxicology

Members may view the full candidate biographies online at https://vote.associationvoting.com/aspet/ when the election opens.

As the bylaws require, the election will be open for a minimum of thirty (30) days from the day of notification. The election will close on February 9, 2018.

#### Wayne L. Backes, PhD Candidate's Statement

ASPET is a vitally important organization that plays critical roles in educating the public and policy makers regarding the importance of pharmacology and fostering the training and development of educators and scientists in the pharmacological sciences. Personally, ASPET has been instrumental in my career development. I recall the excitement of attending my first Federation meetings, and finally seeing the faces of the names that appeared on the papers I had read. I mention this because we all have memorable experiences from these annual meetings, and these moments were formative events in our careers. For young scientists, ASPET plays important roles, whether it involves being asked to present work at the annual meeting, to review a paper for an ASPET journal, organize a symposium, or participate in division activities. These all represent important ways that ASPET contributes to fostering our careers.

I have served ASPET at the division level in both Toxicology and Drug Metabolism and Disposition, as a member of the ASPET Finance Committee, and as councilor. During this time, there have been numerous changes and challenges in the scientific landscape. These include the proliferation of open access journals, tightening of the National Institutes of Health (NIH) pay lines, and consolidation of medical school pharmacology departments into biological sciences programs. Over the past year, under the leadership of Dave Sibley, Council has completed our strategic planning initiative to diminish the impact of these changes and guide the Society through the next several years. There are six specific goals that comprise the ASPET strategic plan, but these goals can be summarized as (1) strengthening ASPET with regard to both finances and membership and (2) continuing to provide benefits to our members.

#### **Providing Benefits to ASPET Members**

This is one of the central roles of ASPET. These benefits include organizing the program for the Annual Meeting at Experimental Biology, managing the journals, coordinating review of annual scientific awards and travel awards, and providing mentoring services. Some benefits are tangible (such as discounts for meeting attendance and journal submission), but the greatest value of ASPET membership may be intangible, with the meetings serving as a forum for scientific discussion, networking, career development, and advocacy for pharmacology. Over the years, ASPET has been able to provide these and other benefits. It is important for the Society and its members that these benefits continue.

#### Strengthening ASPET

Financial stability is a key aspect to keeping ASPET vibrant. ASPET currently is financially strong, which is essential for us to continue providing benefits to the membership. The primary sources of funding are through the journals, our investment portfolio, and dues. There are several challenges that many of us believe need to be addressed for ASPET to continue to strengthen. One of the strengths of ASPET is the quality of our journals, which also affords financial stability. Although journal revenues peaked in 2014, since then, revenues have declined by about 12%. It is uncertain whether this trend will continue, but we need to continue to provide support for our journals. ASPET journals continue to publish high-guality research, and maintain strong citation and impact statistics. Submitting papers to ASPET journals is one of the best ways to support our Society, and will help maintain this source of support to ASPET. Future support for pharmacology research is a second

challenge for ASPET, as well as the other societies. Cuts to the NIH budget and tightening pay lines have made it more difficult to maintain extramural support. Again, ASPET continues to play an active role in advocacy to increase recognition of the value of pharmacological research and to increase support from funding agencies.

The third challenge is a consequence of changes in teaching curricula. Most undergraduate institutions do not have pharmacology majors or even courses that introduce students to pharmacology, making it more difficult to recruit young scientists. Also, several medical school programs have consolidated their discipline-based departments into a single basic science department, making it more difficult for young faculty to identify as pharmacologists. Although several strategies are in place to recruit our next generation of pharmacologists, these efforts need to be augmented. Successfully meeting these challenges will help us develop our next generation of pharmacologists, continue to provide value to our membership, and maintain ASPET as a vibrant society. If elected, I plan to continue the ongoing efforts of the ASPET leadership to maintain its financial viability, to support and increase awareness of pharmacology, and to strengthen the Society by enhancing the meeting experience and provide support for the career development of our younger members.

#### Charles P. France, PhD Candidate's Statement

I have genuinely enjoyed and benefited enormously from my 25 years as an ASPET member, especially the last 10 years during which I have had the privilege of serving on various committees as division chair, elected councilor, and most recently secretary/treasurer. I have seen first-hand the dedication and passion of the diverse set of educators, scientists, policy makers, and others that comprise the Society. It is truly a great honor for me to be nominated to run for president.

The next president of ASPET will be fortunate to take over the helm of a ship that is on a steady course, thanks to the hard work and vision of prior and current ASPET leaders and staff. A major responsibility and opportunity of the next president will be to advance the strategic plan that was

crafted by ASPET leadership, staff, and many of our members. I enthusiastically supported the initiation and development of the plan, and as president I will vigorously promote its implementation. The goals of the plan are thoughtful, forward thinking, andmost importantly-achievable, providing a roadmap of how the Society can and should evolve in order to remain relevant, attractive, and contemporary. While all six major goals of the plan deserve and will receive our attention, I am most passionate about and dedicated to the goal of "attracting and developing the next generation." In many respects, ASPET, as a society, is in a very good place; however, to remain an attractive and viable scientific organization, the Society and the discipline need a constant infusion of bright, young scientists who are ready and able to carry the torch of pharmacology into the future. To that end, we must continue to improve the annual meeting, provide funding for young people to experience pharmacology (SURF programs) and to attend the annual meeting (travel awards), and take every opportunity to promote education in pharmacology, the ultimate translational discipline. Competition is keen among scientific societies and meetings, and we need to ensure that the Society provides significant value to its members and that the annual meeting remains a showcase for cutting-edge science.

While science and education are at the core of pharmacology, the Society and the discipline must have adequate financial resources for sustained success. The current excellent financial health of the Society will protect the organization and its members from unforeseen challenges in the future. This financial strength is also paying great dividends in terms of significant reinvestment in the membership and the discipline. New initiatives such as the Big Ideas and increasing undergraduate travel fellowships and activities at the annual meeting have generated much enthusiasm among our youngest members and reinvigorated many members who are not so young! Thanks to thoughtful stewardship by the Financial Committee, the Investment Subcommittee, and ASPET staff, the future looks bright in terms of financial security and continued opportunities to reinvest in our members and the discipline of pharmacology.

Notwithstanding the current excellent health of the Society, there are and will continue to be challenges for the organization and the discipline. We must be particularly attentive to open-access journals and the rapidly changing publication environment both to protect and maintain the historically rich and highly respected contributions to science that are routinely made through publications in our journals, and to ensure that the journals continue to do well financially, since they provide a significant portion of the operating expense of the Society. As president, I will work closely with the Board of Publication Trustees to protect and carefully plan for the future of our journals.

As the ultimate translational science, pharmacology is in a unique position to advocate for research and education in the biomedical sciences. Through the hard work of the Science Policy Committee, ASPET staff, individual members who reach out to the public and policy makers to speak on behalf of science and the Society, and many of our younger members who advocate for science through the Washington Fellows Program, ASPET is on the frontlines of promoting the importance of sustained investment in science. ASPET must continue advocating for science and educating nonscientists about the value and the high return on investment of biomedical research. At the same time, we must take responsibility for advancing policies that address concerns regarding rigor and reproducibility in science.

ASPET is a member-driven society. Through divisions, members create the program for the annual meeting, they shape the policies that ASPET addresses through its various committees, and they elect ASPET leadership, from division officers to the Council members. If elected, I will serve the members and the Society in the spirit of what I believe ASPET represents—excellence in, and advocacy for, science and science education—in a manner that best serves the individuals who have dedicated their careers to pharmacology.

### **Nominees for Secretary/Treasurer-Elect**



Michael F. Jarvis, PhD Volwiler Senior Research Fellow & Scientific Director, Global Medical Affairs, AbbVie; Adjunct Professor of Biopharmaceutical Sciences, University of Illinois



#### Jin Zhang, PhD

Professor, Department of Pharmacology, University of California, San Diego (UCSD); Member, Moores Cancer Center at UCSD; Adjunct Professor, Department of Pharmacology & Molecular Sciences, Johns Hopkins University School of Medicine

### **Nominees for Councilor**



#### Kathryn A. Cunningham, PhD

Chauncey Leake Distinguished Professor of Pharmacology, Vice Chair of the Department of Pharmacology, and Director of the Center for Addiction Research, University of Texas Medical Branch, Galveston



Susan L. Ingram, PhD Associate Professor, Department of Neurological Surgery, Oregon Health and Science University

The ASPET 2018 election will open on January 8, 2018. All eligible voters will be sent notification with your login credentials to vote. If you have any questions, please contact membership@aspet.org.



### **ASPET Annual Meeting Program**

For speakers and full session descriptions, visit www.aspet.org/eb2018. Schedule subject to change. All ASPET events will be held at the San Diego Convention Center and the adjacent Marriott Marquis San Diego Marina.

#### Friday, April 20, 2018

Session/Event		Time
Give a Day of Service to San Diego at EB 2018 Contact Dr. Charles	UG PB GS PD	7:00 am – 3:00 pm
France to participate (france@uthscsa.edu or 210-567-6969)		

#### Saturday, April 21, 2018

Session/Event		Time
<b>Teaching Institute: Flipping Not Flopping: Active Learning Strategies</b> <b>for Graduate and Healthcare Pharmacology</b> Chairs: L. Gorman and S. Rahman		10:30 am – 1:00 pm
Assessing Pharmacology in Integrated Curricula Chairs: R. L. Carrier and J. S. Reuben		1:30 pm – 4:00 pm
Clinical Paths for Soluble Epoxide Hydrolase Inhibitors Chairs: J.D. Imig and B. Hammock		1:30 pm – 4:00 pm
Graduate Student – Postdoctoral Colloquium: Tools and Tricks for Success in Science Chair: J. E. Clark	GS PB PD	1:30 pm – 4:00 pm
ASPET Business Meeting and Awards Presentation	UG PB GS PD	4:30 pm – 6:00 pm
Tang Prize Lecture         Keynote: Feng Zhang       (All Society EB lecture on CRISPR)		6:00 pm – 7:00 pm
All Society EB Welcome Reception	UG PB GS PD	7:00 pm – 8:30 pm

#### Sunday, April 22, 2018

Session/Event		Time
Diversity and Inclusion Breakfast Facilitator: Iris Wagstaff	UG PB GS PD	7:30 am – 9:30 am
John J. Abel Award in Pharmacology Lecture Keynote to be announced in January		8:30 am – 9:15 am
ASPET Presidential Symposium: Deadly Liaisons: Squeezing the Life Out of Cancer Chairs: J. Schuetz and M. A. Bjornsti		9:30 am – 12:00 pm
Nancy Zahniser Memorial Symposium: The Dopamine Transporter in Health and Disease Chairs: L. Daws and H. Khoshbouei		9:30 am – 12:00 pm
Ray Fuller Lecture and Symposium: <i>State-of-the-Art on Regenerative Pharmacology: The Future is Now</i> <i>Award Lecturer: George Christ</i> <i>Symposium Chairs: G. Christ and K. Marra</i>		9:30 am – 12:00 pm
<i>Placental Xenobiotic Metabolism and Transport</i> Chairs: Q. Mao and L. Aleksunes		9:30 am – 12:00 pm
Humanized in vitro and in vivo Models in Drug Discovery and Development Chairs: X. Ding and A. Sawant-Basak		9:30 am – 12:00 pm
Undergraduate Networking and Career Development Luncheon	UG PB	12:15 pm – 2:00 pm
ASPET Poster Presentations	UG PB GS PD	12:30 pm – 2:30 pm
Daily Poster Datablitz	UG PB GS PD	1:00 pm – 2:00 pm
Goodman and Gilman Award in Receptor Pharmacology Lecture Keynote to be announced in January		2:30 pm – 3:15 pm

### **ASPET Welcomes our Guest Societies!**

The following are ASPET guest societies at EB 2018. Members of these organizations can register for EB using the ASPET member discount and can sponsor their own abstracts.

Behavioral Pharmacology Society British Pharmacological Society Global GI Club International Transmembrane Transporter Society

#### Sunday, April 22, 2018, continued

Adhesion GPCRs as Neurotherapeutic Targets Chairs: G. Tall and X. Piao		3:30 pm – 6:00 pm
<i>Epigenetics in Drug Discovery</i> Chairs: V. Vaka and J. Jilek		3:30 pm – 6:00 pm
<b>Pro-Psychotic Effects of Drugs of Abuse</b> Chairs: M. D. Berquist and M. W. Wood		3:30 pm – 6:00 pm
<i>The Microbiome and Cancer</i> Chairs: M. A. Bjornsti and H. Jeong		3:30 pm – 6:00 pm
<b>Update on the Gaseous Signaling Molecules NO, H2S, and CO</b> Chairs: A. Papapetropoulos and N. S. Bryan		3:30 pm – 6:00 pm
ASPET Student / Postdoc Poster Competition	UG PB GS PD	6:30 pm – 8:30 pm
ASPET Student / Postdoc Mixer	UG PB GS PD	8:30 pm – 11:00 pm

### Give a Day of Service to San Diego at EB 2018

Join us for a day of volunteer service on Friday, April 20, 2018

Since 2009, ASPET members attending Experimental Biology have given a day of volunteer service in the local communities where we convene. Volunteer activities have ranged from home construction to painting, cleaning, stocking, food preparation, and food service.

At EB 2018, EB attendees will spend the day at St. Vincent de Paul Village, doing whatever we can to help the dedicated people at Father Joe's Villages provide assistance to San Diegans.

If you plan to join us, please contact Charles P. France at your earliest convenience at france@uthscsa.edu or 210-567-6969. Space is limited and further details will be provided to those who volunteer.

> At EB 2017 in Chicago, ASPET members spent the day volunteering at Pacific Garden Mission, helping to provide food and shelter for individuals in need.



#### Monday, April 23, 2018

Session/Event		Time
Otto Krayer Award in Pharmacology Lecture Keynote to be announced in January		8:30 am – 9:15 am
Surmounting the Insurmountable: Obstacles in Drug Discovery and Development – Real World Case Studies Chairs: K. He and P. Hollenberg	PB GS PD	9:30 am – 12:00 pm
<b>G Proteins and G Protein-Coupled Receptors in Cancer</b> Chairs: J.S. Gutkind and P. Insel		9:30 am – 12:00 pm
<b>RNA Binding Proteins in Cardiovascular Disease</b> Chair: M. Tranter		9:30 am – 12:00 pm
<b>The Bright and Dark Side of Nrf2 for Tissue Protection</b> Chair: Q. M. Chen		9:30 am – 12:00 pm
<b>Transporters at the Blood-CNS Barriers</b> Chairs: J. Wang and P. T. Ronaldson		9:30 am – 12:00 pm
ASPET Poster Presentations	UG PB GS PD	12:30 pm – 2:30 pm
Daily Poster Datablitz	UG PB GS PD	1:00 pm – 2:00 pm
P.B. Dews Lifetime Achievement Award for Research in Behavioral Pharmacology Lecture Keynote to be announced in January		2:30 pm – 3:15 pm
Division for Translational and Clinical Pharmacology – Young Investigator Awards Platform Session and Early Career Faculty Showcase	UG PB GS PD	3:00 pm – 6:00 pm
Division for Pharmacology Education – Bringing Basic Sciences into Clinical Education Chairs: R. J. Theobald and K. J. Karpa		3:30 pm – 6:00 pm
Division for Behavioral Pharmacology – Looking to the Future of Behavioral Pharmacology Chairs: R. I. Desai and E. M. Jutkiewicz		3:30 pm – 6:00 pm
Division for Cancer Pharmacology – Young Investigators Symposium	UG PB GS PD	3:30 pm – 6:00 pm
Division for Neuropharmacology – Postdoctoral Scientist Award Finalists	UG PB GS PD	3:30 pm – 6:00 pm
Division Annual Meetings for:• Behavioral Pharmacology• Pharmacology Education• Cancer Pharmacology• Translational and Clinical Pharmacology• Neuropharmacology	UG PB GS PD	6:00 pm – 6:30 pm
<ul> <li>Division Joint Mixers for:</li> <li>Behavioral Pharmacology and Neuropharmacology</li> <li>Cancer Pharmacology, Drug Discovery and Development, Pharmacology Education, and Translational and Clinical Pharmacology</li> </ul>	ug pb gs pd	6:30 pm – 8:30 pm
Young Experimental Scientists Y.E.S. Mixer (All Society EB event for students and postdocs)	UG PB GS PD	9:00 pm – 11:00 pm

#### Tuesday, April 24, 2018

Session/Event		Time
Julius Axelrod Award in Pharmacology Lecture Keynote: Michel Bouvier		8:30 am – 9:15 am
Julius Axelrod Symposium: The Pluridimensionality of G Protein-Coupled Receptor (GPCR) Signaling Chairs: M. Bouvier and A. Salahpour		9:30 am – 12:00 pm
<b>'Bath Salts': The Ever-Changing Landscape of Synthetic Cathinones</b> Chairs: S. J. Kohut and M. A. Taffe		9:30 am – 12:00 pm
<b>Can Metabolic Vulnerabilities in Tumors be Therapeutically</b> <b>Exploited?</b> Chairs: S. Cole and K. van de Wetering		9:30 am – 12:00 pm
<b>Challenges and Promises of CNS Orphan Drug Development: Stories</b> <b>from Bench to Clinic</b> Chairs: D. Davies and J. Paul		9:30 am – 12:00 pm
<b>There's Always Room for Dessert: Examining the Effect of Insulin</b> <b>and High Fat Diet on Neurotransmission, Motivation and Cognition</b> Chairs: C. R. Ferrario and L. P. Reagan		9:30 am – 12:00 pm
Division for Translational and Clinical Pharmacology – Trainee Mentoring and Career Development	UG PB GS PD	12:30 pm – 2:00 pm
ASPET Poster Presentations	UG PB GS PD	12:30 pm – 2:30 pm
Daily Poster Datablitz	UG PB GS PD	1:00 pm – 2:00 pm

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#### Tuesday, April 24, 2018 continued

Bernard B. Brodie Award in Drug Metabolism Lecture Keynote to be announced in January		2:30 pm – 3:15 pm
<ul> <li>Division for Cardiovascular Pharmacology Programming</li> <li>Paul M. Vanhoutte Distinguished Lectureship in Vascular Pharmacology</li> <li>Trainee Showcase</li> <li>Hot Topics in Cardiovascular Pharmacology</li> </ul>		2:30 pm – 6:00 pm
<b>Computational Approaches to G Protein-Coupled Receptor Structure</b> <b>and Function</b> Chairs: E. Kelly and A. Conibear		3:30 pm – 6:00 pm
Division for Cardiovascular Pharmacology Trainee Showcase Chair: M. Tranter		3:30 pm – 6:00 pm
Division for Drug Metabolism and Disposition Gillette Awards and Junior Investigator Platform Session		3:30 pm – 6:00 pm
Division for Molecular Pharmacology Postdoctoral Scientist Award Finalists		3:30 pm – 6:00 pm
Division for Toxicology – Novel Genetic-based Tools for Toxicity Screening, Precision Medicine, and Mode of Action Analysis Chair: A. Harrill and B. Cummings		3:30 pm – 6:00 pm
Division Annual Meetings• Cardiovascular Pharmacology• Drug Discovery and Development• Drug Metabolism and Disposition		6:00 pm – 6:30 pm
<ul> <li>Division Mixers for:</li> <li>Drug Metabolism and Disposition and Toxicology</li> <li>Cardiovascular Pharmacology</li> <li>Molecular Pharmacology</li> </ul>	UG PB GS PD	6:30 pm – 8:30 pm

### **Sponsorship Opportunities**

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#### Wednesday, April 25, 2018

Session/Event		Time
Journals Workshop: Hear It from the Editors Chairs: R. C. Dodenhoff and M. Vore	PB GS PD	8:30 am – 11:00 am
<b>Cardiovascular Consequences of Metabolic Targeting in Obesity</b> Chairs: A. C. Arnold and D. I. Diz		8:30 am –11:00 am
<b>The Organization of Signal Transduction and Its Impact on Receptor</b> <b>Function</b> Chair: J. M. Streicher		8:30 am – 11:00 am
<b>Tissue Free Drug Concentrations</b> Chair: D. Zhang		8:30 am – 11:00 am
University Startups: From Invention to Commercialization Chairs: H. Neelakantan, K. Tonsfeldt, and S. Umar	UG PB GS PD	8:30 am – 11:00 am

### **EB** Programming



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### **Important Dates**

Tuesday | February 27, 2018 Discounted Registration Deadline

Tuesday | March 28, 2018

**Discounted Housing Deadline** 

#### Saturday | April 21, 2018

ASPET Annual Business Meeting from 4:30 pm – 6:00 pm in San Diego

April 21 – April 25, 2018 EB 2018 in San Diego



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### **Division Meetings and Activities**

View the full schedule of sessions by division online at: http://bit.ly/2iS3rvZ.

Ş		Behavioral Pharmacology	or Asset
Monday, April 23 7:00 am – 8:15 am			BEH Executive Committee Meeting (invitation only)
Ν	1onday, April 23	2:30 pm – 3:15 pm	P.B. Dews Lifetime Achievement Award for Research in Behavioral Pharmacology Lecture
Ν	londay, April 23	3:30 pm – 6:00 pm	Division Programming: "Looking to the Future of Behavioral Pharmacology"
Ν	londay, April 23	6:00 pm – 6:30 pm	BEH Annual Division Meeting
Ν	1onday, April 23	6:30 pm – 8:30 pm	Joint Mixer: BEH with Neuropharmacology
.00	<b>* ( )</b> (	Cancer Pharmacology	ST ASPET
S	unday, April 22	7:00 am – 8:15 am	DCP Executive Committee Meeting (invitation only)
Ν	londay, April 23	3:30 pm – 6:00 pm	Division Programming: Young Investigators Symposium
Ν	londay, April 23	6:00 pm – 6:30 pm	DCP Annual Division Meeting
Ν	1onday, April 23	6:30 pm – 8:30 pm	Joint Mixer: DCP with Drug Discovery and Development, Pharmacology Education, and Translational and Clinical Pharmacology
	the second second	Cardiovascular Pharmacology	HASPET
S	iunday, April 22	7:00 am – 8:15 am	CVP Executive Committee Meeting (invitation only)
Т	uesday, April 24	2:30 pm – 6:00 pm	Division Programming: Paul M. Vanhoutte Distinguished Lectureship in Vascular Pharmacology, Trainee Showcase, Hot Topics in Cardiovascular Pharmacology
ζт	uesday, April 24	6:00 pm – 6:30 pm	CVP Annual Division Meeting
Т	uesday, April 24	6:30 pm – 8:30 pm	CVP Mixer
		Drug Discovery and Developme	
Ν	londay, April 23	7:00 am – 8:15 am	DDD Executive Committee Meeting (invitation only)
Ν	1onday, April 23	6:30 pm – 8:30 pm	Joint Mixer: DDD with Cancer Pharmacology, Pharmacology Education, and Translational and Clinical Pharmacology
Т	uesday, April 24	6:00 pm – 6:30 pm	DDD Annual Division Meeting
	Vednesday, April 25	8:30 am – 11:00 am	Division Programming: "University Startups: From Invention to Commercialization"
6		Drug Metabolism Disposition	
Ν	londay, April 23	7:00 am – 8:15 am	DMDD Executive Committee Meeting (invitation only)
Т	uesday, April 24	2:30 pm – 3:15 pm	Bernard B. Brodie Award in Drug Metabolism Lecture
Т	uesday, April 24	3:30 pm – 6:00 pm	Division Programming: Gillette Awards and Junior Investigator Platform Session
Т	uesday, April 24	6:00 pm – 6:30 pm	DMDD Annual Division Meeting
Т	uesday, April 24	6:30 pm – 8:30 pm	Joint Mixer: DMDD with Toxicology

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	YN U	
	Molecular Pharmacology	of ASPET
Sunday, April 22	7:00 am – 8:15 am	MP Executive Committee Meeting (invitation only)
Tuesday, April 24	3:30 pm – 6:00 pm	Division Programming: Postdoctoral Scientist Award Finalists
Tuesday, April 24	6:00 pm – 6:30 pm	MP Annual Division Meeting
Tuesday, April 24	6:30 pm – 8:30 pm	MP Mixer
	Neuropharmaco	of ASPET
Monday, April 23	7:00 am – 8:15 am	NEU Executive Committee Meeting (invitation only)
Monday, April 23	3:30 pm – 6:00 pm	Division Programming: Postdoctoral Scientist Award Finalists
Monday, April 23	6:00 pm – 6:30 pm	NEU Annual Division Meeting
Monday, April 23	6:30 pm – 8:30 pm	Joint Mixer: NEU with Behavioral Pharmacology
	Pharmacology Education	of ASPET
Monday, April 23	7:00 am – 8:15 am	DPE Executive Committee Meeting (invitation only)
Monday, April 23	3:30 pm – 6:00 pm	Division Programming: "Bringing Basic Sciences into Clinical Education"
Monday, April 23	6:00 pm – 6:30 pm	DPE Annual Division Meeting
Monday, April 23	6:30 pm – 8:30 pm	Joint Mixer: DPE with Cancer Pharmacology, Drug Discovery and Development, and Translational and Clinical Pharmacology
	Toxicology	of ASPET
Tuesday, April 24	7:00 am – 8:15 am	TOX Executive Committee Meeting (invitation only)
Tuesday, April 24	3:30 pm – 6:00 pm	Division Programming: "Novel Genetic-based Tools for Toxicity Screening, Precision Medicine, and Mode of Action Analysis"
Tuesday, April 24	6:00 pm – 6:30 pm	TOX Annual Division Meeting
Tuesday, April 24	6:30 pm – 8:30 pm	Joint Mixer: TOX with Drug Metabolism and Disposition
	Translational & Clinical Pharmaco	
Sunday, April 22	7:00 am – 8:15 am	TCP Executive Committee Meeting (invitation only)
Sunday, April 22	9:30 am – 12:00 pm	Ray Fuller Lecture and Symposium
Monday, April 23	3:00 pm – 6:00 pm	Division Programming: Young Investigator Awards Platform Session and Early Career Faculty Showcase
Monday, April 23	6:00 pm – 6:30 pm	TCP Annual Division Meeting
Monday, April 23	6:30 pm – 8:30 pm	Joint Mixer: TCP with Cancer Pharmacology, Drug Discovery and Development, and Pharmacology Education
Tuesday, April 24	12:30 pm – 2:00 pm	TCP Trainee Mentoring and Career Development

**BEH** = Behavioral Pharmacology, **CVP** = Cardiovascular Pharmacology, **DCP** = Cancer Pharmacology, **DDD** = Drug Discovery and Development, **DMDD** = Drug Metabolism and Disposition, **MP** = Molecular Pharmacology, **NEU** = Neuropharmacology, **DPE** = Pharmacology Education, **TCP** = Translational and Clinical Pharmacology, **TOX** = Toxicology 234

### **ASPET Meetings**

The following are *invitation-only* meetings. Schedule is subject to change.

#### Thursday, April 19, 2018

			//	
5:00 pm – 10:00 pm	Finance Committee Me	eting		

#### Friday, April 20, 2018

8:00 am – 6:00 pm	Council Meeting
11:00 am – 8:00 pm	Mentoring Network: Coaching for Career Development (mentors)
1:00 pm – 8:00 pm	Mentoring Network: Coaching for Career Development (mentees)
2:00 pm – 5:00 pm	Council of Division Chairs
6:30 pm – 9:00 pm	Council Dinner

#### Saturday, April 21, 2018

8:30 a <mark>m – 1:30</mark> pm	Mentoring Network: Coaching for Career Development (mentors and mentees)
2:00 pm – 3:00 pm	Science Policy Committee
8:30 pm – 10:00 pm	President's Reception (by invitation only)

#### Sunday, April 22, 2018

7:30 pm – 10:00 pm	Board of Publications Trustees Joint Editorial Boards Dinner
12:30 pm – 2:30 pm	Board of Publications Trustees Meeting
12:15 pm – 2:00 pm	Undergraduate Networking and Career Development Luncheon
7:30 am – 9:30 am	Diversity and Inclusion Breakfast
7:30 am – 9:30 am	JPET Associate Editors Meeting
7:00 am – 8:15 am	Executive Committee – Div. for Cancer Pharmacology
7:00 am – 8:1 <mark>5</mark> am	Executive Committee – Div. for Molecular Pharmacology
7:00 am – 8:1 <mark>5</mark> am	Executive Committee – Div. for Cardiovascular Pharmacology
7:00 am – 8:15 am	Executive Committee – Div. for Translational and Clinical Pharmacology

### **EB** Career Center

#### Over 30 workshops to help:

- choose a career
- search for a job
- improve networking skills
- enhance your professional skills

#### **One-on-one appointments to:**

- critique your resume / CV
- assess your personal statement essay
- practice your poster/oral presentation with a mentor
- general career counseling

#### Monday, April 23, 2018

Executive Committee – Div. for Drug Metabolism and Disposition
Executive Committee – Div. for Drug Discovery and Development
Executive Committee – Div. for Neuropharmacology
Executive Committee – Div. for Pharmacology Education
Executive Committee – Div. for Behavioral Pharmacology
Molecular Pharmacology Editorial Board Meeting
Pharmacological Reviews Editorial Board Meeting
Division Communications Officers
Past President's Dinner

#### Tuesday, April 24, 2018

7:00 am – 8:15 am	Executive Committee – Div. for Toxicology
7:00 am – 8:15 am	Nominating Committee Meeting
7:00 am – 8:15 am	Mentoring and Career Development Committee
7:30 am – 9:30 am	Drug Metabolism and Disposition Editorial Board Meeting
2:15 pm – 3:15 pm	Young Scientists Committee
3:00 pm – 5:00 pm	Pharmacology Research & Perspectives Management Committee

#### Wednesday, April 25, 2018

11:30 am – 2:30 pm

Program Committee

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# **Enbrel:** A biotechnology breakthrough

Rebecca J. Anderson, PhD

When they called her name, Elizabeth Petersen navigated her way to the microphone. The ballroom at the Holiday Inn in Gaithersburg, Maryland, was packed with researchers,

industry executives, and government officials. Elizabeth, by contrast, was just an ordinary citizen, permitted a few minutes to speak during the open public hearing part of this meeting (1).

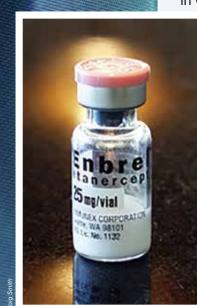
The impressive thing was not that Elizabeth came as an unsolicited participant, nor that she had paid her own travel expenses from Chicago. The impressive thing was that she walked effortlessly to the microphone, free of the crippling and painful arthritis that she had suffered for 36 years. She had been taking an experimental drug, and she wanted to tell the US Food and Drug Administration (FDA) officials—in person—that they should approve this drug for all rheumatoid arthritis patients.

Enbrel's success in treating patients like Elizabeth was all the sweeter because it had survived, despite skeptical experts and several serious setbacks.

#### A New Era

In 1980, the US Supreme Court ruled that genetically engineered microorganisms could be patented. Immediately, a generation of pioneering molecular biologists, full of bright ideas and entrepreneurial spirit, left academia and launched the biotechnology industry.

Among them were Steven Gillis and Christopher Henney, immunologists who aimed to make immune-response-based



Enbrel vial



medicines (2, 3). In 1981, they left the Fred Hutchinson Cancer Research Center and founded Immunex in Seattle, WA. Gillis recruited the best researchers in their fields and fostered a "collegialcritical" environment. He defined "the boundaries of the sandbox" and

Steven Gillis

encouraged everyone to be creative within those boundaries (3).

Energized researchers at Immunex would meet by chance in the hallway and end up discussing science for hours (4). They employed a broad suite of innovative technologies, cloned a long list of genes, and expressed the corresponding recombinant proteins (2). Among their early products were interleukin-based drugs and GM-CSF (granulocyte macrophage colony stimulating factor).

Stephen Duzan, an entrepreneur with no science background, joined the management team and used his business savvy to keep Immunex solvent (2, 3). Through the 1980s, Duzan sold or licensed the company's proprietary technologies, which funded the ambitious research program, but profits remained elusive (2).

Clinical trials of GM-CSF began in 1987, with Hoechst Roussel Pharmaceuticals assisting the young Immunex clinical team (2, 5, 6). GM-CSF proved to be effective in accelerating white cell recovery following bone marrow transplantation in cancer patients and was approved by the FDA in 1991 (2).

Immunex's stock skyrocketed (2). Anticipating demand, the company had invested heavily in a large GM-CSF manufacturing plant (3). Unfortunately, Amgen's Neupogen, a direct competitor product, was approved a month before GM-CSF for the much larger chemotherapy market. Neupogen maintained a 10-fold sales advantage over GM-CSF, and Immunex's new manufacturing facility sat underutilized (2, 3).

Immunex next concentrated on developing PIXY 321, a synthetic molecule that incorporated the properties of GM-CSF and Interleukin-3. PIXY 321 was intended to stimulate platelet and white cell counts (2).

#### Climbing the TNF Wall

When Craig Smith joined Immunex in 1988, researchers in the Receptor Biochemistry and Biophysics Department were focused on Interleukin-2 (7). But Smith was intrigued with another cytokine, tumor necrosis factor (TNF).

"Tumor necrosis factor" had been coined as a term in the 1960s by researchers who found evidence of something that induced tumor regression. In 1984, Bharat Aggarwal and colleagues finally succeeded in isolating two cytotoxic substances, subsequently named TNF- $\alpha$  and TNF- $\beta$ —the first members of what was to become a superfamily of cytokines that can cause cell death *(8, 9)*.

Enbrel structure – a molecule of TNF (red) bound to Enbrel (yellow and green)

After researchers confirmed that TNF causes rapid necrosis

of experimental cancers, they cloned the gene and produced recombinant TNF for clinical trials (9, 10). Unfortunately, rather than attacking the patients' tumors, TNF had a paradoxical tumor-promoting effect (7, 10). Consequently, biotech companies saw no commercial value in TNF, and researchers turned to other biologic drug candidates.

To Smith, "tumor necrosis factor" was really a misnomer. Less than 1% of primary tumor cells or tumor cell lines are killed by TNF (7). Instead, TNF's primary role is to orchestrate the immune response to any challenge—whether it be a virus, bacteria, or fungus. In the oncology clinical trials, recombinant TNF had sent the patients' immune system into pathological overdrive, producing a condition similar to shock (11).

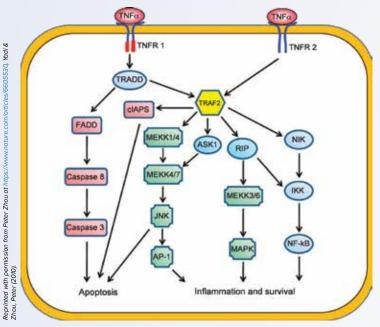
Similarly, up-regulation of TNF could explain the chronic inflammation seen in autoimmune diseases (7, 11). Immunex's ongoing immune-suppressor-factor program focused primarily on the interleukins (3). Smith thought that suppressing TNF would also be therapeutic (11).

At that time, TNF was not commercially available, and production of monoclonal antibodies was still in

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its infancy (7). Researchers at Centacor had created a chimeric TNF antibody called infliximab (Remicade<sup>®</sup>) by attaching the variable region of the mouse TNF antibody to the Fc region of human IgG1 (12).

Taking advantage of the Gillis-authorized sandbox, Smith, in his spare evenings, began expressing and purifying recombinant forms of TNF (7). Then, he used radiolabeled TNF to isolate, clone, and express the TNF receptor (13).



TNF signaling pathways

TNF binds to two receptors: TNFR-1 and TNFR-2. The extracellular (i.e., the binding site) portion of these membrane-bound receptors is functional, like the intact receptors. Extracellular TNFR-1 (p55) and TNFR-2 (p75) circulate as "soluble receptors" and can bind to TNF everywhere in the body (*13, 14*). In a similar manner, the soluble (extracellular) portion of the IL-1 receptor specifically binds to IL-1 (*15*).

The soluble TNF receptors expressed by Smith and his colleague, Ray Goodwin, bound to TNF with relatively low affinity (14). TNF is a homo-trimer, and on the cell surface it normally binds to 2-3 receptor molecules. This multiplicity increases receptor affinity for TNF through interlocking "cooperative binding" (7). Smith aimed to construct a molecule that mimicked the membrane-bound receptor configuration and would have much higher affinity for TNF than the monomeric soluble receptor.

Smith clipped human IgG1, leaving just the Fc stem and a portion of the two hinge regions. He then fused a human p75 soluble TNF receptor to each of the hinges and called the resulting molecule a "TNFR:Fc fusion protein" *(11, 16)*. The two soluble receptors in this configuration accommodated 1-2 binding domains of the TNF molecule *(7)*. As predicted, TNFR:Fc had up to a 1000-fold greater affinity for TNF than the monomeric p75 soluble receptor and was equivalent to the interlocking membrane-bound receptors' affinity for TNF *(7, 14)*.



Craig Smith (left) and Raymond Goodwin



Cindy Jacobs

#### **Assessing Activity**

To determine the biological activity of his molecules, Smith collaborated with Cindy Jacobs in Immunex's preclinical labs. Jacobs had joined Immunex in 1985 as a part-time scientist while she was still in medical school and initially supported the GM-CSF and interleukin projects *(17)*.

Jacobs, who held a PhD in veterinary pathology/ microbiology, set up animal models to test the efficacy of the soluble IL-1 receptor and TNFR:Fc. Each of the molecules was effective in animal models of antigeninduced arthritis, and they were more effective given together than either one alone (15). TNFR:Fc also protected mice from otherwise lethal injections of lipopolysaccharide, an animal model of sepsis (14).

Using radiolabeled TNFR:Fc, Jacobs followed its pharmacokinetics and distribution in serial blood and tissue sections collected from the animals. She found that TNFR:Fc had a 5-fold longer serum half-life than the soluble p75 receptor (14, 15). Smith and Jacobs moved quickly to secure Immunex's patent rights to TNFR:Fc (16).

#### **Looking for Winners**

Despite Duzan's efforts, GM-CSF's flagging sales disappointed investors. At the same time, Immunex's research expenditures were, if anything, increasing. In 1993-1994, in rapid succession, American Cyanamid acquired majority ownership of Immunex, and then American Home Products purchased American Cyanamid (2).

In parallel, clinical trial results indicated that PIXY 321 was ineffective – a crushing blow to both the clinical team and the new managing partners. In October 1993, the project team shut down the PIXY 321 program (6).

Immunex researchers continued interleukin development, exploring the soluble IL-1 receptor for asthma/allergy, rheumatoid arthritis, and inflammatory bowel disease (15). Preliminary clinical trials showed that the molecule protected healthy volunteers from a cutaneous allergic challenge (18).

With TNFR:Fc, the animal model results justified clinical trials in several therapeutic areas, but Immunex's decision makers gave sepsis top priority.

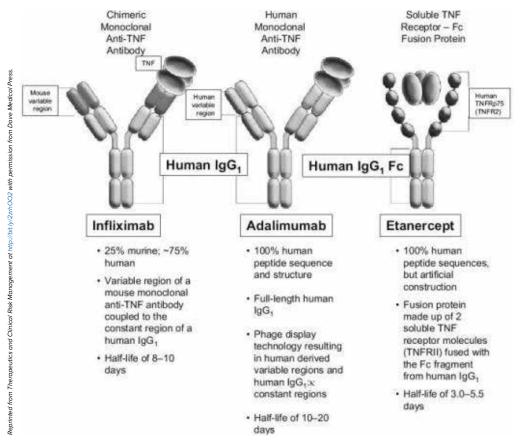


Figure 1: Etanercept structure in comparison with other TNF antagonists.

The sepsis mortality rate was about 40%, and clinicians had virtually nothing to treat it *(19, 20)*.

Immunotherapy was just emerging as a promising new approach to tackle sepsis, and many companies were developing immunology-based treatments (7, 17). Some of those companies, like Immunex, had created fusion proteins by mix-and-match combinations of the p55 or p75 TNF receptor with the Fc region of IgG1 or IgG3. These fusion proteins were effective in animal models, but no one knew whether the animal results predicted efficacy in sepsis patients (14).

Clinical trials for sepsis were usually completed rapidly, with a clear endpoint that required relatively few patients. If TNFR:Fc worked, it would be quickly approved (7, 17). Then, Immunex could consider clinical trials for rheumatoid arthritis, inflammatory bowel disease, and other disorders (15).

#### **Sepsis**

The initial clinical results were encouraging (19). In healthy subjects, TNFR:Fc was safe at doses that were subsequently used in sepsis patients. In addition, when the subjects were challenged with endotoxin, TNFR:Fc bound to all TNF- $\alpha$  circulating in their blood (21).

Immunex's clinical team, led by Janis Agosti, moved quickly to launch a large blinded, randomized, placebo-controlled trial (19, 21). Because sepsis is lifethreatening and progresses rapidly, the lag between enrolling and treating patients was short. Throughout the winter-summer of 1992-1993, Immunex clinical associates traveled continuously from coast to coast to monitor and support the 15 clinical sites (19).

Immunex had also chartered an independent Data Monitoring Committee, which was charged with ensuring the safety of these critically ill patients and periodically reviewing the incoming trial data. The clinical investigators had enrolled about half of the targeted number of patients when the Committee became concerned (5). Immunex's data management group was asked to decode the treatments of the patients who had died.

Unfortunately, most of the deaths occurred in TNFR:Fc-treated patients. And it was a dosedependent effect (21). For the clinical team, it was "very scary to think that the drug may be causing deaths" (5). Immunex immediately stopped the trial. Steve Gillis, as acting CEO, had the unenviable task of notifying American Cyanamid, the FDA, and the public of the results (3).

### ...it was "very scary to think that the drug may be causing deaths".

Through the 1990s, dozens of clinical trials of various anti-inflammatory agents failed to show a benefit in roughly 15,000 sepsis patients, despite impressive efficacy in animal models (20). It now appears that TNF's predominant role in sepsis is protective, helping the patient combat systemic bacterial toxicity (1, 20). One by one, each of the sponsoring drug companies, including Immunex, moved away from sepsis therapeutics.

At Immunex, it was a tumultuous time (6). The company had invested heavily in the sepsis trial, and its failure was an especially hard blow—more than PIXY 321 (6, 7). Further investment in TNFR:Fc did not make good business sense. "There were discussions whether to run or walk away" (17). The company decided to sell its ownership of the product, and researchers moved to more promising drug candidates (5, 22).

#### **Limping Along**

Despite the company's focus on sepsis, Craig Smith thought of TNFR:Fc as an innovative treatment for autoimmune diseases, and rheumatoid arthritis (RA) was always at the top of his list (7). He vividly remembered his Irish-Catholic grandmother, who had raised a large family in the Midwest during the Depression, despite suffering from severe rheumatoid arthritis. She made a deep impression on her young grandson, and now his TNFR:Fc might conquer the disease that had plagued her (7).

Disease-modifying antirheumatic drugs (DMARDs), such as methotrexate, sulfasalazine, and hydroxychloroquine, were available and could retard disease progression. But many patients did not adequately respond, and many stopped treatment due to toxicity *(23)*.

In parallel with the sepsis trial, Cindy Jacobs (at this time a clinical research director) oversaw small clinical trials to probe IL-1-receptor and TNFR:Fc efficacy in rheumatoid arthritis (15). Seeking interested investigators, Immunex representatives attended the



Keystone Symposium in Colorado. Among those they approached was Larry Moreland, a young rheumatologist from the University of Alabama (24).

Moreland headed the university's RA intervention program and had been a clinical investigator for trials of several

Larry W. Moreland

biologic drug candidates. "None of them worked very well" (24). But the results were presented or published, and Moreland, along with his chairman, William Koopman, became widely recognized as rheumatology clinical investigators (24).

At the Keystone meeting, the Immunex representatives asked Moreland which molecule he wanted to test. He picked TNFR:Fc (24). Richard Pope, a rheumatologist at Northwestern University, took the IL-1-receptor. The main objectives of these phase 1 trials were safety and pharmacokinetics, but Moreland and Pope also collected efficacy data on the patients' pain and swollen joints, as well as biochemical markers of arthritis (i.e., erythrocyte sedimentation rate and C-reactive protein) (25, 26).

After receiving the sepsis trial results, American Cyanamid executives wanted to cease all work on TNFR:Fc. Gillis convinced them to at least continue the ongoing trials, and the FDA agreed (3). Most of that work was outsourced to contractors.

Unfortunately, the results from Northwestern only added to the gloom at Immunex. The soluble IL-1 receptor provided no benefit to Pope's arthritis patients, up to doses that produced dose-limiting toxicity (26).

Moreland's TNFR:Fc trial gave "a glimmer of hope" (24). But Immunex needed more than a "glimmer" of RA data to attract a pharmaceutical buyer. Gillis explained, "We had the guts to go ahead" (3). They used their remaining clinical supplies of TNFR:Fc to conduct a phase 2 trial (22).

Consuelo Blosch, the Immunex clinician now in charge of the RA program, called Moreland and asked some very specific questions (24). Over the

phone, they reviewed the results of the phase 1 trial: First and foremost, the drug was safe. The only significant finding was that some patients experienced an injection-site reaction, but that was mild and manageable. Second, the patients had exhibited an overall 45% clinical improvement, and TNFR:Fc decreased the patients' C-reactive protein levels. When drug treatment stopped, these effects reversed (25).

In that half-hour phone call, Moreland and Blosch designed the phase 2 clinical trial, which would include three dose levels of TNFR:Fc (24). At Immunex, Blosch finalized the randomized, double-blind, placebo-controlled clinical protocol (27). Within a few days, Moreland received it—the fastest he had ever initiated a new clinical trial (24).



But Ann Dugan, the sole Immunex clinical associate assigned to the study, had difficulty persuading other rheumatologists to participate (22). The positive data on TNFR:Fc were slim, biologic drugs from other companies had performed poorly, and rheumatologists, in general, were

Ann Dugan

reluctant to use an injectable biologic drug. "Most of the published rheumatologists wouldn't even return my calls" (22).

Aside from the trial's co-leads (Moreland and Scott Baumgartner at the Physician's Clinic of Spokane), most of the investigators whom Dugan successfully persuaded "just wanted to be on the cutting edge of research for their patients" (22). Moreland and Blosch specifically set criteria that would attract patients: "They were the worst of the worst" (24). Still, Dugan constantly traveled to the clinical sites, urging reluctant investigators to enroll patients in the trial (22).

#### I Feel So Good

One of those patients was Elizabeth Petersen in Chicago (1). She had been diagnosed with rheumatoid arthritis at the age of 29 and was told there was no cure. Her joints were so tender she avoided walking

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and shaking hands. Sometimes, her attacks eased, only "because it's hurting more someplace else" (1).

Her doctors first prescribed vitamin B<sub>12</sub> injections to alleviate the anemia that accompanied her arthritis. Then, she tried a variety of NSAIDs (nonsteroidal anti-inflammatory drugs). Some of them provided no relief. Others made her violently ill. She took gold injections until she tasted metal, then prednisone, which made her moon-faced and depressed, and finally cortisone, which contributed to bone loss (1). When her "preexisting condition" resulted in a loss of insurance coverage, she resorted to home remedies: aspirin, vitamins, exercise, and "healthy" foods.

In 1994, Elizabeth enrolled in Immunex's phase 2 trial, and by chance she landed in the group receiving the highest drug dose. The only side effect she experienced was an injection-site reaction, consisting of "a minor itch that lasted about 5 minutes" (1). Soon, she found herself skipping down the alley while walking her dog. "I couldn't stop grinning...I think I was smiling in my sleep. I felt so good" (1).

After 12 weeks, Elizabeth and the other patients stopped treatment and were monitored until their symptoms returned to pre-treatment levels (28). Elizabeth's symptoms returned slowly. She was then offered methotrexate but feared its side effects (1).

#### In a way, the drug worked too well.

Most patients in the high-dose group, like Elizabeth, experienced noticeable symptom relief after the first few doses. In a way, the drug worked too well. Critics later challenged the study design, claiming it really wasn't blinded, because patients improved so much they knew they were not in the placebo group (24, 27). "There was no subtlety in the response" (24). Some patients asked to meet Dugan to say thank you—but for confidentiality reasons, she could not see them (6, 22).

Blinded or not, the endpoints chosen by Blosch were definitive and withstood all criticism (27). The primary endpoint was ACR 20, a quantitative assessment of clinical function. The American College of Rheumatology (ACR) had just published this tool and encouraged its use in RA clinical trials (29).The scheme had been validated using data from previous methotrexate clinical trials, but it had not yet been used to evaluate experimental drugs. The ACR said that drug efficacy could be claimed if a patient experienced a 20% reduction in tender and swollen joint counts and a 20% improvement in 3 of 5 other "core" measures: patient and physician global assessments, pain, disability, and an acute-phase reactant biomarker such as C-reactive protein (29).

By the end of 1994, Gillis, Henney, and Duzan had all left Immunex for other opportunities, but the RA trial continued. With the rest of the company assigned to other projects, Dugan almost single-handedly kept the phase 2 trial on track. "I knew the clinical details of every patient on that study" (22). She ensured that the sites accurately recorded the patients' data, and then statisticians at Statprobe, Immunex's contractor in Michigan, conducted the final analysis – all according to standard procedures (5, 22).

#### **The Turning Point**

Abbe Rubin, Immunex's head of statistics and data management, still remembers the day in 1995 when the Statprobe statistician called to report the TNFR:Fc results (5). Three-fourths of the patients in the highdose group achieved ACR 20 improvement (28). In fact, the clinical improvement was so great that the Immunex team added another level, ACR 50, which represented a 50% improvement in the ACR-defined criteria. "We created that endpoint. No one had ever seen this level of efficacy before" (6).

Remicade had been reported to improve RA symptoms, but the mouse-human chimeric molecule also induced antibodies that attenuated the drug's effect and produced an allergic response in some patients. None of the TNFR:Fc-treated patients generated detectable antibodies (25, 28). This suggested that TNFR:Fc might actually be better than Remicade in RA.

Rubin gave the results to Ann Hayes, Immunex's Senior Vice President of Medical Development, and Hayes rushed the news to Immunex's senior management (5). "Everything changed overnight" (27). The company decided to keep TNFR:Fc rather than sell its ownership rights, and resources were shifted to aggressively continue the RA clinical trials for fasttrack approval (5, 19, 22, 27).

After completing her experimental treatment, Elizabeth learned that the drug—previously known by its code, TNFR:Fc—was called etanercept (Enbrel<sup>®</sup>), and she wanted to continue taking it *(1)*. Fortunately, she would not have long to wait. 243

#### **Enbrel Strategy**

Coming as it did on the heels of the failures with PIXY 321 and the sepsis trial, the RA results greatly boosted morale (6). To manage the rapidly expanding team, Leslie Garrison was designated the Enbrel project leader. She joined Immunex in 1989 and had been involved with multiple clinical development projects, including GM-CSF (6).

Unfortunately, the Enbrel team faced a major hurdle. Because Immunex had planned to hand off Enbrel to another company, the drug inventory was depleted. Clinical supplies for the phase 1 and 2 trials had been produced in Immunex's Seattle laboratories (22). The ambitious phase 3 program required larger batches, and scaling up production at the company's manufacturing plant in Bothell, WA, was not trivial. It delayed the trials by many months (22).

Although frustrating, Garrison and the team used this time wisely. Constantly mindful of the patients, they established cutting-edge efficacy endpoints and defined detailed categories for all adverse events (6, 27). "We never lost sight of who we were working for" (27). They added ACR 70 to the ACR 20 and 50 endpoints—an unprecedented level of symptom relief, but one that Enbrel achieved (6).

In addition, Barbara Finck, a rheumatologist who joined Immunex in 1994, implemented a definitive set of radiographic endpoints based on the Sharp score. First proposed in the 1970s by John Sharp, the Sharp score quantified the erosions and joint space narrowing seen in X-ray films (*30*). Previous clinical trials had followed radiographic progression of RA using the Sharp score, but Immunex took it a step further (*4*).

Finck closely collaborated with Sharp, who was retired but coincidently lived in the Seattle area, to adapt his method for digital reading machines (4). They selected experienced radiologists as their "readers," and Sharp personally trained them to read and score the digital films (4, 31). Each of the readers was then given a remote X-ray station, so that they could read the films at home (4).

Immunex engaged BioImaging, a vendor specializing in digital imaging, to collect, digitize, blind, randomize, distribute, and archive the X-ray films. RA radiographs had never before been managed at this level of detail.

Immunex also kept the FDA informed of these procedures, and the agency was fully engaged in the method development. The Enbrel submission was the first time that the FDA reviewers received indexed digital RA films, which greatly facilitated their data review (4, 6). Subsequently, this procedure became the standard for assessing disease progression in RA drug trials (6, 31).

#### **Safety First**

Critics had good reason to raise safety concerns about every biologic drug that acted on the immune system. Genentech's lenercept (a fusion protein that combined the p55 soluble TNF receptor with IgG1) was only transiently effective in RA patients because of the rapid appearance of anti-lenercept antibodies (32).

In addition to producing anti-Remicade antibodies and inducing an allergic hypersensitivity response, Remicade could increase infection susceptibility and unmask latent infections like tuberculosis *(12)*.

Anticipating such questions about Enbrel's safety, the Immunex team diligently documented the exact type and severity of each injection-site reaction and allergic response (supplemented with photos), as well as infections and other side effects (6, 33). They also collected comprehensive antibody data (6, 23).

#### No Days Lost

The phase 3 trials of Enbrel alone and in combination with methotrexate completed enrollment very quickly because now physicians wanted to participate, and RA patients rushed to sign up (5, 19, 22). Initially, though, drug supplies were very limited. Dugan kept track of every vial, juggling shipments to match enrollment (6, 22). Excitement at Immunex ran high, where the team, pioneers in adopting electronic data capture, followed the trials' progress almost in real time. "We didn't waste any time" (6).

At first, patients came to the clinic twice a week for their injections. Later, nurses at the clinical sites trained the patients to deliver their own subcutaneous injections and gave them a bag containing ice and vials of the prepared drug solution *(19)*. Patients willingly complied with the detailed written instructions for refrigerating the vials and injecting themselves because Enbrel worked.

The phase 3 trials confirmed the earlier findings. Patients experienced rapid and sustained symptom relief. An injection-site reaction was the most common side effect, but in most patients, it was mild, infrequent, and resolved quickly. Auto-antibodies were found in a few serum samples, but none of the patients developed immunogenicity, signs of autoimmune disease, or loss of efficacy (23).

To address questions about Enbrel's long-term safety, Immunex launched an open label safety trial (34). When patients completed their 6-month blinded trial, they were invited to continue treatment in the open label trial, and most patients did. Patients who had participated in the phase 2 trial were also invited to enroll, and Elizabeth signed up (1).

#### **Don't Forget the Kids**

As soon as drug supplies became available, the team began staging expansion of Enbrel's therapeutic indications. In parallel with the RA trials, they conducted clinical trials for psoriatic arthritis, plaque psoriasis, ankylosing spondylitis, Crohn's disease, and juvenile rheumatoid arthritis.

Rheumatoid arthritis can affect children as young as 1 year old, and it is devastating. Inflamed joints can accelerate bone growth, leading to differences in leg length during childhood development, and consequently, to significant long-term disability. The standard of care for these children had been NSAIDs and low dose methotrexate, but they needed something better (4).

The FDA encouraged all drug companies to collect pediatric data in their development programs if the medical condition affected children as well as adults. But pediatric clinical trials are quite challenging for both ethical and feasibility reasons, and most companies delayed – or even avoided – this work.

As a rheumatologist who had seen juvenile RA firsthand, Barbara Finck became a strong advocate within Immunex to start the pediatric trials earlier rather than later. She succeeded in getting corporate support. It was a risky and bold management decision, given the company's already heavy investment in Enbrel, and considering that a bad outcome in a pediatric trial could derail the entire development program (4).

Daniel Lovell and Edward Giannini at the Children's Hospital Medical Center in Cincinnati spearheaded the pediatric trial (35). The main objective was to collect pharmacokinetic data. Because the children were too small to draw multiple blood samples, the study employed a population-PK design (4, 35).

The Cincinnati group saw some of the most severe cases of juvenile RA, and in the first segment of the trial, all children received Enbrel (4). Then, in the

second and blinded segment, some children received placebo injections while the rest continued taking Enbrel. If children in the placebo group experienced a flare response, they resumed Enbrel treatment (4, 35). This innovative study design had never been previously used for pediatric pharmacokinetics trials, but it is now standard (4).

#### The Path to Approval

Enbrel faced stiff competition from other biologic drug candidates. In addition to Remicade, Abbott Laboratories was proceeding with adalimumab (Humira<sup>®</sup>), a fully humanized TNF- $\alpha$  antibody. The Immunex team presented Enbrel data at every rheumatology-related venue – large and small – and published a steady stream of clinical study reports *(6, 36)*.

But by far, the most important document the Enbrel team prepared was the Biologics License Application (BLA), requesting market approval from the FDA. The most important presentation they made was to the FDA's Arthritis Advisory Committee.

Immunex submitted the BLA to the FDA on May 7, 1998 (33). As part of the BLA review and approval process, the FDA requested input and recommendations from its Arthritis Advisory Committee, an independent panel of experts. It was customary for the Advisory Committee to invite the sponsoring company to present summarized data and respond to their questions.

For the Enbrel team, this was a critical meeting, and they did their homework. Many of them had no experience with the regulatory process, though some, including Leslie Garrison, had worked toward GM-CSF's approval. They attended Advisory Committee meetings where other products were discussed, including Centacor's Remicade presentation in May 1998 (5, 6).

Through the summer of 1998, they diligently prepared (5, 6, 36). Ann Hayes and Garrison would make the formal slide presentation and field the Advisory Committee's questions. Many of the Advisory Committee members were rheumatologists who were familiar with Remicade and knew its problems. Their questions would reflect that experience, as well as concerns about investigational biologic drugs in general.

In a series of practice sessions, the Enbrel team and their clinical consultants brainstormed every possible contingency. Sometimes, that required additional statistical analyses and new slides (5). In addition to a concise presentation slide deck, they compiled a mind-boggling set of 1,000 backup slides (36). Each one addressed a single, clearly stated and visually crisp result or data summary (6).

Then, they "drilled like crazy" (36). It was a close and supportive group, and they turned it into a kind of game, practicing quick retrieval of the right slide, as Hayes or Garrison answered each question (19, 36). After many hours of rehearsals over weeks of finetuning, Hayes and Garrison knew every nuance of the Enbrel data (19). They could request from memory the number of the specific slide to accompany their response to any question (1).

After many hours of rehearsals over weeks of fine-tuning, Hayes and Garrison knew every nuance of the Enbrel data.

#### **D-Day: The Meeting**

On Wednesday, September 16, 1998, the Immunex contingent, along with four of their clinical consultants, arrived at the Holiday Inn in Gaithersburg for the FDA's Arthritis Advisory Committee meeting. In Seattle, the rest of Immunex anxiously watched the proceedings via a live-streamed video link (6, 22). They all had a lot riding on the Committee's recommendations.

The morning session ran like clockwork. Hayes and Garrison made their presentations and responded to the Advisory Committee's questions, just as they had rehearsed. In the afternoon, the Advisory Committee discussed six questions posed by the FDA reviewers regarding Enbrel's efficacy, safety, and precautions for use *(1)*. It quickly became clear that some Advisory Committee members were not satisfied with the size of the safety database.

Side effects from Enbrel were few and infrequent, but assessment of safety was confounded by a smaller-than-traditional placebo-control group. As often happens, many placebo patients voluntarily withdrew from the clinical trials because they were not improving and wanted to explore other treatment options (1). Consequently, Immunex compared Enbreltreated patients to the long-term natural course of RA in an appropriately matched demographic group—data that had been collected by the Mayo Clinic (6). Ironically, the Advisory Committee's greatest concerns were the lack of serious side effects and the absence of serum antibodies. Had Enbrel been given to enough patients and had it been given long enough to assess the drug's safety? Jeffrey Seigel, the FDA's medical reviewer, said, "Because TNF plays a role in host defenses, blocking TNF could theoretically have an effect on the number of infections and the severity of infections" (1). Immunex's ongoing long-term safety trial would eventually either refute or confirm this theory, but for now, all they could say for sure was: so far, so good (34).

Elizabeth Petersen injected some humor into the proceedings. She had been taking Enbrel for 3 years, and "the only side effect that I've noticed is that I seem to be deeply in love with the entire Immunex Corporation, especially the scientists" *(1)*.

After a long discussion that afternoon, the Advisory Committee chairman concluded by saying, "Sometimes we get so bogged down in the safety issues that we forget to say how enthusiastic we are, and I think everyone on the committee is extremely enthusiastic about seeing Enbrel being developed and becoming available to our patients with rheumatoid arthritis"(1).

The Advisory Committee unanimously recommended Enbrel approval for patients with moderate to severe rheumatoid arthritis who had failed DMARDs, and a majority recommended its use both alone and in combination with methotrexate (1).

The Immunex team was elated. Later that day, the company's senior vice president invited everyone to her Gaithersburg hotel room. Champagne corks popped. Emotions ran high *(5, 6)*. Enbrel was finally nearing the finish line.

#### **Approval and Beyond**

On November 2, 1998, Enbrel became the first biologic drug approved by the FDA for rheumatoid arthritis in adults. Six months later, approval was expanded to include juvenile rheumatoid arthritis. FDA officials required only one contraindication in the label: "Enbrel should not be given to patients with sepsis" (37).

Enbrel represented a groundbreaking achievement (31). From the first RA trials onward, it had transformed patients' lives (27). But Enbrel's unprecedented efficacy was a double-edged sword.

#### **Biosketch:**



Rebecca J. Anderson holds a bachelor's in chemistry from Coe College and earned her doctorate in pharmacology from Georgetown University. She has 25 years of experience in pharmaceutical research and development and now works as a technical writer. Her most recent book is *Nevirapine and the Quest* to End Pediatric AIDS. Email rebeccanderson@msn.com.

### In the next issue of *The Pharmacologist...*

Dr. Anderson will share the story of treating malaria – from gin & tonic to Chinese herbs.

Don't miss the March 2018 issue.

The Immunex Board had considered building a large Enbrel

manufacturing plant, but remembering the GM-CSF experience, they decided this budget-busting capital investment was unwise (3). After Enbrel's approval, patients demanded the drug, and once they started treatment, they didn't stop. The Bothell, WA, manufacturing plant's capacity was insufficient. Immunex and American Home Products scrambled to set up manufacturing contracts with plants in Germany, Ireland, and Rhode

Island *(3, 38).* It took several years for those facilities to become operational and satisfy the overwhelming demand.

In the meantime, Immunex's top priority was to ensure that patients who were already taking Enbrel could continue uninterrupted treatment *(36)*. Those patients were issued patient Champagne corks popped. Emotions ran high. Enbrel was finally nearing the finish line.

ID numbers, which were required to fill their prescriptions. As production increased, additional patients received ID numbers *(36)*.

After Enbrel, Remicade and Humira were also approved for rheumatoid arthritis. However, they are co-administered with methotrexate to decrease and delay the production of anti-drug antibodies and an allergic response (12). Anti-drug antibodies are less problematic with Enbrel, but methotrexate boosts its efficacy, compared to single-drug treatment (39).

Enbrel, followed by Remicade and Humira, was also approved for psoriatic arthritis, plaque psoriasis, and ankylosing spondylitis. But further clinical trials revealed differences between them. Enbrel is approved for juvenile RA, whereas Remicade and Humira are not. Remicade and Humira are effective in treating Crohn's disease, whereas Enbrel is not (40, 41). All three drugs now rank in the top 10 for worldwide drug sales.

TNF inhibitors revolutionized the treatment of rheumatoid arthritis. More than relieving symptoms, they sent the disease into remission (24). And some of the adults and children who took their first dose as experimental subjects 20 years ago are still taking Enbrel, with no loss of efficacy (4, 36).

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## ASPET Celebrates the 25th Anniversary of the SURF Program

ASPET's SURF program has a rich network of over 2200 alumni, with some former participants serving as mentors to the next generation of researchers. In celebration of SURF's 25<sup>th</sup> anniversary, we have been sharing stories all year from SURF programs that highlight their potential as transformative experiences. In addition to the final installment below, more stories are available in previous 2017 issues of *The Pharmacologist* at http://bit.ly/2iA1kZD and in the booklet celebrating this SURF milestone at http://bit.ly/2ntx2vs.



Mark Westbroek Participation year: 2009 Fellowship type and location: Institutional, University of Utah Current title: PhD candidate, Purdue University

My participation in the SURF program has had a large impact on where I am today. It helped solidify experimental procedures I had learned about

but had not completely understood. It gave me a glimpse of what graduate student life is really like. I was able to do a small amount of work with mice and learn new instrumentation, all of which helped me in graduate school. More than anything, the experience provided a trusted mentor who was able to help me through the process of applying to graduate school. Thanks to his superior mentoring, I was able to realize that I want a career developing new therapeutics. I also learned that I especially enjoy the basic biological and biochemical aspects of pharmaceutical research. These and other





insights gained from SURF guided me to graduate school at Purdue University, where I will soon graduate with my PhD. I look forward to applying my knowledge and skills in the pharmaceutical/ biotech industry to help improve lives.



Marisa Hornbaker Participation year: 2009 Fellowship type and location: Institutional, University of Pittsburgh

Current title: MD/PhD student, University of Texas Health Science Center at Houston

I applied for a SURF fellowship with the intention of bolstering a medical school application. In reality, this experience drastically changed my career trajectory. Under the mentorship of Dr. Jack Yalowich at the University of Pittsburgh, I began to explore the mechanism underlying a devastating hematologic malignancy. At first, I didn't have the background to understand why what we were studying was so important. That was, until a senior MD/PhD student at the time took me to see a child who had the disease. This immediately instilled a sense of urgency in my work. Throughout the summer, my desire to practice clinical medicine evolved to also encompass understanding the basic science underlying clinical problems. I continued doing research throughout college and applied to MD/PhD programs during my senior year. My SURF experience was truly life changing, and I could not be more thankful to ASPET for making this possible.

We thank our SURF alumni for sharing what the fellowship experience meant to them and look forward to continuing to provide these enriching opportunities for future pharmacologists. Programs like SURF are not possible without the continued support of our members. To donate to SURF, visit https://www.aspet.org/donate.

## Hollie Swanson Discusses the SURF Program at the University of Kentucky



Hollie Swanson

In the final installment of our year-long series commemorating the 25<sup>th</sup> anniversary of ASPET's Summer Undergraduate Research Fellowship (SURF) program, Catherine Fry, PhD, Director of Education at ASPET, interviewed Hollie Swanson, PhD, Professor of

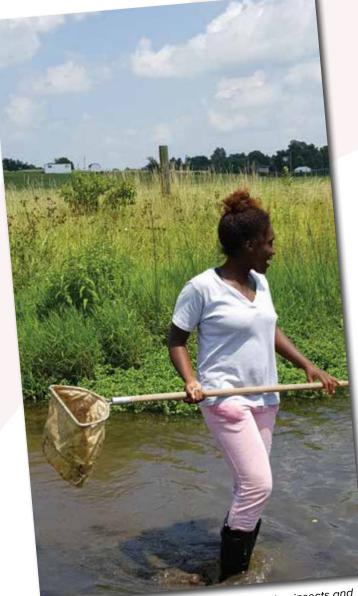
Pharmacology and Nutritional Sciences and Director, Summer Undergraduate Research Fellowship Programs in Pharmacology and Environmental Health Sciences, at the University of Kentucky about the SURF program she established in 2016.

## CF: What was the motivation for starting a new SURF program at the University of Kentucky?

HS: On our campus, there is a renewed focus on undergraduate education. Since our College of Medicine is contiguous with our undergraduate campus, it was a natural for us to reach out and work together. Our provost is very focused on student success, and we know that undergraduate research can be a big part of that. The importance of undergraduate research is definitely growing here. In its first year, SURF was a stand-alone program, but then I got a second program funded in environmental health sciences. I'm the director of both, and I am trying to maintain each program's separate identity while having joint programming wherever it makes sense.

## CF: Do you have any advice for others who are looking into starting a SURF program?

HS: One thing that really needs to be considered is the target audience. For example, do you want a national program where you take students from all over the country, or do you want it to be more local? We have so many students in need here in Kentucky that I wanted to serve as many of those students as I could. Many of the local students come from socioeconomically disadvantaged populations, and I want to be able to encourage and support them. The most effective avenue to recruit so far has been to ask individual faculty for recommendations.



One of Dr. Swanson's SURF students collecting insects and measuring water quality.

Next week I am going to the Kentucky Academy of Sciences and I hope to get some good contacts there as well. I also have some great partners at Eastern Kentucky University; they had a biomedical science program and were looking for these kinds of opportunities, so that was a natural fit. One thing I've learned about recruiting is that you have to be early. I get the process up and running before the students leave on Christmas break. Our university PR department did a short video for us, which also helps us with recruitment. Now that we are in our second year, we're getting more word of mouth effects with students encouraging their friends to apply.

## **CF:** How do you help set expectations about the summer research experience?

HS: We do several days of orientation to discuss ethics, lab books, communication, and related topics. Because I want them to develop good group dynamics, I send them on a campuswide scavenger hunt at the beginning of their experience. They had a lot of fun getting to know both the campus and each other.

## CF: What kind of activities and interactions are available for students outside the lab?

HS: We generally had a weekly activity. For example, I set up a hike at Red River Gorge through our outdoor center. My personal favorite was a visit from rapper Farmer Brown. He was a rapper in his former career and now he raps about nutrition and sustainable farming. We had a great conversation about outreach and using culturally appropriate ways to reach an audience. We also worked with our agriculture extension agent to check stream health by collecting insects and measuring water quality. We talked about runoff and all the substances that can get into our water supply. We want them to see how science is used in their own community while getting some exposure to possible career paths. One of the students' major concerns is careers, so we've had lunches where researchers come in and talk about their research and their career paths. We've set up shadowing opportunities, and we stress for them how important it is to establish networks.



Dr. Swanson and her SURF students wearing the tie-dyed lab coats they created.

## CF: How do the students cap off their summer research experiences?

HS: They all present their research as a poster at our faculty club. We have a nice event with about 50 attendees. I recruit graduate students to visit the posters to conduct an evaluation. I created a rubric for them to use so they knew what to be looking for. That way, the undergraduates get feedback and the graduate students also get experience in offering constructive comments. At the end of our summer, I give the students a token to remember their experience – I found a little mortar and pestle on which I put SURF and the year of their fellowship. For one of our last summer activities, we tie-dyed lab coats. For their poster presentations, they all wore their tie-dyed lab coats, which was a lot of fun. We also have a campus-wide showcase in April, and some of our SURF students have participated in that.

## CF: What do you envision for the future of the program?

HS: We're finding that our students from the first year have stayed in the lab and continued

to work on their research. I've been impressed at their motivation to keep going - some of them have really begun to think of their labs as their academic home. One of our students from last summer was also involved in training a new student this summer. I had one student come to me saying he had such a great time - could he do it again next summer? We started talking about what a phase 2 of the fellowship might look like. I've thought about going to Woods Hole for a week, or taking a smaller group for a shorter-term follow-up experience. I'd like to have someone from the Alan Alda Center for Communicating Science come work with us, and I'd like to have the students do some improvisation exercises to get more comfortable with communication.

We thank Hollie for taking the time to speak with us about her SURF program at the University of Kentucky. More information is available at https://surfsures.blogspot.com/2017/07/aboutprograms.html and at https://pharmns.med.uky.edu/.



## Fueling Innovation: Public Programs Driving Drug Discovery

Submitted by Janet Clark, PhD and Michael Wood, PhD

ASPET in collaboration with the Academic Drug Discovery Consortium (ADDC) recently convened the 2<sup>nd</sup> ASPET/ADDC Colloquium on Academic Drug Discovery. The program, entitled *Fueling Innovation: Public Programs Driving Drug Discovery*, began on October 12, 2017 and concluded mid-afternoon on the 13<sup>th</sup>. The event was held on the campus of the



From Left to Right: ASPET/ADDC Colloquium Co-Organizers Michelle Arkin, Michael Wood, and Janet Clark

National Institutes of Health (NIH) at the beautiful Natcher Conference Center and attracted several hundred registrants. Once again, the energy and drive of the ASPET staff that focused on the meeting logistics delivered flawlessly. As co-organizers, we were enabled at every stage of the process by the competence of ASPET's meetings management staff and the able support of the NIH staff that facilitated access to the venue. We also wish to acknowledge the financial support of Millipore Sigma, Eli Lilly & Co., Discovery | Charles River, Pfizer Inc., Janssen Research & Development, LLC, Waters Corporation, Wilson Sonsini Goodrich & Rosati, AbbVie Inc. and ChemBridge Corporation which made the colloquium possible.

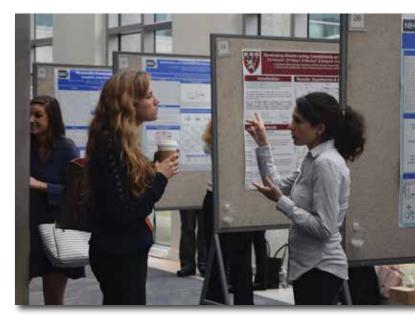
While the first collaborative colloquium, held April 6-7, 2016 in San Diego, CA, was focused on sharing success stories, the second spotlighted funding mechanisms designed to foster academic drug discovery. Basic research in universities and institutes has always provided the fundamental insights that inspired the search for new therapies, but typically these advanced as applied research through investments made by commercial enterprises like biotechnology or pharmaceutical companies. There has been a rising interest in converting the fundamental insights made within academic laboratories into treatments within the same laboratories that drove those discoveries. The participants of the recent colloquium share this interest. To that goal, the colloquium program blended presentations on leading scientific discoveries with discussions on funding mechanisms focused on translating new discoveries to therapies.

Carlos Zarate, MD, of NIMH, presenting "Experimental Therapeutics for Treatment-Resistant Depression."

The second day provided an opportunity for attendees to meet with program officers from nine NIH divisions, unique NIH program personnel and representatives from private foundations. The common interest of these representatives is funding applied research into innovative ideas for therapies.

Keynote speeches from Carlos Zarate, MD and Bryan Roth, PhD bracketed the scientific program and provided compelling insight into the roots of the academic drug discovery experience. Dr. Zarate described a search for the mechanism of ketamine's antidepressant activity and Dr. Roth outlined a systematic exploration of GPCRs – the most richly mined class of drug targets. In between, a collection of excellent presentations highlighted examples of applied research that emanated from novel funding mechanisms like the Chemical Biology Consortium in the NCI Experimental Therapeutics program, Cancer Research UK, the Blueprint Neurotherapeutics Network, the Wellcome Trust, the California Institute for Regenerative Medicine, and the European Lead Factory. The program also included some outstanding examples of how intramural NIH research had enabled therapeutic discovery from Sriram Subramaniam, PhD, of the Center for Cancer Research and Amy Newman, PhD, of NIDA. Jim Wells, PhD, of University of California, San Francisco, Craig Crews, PhD, of Yale University, and Barbara Slusher, PhD, and Jonathan Powell, PhD, of Johns Hopkins University provided detailed insight into their ongoing success in conducting therapeutic discovery programs in academic environments.

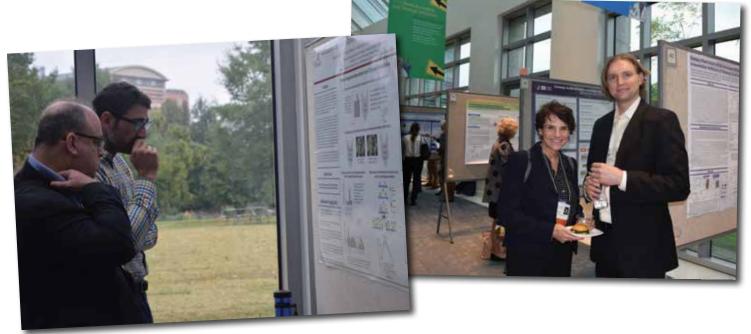
One-third of the attendees learned of the colloquium through communications directly from ASPET, and ASPET was the leading source of information about the colloquium. The remainder learned of the meeting through the ADDC or through direct outreach from those involved in the program or planning. Attendees represented an equal blend from academia, government and industry. 85% of the attendees were quite pleased with the program, although the minority were less enthused and shared concerns that included the desire for increased networking time and more emphasis on poster presentations. The colloquium hosted more than 35 poster presenters, which was more than twice the number presented in the first colloquium. Critiques from participants will surely be considered if another iteration of the colloquium follows, but most of the feedback suggests that the meeting was an

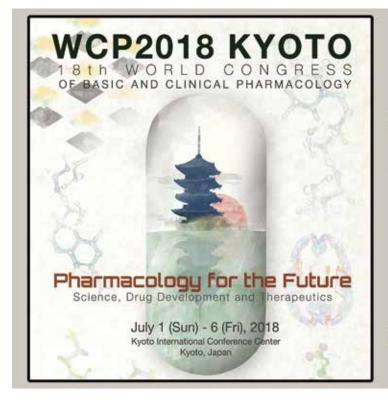


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enormous success. Consistent with that conclusion, 'programming content' was the most cited reason for attending, and the overwhelming majority of respondents felt that the quality of the speaker presentations was excellent or very good.

From the past two experiences, we can conclude that ASPET/ADDC colloquia have provided a valuable venue for information sharing and networking. Moreover, there is little doubt that academic drug discovery is a topic of shared interest among ASPET's membership. For us, the open questions that remain are – should the series continue and if so, what frequency/formats/venues/topics should be in focus? If you've read thus far, it's quite likely that you have an opinion and we'd like to hear it, so please share your comments at drugdiscoverycolloquium@gmail.com.







Proud sponsor of WCP2018 Kyoto

#### Early Registration Deadline: March 30, 2018

Visit www.wcp2018.org for program, abstract submission, registration, and housing information **Science Policy News** 

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## **Congress Finalizes Budget Resolution, Appropriations Still Being Debated**

In late October, the Senate passed its budget resolution and the House adopted the fiscal year (FY) 2018 budget resolution to set the stage for a tax reform push by Republicans. It's important to note that a budget resolution does not have the force of law, and thus will not replace the Continuing Resolution (CR) in place that is currently funding the government at the previous year's levels. The current budget resolution is at odds with the appropriations levels set by the Senate Appropriations Committee, which funded programs at \$5.1 billion greater than the resolution. Therefore, to avoid sequestration and mandatory cuts to spending per the Budget Control Act of

2011, the budget caps for discretionary defense and non-defense spending must be raised to accommodate this excess spending unless some other deal is reached.

ASPET recently signed on to a letter circulated by the Association of American Medical Colleges calling on congressional leadership to reach a bicameral, bipartisan agreement to raise those caps so that the National Institutes of Health (NIH) can be funded at \$36.1 billion for FY 2018. \$36.1 billion would represent a \$2 billion increase over FY 2017, as suggested by the Senate Appropriations Committee (the House Appropriations Committee approved a \$1.1 billion increase), and sharply contrasts with the administration's budget request of \$26 billion less in funding for NIH.

The administration's request for a 21.5% reduction in spending on NIH came mostly from a proposal to cap overhead costs on grants funded by NIH. These so-called "indirect costs" account for approximately 28% of overall extramural research spending. A cap of 10% would be devastating to NIH research. During the spending debate, however, the chairman of the appropriations subcommittee that funds NIH, Sen. Tom Cole (R-OK), inserted a provision into the appropriations bill that blocks the administration's proposal and preserves indirect costs at their current levels.

The next step in the funding process is for the House and Senate to reconcile their competing versions of the appropriations bills. Appropriations bills must pass with 60 votes (i.e., with Democratic votes), and Democrats have stated that they will not raise the cap on defense spending unless there is a raise in the cap on non-defense spending. Thus, to avoid the mandatory cuts from sequestration, the non-defense spending cap that includes NIH will likely have to be raised and the projected increase in the budget of the NIH should fall somewhere between the \$1.1 billion appropriated by the House and the \$2 billion appropriated by the Senate. In the less likely event that a deal cannot be reached, sequestration will force across the board cuts to all discretionary spending.

Whatever happens, it is likely that another Continuing Resolution will be required when the current one expires. A new CR will keep the government funded at the previous year's spending levels until a new budget is enacted.

## Tyler Lamb Joins ASPET as Sr. Manager of Government Affairs and Science Policy



On October 16<sup>th</sup>, Tyler Lamb joined ASPET as the new Senior Manager of Government Affairs and Science Policy. Prior to joining ASPET, he worked as a manager in the government relations department of a national patient advocacy organization on state and federal health care issues. He has also worked as a finance director on several electoral campaigns.

Tyler is a graduate of the Charleston School of Law (JD) and the University of South Carolina (BA, Political Science). With his background and experience, Tyler is excited to jump into his role to further develop our Government Affairs and Science Policy programs.

On October 17<sup>th</sup>, ASPET signed on to a letter with many other scientific societies and organizations that urged President Trump to review his administration's visa and immigration policies so that foreign students will face fewer obstacles to enrolling in U.S. science and engineering programs.

On October 27<sup>th</sup>, ASPET joined 25 organizations in a joint letter to raise concerns about the NIH's new clinical trial definition.

For the full version of this letter, please go to http://bit.ly/2i3knf1.

Francis Collins, PhD, MD, Director National Institutes of Health One Center Drive Bethesda, MD 20892-0160

October 27, 2017

#### Dear Dr. Collins:

The undersigned organizations applaud NIH for its work to improve transparency in clinical trials. We recognize that concerns have been raised with the agency that not enough data elements are being collected on clinical trials, and that the results of NIH-funded clinical trials are not being published in a timely manner. We understand that these are real problems the agency must address

We write, however, to share our concerns that basic science research is being redefined as a clinical trial at NIH. We see this as a distinct matter that does not relate to the problems associated with clinical trials the agency is attempting to address. Yet, basic science investigators will be unnecessarily burdened with requirements relating to conducting clinical trials that have nothing to do with their own research. These include limiting research proposal submissions to funding announcements that are specific to clinical trials, subjecting basic research proposals to new and "more rigorous" review criteria for clinical value constitutions and constitution and subject to the subject to trials, completing new forms, and participating in good clinical practice training. At a time when Congress has asked for reduced burdens on investigators, we are surprised by NIH's actions.

In rolling out the new definition and related policies, NIH created case studies to determine whether a research project will be classified as a clinical trial. We are aware that NIH has revised the case studies to exclude some basic science research, and we see this as a positive step. However, the case studies have exclude some dask science research, and we see this as a positive step. However, the case studies have not gone far enough, still define a large amount of basic science as a clinical trial, and remain confusing to basic science investigators who have studied them. As a result, we remain concerned that the policies, at least as applied to basic research, may destabilize areas of science over the coming year, areas that are important to the NIH mission.

To be clear, we support the goal of transparency in clinical trials. We also support the goal of transparency (including registration and reporting) in basic science research. We part ways, however, in thinking that labeling basic science research as a clinical trial, and including this research in a clinical trial thinking that labeling basic science research as a clinical triar, and including the research to basic science, database, is the best approach. There are alternative ways to collect this information for basic science. In fact, other registration and reporting frameworks have been in development for years and are more amenable to the concerns of basic scientists. With additional attention and input from basic scientists, transparency can be achieved in basic research without eroding trust in the agency.

Our communities of scientists are guided by professional codes of ethics as well as human research protection regulations, both stretching back decades. We owe an ethical obligation to human protection regulations, both stretching bock decades, no one on cancella bangation or handle participants to conduct research that allows us to build upon prior discoveries to advance knowledge. Basic scientists take this obligation seriously. Our interest in building an infrastructure for transparency in basic science that is separate from a clinical trial database should not be misinterpreted as weakening that ethical obligation.

NIH began the process of redefining clinical trials several years ago. Public notices, however, did not signal that basic science research would be redefined as a clinical trial. Regardless, basic scientists are now aware-at least large numbers of them-and are asking NIH to treat basic science as basic science, not as a clinical trial. There may be different pathways to achieving this, and we welcome the

We urge NIH to work with the affected basic science communities to identify a reasonable solution.

#### Sincerely.

American Economic Association Committee on Government Relations American Educational Research Association American Institute for Medical and Biological Engineering American Kinesiology Association American Physiological Society American Psychological Association American Society for Bone and Mineral Research American Society for Pharmacology & Experimental Therapeutics Association for Psychological Science Association for Research in Vision and Ophthalmology (ARVO) Association of Population Centers Cognitive Neuroscience Society Consortium of Social Science Associations Department of Psychology, UNC Greensboro Federation of Associations in Behavioral and Brain Sciences International Congress of Infant Studies Linguistic Society of America Population Association of America Psychonomic Society Society for Behavioral Neuroendocrinology Society for Computers in Psychology Society for Mathematical Psychology Society for Mathematical Psychology Society for Personality and Social Psychology Society for Psychophysiological Research Society of Experimental Social Psychology, Inc. The Histochemical Society

# **Education News**

## ASPET Collaborates With Other Societies on NSF-Funded Project to Improve Diversity

ASPET is collaborating with five other societies on a three-year project funded by the National Science Foundation entitled "Alliance of Scientific Societies for the Development of the Next Generation of Scientists." The founder societies and research group involved in the Alliance are: American Society for Biochemistry and Molecular Biology, American Society for Cell Biology, American Society for Pharmacology and Experimental Therapeutics, Biophysical Society, The Endocrine Society, and the Scientific Careers Research and Development Group.

Building a diverse and inclusive STEM (science, technology, engineering, and mathematics) workforce is a goal shared by many, including professional societies. While many groups have projects and programs focused on inclusion and diversity, efforts to understand effective interventions leading to increased participation remain isolated. The Alliance is focused on building a diverse scientific workforce inclusive of underrepresented minorities by coordinating the efforts of scientific professional societies. The project will draw upon principles from the field of social science to build a community of practice among these societies. The Alliance aims to create innovative and effective plans to offer members of underrepresented groups the opportunity to participate in the scientific enterprise and to

establish robust programs for the recruitment and retention of a diverse scientific workforce. A set of best practices and evaluation metrics will be developed and made available to the scientific community by a variety of mechanisms including conferences, workshops, and online databases. This project will bring together the minority affairs and diversity committees of participating scientific societies (in ASPET's case, the Mentoring and Career Development Committee), society staff, social science professionals, and other stakeholders. The initial partner societies were chosen based on the strength of their efforts to promote diversity. ASPET was brought into this project in part because of our success in running the ASPET Mentoring Network.

The Alliance will be structured around a threemeeting conference series. Participants in the project will create and disseminate a database of diversity programs in STEM and a standard reference set of evaluation metrics in order to share best practices and program outcomes to broaden participation in STEM. This conference series will also be used to develop strategies to manage future efforts of the Alliance in a sustainable way, with an ultimate aim to expand the numbers of societies involved and to establish a model that can be translated to other organizations.

## Individual Summer Undergraduate Research Fellowship (SURF) Program

Applications Due March 1, 2018 for Summer 2018 Fellowships



ASPET's individual SURF program introduces undergraduate students to pharmacology research through a 10-week laboratory research experience. The goal of the program is to use authentic, mentored research experiences in pharmacology to heighten student interest in careers in research and related health care disciplines. The SURF individual awards are intended to support students whose institutions do not have a currently funded institutional SURF program. Research may be conducted at the student's home institution or another institution, as appropriate to the research project.

#### Who Should Apply

Undergraduate students conducting pharmacologyrelated research including, but not limited to, students representing departments of pharmacology, toxicology, pharmaceutical sciences, and/or biological chemistry are invited to apply to the program. Applications from women and underrepresented minorities are particularly encouraged.

#### **Program Overview**

- Students must apply with a mentor who is a regular or affiliate member of ASPET in good standing or an emeritus member who is still active in research.
- Students and mentors must have already identified, and briefly describe, a summer research project that the student proposes to undertake.
- If awarded, ASPET will provide a student stipend of \$2800 for a minimum of 10 weeks' participation.
- The student must apply for membership in ASPET no later than the beginning of their summer research experience.

For more information and to apply, please visit https://www.aspet.org/awards/SURF/. For questions, please contact Catherine L. Fry, PhD at cfry@aspet.org.

## Marilyn Johnson Joins ASPET as Program Coordinator



On October 19<sup>th</sup>, Marilyn Johnson joined ASPET as the new program coordinator. Ms. Johnson brings 10 years of providing administrative support at the National Institutes of Health. She is a graduate of Loyola University in New Orleans (BS, biology). She is passionate about writing and is the membership chair of the Women's National Book Association (WNBA) and serves as a contributing editor for DC SMS (Stop Modern Slavery). She is excited to join the ASPET team.

# Journals News

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## Jeffrey Stevens Named Next DMD Editor



Dr. Jeffrey Stevens has been selected to succeed Dr. Edward T. Morgan as the next editor of *Drug Metabolism and Disposition*. Dr. Stevens will fully assume the editorship in January 2018 when Dr. Morgan's term will end. "I am extremely honored to be selected as the new editor," Dr. Stevens commented, "and want to thank previous editors and board members for the mentorship and providing opportunities to be involved with ASPET."

Read the complete announcement in *DMD* at http://bit.ly/2fjhMg0.

## **New BPT Member**



Dr. Beverley Greenwood-Van Meerveld has been appointed to the Board of Publications Trustees by ASPET's Council. She will fill the at-large position on the BPT being vacated by Jeff Stevens when he becomes the editor of *DMD*. Dr. Greenwood-Van Neuroscience, the Presbyterian Health Foundation Chair in Neuroscience, professor of physiology, and the President's Associates Presidential Professor at the University of Oklahoma Health Sciences Center. She is also the recipient of a Senior Research Career Scientist award from the Department of Veterans Affairs. Dr. Greenwood-Van Meerveld is an associate editor for *JPET* and past chair of the ASPET Division for Neuropharmacology. In addition, she is the president-elect of the American Neurogastroenterology and Motility Society.

Meerveld is director of the Oklahoma Center for

## **New Associate Editors**

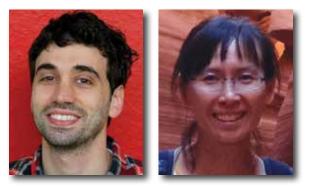


Dr. John D. Hayes has been appointed to serve as an associate editor for *The Journal of Pharmacology and Experimental Therapeutics*. Dr. Hayes is chair of molecular carcinogenesis and deputy director of the Medical Research Institute at the University of Dundee.

Dr. Vivian Hook has been appointed to serve as an associate editor for *Pharmacological Reviews*. Dr. Hook

is a professor with the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California, San Diego. Her other positions at UCSD include director of Graduate Training in Pharmaceutical Sciences and Drug Development with the Biomedical Sciences Graduate Program and adjunct professor with the Department of Neurosciences, Department of Pharmacology, School of Medicine. She serves as director of the NIH Training Program in "Neurosciences Related to Drugs."

## Molecular Pharmacology Highlighted Trainee Authors



The October issue of *Molecular Pharmacology* launched the journal's new Highlighted Trainee Author program. One trainee author (defined as an undergraduate student, graduate student, or post doc) from each issue is highlighted with his or her photograph on the journal's homepage. The image is linked to information about the author such as the trainee's areas of research, current projects, the anticipated impact of the research, and interests outside the lab. There's also a link to the author's paper. Highlighted trainee authors receive a coffee mug that notes their selection for this honor.

Trainee authors may be nominated by a corresponding author or self-nominated. The selection process is managed by Dr. Adriano Marchese, who serves on the *MOL* Editorial and Advisory Board. Each honoree is noted on social media and through other means in addition to the information posted on the website.

The first two highlighted trainee authors are Dr. Andrea Martella at the Leiden Institute of Chemistry (for October) and Dr. Yi-Ting Chiu at the Center for Substance Abuse Research and the Department of Pharmacology, Temple University Lewis Katz School of Medicine (for November). More information about them and their research is at http://bit.ly/2yX1YeH.

## **Altmetric Badges – What's Your Score?**



Articles published in *DMD*, *JPET*, *MOL*, and *PharmRev* now have Altmetric badges that show the attention they have received on social media, blogs, traditional media, and online reference managers such as Mendeley and

CiteULike. The badges are located on the Info & Metrics tab. Monthly usage statistics showing hits to the article's abstract and the full-text HTML and PDF versions are also provided.

ASPET journals added social bookmarking in September 2013, enabling readers to easily note

articles of interest through Twitter, Facebook, and Google+. During the past summer, Kudos was added as a service to authors to make it easy to share their research through social media. The addition of Altmetric brings those features full circle by providing a concise and simple way to track their use and track attention to articles from other sources such as traditional news outlets.

A detailed explanation of Altmetric and its scoring system is given at http://bit.ly/2xSCuyF.

These author services and others make ASPET journals a great place to publish your research.

## **Membership News**

## **New Members**

#### **REGULAR MEMBERS**

Dina A. Aly Labib, Cairo Univ, Egypt David J. Augeri, Rutgers Univ, NJ Pithi Chanvorachote, Chulalongkorn Univ. Thailand Prasoon Chaturvedi, C4 Therapeutics, MA Feihong Chen, Southeast Univ, China James D. Foster, Univ of North Dakota Sch of Med & Hlth Sci Donald Fox. Duke Univ Med Ctr. NC Peter Hecht, Ironwood Pharmaceuticals, Inc., MA Katharine R. Hobbing, Univ of Cincinnati, Coll of Med, OH Scott E. Kanoski, Univ of Southern California Atsushi Kawase, Kindai Univ, Japan Steven Mennerick, Washington Univ Sch of Med in St. Louis, MO

Adam J. Prus, Northern Michigan Univ Kathryn J. Reissner, Univ of North Carolina at Chapel Hill Marilyn E. Thompson Odom, Belmont Univ Coll of Pharmacy, TN
Rheem A. Totah, Univ of Washington
Nikhil M. Urs, Univ of Florida
Xin Xu, NIH, MD

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**Orang Ojong B. Bessem,** Bamenda Univ of Sci and Tech, Cameroon

Ranjeet P. Dash, Johns Hopkins Univ, MD

Michael J. Espiritu, Pacific Univ, OR Brian Fuglestad, Univ of Pennsylvania

Filomene Morrison, Boston Univ Sch of Med, MA

Benard O. Ogola, Tulane Sch of Med, LA

Herana K. Seneviratne, Johns Hopkins Univ, MD Takeshi Suetomi, Univ of California, San Diego Joseph Tillotson, Johns Hopkins Univ Sch of Med, MD

Zachary J. Zimmermann, MPI Research, MI

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## **Renew Your ASPET Membership For 2018**

#### www.aspet.org/membership

We hope you will continue your ASPET membership and take advantage of all of the many benefits ASPET has to offer. Renew by December 31st and you will be entered in a raffle for a \$50.00 American Express gift card. Good luck and thank you for your valued support!



Zdravka Daneva, Virginia Commonwealth Univ

Toluleke O. Famuyiwa, Florida Atlantic Univ

Maria M. Figueroa Rosado, Pontifical Catholic Univ, PR

Erick Galicia, Instituto Politecnico Nacional, Mexico

Moriah Hovde, Univ of North Dakota Rohitash Jamwal, Univ of Rhode Island Coll of Pharmacy

Tyler N. Kambis, Univ of Nebraska Mee Jung Ko, Purdue Univ Lib TSS, IN

Kara A. Lau, Brown Univ, RI

Katherine Leon, Univ of Chicago, IL

**Jinhui Li,** Ohio State Univ

Charlotte P. Magee, Univ of Utah

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Joe O'Brien, Univ of Iowa

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Kajal Risbud, Long Island Univ, NY

Lauren Russell, Univ of Arkansas for Med Sci

Sara Sanjari, Univ of Illinois at ChicagoFatima Sleiman, American Univ of Beirut, Lebanon

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Brian G. Stogsdill, Wright State Univ, OH

Darian Williams, Emory Univ, GA Laura A. Wilt, Univ of Georgia

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Teagan H. Glass, Univ of Colorado-Boulder

Rachel A. Harenchar, Saint Vincent Coll, PA

Madison Harris, Abilene Christian Univ, TX Meghan Jain, Loyola Univ Chicago, IL Adrienne Jo, Claremont McKenna Coll, CA

Sylvia J. Karpio, Loyola Univ, IL Abi Kirubarajan, McMaster Univ, ON John Lawrence N. Kwan, Loyola Univ Med Ctr, IL

Janay I. Little, Hampton Univ, VA Jensan Liu, Rutgers Univ, NJ Remi Looi-Somoye, Univ of Bath, UK Brandon Melendez, Univ of Houston, TX

MariKate Murphy, Loyola Univ Chicago, IL

Nahomie S. Possible, Rutgers Univ, NJ Sanna Rahman, Univ of Arizona Coll of Med

Stephanie Scalia, MCPHS Univ, MA Sera Sermet, Michigan State Univ

Marina M. Shenouda, Univ of Pittsburgh, PA

Dana T. Shively, Univ of Florida

Daniel G. Stuckey, Univ of Arkansas at Little Rock

Emily M. Veach, Olivet Nazarene Univ, IL

**Dorothy Wang,** Whitworth Univ, WA **Ginger L. Washington,** Loyola Univ of

Chicago, IL

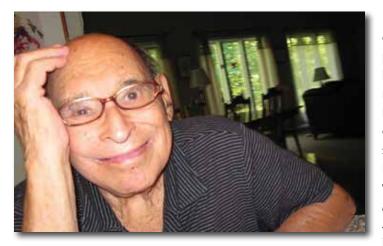
Yusheng Wu, Wheaton Coll, MA Alireza A. Zaravar, Rhodes Coll, TN

Congratulations Audrey Hager, PhD

on being the winner of the \$25.00 Amazon gift card. Dr. Hager located the five web pages where the donkey was hidden on the new ASPET site. Thank you for participating in the ASPET donkey website contest.

## A Tribute to Alexander George Karczmar (1917-2017)

Submitted by Palmer Taylor, PhD, Israel Silman, PhD, and Hermona Soreq, PhD



Alexander Karczmar, known as Alex or Niki, was born in Warsaw. Poland in 1917. His education in Poland was interrupted by anti-semitic outbursts in the late 1930's, but in 1939 Alex emigrated to the United States. After completing his MA and PhD degrees at Columbia University in 1946 and 1947, respectively, he joined the Department of Pharmacology at Georgetown University, where he became interested in the cholinergic nervous system. Alex rose through the academic ranks at Georgetown, spending a portion of his time at Sterling-Winthrop developing cholinesterase inhibitors such as ambenonium (Mytelase) and vasodilators such as amotriphene (Myordil). In 1956, he became professor and chair of pharmacology at Loyola University at the Chicago Medical Center. He served as a pharmacology department chair for close to thirty years, a long term of service as a chair. As an emigrant from Poland coming to the United States before World War II, Alex had an unrivaled history as an active pharmacology leader in both industry and academia through the years. He remained active in scientific endeavor until the very end and gained centenarian status this year. Alex passed away on August 17, 2017. He was a member of ASPET since 1953.

Alex exemplified academic life after being a chair, carrying an active research program, manuscript production, and meeting reviews until the end of his life. He was a primary proponent of the cholinergic nervous system contributing to alertness, cognitive behavior, and perception of "self." He was an organizer of many symposia and an awardee of several citations in the United States, Japan, and Europe. The book that he edited and for which he wrote the majority of chapters a decade ago, entitled *Exploring the Vertebrate Central Cholinergic Nervous System,* published in 2007 by Springer, is found in many libraries and still is a most valuable "opus magnum" and archival reference for students of CNS pharmacology, physiology, and neuroscience.

A more detailed obituary and description of Alex Karczmar's research interests and contributions may be found in the *Journal of Neurochemistry (2017)* https://doi.org/10.1111/jnc.14219.

## **In Sympathy**



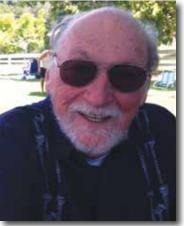
Darrell Abernethy

Dr. Darrell Abernethy passed away as this issue of *The Pharmacologist* went to press. An obituary will be included in a future issue of *The Pharmacologist*.

## A Tribute to Robert Jacobs (1933-2015)

Professor of Pharmacology Emeritus, Department of Ecology, Evolution, and Marine Biology, University of California, Santa Barbara

Submitted by William Fenical, PhD, Keith Glaser, PhD, Peer Jacobson, PhD, Alejandro Mayer, PhD, and Palmer Taylor, PhD



Although Dr. Robert Jacobs passed away in 2015, he is still greatly missed. On the second anniversary of his passing, his friends and colleagues have taken the opportunity to reminisce and prepare this tribute.

Robert Jacobs in his later years enjoying the outdoors.

Rebecca Madigan and Joan Jacobs

Robert Jacobs passed away on August 26, 2015. Bob, as his students would call him, was born April 2, 1933

in Chicago, IL to Robert S. and Betty Ester Jacobs. Bob initiated his pharmacology career by joining G.D. Searle, LLC in 1957 and circa 1960 became head of the Pharmacology Screening Lab there. While at G.D. Searle, he earned his undergraduate degree at Northwestern University in 1964 and PhD in pharmacology at Chicago's Loyola University, Stritch School of Medicine in 1971 (dissertation available at Loyola University of Chicago

eCommons). Alexander Karczmar, a true centenarian in life and likely in the pharmacology literature, served as chair of the Department and chair of the Jacobs Thesis Committee. See the companion obituary on page 264.

Bob moved to Santa Barbara in 1974, was hired as an assistant professor to initiate an undergraduate degree program in pharmacology at the University of California, Santa Barbara (UCSB), which became "the first campus in the nation to offer a full undergraduate pharmacological sciences curriculum." In contrast to professional programs in medicine, nursing, and pharmacy, which emphasize the therapeutic principles and applications of pharmacology, Bob developed

an undergraduate pharmacology program that emphasized pharmacology as a basic science focusing on drug discovery and mechanism of action. An aspect that set this program apart encompassed extensive laboratory preparations demonstrating pharmacological principles using primary tissues and in vivo models. Today, the major includes courses that represent "state of the art" pharmacology for students with research interests in all of health sciences (https://undergrad.biology. ucsb.edu/majors/pharmacology).The program continues as a vigorous undergraduate major, where many of its graduates continue for advanced degrees and hold leadership positions in industry and academia. Other UC campuses and universities, such as UC, San Diego; UC, Davis; SUNY, Stony Brook and Duke, followed Bob's lead in the undergraduate arena. He was ably assisted by the late Jean Devlin in instruction, organizing the major, and mentoring students at UC, Santa Barbara. The major, its courses, and the preparation of students for graduate study or professional school in medicine, pharmacy, and dentistry continue today at UC, Santa Barbara with Drs. Carol Vandenberg and Leslie Wilson providing the continuity and oversight of the major.

Bob's internationally recognized research centered on the pharmacology and toxicology of marine natural products (MNPs) that blossomed after joining UC, Santa Barbara. He built an internationally recognized center of marine pharmacology by developing extensive collaborations with marine natural product chemistry laboratories and pharmaceutical companies around the globe. Bob uniquely integrated his passion for MNPs with teaching pharmacology by developing in vitro and in vivo assays that were taught in the hands-on undergraduate pharmacology laboratory and then used by student volunteers in the lab to screen MNPs. Initially the lab focused on discovering compounds that modulated neuronal transmission at the neuromuscular junction in skeletal muscle, which resulted in the discovery of lophotoxin, isolated from *Lophogorgia sp.*, as an irreversible antagonist of the nicotinic acetylcholine receptor. Broadening the focus of the lab and screening efforts to identify potential anti-cancer, anti-inflammatory, and antipyretic compounds led to the discovery of novel pharmacology of MNPs. Using the sea urchin embryo assay as a model to identify potential inhibitors of cell division led to the discovery of stypoldione, a novel inhibitor of microtubule assembly.

While investigating potential inhibitors of beta bungarotoxin neurotoxicity, a novel antiinflammatory MNP, manoalide, was identified through in vivo evaluation in the PMA-induced ear edema assay. Mechanism of action studies identified irreversible inhibition of phospholipase A2 lipase, a key enzyme in arachidonic acid release, resulting in anti-inflammatory effects similar to nonsteroidal anti-inflammatory agents. Manoalide was eventually evaluated by several pharmaceutical companies for anti-rheumatic and dermatological applications. MNPs became a rich source of antiinflammatory compounds identified in the lab, e.g., sclaradiol, fuscoside, and the pseudopterosins. The pseudopterosins isolated from the sea whip Pseudogorgia elizabethae were found to affect many aspects of inflammatory signaling cascade. These activities were ultimately harnessed as an ingredient in a cosmetic to prevent wrinkles and were found to possess notable wound healing properties. Development of the pseudopterosins for their unique wound healing properties through Phase 2 clinical trials was managed by the biotech company Terosin, co-founded by Bob. Bob used



his passion for pharmacology and MNPs to train his students by guiding them through the discovery of novel mechanisms of action of these MNPs.

Bob retired from UCSB in 2010 at the age of 77. Alejandro Mayer (postdoc 1985-1988), Keith Glaser (graduate student 1985-1987), and Peer Jacobson (graduate student 1987-1990) carried Bob's enthusiasm and legacy in the pharmacology of marine natural products forward by curating a dedicated website (http://marinepharmacology. midwestern.edu/), contributing reviews on marine pharmacology (http://marinepharmacology. midwestern.edu/preclinPipeline.htm) and providing rigorous editorial assistance to the only journal dedicated to the preclinical and clinical pharmacology of marine natural products (http:// www.mdpi.com/journal/marinedrugs).

## Achievements, Awards, Promotions, and Scientific Breakthroughs

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#### V. Craig Jordan, OBE, PhD

University of Texas MD Anderson Cancer Center V. Craig Jordan, OBE, PhD, Living Legend Chair of Cancer Research in the Department of Breast Medical Oncology at the University of Texas MD

Anderson Cancer Center, has been elected to the National Academy of Medicine (NAM) for his discovery of selective estrogen receptor modulators (SERMs), a class of drugs that has wide-ranging impact on women's health. Membership in NAM is considered one of the highest honors in the fields of health and medicine.

Dr. Jordan is recognized internationally for his discovery of SERMs. Dr. Jordan's findings include application of the original SERM (the estrogen-blocking drug tamoxifen) to the treatment and prevention of breast cancer, and the discovery that raloxifene prevents both osteoporosis and breast cancer. Tamoxifen and raloxifene are among five SERMS approved by the US Food and Drug Administration and all five are connected to the basic research conducted in Dr. Jordan's laboratory.

In 2017, the Endocrine Society recognized Dr. Jordan with the Gerald D. Aurbach Award for Outstanding Translational Research. Dr. Jordan also recently had his name placed on the Wall of Honor at the Royal Society of Medicine in London. In 2015, Dr. Jordan was recognized by the British Pharmacological Society with the Sir James Black Award for Contributions to Drug Discovery.

Her Majesty, Queen Elizabeth II, inducted Dr. Jordan into the Order of the British Empire in 2002 for his services to international breast cancer research. Dr. Jordan is a member of the National Academy of Sciences, the Royal Society of Medicine, and the Academy of Medical Sciences.

Dr. Jordan was the recipient of the ASPET Goodman and Gilman Award in Receptor Pharmacology in 2012 and received the Pharmacia-ASPET Award in Experimental Therapeutics in 1993. He has been an ASPET member since 1981 and is a member of the **Divisions for Molecular Pharmacology, Drug Discovery and Development, Drug Metabolism and Disposition, Pharmacology Education, Translational and Clinical Pharmacology**, and **Toxicology**.



#### P. Jeffrey Conn, PhD

Vanderbilt University P. Jeffrey Conn, PhD, the Lee E. Limbird Professor of Pharmacology at Vanderbilt University, was awarded the Research and Hope Excellence in Academic Research Award from the PhRMA Foundation on Oct. 10<sup>th</sup>, 2017 during

PhRMA's annual award dinner in Washington, D.C. for his outstanding research in the area of mental health. The honorees were selected by the Scientific Advisory Board of the PhRMA Foundation.

Dr. Conn received his PhD in pharmacology from Vanderbilt in 1986, after which he received postdoctoral training at Yale University. In 1988, he joined the faculty of Emory University before accepting the position of senior director and head of the Department of Neuroscience at Merck and Co., where he directed drug discovery efforts for the treatment of schizophrenia and movement disorders. In 2003, he returned to Vanderbilt, where he became the founding director of the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD). The primary mission of the VCNDD is to facilitate the translation of findings in basic research to novel therapeutics. The VCNDD recently had a major advance in this effort.

On July 29th, 2017, a potential new drug for the treatment of Alzheimer's disease and schizophrenia, VU319, was administered to the first volunteer enrolled in a phase 1 clinical trial at the Vanderbilt Institute for Clinical and Translational Research. VU319, a positive allosteric modulator of the M1 muscarinic acetylcholine receptor, was developed by a team of scientists at the VCNDD under the direction of Dr. Conn and Craig Lindsley, PhD, codirector of the VCNDD and director of VCNDD Medicinal Chemistry. Animal studies suggest that VU319 may have potential for reducing memory impairments in brain disorders such as Alzheimer's disease and schizophrenia. This randomized, doubleblind and placebo-controlled study, designed and lead by Paul Newhouse, MD, director of the Center for Cognitive Medicine at Vanderbilt University Medical Center, will be conducted in about 50 healthy adult volunteers over the next 12 months to determine the compound's safety, tolerability and bioavailability when taken orally with or without food. If the safety trial proves successful, the next trials will determine if VU319 improves cognitive impairment seen in patients with Alzheimer's disease and possibly schizophrenia. Dr. Conn said "This is a major milestone for us and a rare example of an academic drug discovery group advancing from early concept to clinical development without the help of an industry partner".

Dr. Conn has been an ASPET member since 1992 and is a member of the **Divisions for Neuropharmacology, Drug Discovery and Development,** and **Molecular Pharmacology**.

Dr. Lindsley has been an ASPET member since 2009 and is a member of the **Divisions for Molecular Pharmacology, Drug Discovery and Development,** and **Neuropharmacology**.



#### Robert A. Nicholas, PhD

University of North Carolina

Robert A Nicholas, PhD, professor in the Department of Pharmacology and Microbiology & Immunology at the University of North Carolina (UNC), has won an "Innovations in Research &

Research Education Award" from the Association of American Medical Colleges (AAMC). This award, which was shared with Mohanish Deshmukh, PhD, professor in the Department of Cell Biology and Physiology at UNC, includes a monetary prize as well as a webinar presentation ceremony. The award is in recognition of a short course called "Best Practices for Reproducibility and Rigor in Research" that they developed and taught at UNC. The course was initially developed using a T32 supplement award from the National Institute of General Medical Sciences and the award from the AAMC was awarded based upon the design and the outcomes.

Dr. Nicholas has been an ASPET member since 1990 and is a member of the **Divisions for Molecular Pharmacology** and **Neuropharmacology**.



#### M. N. V. Ravi Kumar, PhD

Texas A&M University M.N.V. Ravi Kumar, PhD, professor of pharmaceutical sciences at Texas A&M University in the Irma Lerma Rangel College of Pharmacy, was recently named as one of

the Royal Society of Chemistry's Faces of Toxicology (https://youtu.be/R4ZjUTCzO9M). In addition, he has recently received an R01 grant from the National Eye Institute at the National Institutes of Health entitled "Systemic anti-inflammatory therapy to prevent or delay diabetic cataracts and treat post-surgical inflammation" (R01EY028169-01). Furthermore, recent work about the mechanism of cisplatininduced kidney toxicity from Dr. Kumar's laboratory has been highlighted as the cover article for the October issue of the Journal of Pharmacology and Experimental Therapeutics. Dr. Kumar has been an ASPET member since 2015 and is a member of the **Divisions for Drug Discovery and Development, Molecular Pharmacology, Cardiovascular Pharmacology, Drug Metabolism and Disposition, Toxicology, and Translational and Clinical Pharmacology.** 



#### Richard van Rijn, PhD

Purdue University

Richard van Rijn, PhD, assistant professor of Medicinal Chemistry and Molecular Pharmacology in the Purdue College of Pharmacy, was recently awarded an R01 from the National Institute on Alcohol Abuse and Alcoholism

entitled "G protein, beta-arrestin, and ERK signaling in alcohol use and anxiety disorders" in order to study the role of ERK signaling induced by G protein or beta-arrestin pathways in the modulation of alcohol and anxiety behaviors. His lab is broadly interested in better understanding how GPCRs function to propagate signal transduction in the modulation of behaviors, with the ultimate goal of identifying and developing new therapeutics with better potency, efficacy, and safety profiles. Their main area of focus is neurological disorders including drug addiction, mood and anxiety disorders, and chronic pain.

Dr. van Rijn has been an ASPET member since 2012 and is a member of the **Divisions for Molecular Pharmacology, Behavioral Pharmacology, Drug Discovery and Development, Neuropharmacology,** and **Pharmacology Education.** 



#### Michael Wood, PhD

Circuit Therapeutics, Inc.

Previously a Principal at Neupharm LLC., Dr. Wood is now senior vice president of Drug Discovery and Strategic Partnerships at Circuit Therapeutics, Inc. Dr. Wood has been an ASPET member since 2010 and is a member of the **Divisions** 

for Neuropharmacology, Drug Discovery and Development, and Molecular Pharmacology.



#### Colleen Niswender, PhD

Vanderbilt University

Colleen Niswender, PhD, was promoted to research professor at Vanderbilt University on September 1, 2017. She also serves as the Director of Molecular Pharmacology for the Vanderbilt Center for

Neuroscience Drug Discovery. Dr. Niswender recently received several new grants which total approximately \$3.2 million in direct and indirect funding. Her lab studies metabotropic glutamate receptors as targets for Rett syndrome and other MeCP2-related disorders.

Dr. Niswender has been an ASPET member since 2007 and is a member of the **Divisions for Molecular Pharmacology, Drug Discovery and Development,** and **Neuropharmacology.** 

Share your achievements, awards, promotions and scientific breakthroughs with fellow ASPET members. Send your news to your division's communications officer:

- Behavioral Pharmacology: Brenda M. Gannon, PhD at GannonB@uthscsa.edu
- Cancer Pharmacology: Jack C. Yalowich, PhD at yalowich.1@osu.edu
- Cardiovascular Pharmacology: David B. Averill, PhD at daverill@tcmc.edu
- Drug Discovery and Development: Przemyslaw Radwanski, PharmD at Przemyslaw.Radwanski@osumc.edu
- Drug Metabolism and Disposition: Aarti Sawant-Basak, PhD at aarti.sawant@pfizer.com, Lindsay M. Henderson at Imhender@uw.edu
- Molecular Pharmacology: Kathryn E. Livingston, PhD at kathrynlivingston@gmail.com, Amy E. Moritz, PhD at amy.moritz@nih.gov
- Neuropharmacology: Luisa Torres, PhD at Ift9@cornell.edu
- Pharmacology Education: Catherine M. Davis, PhD at cdavis91@jhmi.edu
- Toxicology: Alison H. Harrill, PhD at harrill.alison@gmail.com
- Translational & Clinical Pharmacology: Naeem K. Patil, PhD at naeem.patil@vanderbilt.edu



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## **2018 Division Elections**

The 2018 election includes nominees for ASPET Council (president-elect, secretary/treasurer-elect, and councilor), as well as Division officers: Division for Cancer Pharmacology (DCP), Division for Division for Drug Discovery and Development (DDD), Division for Drug Metabolism and Disposition (DMDD), Division for Molecular Pharmacology (MP), Division for Neuropharmacology (NEU), and Division for Toxicology (TOX). Members will receive notification when the election opens on January 8, 2018.

**Nominees for Secretary/Treasurer-Elect** 

#### **Division for Cancer Pharmacology**

#### **Nominees for Chair-Elect**



Larry H. Matherly, PhD Professor of Oncology and Associate Center Director for Basic Science, Wayne State University and the Barbara Ann Karmanos Cancer Institute



Christine E. Canman, PhD Associate Professor of Pharmacology, University of Michigan Medical School



Andrew Thorburn, DPhil Professor and Chair, Department of Pharmacology, University of Colorado



Daniel L. Gustafson, PhD Professor, Department of Clinical Sciences, Colorado State University

#### Division for Drug Discovery and Development

#### **Nominees for Chair-Elect**



**Tom J. Parry, MBA, PhD** Founder and Principal, Skyline Biopharma, LLC



**Donald Button, PhD** Senior Director, R&D, Acorda Therapeutics

**Nominees for Secretary/Treasurer-Elect** 



Przemyslaw Radwanski, PharmD, PhD Assistant Professor, Division of Pharmacy Practice and Science, College of Pharmacy, The Ohio State University



Benita Sjögren, MSc, PhD Assistant Professor, Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University

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#### Division for Drug Metabolism and Disposition

#### **Nominees for Chair-Elect**



John Harrelson, PhD Associate Professor with Tenure, School of Pharmacy, Pacific University



Aiming Yu, PhD Professor, Department of Biochemistry and Molecular Medicine, University of California Davis

**Bhagwat Prasad, MS, PhD** Assistant Professor, Department of Pharmaceutics, University of Washington

**Nominees for Secretary/Treasurer-Elect** 



Xiaobo Zhong, PhD Professor, Department of Pharmaceutical Sciences, School of Pharmacy, University of Connecticut

#### **Division for Molecular Pharmacology**

#### **Nominees for Chair-Elect**



Allyn C. Howlett, PhD Professor of Physiology and Pharmacology, Wake Forest School of Medicine



Nevin A. Lambert, PhD Regents' Professor and Vice-Chair, Department of Pharmacology and Toxicology, Medical College of Georgia, Augusta University

#### **Nominees for Secretary/Treasurer-Elect**



Angeline Lyon, PhD Assistant Professor of Chemistry and Biological Sciences, Purdue University



Adriano Marchese, MSc, PhD Professor of Biochemistry, Medical College of Wisconsin

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#### **Division for Neuropharmacology**

#### **Nominees for Chair-Elect**



#### Irwin Lucki, PhD

Professor and Chair, Department of Pharmacology and Molecular Therapeutics, Uniformed Services University of the Health Sciences



Kelly M. Standifer, PhD Chair and Professor, Department of Pharmaceutical Sciences, College of Pharmacy, University of Oklahoma Health Sciences Center

#### **Nominees for Secretary/Treasurer-Elect**



Shaifali Bhalla, PhD Associate Professor of Pharmaceutical Sciences, Midwestern University, Chicago College of Pharmacy



#### **Daniel Morgan, PhD**

Assistant Professor of Anesthesiology, Pharmacology, and Neural and Behavioral Sciences, Department of Anesthesiology and Perioperative Medicine, Penn State University College of Medicine

#### **Division for Toxicology**

#### **Nominees for Chair-Elect**



**Brian S. Cummings, PhD** Professor and Director, Interdisciplinary Toxicology Program, University of Georgia

#### **Nominees for Secretary/Treasurer-Elect**



**Brendan Stamper, PhD** Associate Professor, Pacific University School of Pharmacy



## **Division for Drug Metabolism** and Disposition

## **Member Spotlight**

#### From Regulation of P450s to ASPET Presidency: Edward Morgan

Submitted by Lindsay Henderson and Aarti Sawant-Basak, PhD

Edward (Eddie) Morgan, PhD is a professor in the Department of Pharmacology at Emory University in Atlanta, Georgia. He earned his PhD in pharmacology at the University of Glasgow, Scotland in 1979. As a postdoctoral fellow in the lab of Minor J (Jud) Coon at the University of Michigan, Dr. Morgan worked with Dennis Koop to purify and characterize CYP2E1 as a novel cytochrome P450 induced by ethanol. At the Karolinska Institute, Dr. Morgan worked as a visiting scientist fellow with Dr. Jan-Åke Gustafsson to purify sex-specific forms of cytochrome P450s and provided the first demonstration that their expression is regulated by growth hormone secretion. He joined Emory University as an assistant professor in 1986 and has been a faculty member since. Today, Dr. Morgan's research is focused on elucidating the mechanisms responsible for regulating cytochrome P450 enzymes in infectious or inflammatory disease states.

Since 1991, Dr. Morgan has been actively involved in ASPET. He served as chair of the Division for Drug Metabolism from 1998 to 2001 and was an at-large member of the Board of Publications Trustees from 2005 to 2010. He is currently the president-elect of the ASPET Council and will be completing his 6-year term as Editor of *Drug Metabolism and Disposition (DMD*) in December 2017.

Dr. Morgan kindly agreed to share his story, providing us with insights into his role as editor of *DMD* and his upcoming term as president of ASPET.

## Q: Can you briefly describe your ASPET journey since joining the Society in 1991?

**A:** After I returned to the US from my postdoc at the Karolinska Institute, the first ASPET meeting I

attended was the fall meeting in Salt Lake City in the late 1980s, where I gave a 10-minute talk in a platform session. The experience of this small, very collegial meeting prompted me to join the Society, and my first experience in Society governance was when Jim Halpert recruited me to help him revive the Division for Drug Metabolism in the mid-90s. Jim's strong leadership was a great example to me and made it relatively easy to transition to chair of the division. I continued to participate in division affairs thereafter, and then I was recruited to serve on the Board of Publications Trustees (BPT). I assume this was at least partly due to my experience as an associate editor of Molecular Pharmacology. The BPT experience was really rewarding due to the rapidly changing publishing landscape and the vital role of the journals in the financial health of the Society. No good deed goes unpunished, and shortly after leaving the BPT, I was elected to the position of Secretary/Treasurer, as well as appointed editor of DMD! Both of these were tremendous honors for me and would have been recognition enough of my contributions to the Society. To be elected president of the society that John J. Abel founded, of whom so many of my esteemed colleagues are members, and to follow so many other illustrious scientists and ASPET luminaries, is an honor of which I honestly never dreamed.

Q: You have been very involved in ASPET leadership during your career. Why do you believe it is important to contribute to professional societies within your field? Can you advise ASPET members on different ways to get involved?

A: There are so many reasons to contribute to professional societies. It's one of the best ways to network and make crucial contacts for collaborations, service opportunities, and letters of reference. ASPET's approach of member-driven scientific programming and emphasis on students, postdocs, and junior scientists provides opportunities to enhance your standing in the field and promote career advancement. As a more senior scientist, society membership and leadership provides you with an opportunity to expand your mentoring role and give back to the discipline while continuing to network and discover new opportunities. And not least, you get to meet and become friends with some wonderful people. The best way to get involved is to engage with your division(s), whose main purpose is to bring society governance close to the membership. Go to your annual division business meeting and contribute to the discussion. Go to your division mixer and talk to the division leadership.

#### Q: What has been the most rewarding part of being editor of *DMD*? What challenges have you encountered during your term?

A: The most rewarding aspect has been to experience the esteem in which the journal is held by scientists in the drug metabolism/transporter/ PK fields. I've also been privileged to have an incredible group of hard-working and insightful associate editors and editorial board members whose dedication has been inspiring. The biggest challenge has been to balance the importance of maintaining

## career scientists and researchers?A: There has been a lot of talk about this becoming

disposition? Any advice to graduates and mid-

a "mature field." However, the transporter field is burgeoning, as are new areas for research into drug metabolizing enzymes, e.g., as drug targets, or in developing novel catalysts for chemical syntheses and bioremediation. There is still much to learn about how genetics, physiology, and the environment interact to determine a person's drug metabolism phenotype. There will also be a continuing need for well-trained drug metabolism scientists in the pharmaceutical industry for the foreseeable future. So my advice would be: it's a rich and interesting field with lots of important contributions to be made, and I'd encourage you to be part of it.

## Q: What in your view are the emerging areas of research in the field of drug metabolism and disposition?

**A:** I've mentioned a couple of them in my previous response. Bioinformatics and modeling. Developing the tools to probe the roles of specific transporters in the disposition of drugs is an important area. As biologics become a bigger part of the therapeutic arsenal, understanding their metabolism, disposition, and PK becomes more challenging and important. And I think we've only skimmed the surface on epigenetic control of drug metabolizing enzymes and transporters.

has been to balance the importance of mainta and improving the impact factor with the important role the journal plays in serving the drug metabolism and disposition community. I think that the previous editors did a good job of that, and I hope that I have too. A second challenge that has arisen recently with the advent of so many new journals is a reduced number of submissions. I'm not sure what we can do about that except to continue to provide rapid and fair expert reviews, and encourage you all to submit to *DMD*!

Q: What advice would you give young investigators who wish to pursue a higher degree in the field of drug metabolism and



The Morgan Lab – October 2017 (from left to right): Nikki Olagbegi, JiWon Park, Eddie Morgan, and Choon Lee.



## **2017 Mid-Atlantic Pharmacology Society Annual Meeting in Review**

Submitted by Catherine C. Moore, PhD

The Mid-Atlantic Pharmacology Society (MAPS) held its annual meeting on October 26, 2017 at Temple University Health Science Center in Philadelphia, PA. Following a long-standing tradition, the meeting showcased the power of pharmacology to combat disease and highlighted recent pharmacological advances through a diverse program. The agenda included research presentations focused around an annual theme by both academic and industry experts, roundtable discussions by a panel of biotech leaders, invited talks and posters covering diverse areas of pharmacology by up and coming trainees, and awards to both mentors (distinguished career) and mentees (best posters).

The research presentations focused on this year's theme, Pharmacology of Metabolic Diseases, and featured recent therapeutic advances and mechanistic insights into metabolic alterations associated with diabetes, cardiac dysfunction, and adipocyte regulation. The keynote address, presented by renowned researcher Sheila Collins, PhD (Prebys Medical Discovery Institute), shed light on brown fat cell energy expenditure and metabolic health. Podium presentations by cuttingedge researchers from the Mid-Atlantic area fueled discussions on PPARy genetic variation and antidiabetic drug response (Mitchell Lazar, MD/PhD, University of Pennsylvania), myocardial GRK2 regulation and adipogenesis (Walter Koch, PhD, Temple University), and GPR40 ligand profiling and glucose/weight regulation (Maria Trujillo, PhD, Merck Research Laboratories).

The biotech roundtable discussion focused on *Biotech Success Stories*, and featured removing

the "un" from undruggable targets, adding the "re" to repositioning drugs, and broadening the drug "space" through collaborative operations. The session was moderated by R. Kyle Palmer, PhD (Opertech Bio and MAPS Councilor), and featured Ahmed Samater (CSO, TheraMet Biosciences), John Geisler (CSO, Mitochon Pharmaceuticals), and Andrew Reaume (President and CEO, Melior Discovery). Questions from meeting



Ellen Unterwald (right) from Temple University received the George B. Koelle Award, presented by Toby Eisenstein, co-director of the Center for Substance Abuse Research at Temple.

attendees also probed into biotech operations, investor targeting phases, and career turning points.

The George B. Koelle Award was presented to Ellen Unterwald, PhD (Temple University), who emulates the outstanding qualities of Dr. Koelle, including "profound commitment to teaching,



Brian Fuglestad (right) from the University of Pennsylvania received a postdoctoral poster award, presented by Marlene Jacobson, president of MAPS.

fondness for encouraging students, excellence in research, and strong devotion to the science of pharmacology." Congratulations Ellen! Continuing the commitment to foster trainee development, MAPS selected Invited Trainee Talks by graduate student Charikleia Kalliora (Temple University) and postdoctoral fellow Jessica Pfleger, PhD (Temple University). Poster topics covered broad areas of pharmacology and poster awards for 1st and 2nd place were given in the following categories: undergraduate student (Attilio Ceretti, Temple University; Nicole Lemon, Temple University); graduate student (Imran Sheikh, Temple University; Danielle Salvadeo, Temple University) and postdoctoral fellow (Brian Fuglestad, University of Pennsylvania; Pooja Jadiya, Temple University).

Thank you to all attendees, presenters, poster judges, and our financial sponsors (grants from ASPET; University of Pennsylvania, Department of Pharmacology; Temple Department of Pharmacology; and Temple University Centers for Substance Abuse Research, Translational Medicine, and Cardiovascular Research) and from the MAPS Officers and Councilors (Marlene Jacobson, President; Bradford Fischer, Vice President; Douglas Tilley, Past President; Linda Console-Bram, Treasurer; R. Kyle Palmer, Secretary; and Councilors Carol Beck, Julie Blendy, Thomas Keck, Catherine Moore, and Ellen Unterwald). See you next year!



The upcoming annual meeting is taking place in "America's Finest City," San Diego. For repeat visitors to San Diego, check out some of the offbeat places you may have missed before. Newcomers will be equally fascinated by these unique things to do in the area:





#### **Whaley House**

Built in 1856 by Thomas Whaley (an early settler of San Diego), the Whaley House is recognized for its historical significance in San Diego's Old Town neighborhood. The Whaley House is also wellknown for its paranormal sightings and reports, with The Travel Channel's "Most Haunted" show having named the Whaley House as the most haunted home in the country.

#### **Women's Museum of California**

The Women's Museum of California is located in a former Navy training facility, and is dedicated to the historic accomplishments and contributions of women. The Museum houses California's only known first edition of Susan B. Anthony and Elizabeth Cady Stanton's *The History of Women's Suffrage*.

#### Spruce Street Suspension Bridge

Located in the residential Bankers Hill neighborhood, the Spruce Street Suspension Bridge is a hidden pedestrian bridge 375 feet long, with a beautiful view of the Sessions Canyon below it.



#### Lemon Grove Mummies at the Museum of Man

"The Lemon Grove Girl", a teenage mummy and her infant companion, are housed at the San Diego Museum of Man. The teen is thought to have died between A.D. 1040 and A.D. 1260.

#### **Fallen Star**

Fallen Star is a little blue house that sticks out over the campus of UC San Diego, seven stories high. Fallen Star is the 18th piece in a series of permanent public art installations of the Stuart Collection at UCSD.

#### **1895** Looff Carousel

The Looff Carousel was first installed in Fair Park, Texas in 1895 and finally made its way to San Diego's Seaport Village area in 2004. The Looff Carousel is one of the few remaining carousels built by master amusement park carver Charles I.D. Looff.



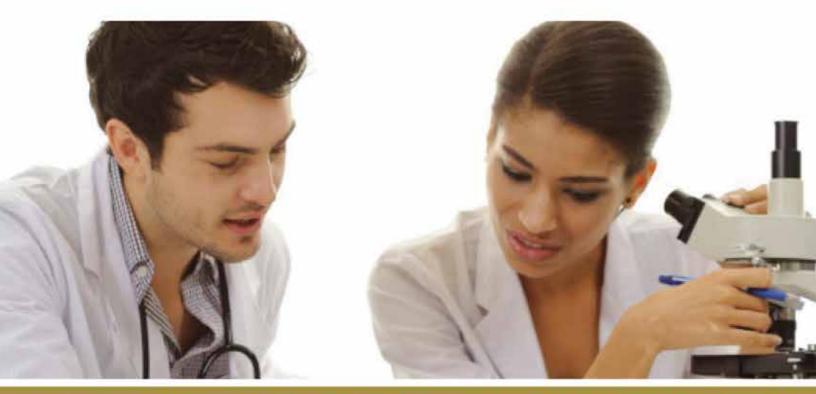


#### San Diego Model Railroad Museum

Located in a basement in San Diego's Balboa Park, the San Diego Model Railroad Museum is the largest indoor model railroad collection in the world and the only accredited museum of its type in the United States.

Be sure to register for the ASPET Annual Meeting at EB 2018 at www.aspet.org/eb2018/register.

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Tall khaki travel mug with silicone lid





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