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Rapamycin:
The fountain of youth?

INSIDE

ASPET
Transforming Discoveries into Therapies

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

Contents

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Message from The President

Dear Members of ASPET,

First of all, I would like to welcome the Canadian Society of Pharmacology and Therapeutics (CSPT) as ASPET's first international chapter, and thank CSPT President Dr. Michael Rieder and President-Elect Kerry Goralski for their work in putting this together. Both Societies are excited about this first step in building a closer relationship that will provide additional opportunities for our members to network, build collaborations, and present their research. This is a very timely development, as ASPET begins to work on our global strategy through our Global Partnerships Task Force.

Those of us who depend on federal grants to support our research programs will be gratified by the $2 billion in increased funding for the NIH in FY2019. ASPET's Science Policy Committee (SPC), under the leadership of Chair Dr. Ken Thummel and ASPET Sr. Manager for Government Affairs and Science Policy Tyler Lamb, partnered with our sister societies and FASEB to communicate with our lawmakers and government to convince them of the need for this increase. The SPC also are committed to helping members engage with their representatives and senators. If you would like to advocate on an ASPET-related issue, please don't hesitate to contact Tyler for assistance.

The SPC is just completing a review of our Washington Fellows Program, and Council has approved funds to improve the experience for the Fellows by bringing them all to Washington at the same time and providing them with more programming during their visit. Please take the time to read the op-eds by some of our Washington Fellows in this issue of *The Pharmacologist*! Here are some of the other achievements of the SPC and our Public Affairs Department in the past year:

- arranged for an ASPET member to testify before the House Energy and Commerce Health subcommittee on research concerns related to opioid legislation;
- amended a bill favorably in the Maryland legislature that would have burdened research institutions with onerous reporting requirements;
- joined the Membership Committee of the Coalition for Health Funding to increase awareness of ASPET;
- redesigned the advocacy section of the ASPET website; and
- over the course of 2018, visited 70+ House offices and 30+ Senate offices to discuss ASPET's policy priorities with legislators and staff.

Also related to science policy, please read the article in this issue by the Board of Publications Trustees Chair, Dr. Mary Vore, and myself, that describes a new Open Access publishing movement called cOAlition S and its implementation of Plan S. There is concern that this plan could radically change the landscape of research publishing and thereby affect the services and activities that ASPET is able to offer our members.

In my last message, I mentioned that Council had approved an ASPET Fellows Program to recognize members for their outstanding contributions to science and our society. I can now share some details with you. Fellows will be ASPET members who have had a significant and sustained impact on the field of pharmacology; who have demonstrated commitment to mentorship and teaching; and who have shown commitment to ASPET through contributions to committees, editorial boards, or scientific meetings. Fellows will be recognized and honored at the ASPET Annual Business Meeting, and in various forums including a profile on the ASPET website, as well as announcements in the membership email newsletter, in *The Pharmacologist*, and on social media. They will also be entitled to use the designation FASPET (Fellow of ASPET) in their signatures. The inaugural Fellows class will be selected by Council, and subsequent Fellows will be selected by a committee of existing Fellows. Look for the announcement of the first cohort of Fellows in August 2019!

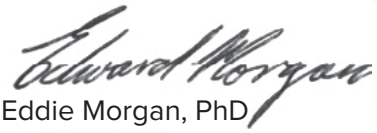
I'm particularly excited about the upcoming EB 2019 meeting in Orlando, when we will get to see the impact of the many different initiatives we have instituted in our drive to reimagine the meeting. As a reminder, these include shortening the meeting to four days (Saturday-Tuesday) and a dedicated poster presentation time providing an outstanding experience for our trainees with no competing talks, meetings, or lunch breaks. And, of course, other recent improvements such as the integration of the meeting through the all-society Tang Prize Award Lecture and opening reception as well as the ASPET datablitz will continue. Don't miss the joint ASPET-APS Presidential Symposium series on the microbiome in physiology and pharmacology! Other reasons to attend EB 2019 include: five disciplines intersecting to bring you cutting-edge scientific sessions; ASPET-specific networking opportunities including division mixers, the poster competition, and the member lounge; and a large exhibit hall where you can check out the latest innovative technology to benefit your research.

Our Young Scientists Committee (YSC) has been very active in helping us reimagine the annual meeting and to reach out to the next generation of pharmacologists. The YSC hosted its second annual undergraduate outreach event in conjunction with EB 2018 at the University of California, San Diego. In 2019, they will team up with the Orlando Science Center to make a visit to Edgewater High School, which has a magnet program directed at students who are interested in pursuing careers in science, engineering, and technology. Among other activities, the visit will be used to educate the students about ASPET's SURF program.

Other activities planned by members of the YSC for EB 2019 include a symposium on the opioid epidemic, participation in a CV-to-resume workshop at the Graduate Student - Postdoctoral Colloquium, continuing and improving their Partnering for Success peer mentoring program, and an improved Poster Bingo experience. The level of enthusiasm, innovation, and commitment to ASPET by Chair Stephanie Davis and all the members of YSC is both amazing and highly gratifying, and I hope you'll have the opportunity to attend and/or participate in some of these events.

I wish you and your families a joyous and safe holiday season, and look forward to seeing you at EB 2019 in Orlando!

Warm regards,



Eddie Morgan, PhD
ASPET President

2018 Year in Review

Membership

4,457
total members
in **73** countries

424
new members
in 2018

Education & Awards

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

68 **poster awards** provided to young scientists at the Annual Meeting

$106,029
provided to ASPET **scientific achievement award** winners

Publications

ASPET's *Journal of Pharmacology and Experimental Therapeutics, Molecular Pharmacology, Drug Metabolism and Disposition,* and *Pharmacological Reviews* had a successful year of publishing.

72 Open Access articles were published.

59% of all articles in the journals (back to 1908) were accessed.

Received manuscripts from **58** different countries.

3,446 manuscript reviews were completed.

Data supplements were accessed an average of **20,671** times per month.

Figures were downloaded to PowerPoint an average of **87,268** times per month.

Articles were accessed through RSS feeds an average of **82,019** times per month.

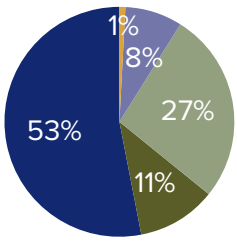
The Pharmacologist continues to be an important publication with **12,538** total hits from December of last year through November of this year.

Annual Meeting at EB 2018

The primary interest of **1,539** attendees at EB 2018 was pharmacology. An additional **9,693** multi-disciplinary scientists participated at EB creating a uniquely collaborative community.

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

- 1% high school students
- 8% undergraduates
- 27% graduate students
- 11% postdocs
- 53% established scientists



The countries with the highest representation of scientists at the ASPET Annual Meeting were:
1. United States **2.** China **3.** South Korea
4. Canada **5.** Brazil **6.** United Kingdom

Once again ASPET saw an increase in the number of abstracts submitted to pharmacology. We accepted **894** abstracts in pharmacology topics at EB 2018.

- **10** top ASPET abstracts were featured EB-wide at the EB Scientific Highlights poster session
- **30** top scoring abstracts from students and postdocs were featured in the ASPET Daily Datablitz
- **65** abstract submitters were selected to present talks at ASPET symposia
- **141** young scientists earned spots to compete in the ASPET student/postdoc poster competition

Pharmacology research presented at the ASPET Annual Meeting attracted coverage in major news outlets including:

- Los Angeles Times
- The Washington Post
- Orlando Sentinel
- UPI
- New Scientist
- Futurism

Science Policy

70+
House office visits

30+
Senate office visits

15
letters to public officials

5
letters of testimony submitted

1
ASPET member invited to testify at a committee hearing

Social Media

2,056
total "likes" and
2,020 follows for ASPET's Facebook page

2,251
ASPET Twitter followers

2,262
ASPET LinkedIn group members

Career Center

The ASPET Career Center averages **112** **jobs available** on the site daily

There have been **19,263** **page views** on the ASPET Career Center

All of the statistics in the "2018 Year in Review" were taken as of November 15, 2018.

2018 Contributions

ASPET gratefully acknowledges the following individuals who made contributions from November 2017 through October 2018:

Amir Askari
James Barrett
Michael Callahan
Ingeborg Hanbauer
Omar Issa
Linda Jones
Christopher Larbie
Robert Pechnick
Elaine Sanders-Bush
Afifah Sutjiatmo
Rita Valentino
Pancras Wong
Michael Wood

Thank you to our Annual Meeting Sponsors:

Association of Medical School Pharmacology Chairs (AMSPC)
La Jolla Alcohol Research, Inc.
UT Health San Antonio
University of California, Irvine
University of Cincinnati
University of Michigan
University of Minnesota
University of North Carolina - Chapel Hill
University of South Florida
University of Wisconsin-Madison
Wake Forest School of Medicine
West Virginia University

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

Tax-deductible donations to ASPET support research, publications, travel scholarships, science advocacy, and career development for scientists. Making a donation is a great way to demonstrate your commitment to the future of ASPET and pharmacology! Thank you for your support!

Donate today at https://www.aspet.org/aspet/utility-nav/donate/donate-to-aspet

2019 Election

The ASPET election for president-elect, secretary/treasurer-elect, and councilor will open on January 7, 2019. Eligible voting members will receive notification when the election opens.

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

- Division for Behavioral Pharmacology
- Division for Cardiovascular Pharmacology
- Division for Drug Metabolism and Disposition
- Division for Molecular Pharmacology
- Division for Pharmacology Education
- Division for Toxicology

Full candidate biographies will be available online when the election opens. Division candidate information is on page 256.

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 8, 2019.

Nominees for President-Elect

Charles P. France, PhD
Professor of Pharmacology and Psychiatry, Robert A. Welch Distinguished Chair in Chemistry, University of Texas Health Science Center

John J. Tesmer, PhD
Walther Professor in Cancer Structural Biology, Purdue University

Charles P. France, PhD

Candidate's Statement

I have benefited enormously from my 26 years of ASPET membership, especially the last few years when I had the privilege of serving on committees, as division chair, councilor, and most recently secretary/treasurer. I have witnessed first-hand the dedication and passion of the educators, scientists, policy makers, and others who comprise the Society, and I am honored to be nominated to run for president.

The next president will inherit leadership of a very healthy organization, thanks to the hard work and vision of ASPET members and staff. One charge of the president's office is to implement the strategic plan crafted by ASPET leadership, staff, and members. I helped construct the plan and as president, I will work to advance its implementation. The plan is thoughtful, forward thinking, and provides a realistic roadmap of how the Society can evolve to remain attractive, relevant, and effective. While all

six goals in the plan demand our attention, I am most passionate about two goals:

1. "Attracting and Developing the Next Generation"—To remain a viable and effective scientific organization, the Society and the discipline need to attract bright, young scientists and educators who are ready, willing, and able to carry the torch of pharmacology into the future. To that end we must continually work to improve the annual meeting, provide funding for young people to experience pharmacology (SURF programs) and attend the annual meeting (travel fellowships), and at every opportunity promote education in pharmacology. We need to ensure that the Society provides value to its members and that the annual meeting remains an attractive destination for young scientists as well as a showcase for cutting-edge science.
2. "Advocating for Critical Science Policies"—As the ultimate translational discipline, pharmacologists must advocate for research and education in biomedical science. As a member of the Science Policy Committee, I witnessed the passion and dedication of ASPET staff and members who reach out to the public and policymakers, advocating for biomedical science and the Society. The enthusiasm of our Washington Fellows is contagious and one of the most effective ways we can communicate with policymakers. If elected, I will use the office of the president to advocate for sustained investment in biomedical science and I will use the resources and stature of ASPET to educate non-scientists about the value as well as the high return on investment (improved public health) of biomedical research. Science is under attack (e.g., use of animals in research, rigor, and reproducibility) and we all share the responsibility of educating the public about our goals, our dedication, and the high ethical standards that guide us in our daily work.

The current financial health of the Society will help protect the organization and its members from unforeseen challenges in the future. The financial health of the Society continues to pay dividends in terms of reinvestments in the membership and the discipline. Initiatives such as Big Ideas, student (including undergraduate) travel fellowships, and new activities at the annual meeting are generating enthusiasm throughout our membership. Thanks to thoughtful stewardship by the Financial Committee, the Investment Subcommittee, and ASPET staff, the future of the Society looks bright in terms of financial security, and there will continue to be opportunities to reinvest in our members and the discipline of pharmacology.

Notwithstanding the excellent financial health of the Society, there are sure to be challenges ahead that will demand creative and thoughtful action. We must be particularly attentive to open-access journals and the rapidly changing publication environment to both protect and maintain the historically rich and highly respected contributions to science 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 budget. As president, I will work with the Board of Publications Trustees to protect and plan for the future of our journals.

Although the Society is in excellent financial health and the journals are doing very well, ASPET is not defined by money or publications, but by its members who determine programming for the annual meeting, select the policies ASPET addresses through its various committees, and shape the future by electing ASPET leadership. If elected I will serve the Society in the spirit of what I believe ASPET represents—excellence in and advocacy for biomedical science and education. To the best of my ability, I will work for the Society in a manner that serves the individual members who have dedicated their careers to pharmacology.

John J. Tesmer, PhD

Candidate's Statement

ASPET has been instrumental to the development of my career and of the trainees in my lab, and I seek to return the favor by working to ensure that others have the same opportunities. As your candidate for president, I pledge to work toward maintaining the overall intellectual and financial health of our Society, and providing the membership with innovative and high content programs. Toward these overarching goals, I would emphasize several specific objectives that should be achievable over the course of the next three years:

- Integration of ASPET programming activities at the Experimental Biology meeting with the content of other FASEB societies, in particular

ASBMB and APS, to minimize overlap and identify common thematic material, thereby enhancing the experience of attendees and generating cost savings.

- Refinement of the meeting format and increasing the number of travel awards to better highlight the research of our junior investigators. Not only are these individuals engaged in some of the most cutting-edge research activities, but also their success would ensure the generation of many future ASPET members within their laboratories. Promoting the careers of these individuals is thus key to the continued viability and evolution of our society.
- Increasing the voice of trainees and junior faculty in ASPET governance by establishing mechanisms by which they may serve on ASPET executive committees and on Council. This would be part of my overall effort to identify ways to instill more diversity of all kinds in our leadership and membership.

These outcomes are all consistent with the 2017 ASPET strategic plan.

Nominees for Secretary/Treasurer-Elect

Carol L. Beck, PharmD, PhD
Associate Professor, Department of Pharmacology & Experimental Therapeutics, Sidney Kimmel Medical College; Associate Dean for Curriculum, Jefferson College of Life Sciences, Thomas Jefferson University

Mary-Ann Bjornsti, PhD
Professor and Chair, Department of Pharmacology and Toxicology, University of Alabama at Birmingham; Associate Director for Translational Research, University of Alabama at Birmingham Comprehensive Cancer Center

Carol L. Beck, PharmD, PhD

Candidate's Statement

With the involvement of a cross-section of members at all levels, division leadership, Council, and staff, ASPET finalized a new strategic plan in 2017. Our strategic plan is a critical document in helping us make decisions that focus on the agreed upon mission of being the professional home for scientists at all levels working in the broad field of pharmacology.

The Secretary/Treasurer, the Finance Committee, and the Investment Subcommittee are responsible for making recommendations related to the fiscal health of ASPET. As professional and volunteer organizations everywhere are experiencing declining membership numbers and thus declining dues revenue, we must realize that this may affect funding of programs. We need to carefully assess which programs align with our mission and continue to fund those programs. ASPET is fortunate to have investment income to supplement dues and publication revenues, but it is important to use these funds wisely and not as a routine part of the budget. The strategic plan is our roadmap for staying focused on programs that relate to our mission; we may not be able to fund all good and noble projects. We must be prepared to use our funds to benefit our members and to promote pharmacology to the next generation of scientists.

My career-long involvement in professional and community organizations at all levels, including service on the Finance Committee of the Biophysical Society (2013-2016), gives me a good perspective to serve in the role of ASPET secretary/treasurer. I would welcome this opportunity to serve ASPET in this capacity.

Mary-Ann Bjornsti, PhD

Candidate's Statement

I am honored to be nominated to serve as the secretary/treasurer of ASPET. This is an exciting time for the discipline of pharmacology, and ASPET has embarked on a new strategic plan that promises to promote excellence in pharmacology research, education, and public policy and provide a world class annual meeting for the presentation and discussion of the very best scientific accomplishments of our scientific community. During the past several years, I have actively participated in science policy efforts to advocate for increased federal support and funding of pharmacology and biomedical research, and have worked closely with colleagues on the ASPET Program Committee to improve the quality of the ASPET Annual Meeting at EB. I have also had the privilege as chair of the Division of Cancer Pharmacology to work with the former chair, Susan Cole, the incoming chair, Andrew Thorburn, the secretary/treasurer, Jack Yalowich, and other members of the executive committee to help establish this relatively new division as a vibrant part of ASPET, with increasing engagement with the cancer community and a track record of exceptional science symposia and poster presentations at the annual meeting.

As chair of the Department of Pharmacology and Toxicology at the University of Alabama at Birmingham since 2009, I fully appreciate the challenges of providing the resources and support critical to promoting the development of robust research and educational programs, in a fiscally responsible manner. Achieving each of these goals requires financial planning to ensure operational costs are managed efficiently and that resources are also available to support innovative programs. If I am fortunate to be elected secretary/treasurer, I look forward to working with the ASPET president, Council, divisions, committees, and membership to achieve the strategic goals of the society and to assist with the financial management, business planning, and budgetary functions that are critical for the success of the organization.

Nominees for Councilor

Namandjé N. Bumpus, PhD
Associate Dean for Basic Research; Associate Professor of Medicine and Pharmacology & Molecular Sciences, Johns Hopkins University School of Medicine

Emily E. Scott, PhD
Professor, Departments of Medicinal Chemistry and Pharmacology and Programs in Biophysics and Chemical Biology, University of Michigan

Namandjé N. Bumpus, PhD

Candidate's Statement

ASPET has been my professional home since I was a trainee. During my time in ASPET, I have served on the Public Affairs Committee, Awards Committee, and as a councilor and subsequently secretary/treasurer in the Division for Drug Metabolism and Disposition. Through these service opportunities, ASPET has nurtured my growth as both a pharmacologist and a member of our pharmacology community. I would like the chance to actively participate in doing the same for others through playing a role in continuing to expand the space and the platforms that we provide for trainees and early stage investigators to showcase their work and to grow both professionally and scientifically.

My collective professional experience will enable me to make unique and meaningful contributions to

ensuring that ASPET achieves the goals outlined in the strategic plan. My background as a leader, with responsibilities in both graduate education and basic science more broadly, positions me to be a strong contributor to ASPET's efforts to attract and develop the next generation of pharmacologists. I have a deep interest in and history of actively working in full service of providing emerging and early stage investigators with support and high-quality educational experiences while aggressively addressing issues related to their success. My time on the Public Affairs Committee of ASPET as well as my personal interactions with legislators on Capitol Hill including delivering a briefing on pharmacology this year to the Congressional Biomedical Research Caucus, have provided me with valuable perspectives that I will leverage in working to promote pharmacology and ASPET, in addition to advocating for critical science policies. To achieve the goals of reimagining the annual meeting experience, enhancing the ASPET journals, and strengthening ASPET overall, the application of assessment measures will be an important consideration. Through my leadership experience I have established a track-record of employing assessment and accountability measures to help to guide and enhance strategic planning goals. Finally, I truly value that ASPET is an environment of shared governance. My experience as a leader and diplomat with strong organizational and consensus-building skills equip me to positively and enthusiastically participate in our shared governance.

Emily E. Scott, PhD

Candidate's Statement

The councilor duties are to serve as 1) Council liaison to the divisions and other subgroups and 2) a reviewer for various award committees. I see serving as a liaison as a privilege of not just involving maintaining clear communication and mutual understanding across different areas of our society, but also working with multiple parties to help creatively solve problems and advance the profession and profile of pharmacology, both within our society and externally. This includes reaching out to the next generation of researchers and pharmacologists broadly defined. Most recently I have had significant experience bringing together diverse interests, agendas, and visions to establish the first cross-campus Core facility at the University of Michigan, a BioNMR facility that successfully serves and is responsive to researcher needs. With respect to commitment to reviewing on award committees, I strive to be thorough, confidential, fair, and timely. My previous experience includes service on numerous award committees for trainees at multiple institutions, for ASPET in the Drug Metabolism and Disposition Division and for the Bernard B. Brodie Award in Drug Metabolism, for the International Society for the Study of Xenobiotics in North America and Asia, for the Herb Tabor Young Investigator Award given by the *Journal of Biological Chemistry*, and as a reviewer for NIH, NSF, and international granting organizations.

The ASPET 2019 election will open on January 7, 2019. 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/eb2019-TPharmDec. *Schedule subject to change.*

All ASPET events will be held at the Orange County Convention Center (OCCC) and the adjacent Rosen Centre Hotel.

Friday, April 5, 2019

Session/Event	Time
Give a Day of Service to Orlando at EB 2019	8:00 am - 2:00 pm

Saturday, April 6, 2019

Session/Event	Time
An Apel(-in) a Day Keeps Cardiovascular Disorders at Bay? *Chairs: R. Maitra and H. Chun*	11:00 am - 1:00 pm
Mechanisms of Drug-Induced Liver Injury: From Bedside to Bench and Back *Chairs: X. Ma and N. Kaplowitz*	11:00 am - 1:00 pm
New Strategies for Augmenting Immune Checkpoint Blockade in Cancer Therapy *Chairs: C. Canman and J. Lazo*	11:00 am - 1:00 pm
Teaching Institute: Pharmacology Education ADME: Audience, Design, Modality and Experimentation *Chairs: M. Bush and K. Summers*	11:00 am - 1:00 pm
ASPET-APS Presidential Symposium Workshop: Microbiome Research: What You Need to Know *Chairs: A.D. Patterson and M. Hullar*	1:00 pm - 3:00 pm
Graduate Student - Postdoctoral Colloquium: Building Winning Career Connections: The Art of Self-Promotion *Chair: L. Devi*	2:00 pm - 4:00 pm
Balancing Content, Critical Thinking, and Creativity in Graduate Education *Chair: M. Nieman*	2:00 pm - 4:00 pm

Leveraging Novel Insights into Allosteric Modulator Pharmacology for CNS Disorders *Chair: K. Gregory*	2:00 pm - 4:00 pm
Natural Product-Drug Interactions: Complex Mechanisms and Public Health Impact *Chairs: M. Paine and A. Roe*	2:00 pm - 4:00 pm
Renal Development and Disease *(EB multi-discipline symposium)*	3:00 pm - 4:30 pm
ASPET Business Meeting and Awards Presentation	**4:30 pm - 6:00 pm**
All Society EB Lecture - Tang Prize *Keynote: Brian J. Druker* *Imatinib as a Paradigm of Targeted Cancer Therapies*	6:00 pm - 7:00 pm
All Society EB Welcome Reception *Including Scientific Highlights Posters*	7:00 pm - 8:30 pm

Sunday, April 7, 2019

Session/Event	Time
Diversity and Inclusion Breakfast	7:30 am - 9:30 am
ACE2/Angiotensin-(1-7)/Mas Receptor Axis: Look How Far We've Come! *Chairs: Y. Jarajapu and R. Valentino*	8:00 am - 10:00 am
Addressing the Opioid Epidemic Through Science and Policy *Chairs: S. Kaska and C. Paronis*	8:00 am - 10:00 am
G protein-β -arrestin Interplay: Molecular and Therapeutic Implications *Chairs: D. Tilley and Y. Xiang*	8:00 am - 10:00 am
ncRNAs in Drug Metabolism and the Translation of Gene Silencing Technology into Therapeutics *Chairs: B. Ning and J. Lade*	8:00 am - 10:00 am

= Lectures = Networking

ASPET Welcomes Our Guest Societies!

The following are ASPET guest societies at EB 2019. Members of these organizations can register for EB using the ASPET member discount and can sponsor their own abstracts.

Behavioral Pharmacology Society
Catecholamine Society
Chinese Pharmacological Society (CNPHARS)
Global GI Club

Sunday, April 7, 2019 *continued*

ASPET-APS Presidential Symposium I: Gut Microbiome and Metabolic Disorders *Chairs: E. Morgan and J. Sands*	8:30 am - 10:00 am
ASPET Poster Presentations	10:00 am - 12:00 pm
ASPET Daily Datablitz *Sponsored by* Pharmacology Research & Perspectives	10:30 am - 11:00 am
Networking in the Exhibit Hall *Visit with exhibitors, grab lunch, explore Career Central*	12:00 pm - 1:00 pm
Undergraduate Networking and Career Development Luncheon	12:15 pm - 2:00 pm
John J. Abel Award in Pharmacology Lecture *Keynote to be announced in January*	1:00 pm - 1:45 pm
Julius Axelrod Award in Pharmacology Lecture *Keynote: Joe A. Beavo* *Cyclic AMP Coordination of Signaling Pathways: What Does Phosphoproteomic Analysis with PDE Inhibitors Suggest?*	1:45 pm - 2:30 pm
Axelrod Symposium: Phosphoproteomic Analysis of G Protein-Coupled Pathways *Chairs: J. Beavo and M. von Zastrow*	3:00 pm - 5:00 pm
Journals Workshop: An Interactive Guide to Publishing, Reviewing, and Ethics Issues *Chairs: M. Vore and R. Dodenhoff*	3:00 pm - 5:00 pm

= Lectures = Networking

EB Programming

Unlock the full EB program!

Did you know your registration fee to the ASPET Annual Meeting includes the full EB program with 5 host societies' annual meetings and 25 guest societies?

This opportunity for transdisciplinary exploration and collaboration in the life sciences community is unmatched. Explore the EB program here: https://bit.ly/2Pxjfnq.

Sunday, April 7, 2019 *continued*

ASPET-CNPHARS Joint Symposium: Parkinson's and Alzheimer Diseases: Neuronal Mechanism and Therapeutic Discoveries to Combat Neurodegenerative Diseases *Chairs: Y. Zhang and H. Khoshbouei*	3:00 pm - 5:00 pm
Companion Animals in the Cancer Therapeutic Development Pipeline *Chair: D. Gustafson*	3:00 pm - 5:00 pm
Virtual Pharmacology and Experimental Therapeutics: Near or Distant? *Chair: C. A. Hunt*	3:00 pm - 5:00 pm
David Lehr Research Award Lecture *Keynote: Paul A. Insel* *GPCRs as Novel Therapeutics for Pancreatic Cancer*	5:15 pm - 6:00 pm
ASPET Student / Postdoc Poster Competition *Including display tables for university graduate programs*	6:30 pm - 8:30 pm
ASPET Student / Postdoc Mixer	8:30 pm - 11:00 pm

= Lectures = Networking

Give a Day of Service to Orlando at EB 2019

Join us for a day of volunteer service on Friday, April 5 from 8:00 am – 2:00 pm.

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 shelves, food preparation and service, and building maintenance. The ASPET Division for Behavioral Pharmacology will again sponsor this volunteer opportunity.

At EB 2019, we will spend the day working with Habitat for Humanity Greater Orlando & Osceola County https://habitatorlandoosceola.org.

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

ASPET volunteers build homes with Habitat for Humanity New Orleans in 2009

Monday, April 8, 2019

Session/Event	Time
Drugging DNA Damage Response and Repair: A Layered Therapeutic Approach for Cancer Treatment *Chair: R. van Waardenburg*	8:00 am - 10:00 am
Genetic Polymorphisms in Drug Metabolizing Enzymes *Chairs: M. Shah, L.M. Henderson and A. Ramamoorthy*	8:00 am - 10:00 am
New Roles and Mechanisms of RGS Proteins in Physiology and Disease *Chairs: K. Martemyanov and R. Fisher*	8:00 am - 10:00 am
Targeting Adipose Inflammation in Diabetic Vascular Complications *Chairs: A. El-Yazbi and R. Touyz*	8:00 am - 10:00 am
ASPET-APS Presidential Symposium II: Gut Microbiota: A Chemical Factory *Chairs: Y. Jeong and J. Pluznick*	8:30 am - 10:00 am
ASPET Poster Presentations	10:00 am - 12:00 pm
ASPET Daily Datablitz *Sponsored by* Pharmacology Research & Perspectives	10:30 am - 11:00 am
Networking in the Exhibit Hall *Visit with exhibitors, grab lunch, explore Career Central*	12:00 pm - 1:00 pm
Reynold Spector Award in Clinical Pharmacology Lecture *Keynote to be announced in January*	1:00 pm - 1:45 pm
Scientific Achievement Award in Drug Discovery and Development Lecture *Keynote to be announced in January 2019*	1:00 pm - 1:45 pm
Enteric Drug Metabolism and Drug-Drug Interactions *Chair: A. Li*	2:00 pm - 3:30 pm
New Opportunities in Targeting WNT Signaling *Chairs: W. M. Blankesteijn and G. Schulte*	2:00 pm - 3:30 pm
Novel Neuropeptides that Regulate Motivational and Reward-Related Behaviors *Chairs: E. Bobeck and S. Clark*	2:00 pm - 3:30 pm
The Need for Scientists in Regulation and Policy: Academia, Government, and Industry *Chairs: B. Gannon and M. Delatte*	2:00 pm - 3:30 pm
What Does Sex Have to Do With It? Implications for Pharmacotherapy *Chairs: S. Wood and C. Northcott*	2:00 pm - 3:30 pm
Division for Pharmacology Education: Surviving an Existential Threat - Creating a Niche for Basic Science Educators *Chairs: A. Ram and L. Cohen*	4:00 pm - 5:30 pm
Division for Drug Metabolism and Disposition Gillette Awards and Junior Investigator Platform Session	4:00 pm - 6:00 pm

= Lectures = Networking

Monday, April 8, 2019 *continued*

Division for Molecular Pharmacology **Postdoctoral Award Competition**	4:00 pm - 6:00 pm
Division for Neuropharmacology **Postdoctoral Scientist Award Finalists**	4:00 pm - 6:00 pm
Division for Toxicology - Division Programming Symposium	4:00 pm - 6:00 pm
Annual Division Meeting for: • Division for Pharmacology Education	5:30 pm - 6:30 pm
Annual Division Meetings for: • Drug Metabolism and Disposition • Molecular Pharmacology • Neuropharmacology • Toxicology	6:00 pm - 6:30 pm
Division Mixers for: • Drug Metabolism and Disposition, Pharmacology Education, and Toxicology • Molecular Pharmacology	6:30 pm - 8:30 pm

= Lectures = Networking

First Timers' Navigation Guide

Is this your first time to EB or haven't been in a while?

ON DAY 1

We kick things off mid-morning **Saturday** and offer 9 symposium options before our big event, the **ASPET Business Meeting and Awards Presentation**, a place to catch up on the latest ASPET member initiatives and celebrate our award winners.

We then join the other EB host societies for two multi-disciplinary events - the **Tang Prize Lecture** and a **Welcome Reception** which includes the top posters across all EB.

ON DAY 2

Sunday is a full day packed with great science from 8:00 am until 8:30 pm. Choose from a variety of symposia, award lectures, posters, and career development sessions like the **Journals Workshop**, an interactive guide to publishing, reviewing, and ethics.

The **Student/Postdoc Poster Competition** that ends the day includes refreshments along with top research presented by our young scientists in every divisional topic area.

ON DAY 3

In addition to another full day of symposia, posters, and award lectures, on **Monday** afternoon the first half of ASPET's 10 divisions will host special programming focused on their topical area. These are immediately followed by their annual business meetings where you can learn how becoming involved in division activities can help your career.

In the evening, the division-hosted **mixers** provide a prime opportunity for networking and fostering collaborations in your research area.

ON DAY 4

Don't be fooled into thinking you've seen it all by the last day. **Tuesday** is another day packed with over 10 symposium options, 200+ new posters, award lectures, and division-hosted special programming, business meetings, and mixers from the other 5 divisions. It doesn't wrap up until 8:30 pm. You'll want to be sure to spend the night!

EVERY DAY TIPS

Stop in the **ASPET member lounge** for a comfy chair, a cup of coffee, wifi, and fellowship!

Attend the **Daily Datablitz** for a fast-paced overview of the most exciting science of the day. Ten poster talks in 30 minutes!

Career Central is open throughout EB, offering a variety of services and educational opportunities.

Check out our website for all the up-to-date program and schedule information.
www.aspet.org/eb2019-TPharmDec

Tuesday, April 9, 2019

Session/Event	Time
Cardiovascular Signaling via the G Protein-Coupled Estrogen Receptor *Chairs: K. Tran and S. Lindsey*	8:00 am - 10:00 am
Functional Output of Sexual Dimorphism of Neuroimmune Cells *Chairs: L. Torres and S. Tsirka*	8:00 am - 10:00 am
Maximizing the Therapeutic Value of Psychedelics: Recent Preclinical Studies *Chairs: C. Canal and P. Hendricks*	8:00 am - 10:00 am
Strategies to Assess Drug-Drug Interactions when Developing Fixed Dose Combinations *Chairs: Y. Lai and P. Zhao*	8:00 am - 10:00 am
ASPET-APS Presidential Symposium III: Microbiota in Action: The Gut and Beyond *Chairs: L. McCabe and J. Cui*	8:30 am - 10:00 am
ASPET Poster Presentations	10:00 am - 12:00 pm
ASPET Daily Datablitz *Sponsored by* Pharmacology Research & Perspectives	10:30 am - 11:00 am
Networking in the Exhibit Hall *Visit with exhibitors, grab lunch, explore Career Central*	12:00 pm - 1:00 pm
Norman Weiner Lecture *Keynote: Mary Vore* *Cancer Chemotherapy, Oxidative Stress, and ATP-Dependent Efflux Transporters*	1:00 pm - 1:45 pm

= Lectures = Networking

Tuesday, April 9, 2019 *continued*

Bridging the Translational Gap in Ischemic Stroke Research *Chair: K. Pennypacker*	2:00 pm - 3:30 pm
New Paradigms for Targeting Adenosine Receptors: Basic and Translational Applications *Chairs: L. May and R. Corriden*	2:00 pm - 3:30 pm
Pharmacology of Taste: From Receptors to Behavior *Chair: K. Palmer*	2:00 pm - 3:30 pm
Pharmacology Repurposed: Novel Uses for Current Therapies *Chairs: M. Zimmerman and J. Provost*	2:00 pm - 3:30 pm
Teaching Blitz *Chairs: N. Kwiek and B. Cummings*	2:00 pm - 3:30 pm
Division for Behavioral Pharmacology - Team Science: from Molecules to Test Tubes to Behavior	4:00 pm - 6:00 pm
Division for Cancer Pharmacology - Young Investigators Symposium	4:00 pm - 6:00 pm
Division for Cardiovascular Pharmacology Trainee Showcase	4:00 pm - 6:00 pm
Presentations of Noteworthy 2019 Abstracts from Drug Discovery and Development	4:00 pm - 6:00 pm
Division for Translational and Clinical Pharmacology - Young Investigator Awards Platform and Early Career Faculty Showcase	4:00 pm - 6:00 pm
Annual Division Meeting for Cardiovascular Pharmacology	5:30 pm - 6:00 pm
Annual Division Meetings for: • Behavioral Pharmacology • Cancer Pharmacology • Drug Discovery and Development • Translational and Clinical Pharmacology	6:00 pm - 6:30 pm
Benedict R. Lucchesi Young Scientist Award in Cardiac Pharmacology *Awardee to be announced in January 2019*	6:00 pm - 6:30 pm
Division Mixers for: • Behavioral Pharmacology and Neuropharmacology • Cancer Pharmacology, Drug Discovery and Development, and Translational and Clinical Pharmacology • Cardiovascular Pharmacology	6:30 pm - 8:30 pm
DMDD Meet-the-Experts Dinner and Reception for Richard Okita Early Career Award (tickets required)	6:30 pm - 9:00 pm

= Lectures = Networking

Division-Specific Meetings and Activities

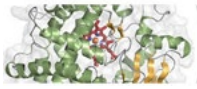
Explore the new division filter to see a full schedule of sessions of interest to your division at EB 2019.
www.aspet.org/eb2019-program-TpharmDec

Tuesday, April 9	12:00 pm - 1:00 pm	BEH Executive Committee Meeting (invitation only)
Tuesday, April 9	4:00 pm - 6:00 pm	BEH Division Programming: *Team Science: from Molecules to Test Tubes to Behavior*
Tuesday, April 9	6:00 pm - 6:30 pm	BEH Annual Division Meeting
Tuesday, April 9	6:30 pm - 8:30 pm	Joint Mixer: BEH with Neuropharmacology

Tuesday, April 9	12:00 pm - 1:00 pm	DCP Executive Committee Meeting (invitation only)
Tuesday, April 9	4:00 pm - 6:00 pm	DCP Young Investigators Symposium
Tuesday, April 9	6:00 pm - 6:30 pm	DCP Annual Division Meeting
Tuesday, April 9	6:30 pm - 8:30 pm	Joint Mixer: DCP with Drug Discovery and Development and Translational and Clinical Pharmacology

Tuesday, April 9	12:00 pm - 1:00 pm	CVP Executive Committee Meeting (invitation only)
Tuesday, April 9	4:00 pm - 5:30 pm	CVP Trainee Showcase
Tuesday, April 9	5:30 pm - 6:00 pm	CVP Annual Division Meeting
Tuesday, April 9	6:00 pm - 6:30 pm	Benedict R. Lucchesi Young Scientist Award in Cardiac Pharmacology
Tuesday, April 9	6:30 pm - 8:30 pm	CVP Mixer

Monday, April 8	12:00 pm - 1:00 pm	DDD Executive Committee Meeting (invitation only)
Monday, April 8	1:00 pm - 1:45 pm	Scientific Achievement Award Lecture in DDD
Tuesday, April 9	4:00 pm - 6:00 pm	Presentations of Noteworthy 2019 Abstracts from Drug Discovery and Development
Tuesday, April 9	6:00 pm - 6:30 pm	DDD Annual Division Meeting
Tuesday, April 9	6:30 pm - 8:30 pm	Joint Mixer: DDD with Cancer Pharmacology and Translational and Clinical Pharmacology



Sunday, April 7	12:00 pm - 1:00 pm	DMDD Executive Committee Meeting (invitation only)
Monday, April 8	4:00 pm - 6:00 pm	DMDD Gillette Awards and Junior Investigator Platform Session
Monday, April 8	6:00 pm - 6:30 pm	DMDD Annual Division Meeting
Monday, April 8	6:30 pm - 8:30 pm	Joint Mixer: DMDD with Pharmacology Education and Toxicology
Tuesday, April 9	6:30 pm - 9:00 pm	DMDD Meet-the-Experts Dinner and Reception for Richard Okita Early Career Award (tickets required)

Monday, April 8	12:00 pm - 1:00 pm	MP Executive Committee Meeting (invitation only)
Monday, April 8	4:00 pm - 6:00 pm	MP Postdoctoral Award Competition
Monday, April 8	6:00 pm - 6:30 pm	MP Annual Division Meeting
Monday, April 8	6:30 pm - 8:30 pm	MP Mixer

Monday, April 8	12:00 pm - 1:00 pm	NEU Executive Committee Meeting (invitation only)
Monday, April 8	4:00 pm - 6:00 pm	NEU Postdoctoral Scientist Award Finalists
Monday, April 8	6:00 pm - 6:30 pm	NEU Annual Division Meeting
Tuesday, April 9	6:30 pm - 8:30 pm	Joint Mixer: NEU with Behavioral Pharmacology

Monday, April 8	12:00 pm - 1:00 pm	DPE Executive Committee Meeting (invitation only)
Monday, April 8	4:00 pm - 5:30 pm	Division Programming: *Surviving an Existential Threat - Creating a Niche for Basic Science Educators*
Monday, April 8	5:30 pm - 6:30 pm	DPE Annual Division Meeting
Monday, April 8	6:30 pm - 8:30 pm	Joint Mixer: DPE with Drug Metabolism and Disposition and Toxicology

Sunday, April 7	12:00 pm - 1:00 pm	TOX Executive Committee Meeting (invitation only)
Monday, April 8	4:00 pm - 6:00 pm	TOX Division Programming Symposium
Monday, April 8	6:00 pm - 6:30 pm	TOX Annual Division Meeting
Monday, April 8	6:30 pm - 8:30 pm	Joint Mixer: TOX with Drug Metabolism and Disposition and Pharmacology Education

Sunday, April 7	12:00 pm - 1:00 pm	TCP Executive Committee Meeting (invitation only)
Tuesday, April 9	4:00 pm - 6:00 pm	TCP Young Investigator Awards Platform and Early Career Faculty Showcase
Tuesday, April 9	6:00 pm - 6:30 pm	TCP Annual Division Meeting
Tuesday, April 9	6:30 pm - 8:30 pm	Joint Mixer: TCP with Cancer Pharmacology and Drug Discovery and 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

ASPET Meetings

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

Thursday, April 4, 2019

1:00 pm - 4:00 pm	Finance Committee Meeting
5:00 pm - 10:00 pm	Council Meeting

Friday, April 5, 2019

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

Saturday, April 6, 2019

8:30 am - 12:00 pm	Mentoring Network: Coaching for Career Development (mentors and mentees)
12:00 pm - 1:30 pm	Mentoring Network Lunch
1:00 pm - 2:00 pm	Science Policy Committee Meeting
8:30 pm - 10:00 pm	President's Reception *(by invitation only)*

Sunday, April 7, 2019

7:00 am - 8:00 am	Division Communication Officers Meeting
7:30 am - 9:30 am	*JPET* Editorial Board Meeting
7:30 am - 9:30 am	Diversity and Inclusion Breakfast
12:00 pm - 1:00 pm	Executive Committee - Div. for Drug Metabolism and Disposition
12:00 pm - 1:00 pm	Executive Committee - Div. for Toxicology
12:00 pm - 1:00 pm	Executive Committee - Div. for Translational and Clinical Pharmacology
12:15 pm - 2:00 pm	Undergraduate Networking and Career Development Luncheon
12:00 pm - 2:00 pm	Board of Publications Trustees Meeting
7:30 pm - 10:00 pm	Board of Publications Trustees Joint Editorial Boards Dinner

Monday, April 8, 2019

7:00 am - 8:00 am	Nominating Committee Meeting
7:00 am - 8:00 am	Young Scientists Committee Meeting
7:30 am - 9:30 am	*Molecular Pharmacology* Editorial Board Meeting
12:00 pm - 1:00 pm	Executive Committee - Div. for Drug Discovery and Development
12:00 pm - 1:00 pm	Executive Committee - Div. for Molecular Pharmacology
12:00 pm - 1:00 pm	Executive Committee - Div. for Neuropharmacology
12:00 pm - 1:00 pm	Executive Committee - Div. for Pharmacology Education
12:00 pm - 2:00 pm	*Pharmacological Reviews* Editorial Board Meeting
6:30 pm - 9:00 pm	Past President's Dinner

Tuesday, April 9, 2019

7:00 am - 8:00 am	Mentoring and Career Development Committee
7:30 am - 9:30 am	*Drug Metabolism and Disposition* Editorial Board Meeting
12:00 pm - 1:00 pm	Executive Committee - Div. for Cancer Pharmacology
12:00 pm - 1:00 pm	Executive Committee - Div. for Cardiovascular Pharmacology
12:00 pm - 1:00 pm	Executive Committee - Div. for Behavioral Pharmacology
3:00 pm - 5:00 pm	*Pharmacology Research & Perspectives* Management Committee

Wednesday, April 10, 2019

8:00 am - 12:00 pm	Program Committee Meeting

EB Career Central

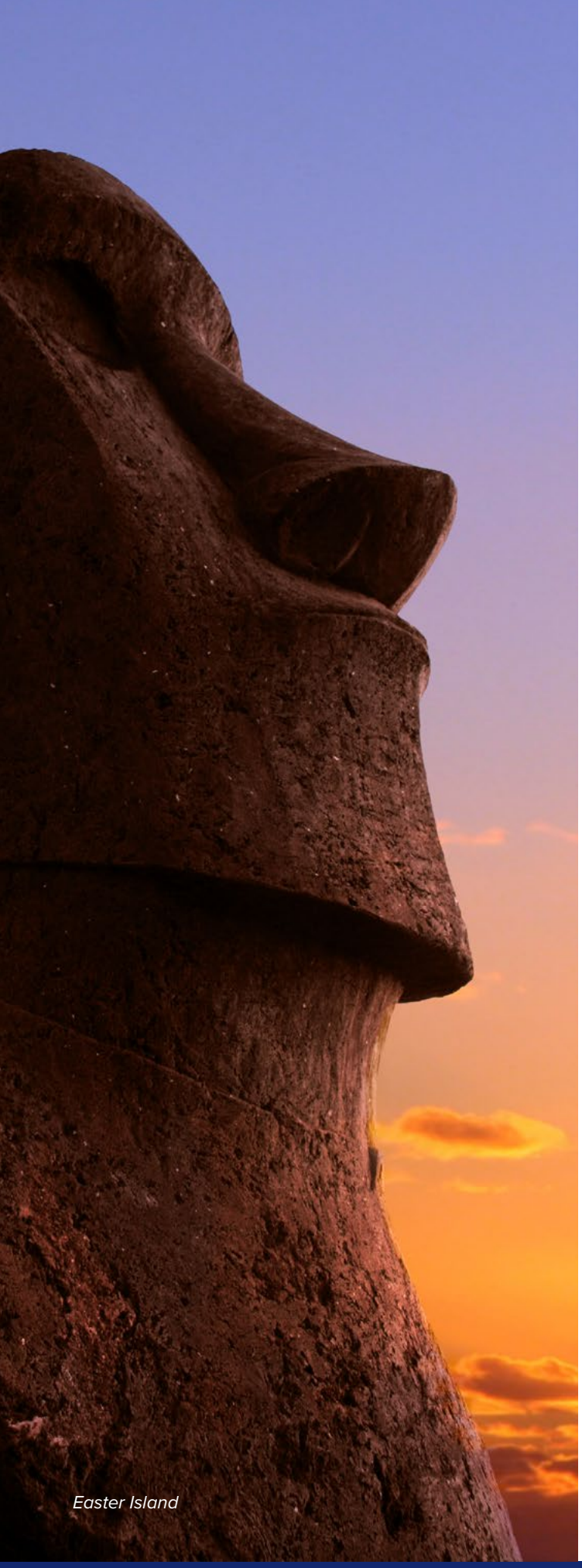
Take the next step in your career with the help of Experimental Biology's new Career Central!

- **Micro-learning Hubs**
  Quick 10 minute nuggets of professional development
- **Career Development Workshops**
  Longer form workshops on specialized topics
- **Job Listings**
  View the latest openings
- **Resume/CV Critiques**
  During personalized appointments
- **Poster Presentations**
  Practice with a mentor
- **Doctoral Program Outreach**
  Learn about university programs and speak with their reps

Missed out on abstract submission? It's not too late!

There's still time to showcase your cutting-edge science by submitting your abstract to be presented as a late-breaking poster. Submit your late-breaking abstract at https://bit.ly/2Rm4qAF

Late-Breaking Abstract Submissions are due by January 30.



Easter Island

Rapamycin: The Fountain of Youth?

Rebecca J. Anderson, PhD

Sometimes the greatest discoveries come when you're looking for something else. Such was the case for Georges Nógrády. When he signed up for an expedition to Easter Island, the furthest thing from his mind was finding the Fountain of Youth.

Nógrády's colleague, Stanley Skoryna, a professor at McGill University, led the expedition, which was sponsored by UNESCO's International Biology Program and the Canadian government *(1-3)*. Under the United Nation's umbrella of human adaptability research, Skoryna had devised a comprehensive study of the factors (climate, geology, genetics, and endemic diseases) that affect human health *(1, 2)*.

Easter Island was the ideal study site. Known primarily for its massive *moai* statues, Easter Island in the mid-twentieth century was considered the "loneliest place on Earth" *(1, 3)*. The island's inhabitants comprised the world's most remote community, residing 1,400 miles from the nearest port in an "empty" part of the Pacific Ocean. Their only connection with the rest of the world was an annual visit by a Chilean supply ship *(1, 4, 5)*. Scientifically, Easter Island represented a self-contained biosphere in dynamic equilibrium—for Skoryna, a living laboratory *(1, 3)*.

His multinational team of 38 physicians, scientists, and support staff landed on Easter Island on December 13, 1964. Over the next 2 months, they conducted comprehensive physical exams, blood tests, and X-rays on all 949 islanders *(1-3)*. They also collected data on the islanders' diet, lifestyle, genealogy, and work habits, as well as samples of all the flora and fauna on the island and in the surrounding waters.

Georges Nógrády, a microbiologist at the University of Montreal, was among the most active and energetic members of the expedition *(2)*. He collected 5,600 clinical specimens from the islanders to analyze for tetanus, tuberculosis, whooping cough, leprosy, and fungal diseases *(2, 4)*.

In his spare time, Nógrády assisted the expedition's veterinarians, who were interested in the health status of the island's large population of sheep, horses, and cattle. He analyzed nearly 2,000 specimens for common livestock diseases *(2)*.

The islanders should have been at high risk for tetanus. Horses outnumbered people on the island, and many islanders went barefoot *(2, 5)*. Tetanus spores should have been easily transmitted, but there was no evidence of lockjaw *(2)*. To investigate why, Nógrády divided the island into 67 one-mile squares and collected a core soil sample from the center of each square *(2, 5)*.

Reprinted with permission from the Sehgal Family.

Dr. Surendra Sehgal

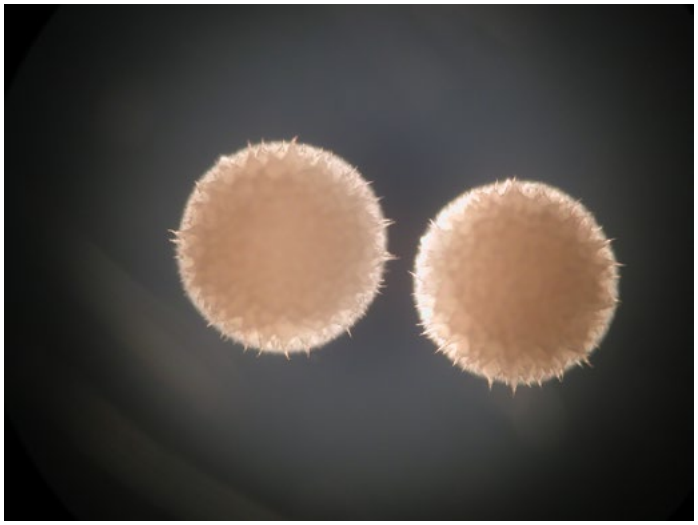
When he returned to Canada in March 1965, Nógrády sent his soil samples to Louis Smith in Virginia for analysis *(4, 6)*. Smith found tetanus in only one sample *(5, 6)*. Satisfied that tetanus was almost entirely absent on Easter Island, Nógrády put the samples in frozen storage *(4, 6)*.

Dirt to Drug

In 1969, Nógrády donated his sample collection to Ayerst Pharmaceuticals in Montreal *(5, 7)*. The microbiology team at Ayerst, headed by Surendra Sehgal, systematically isolated microorganisms from the soil samples and grew them in culture. Then, they extracted the chemicals produced by those organisms and tested each one for pharmacological activity.

One organism, *Streptomyces hygroscopicus*, produced a compound that could kill fungi *(1, 5, 7)*. In 1972, Sehgal elucidated the compound's chemical structure *(4, 8)*. He called it rapamycin, after Rapa Nui, the natives' name for Easter Island *(4, 9)*. Unfortunately, the compound also suppressed the immune system, an undesirable property for an antifungal agent *(9)*.

Sehgal had also sent the compound to the National Cancer Institute (NCI) for evaluation in its drug screening program. Rapamycin had "fantastic activity" against solid tumors *(8, 9)*. According to Sehgal, "We had the notion we were dealing with something novel" *(9)*. NCI designated it a priority drug and wanted to study it further, but Ayerst did not *(4, 8, 9)*.



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Streptomyces hygroscopicus

Sehgal elucidated the compound's chemical structure. He called it rapamycin, after Rapa Nui, the natives' name for Easter Island.

In 1983, to ease its financial burden, Ayerst decided to close its Canadian operations, which included the company's natural products division *(4, 5, 8)*. Before the large-scale fermenters were shut down, Sehgal prepared one final batch of *S. hygroscopicus (5, 8)*. He packed the bacterium into some vials and stuck them in the family's freezer. The package (next to the ice cream) was labeled, "DON'T EAT!" *(5)*.

Sehgal was among about 30 Montreal scientists who remained with Ayerst *(5)*. When he relocated to the company's laboratories in Princeton, New Jersey, his son, Ajai, came home from college to help the family move. Ajai's job was to stuff the freezer (containing the vials) with dry ice and seal it with duct tape "so that the movers wouldn't open it" *(5)*. The vials of bacteria stayed in the Sehgal family freezer in New Jersey for the next 5 years.

In 1987, Ayerst merged with Wyeth, and a new management team took charge of Wyeth-Ayerst Laboratories *(5, 8, 9)*. Thinking his new bosses might be receptive, Sehgal wrote a memo proposing to restart rapamycin research. Of rapamycin's biological effects, the management team was most intrigued by its immunosuppressant properties *(5, 9)*.

In 1983, Sandoz's cyclosporin A had been approved to prevent organ rejection in transplant patients, and that facilitated expansion of organ transplant procedures *(5)*. Cyclosporin's success and impressive sales also stimulated the search for stronger immunosuppressant drugs *(4)*.

Researchers at Fujisawa Pharmaceutical Co. discovered FK 506, another immunosuppressant compound. Interestingly, half of its chemical structure was identical to rapamycin *(5, 10)*. Wyeth-Ayerst's management told Sehgal to contact outside investigators who could test rapamycin in animal models of organ transplant *(5, 8)*.

This led to Wyeth-Ayerst's fast-tracked clinical trials. The Food and Drug Administration (FDA) approved rapamycin (Rapamune®) in 1999 for prevention of organ transplant rejection, and approvals around the world soon followed *(4, 5, 8)*. Wyeth-Ayerst also licensed Rapamune to Johnson & Johnson for coating stents to prevent arterial blockage due to restenosis in heart patients *(8, 11)*.

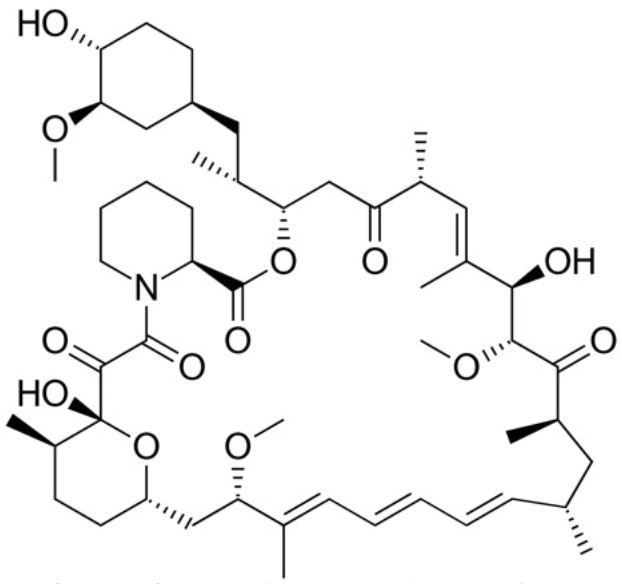
Rapalogs, Too

In parallel with the clinical trials, Sehgal contacted NCI, and the anticancer research on rapamycin resumed after a 6-year hiatus. NCI's interest remained high. According to Janet Dancey, a senior clinical investigator at NCI, "It didn't really look like any other drug in the cell line screen. Its pattern of activity was unique" *(9)*. At that time, all chemotherapy agents were cytotoxic. Rapamycin was cytostatic *(9)*.

Because the original rapamycin patent expired in 1992, Wyeth-Ayerst researchers conducted structure-activity studies to find an active analog that would be proprietary *(5)*. They synthesized and tested hundreds of compounds. The best one was CCI-779 (temsirolimus). It was active against a wide variety of tumor types *(9)*. The FDA approved temsirolimus (Torisel®) for treating kidney cancer in 2007 *(5, 11)*.

Chemists at Novartis used a similar structure-activity strategy to create everolimus (Afinitor®), which was approved for advanced kidney cancer in 2009 *(5)*. These "rapalogs" were subsequently approved for other cancers. Everolimus is also used in transplant patients. Other rapalogs are being developed as cancer drugs or for drug-eluting stents *(5)*.

Monotherapy with rapamycin or rapalogs has been only modestly successful against cancer because they result in stable disease (i.e., cytostatic) rather than tumor regression *(12)*. Combining rapalogs with other anticancer agents seems to give better results. Several combos (e.g., with paclitaxel, carboplatin, or doxorubicin) have yielded additive or synergistic effects *(12)*.



Skeletal formula of sirolimus (brand name Rapamune) — an mTOR inhibitor.

In the public domain

The New sTORy

In 1996, rapamycin pharmacology shot in a completely new direction, thanks to Michael Hall. After completing his postdoctoral work at UC San Francisco in the

late 1980s, Hall became an assistant professor at the Biozentrum of the University of Basel, Switzerland *(13)*. He was studying how proteins are transported across the cell's nuclear membrane—a process that at the time was a black box—and the work was not going well *(13)*.

Among Hall's collaborators was Rao Movva, group leader at Sandoz in Basel. Movva was interested in determining the mechanism of Sandoz's blockbuster new drug, cyclosporin A *(13)*. Little was known about how cyclosporin A and FK 506 worked, except that they blocked import of something—perhaps a protein—into the nucleus of T-cells *(13, 14)*. Because his own studies were going nowhere, Hall was willing to use Movva's drug as a tool to probe cell signaling pathways *(13)*.

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Michael N. Hall

Hall chose a simple organism (baker's yeast) as his model system—an unusual choice for studying drugs that were destined for use in people. According to Hall, "Some viewed these experiments as tantamount to giving aspirin to yeast—why would we do something so physiologically irrelevant?" *(13)*.

Hall chose a simple organism (baker's yeast) as his model system—an unusual choice for studying drugs that were destined for use in people.

His first experiments only seemed to justify the critics' skepticism. Cyclosporin A and FK 506 had little effect on the yeast cells *(13)*. Then, Movva told Hall about rapamycin, a brand-new FK 506-lookalike. Rapamycin had not yet been approved and was not commercially available, but fortunately, Sandoz was one of the few places in the world that could provide it. Hall found that rapamycin blocked proliferation of yeast cells *(13)*.

Using various yeast mutants, Hall's group soon isolated and characterized two genes, which they called TOR1 and TOR2 (for "target of rapamycin"). Those genes encoded a couple of closely related proteins, and further experiments confirmed that the TOR1 and TOR2 proteins were inhibited by rapamycin *(13)*. Hall and his postdoctoral fellow, Joseph Heitman, published these results in 1991 *(14)*.

Subsequently, TOR, the first in a new family of kinases, was also found in other invertebrates, including nematode worms (*C. elegans*) and fruit flies (*Drosophila*). Using mice, other research groups found a mammalian molecule that resembled the invertebrate TOR *(13, 14)*. This was subsequently named mTOR (for "mammalian" or "mechanistic" TOR).

By 1994, it was clear that TOR was highly conserved and that it performed similar tasks across the evolutionary spectrum. But the physiological role of TOR remained unknown *(13, 14)*.

A New Paradigm

At first, Hall thought that TOR controlled cell division because rapamycin had prevented his yeast cells from proliferating *(13)*. But in subsequent experiments, Hall showed that when TOR is not functioning, yeast cells generate unusually small quantities of protein. The yeast failed to duplicate—not because nonfunctional TOR disrupted a specific job in cell division, but rather because protein manufacture plummeted in general, including the proteins involved in cell division *(14)*. Without TOR, cells behave as if they are starving.

Without TOR, cells behave as if they are starving.

Conventional wisdom at the time asserted that cell growth was a spontaneous process *(13)*. If raw materials such as amino acids and fatty acids were present, the cells would automatically manufacture the corresponding proteins and lipids. A growth regulator was not necessary *(14)*.

However, in an elegant series of experiments in yeast, Hall's team demonstrated that cell growth is, indeed, an actively controlled process, and that TOR is the controller. When nutrients are scarce, yeast cells scale down production of proteins and most mRNA; they remain alive but metabolically dormant *(13)*. Hall proposed that TOR's role is to stimulate cell growth when the appropriate nutrients are available *(13, 14)*. This jarring new paradigm—that cell growth, as well as cell division, is a regulated process—was published in 1996.

Hall's discovery led to an explosion of work by many investigators who confirmed and expanded Hall's findings *(13)*. They reported that TOR responds not only to nutrients but also to the presence of growth factors and various stress conditions such as hypoxia and mechanical stress. By integrating all of these different environmental conditions, TOR ensures that cells grow only when the conditions are right *(5, 15)*.

By integrating all of these different environmental conditions, TOR ensures that cells grow only when the conditions are right.

Researchers now know that, in both invertebrate and mammalian systems, TOR combines with other proteins to form at least two structurally distinct multiprotein complexes *(12)*. The mTOR complex 1 (mTORC1) comprises six companion proteins in addition to mTOR. The mTOR complex 2 (mTORC2) has seven accessory proteins in addition to mTOR *(12)*. The structural differences between these two complexes affect their function, activation, and sensitivity to rapamycin.

mTORC1, which has been more widely studied, is a master controller, integrating numerous upstream and downstream signals in the cell *(12)*. It is acutely sensitive to environmental stimuli (amino acids, glucose, growth factors, insulin, cytokines, and oxygen). Downstream, mTORC1 promotes protein, lipid, and nucleotide synthesis (regulating cell growth), promotes mitochondria biogenesis (driving cell metabolism), and inhibits the breakdown and recycling of macromolecules *(10, 12, 14)*.

Rapamycin potently inhibits mTORC1. Under rapamycin exposure, cell growth ceases, and this pause in growth-related tasks allows cells to focus on repairing and recycling damaged components and cleaning out cellular "junk."

On the other hand, mTORC2 is required for maximal activation of numerous kinases and is not responsive to nutrient stimulation *(10, 12)*. Rather, it responds to growth factors, influences cell survival, growth, and proliferation, and regulates the actin cytoskeleton and cell migration *(12)*. Only chronic, high doses of rapamycin will inhibit mTORC2.

Life Saver

The most intriguing observation of Hall's research was that inactivating TOR—either through genetic mutations or inhibition with rapamycin—increased the lifespan of yeast cells. This effect was also seen in nematode worms and fruit flies *(5, 16)*. Because TOR is conserved across species, scientists were keen to know whether rapamycin would produce the same life-extending effect in mammals.

At the National Institute on Aging (NIA), the Interventions Testing Program was set up to evaluate a variety of agents for their potential to extend lifespan and delay disease *(15, 17)*. The mice in these studies were genetically heterogeneous to avoid gene-specific effects on disease susceptibility. Of the 26 compounds tested in the NIA program, only 6 (including rapamycin, metformin, acarbose, and 17α-estradiol) gave positive results *(17, 18)*.

Rapamycin was the only compound that showed a substantial anti-aging effect in both male and female mice. It increased lifespan by 12-25%, and the effect was dose-dependent *(19, 20)*. Interestingly, the beneficial effect was seen not only in young adult mice (9 months)—equivalent to a 35-year-old person—but also in older mice (20 months), which equates to about 60 human years *(19, 21)*. This suggested that an effective anti-aging intervention could be initiated later in life and still be effective in slowing, if not reversing, the aging process.

Rapamycin also seemed to improve the mice's overall health status. It retarded age-dependent declines in spontaneous in-cage activity *(21)*. Histopathology of the mouse tissues showed evidence that rapamycin diminished age-associated changes in liver, myocardium, endometrium, adrenal, and tendons, as well as suggestive beneficial effects on ovary, thyroid, and lung *(21)*.

End-of-life necropsies on the mice showed that the spectrum of specific lethal illnesses (mostly from cancer) was not altered by rapamycin, even though the treated animals lived longer. This suggested that rapamycin postponed tumor induction, progression, or lethality—consistent with the drug's known anti-cancer effects *(21)*.

These results, published in 2009, triggered massive interest. More than a dozen investigators subsequently reproduced and extended the NIA findings *(10, 11, 16)*.

Understanding Aging

Aging is a complex process involving thousands of genes. And it is becoming more complex, as scientists uncover new layers of biology, such as epigenetics, micro-RNA, and the microbiome, all of which influence aging *(22)*.

In the 1960s, Leonard Hayflick discovered that some human cells divide 40-60 times before stopping at what is now called the Hayflick Limit *(23)*. Researchers have since discovered that all cells age, even if they keep dividing, and they become increasingly inefficient at basic functions such as repairing DNA and recycling proteins, lipids, and other key molecules.

Matt Kaeberlein

Reprinted with permission from Matt Kaeberlein.

Unable to maintain themselves, aging cells slowly accumulate damage, which impedes their ability to function normally and facilitate tissue repair. Senses diminish, skin goes slack, joints creak, and muscles atrophy *(23)*. Eventually, the diseases associated with old age, disability, and death creep in: stroke, Alzheimer's and cognitive decline, pulmonary fibrosis, kidney disease, arthritis, osteoporosis, immune decline, diabetes, heart disease, and cancer *(7, 23)*.

Although human lifespan has doubled over the past few centuries, many elderly individuals suffer for years or decades from diseases or disorders that reduce their quality of life *(22)*. According to one geriatric researcher, Matt Kaeberlein, "There is something about the aging process and getting older that increases the risk of getting these diseases/disorders" *(7)*. Experts have estimated that by slowing aging, human life expectancy would increase by 15-25 years—and those extra years would be spent in relatively good health *(7)*.

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Encouraged by the early results with rapamycin, researchers now think that pharmacologic interventions can help the aging population live healthier for longer *(18, 22)*.

Mighty Mice

Using mice of varying ages and genetic backgrounds, researchers have shown that rapamycin has many beneficial effects on health. Rapamycin has a stimulatory effect on locomotor behavior and improves memory and learning in mice *(11)*. The drug also slows the development of kidney disease and obesity, as well as some cancers *(24, 25)*.

In mouse models of diseases, rapamycin ameliorates the progression of atherosclerosis, Alzheimer's disease, and muscular dystrophy *(10, 21, 25, 26)*. In one study, the hearts of mice functioned better for longer *(24)*. Rapamycin actually reversed the age-dependent defects in cardiac function and rejuvenated tissues in the aging heart *(10, 11)*.

On the other hand, rapamycin has limited effects on motor coordination and balance, muscle strength, and age-related pain perception *(11)*. There are also some age-dependent changes in male mice that are not prevented by rapamycin *(20)*.

Overall, though, the conclusion from these studies is clear. Rapamycin slows down the aging process, not only increasing lifespan but also generally improving health span—at least in mice *(7)*.

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Dog Years

Studies in other mammalian species would boost support for rapamycin as a clinically relevant anti-aging agent. Dogs are a good candidate for bridging the gap between mice and people because they age about 7 times faster than humans. For studies on aging, dogs can provide results in 3-5 years *(7)*.

Dogs have always been an attractive experimental species for evaluating human-destined drugs because they have a similar genome and develop many of the same diseases that humans do *(25)*. In conventional laboratory experiments, inbred dogs of uniform size (usually beagles) are kept in a controlled environment. But Matt Kaeberlein's laboratory in Seattle has taken a different approach, recruiting companion (pet) dogs. This approach, which has been used mostly for studies of investigational cancer drugs, employs the same procedures that are used to recruit, enroll, and treat people in a clinical trial. Pet dogs are especially attractive for studies on aging (and cancer) because they are subject to similar risk factors, share the human environment, and receive comparable medical care to humans *(25)*. Also, their detailed medical records are often available.

In 2017, Kaeberlein published the results from a Phase 1 study to determine the effects of rapamycin in companion dogs *(25)*. Rather than following the dogs until death, Kaeberlein monitored several cardiac biomarkers associated with aging. The blinded study included 24 "middle-aged" pet dogs, which were randomized to one of two rapamycin doses or placebo *(25)*.

Reprinted with permission from Tammi Kaeberlein.

Matt Kaeberlein with dogs Chloe and Dobby.

The dogs treated with rapamycin for 10 weeks showed improvement in age-related measures of heart function, indicating that their hearts were pumping blood more efficiently *(24, 25)*. The greatest improvement was in dogs that had lower baseline cardiac function *(25)*. These results were comparable to the cardiac improvement previously reported in middle-aged mice.

Rapamycin produced no clinical side effects and only minor changes in the dogs' blood chemistry *(25)*. Interestingly, although the dog owners did not know the treatment assignment, in 70% of dogs receiving the rapamycin higher dose and 40% of those in the lower dose group, owners reported that their dog displayed increased activity and energy *(25)*. Also, for 20% of dogs in the higher dose and 40% in the lower dose group, owners reported that their dogs' behavior was more affectionate. None of the placebo-treated dogs exhibited these changes. Kaeberlein speculated that this might be related to the anti-inflammatory effect of rapamycin, reducing pain associated with arthritis *(25)*.

Although not definitive proof of an anti-aging effect, these observations were encouraging and led to follow-up studies. Kaeberlein is currently conducting a Phase 2 trial, using more dogs, treated for 6 months, and assessing additional endpoints including motor activity. This will be followed by a 5-year study in 600 pet dogs *(7)*.

What about People?

The results in animals offer a compelling rationale for conducting clinical trials to examine the anti-aging effects of rapamycin. Considering that human life expectancy is now around 80 years, clinical trials to demonstrate a convincing anti-aging effect would take decades and would be prohibitively expensive *(22, 27)*. In addition, receiving regulatory approval may be challenging because the FDA does not formally consider aging a disease *(22, 27)*.

The FDA has allowed clinical trials in older adults who already have a diagnosis of at least one age-related disease *(24, 28)*. But drug intervention to retard or reverse aging may not work in people who are already showing symptoms. For example, patients with clinically diagnosed Alzheimer's disease have already developed significant brain pathology, which is probably irreversible *(7)*.

Finally, there are ethical concerns about long-term drug exposure in healthy older individuals *(27)*. They are, in general, at greater risk of adverse drug reactions than young adults, due both to age-related physiological changes (e.g., lower liver and kidney function) and increased use of other medications *(29)*.

The first evidence that drug intervention might have a beneficial effect on human lifespan came from a retrospective metanalysis of metformin exposure. British researchers reviewed the medical records of 90,000 diabetic patients, some taking metformin and others taking a sulfonylurea as first-line therapy. These patients were matched to 90,000 control subjects who did not have diabetes *(30)*.

The observed survival time was 38% longer in metformin-treated patients compared to patients taking a sulfonylurea. This was consistent with clinical experience, which suggests that sulfonylurea drugs have a detrimental effect on cardiovascular function *(30)*. More surprising—and intriguing—the British analysis revealed that diabetic patients taking metformin had a 15% longer survival time than the matched control subjects, who were not diabetic and not taking metformin *(30)*.

Metformin's primary mechanism of action is thought to be the alteration of cellular energy metabolism by stimulating 5-AMP-activated protein kinase *(31)*. Interestingly, metformin also inhibits mTORC1 *(7, 21, 31)*.

Unlike rapamycin and the rapalogs, metformin inhibits mTORC1 indirectly by interfering with two major input pathways. The downstream effect of inhibiting those pathways is to decrease insulin resistance and hepatic gluconeogenesis, which probably contributes to metformin's efficacy in diabetes *(31)*. In addition, this decreased mTORC1 activity may explain metformin's apparent beneficial effect on aging *(31)*.

Many other researchers have provided supportive evidence that metformin might protect against basic aging processes, not just diabetes *(18, 22)*. This leads to the converse theory that drugs used to treat early-stage chronic disease may be effective, at least in part, because they target the biggest risk factor for these diseases: aging itself *(18, 22)*.

Other supportive data come from patients who have been treated with rapamycin or a rapalog. One study assessed cognitive function and other psychiatric endpoints in heart transplant patients *(32)*. After being

treated with immunosuppressant doses of the rapalog everolimus, patients exhibited significant improvement on several standard tests of memory, cognition, depression, and psychiatric health *(32)*.

In another study, several biomarkers associated with cellular aging were measured in 13 elderly patients with coronary artery disease *(33)*. Aged cells (i.e., those beyond the Hayflick Limit) express a complex biochemical profile driven by mTOR that, in turn, alters the tissue microenvironment, produces persistent inflammation, and contributes to degenerative diseases *(33)*. In animals, rapamycin (by inhibiting mTOR) produces a favorable, dose-dependent shift in these biochemical markers *(28)*. The clinical investigators showed that rapamycin favorably shifted the levels of several cell-aging biochemical markers, and those changes correlated with improvement in the heart patients' physical performance *(33)*.

Only a few clinical trials have been conducted to assess the anti-aging properties of rapamycin in healthy elderly subjects, but the results so far have been encouraging.

In a randomized, controlled trial of 25 healthy adults (70-95 years), rapamycin at nonimmunosuppressant doses produced no significant differences in cognitive function between the control and treated groups *(29)*. But interestingly, the person who scored most poorly on the pretreatment tests demonstrated improvement on cognitive measures after rapamycin treatment in this blinded trial. He also increased his walking speed by nearly 10 seconds on the 40-foot walk test. Anecdotally, his family reported improvement in his cognitive and memory abilities while he was in the study; after ending rapamycin treatment, his short-term memory grew much worse *(29)*.

The Downside

Because rapamycin and several rapalogs have received regulatory approval, they are widely available, and physicians can legitimately prescribe them for any indication, including as an antiaging therapy. Given the large and growing body of preclinical data, few researchers doubt rapamycin's antiaging efficacy. But they are reluctant to give rapamycin or a rapalog to healthy individuals because of diverse and severe side effects *(10, 34)*.

Most of the reported adverse effects come from treatment of patients who received high, immunosuppressant doses. Mouth ulcers (canker sores) are a telltale sign of rapamycin in transplant medicine and an indicator that it is suppressing the patient's immune system *(34, 35)*.

In transplant and cancer patients, rapamycin and the rapalogs can cause high blood lipids, high cholesterol (HDL and LDL), high triglycerides, glucose intolerance, insulin resistance and new-onset diabetes, anemia, thrombocytopenia, skin rashes, gastrointestinal disorders, sinusitis, respiratory and urinary infections, and testicular dysfunction *(10, 12, 24, 25, 29, 35)*.

Many of these effects are transient and reversible (especially the skin and testicular effects), but the immunological consequences are extremely serious and occasionally result in death from infections *(10)*.

Intermittent Dosing

The beneficial effects of rapamycin as an antiaging agent have been attributed to its inhibition of mTORC1, which in turn dampens a number of factors that mediate cell growth and aging *(10-12)*. Researchers have attributed many of the negative side effects to inhibition of mTORC2. Fortunately, mTORC2 is inhibited only by chronic, high doses of rapamycin *(10)*.

In one clinical study of healthy elderly subjects, rapamycin at low, nonimmunosuppressant doses produced no adverse changes in most clinical lab endpoints. No changes were seen in glucose metabolism or insulin, which differed from the increased risk of type 2 diabetes reported in transplant patients *(29)*. Similarly, they exhibited no increases in plasma lipids, which have been reported in younger patient populations, and immune parameters were largely unchanged *(29)*. There were several statistically significant decreases in red blood cell parameters (e.g., hemoglobin, hematocrit)—well known effects of mTOR inhibitors—but the changes were not judged to be clinically significant *(29)*.

Rapamycin has a relatively short half-life in humans, but the terminal half-life has been reported to be 80 hours *(10)*. This suggests that a single dose can remain in the circulation at a beneficial level for a minimum of a week *(10)*.

Modulation of mTOR using inhibitors like rapamycin is unquestionably complicated. But the pharmacokinetics, relative inhibitory potency of rapamycin, and slow emergence of aging cells

suggest that a dosing regimen consisting of single low doses of rapamycin, given at sufficiently lengthy intervals, would selectively inhibit mTORC1 and arrest aging *(10, 12)*. Initial research results seem to support this notion *(12, 34)*.

A 2 mg/kg dose once every 5 days has been used most frequently in animal studies. This regimen produces no impairment of glucose homeostasis and reduces the impact on the immune system, while still significantly inhibiting mTORC1 in many tissues *(10)*. This regimen of rapamycin significantly increased lifespan in female mice, suggesting there is a therapeutic window in which the antiaging effects (mediated by mTORC1 inhibition) can be achieved while minimizing mTORC2-related side effects *(10)*.

Investigators at Novartis evaluated the effects of the company's rapamycin analog, everolimus, in 211 healthy elderly subjects *(35)*. Subjects were randomly assigned to a placebo, a low dose of everolimus administered daily, or one of two nonimmunosuppressant doses administered weekly.

Rather than monitoring time to death (which was not feasible), the investigators used a biomarker as an indicator of aging status: immune responsiveness to vaccination. Adults over 65 have a lower antibody response to influenza vaccination compared to younger adults, due to an accumulation of age-related immune defects *(35)*.

Subjects in the Novartis study were treated for 6 weeks. Two weeks after the end of treatment, they received an influenza vaccination. Everolimus enhanced the antibody response to influenza vaccination by about 20% compared to the placebo group *(35)*. This was consistent with previous studies that showed the same beneficial effect in aged mice.

The Novartis researchers confirmed the vaccine-responsiveness effect in a follow up placebo-controlled study of 264 elderly subjects *(36)*. Two mTORC1 inhibitors (everolimus or dactolisib) were given for 6 weeks. Interestingly, the subjects in the drug-treated groups also exhibited a significantly lower rate of infections for 1 year following treatment, compared to the placebo group *(36)*.

It may seem paradoxical for a drug, which (like rapamycin) is known and used clinically as an immunosuppressant, to enhance immune responsiveness *(35)*. But the immunomodulatory effects of the rapalogs appear to depend on several factors, including dose.

The goal in transplant patients is to completely suppress mTOR activity (and immune function) with high-dose rapamycin. In aged tissues, the activity of mTOR progressively increases, impeding normal function and repair compared to younger tissues and organs *(5, 35)*. The beneficial effects on immune response to vaccination and infection rate in the elderly subjects was achieved with low, short, and intermittent dosing regimens, which apparently shifted mTOR activity down to the "healthy" levels that are typical of young tissues *(35)*. That is, the treatment regimens used in the Novartis studies helped the elderly subjects' immune system to work better *(5)*.

The Pudding's Proof

The extensive preclinical data and limited clinical findings provide convincing evidence to justify further research. Based on that evidence, Kaeberlein predicts that an appropriate mTOR inhibitor could add a couple of decades to human lifespan, "with the expectation that those years are going to be spent in relatively good health" *(24)*.

But there is a lack of clarity regarding the optimal dose and treatment schedule needed to maximize the benefit/risk ratio *(10, 16)*. Some researchers are optimizing rapamycin's anti-aging properties by creating more selective rapalogs. Other researchers are devising selective mTORC1 inhibitors that have novel chemical structures *(7)*. Torin 1 and dactolisib, which block the mTOR catalytic subunit, represent yet another approach.

A few passionate physicians are already convinced that rapamycin is the Fountain of Youth. Dismissing the need for definitive proof, they have begun prescribing low-dose intermittent rapamycin off-label for their patients or themselves.

But most mTOR researchers, given the option, say they wouldn't take it. They see rapamycin's potential, but they are waiting for an appropriately selective compound and dosing conditions that demonstrate a bona fide clinical response *(5)*. Until then, Judith Campisi, a professor at Buck Institute for Research on Aging, says, "When people ask me how to stay young, I say: exercise, don't smoke, eat your veggies, and choose your grandparents wisely" *(22)*.

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Biosketch:

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

In the next issue of The Pharmacologist:
Dr. Anderson will share the story of Leo Sternbach and the discovery of the benzodiazepines.

Don't miss the March 2019 issue.

Meeting News

Neuroscience 2018

November 3–7, 2018

San Diego Convention Center, California

ASPET exhibited at *Neuroscience 2018*, the annual meeting of the Society for Neuroscience. We shared with attendees information about ASPET's membership benefits and publishing opportunities in ASPET's five journals.

We also held a Sunday evening reception, hosted by the ASPET Division for Neuropharmacology. Over 60 conference attendees joined ASPET members and prospective members at the House of Blues for an evening of networking and conversation.

Members at the ASPET Division for Neuropharmacology mixer.

ASPET booth at Neuroscience 2018.

2018 Annual Biomedical Research Conference for Minority Students

November 14–17, 2018

Indiana Convention Center, Indianapolis

ASPET exhibited at ABRCMS—the Annual Biomedical Research Conference for Minority Students—held in Indianapolis this year. The meeting presented an opportunity to engage with an audience dedicated to advancing the education and careers of minority scientists.

ASPET booth at ABRCMS 2018.

Annual British Pharmacological Society Meeting: Pharmacology 2018

December 18-20, 2018

Queen Elizabeth II Centre, London, UK

ASPET will attend the British Pharmacological Society's (BPS) annual meeting, *Pharmacology 2018,* in London this December.

We'll exhibit at Stand 30 in the BPS exhibition space and share with attendees information about ASPET's journals and membership benefits that may appeal to scientists based outside the U.S.

Visit us at Stand 30 if you're in London for the conference.

Science Policy News

ASPET Washington Fellows Alumni Share Op-eds

The ASPET Washington Fellows Program allows developing and early career scientists interested in science policy to learn about and become more engaged in public policy issues.

Last spring, the 2018 class of Washington Fellows traveled to Washington, D.C. to meet with legislators and staff to advocate on behalf of the biomedical sciences. Following their return home, they were asked to write an opinion editorial (op-ed) that drew on their experiences on Capitol Hill.

The following three op-eds are on two subjects: animal research and drug scheduling. Both issues are central to the mission of ASPET's public affairs department, and both issues are regularly featured in policy discussions.

There are also likely to be many opportunities for advocates to engage on these issues in the next few years. With the skills and knowledge that our 2018 class acquired during their fellowship, they will be strong advocates for science policy throughout their careers. To read more op-eds from the 2018 Washington Fellows class, please visit https://www.aspet.org/aspet/advocacy/aspet-washington-fellows-program.

Animal Research: A Keystone of Curative Medicine

Ryan Staudt *University of Pittsburgh*

Some of the most important work in the fight against HIV was performed by scientists who had no idea that the virus existed.

It would be animal research into a family of viruses in the 1960s and 1970s that allowed researchers in the 1980s to identify HIV as the cause of AIDS.

It would be the 1970 discovery of a protein called reverse transcriptase in livestock-infecting viruses that would enable scientists in the next decade to understand how HIV spreads copies of itself throughout the body.

And it was an early group of scientists looking for cancer drugs in leukemic mice who first synthesized azidothymidine (AZT), the drug that would go on to be the first HIV treatment.

With an almost serendipitous pooling of knowledge from this prior research, the biomedical community was able to transform HIV infection from a guaranteed death sentence to a treatable chronic condition within the span of about a decade.

An essential part of that progress, from those initial insights into similar viruses to the development and validation of drugs like AZT, was animal research.

Today, with over 36 million people infected with HIV worldwide, animal research in mice and non-human primate models of HIV infection remain essential to finding a permanent cure.

Because as effective as HIV treatments are at preventing the spread of HIV, they cannot cure individuals infected with the virus, and any lapse in treatment means a resurgence of the virus.

Think of it this way: if HIV is a printer feverishly making copies of itself, AZT and other drugs are an irritatingly crumbled paper which jams the machine. However, as long as there is even a single functional copy of the virus, an unlimited number of copies can be created once the source of the jam is bypassed or removed.

During initial infection with HIV, these copies of the virus travel to remote locations within the human body. Eradicating the virus requires understanding where

these copies hide in the body, which requires studying HIV infection in entire organisms, not just within a test tube. Since we cannot ethically delay treatment in HIV-infected humans to study infection dynamics, and since testing novel treatments in humans without prior validation would be extremely dangerous, the use of animal models is essential.

Along with its role in improving our understanding of HIV/AIDS, animal research has been an essential part of nearly every medical breakthrough in history. In fact, 180 out of 216 recipients for the Nobel Prizes in Medicine relied on animal models to publish their research.

Complex diseases like Alzheimer's, cancer, and atherosclerosis still represent a major public health challenge, and animal research remains a critical resource in finding their cures.

However, despite this continual need for animal research, we are in the midst of a troubling shift in public opinion. According to a recent Gallup poll, public support for animal research has fallen 14% within the past decade, with just 51% of Americans today agreeing that biomedical animal research is morally acceptable compared with 65% of Americans in 2001.

Animal research is a lynchpin of medical progress, and if public and political support for animal work stalls, the development of important discoveries and life-saving therapies could stop as well.

It's up to scientists to be candid about the role of animals in not only the medical triumphs in the past, but the trenches of ongoing critical research. For too long we've presented the general public with a stale image of biomedical research as a black box from which medical breakthroughs occasionally shake through.

The role of animal research in these breakthroughs is a key part of that black box, and we need to do a better job of discussing candidly why these animals are essential for our research and the careful regulations surrounding their use.

For example, every federally funded lab is overseen by an Institutional Animal Care and Use Committee (IACUC), and labs are only able to work with animals after submitting an extensive application for approval. This document, called an IACUC protocol, requires researchers to explain why the use of an animal model is required, what specific experiments will be conducted, and how animals will be provided with the best possible facilities and veterinary care during these experiments. Also, every committee is federally mandated to have community members on them to ensure that animals are treated humanely.

Honestly, if scientists could accurately conduct their research without using animal models they would do so in an instant, as working with alternative models is both easier and less expensive than working with animals. But solving complex biological questions requires complex biological models, and we are unfortunately just not at a point where "organs-a-chip" and computational models can faithfully recreate complex and life-threatening disease states.

Scientists, along with individuals concerned with animal welfare, actively look forward to a future where alternative technologies can eclipse the use of animals in biomedical research.

In the meantime, animal research remains vital to confront an ever-growing list of challenges to our collective health.

Animal Research: A [Sometimes] Necessary Evil

Sterling Glass *University of Connecticut*

Let me ask you this: would you want to be operated on by a surgeon who had never performed a surgery before? Well that's precisely how much of the scientific community feels about the use of animals in research.

Now before you roll your eyes, I already know what you're thinking. But I assure you I am not here to shill Big Pharma and shove statistics and pretentious science-speak down your throat. Too much of that goes on already, and frankly I think it has helped destroy the rapport between science folk such as myself and the rest of the world. Instead, what I intend to do is present to you a view of animal research from the perspective of a young pharmaceutical scientist (and animal lover, I swear!), with a few tidbits of evidence thrown in for good measure.

As pharmaceutical scientists, showing that drugs have the potential to work in people is our bread and butter. Without having some sense of what a drug does in a living organism, it is near impossible to figure out how the heck it *might* work (or not) in a human being. I lied. I need to shove one statistic down your throat—about 7 out of 10 long-term side effects in humans can be predicted by using two different animal species to study the toxicity of new drugs. That's pretty good. I will admit, though, that it's not perfect and that there is a lot of room for improvement. When it comes to cancer, everyone's favorite animal model is the mouse. Unfortunately, as it turns out, it's *really* hard to mimic human cancer in mice, therefore making mouse models not necessarily predictive of how humans might respond to a particular treatment. While improvements have been made with regard to computer (often referred to as *in silico*) models and cell-based (*in vitro*) models, using animals such as mice is still typically our best shot at making progress within many fields of pharmacology. Believe me, I wish it were different, but the reality is that we don't know a whole lot about how diseases and the body work (spoiler alert: we don't have the cure for cancer hidden in an underground vault somewhere in Oklahoma). Thus, the general consensus is that in many cases, though they may not exactly represent reality, animals can often give us significant clues as to how we can ultimately improve the lives of actual people.

While the jury might still be out on whether animal models continue to be our best bet, the fact of the matter is that the use of animals in pharmaceutical research has drastically changed both human *and* animal health for the better. What I'm getting at is this: would you have wanted to be the first person to try out a new general anesthetic or would you want your beloved Fido to be the guinea pig for that new heartworm medication? I didn't think so.

At this point, you have likely gathered that I'm pro-animal research, but that does not make the subject an easy pill for me to swallow. I shudder every time I think about the fact that Beagles are the best predictor for cardiac toxicity. I loathe having to kill (we self-righteously call it "sacrificing") a mouse after treating it with an experimental cancer drug. But I know that these things have, do, and will continue to help lots of people in pain and in need. I am also able to sleep at night knowing that animal research is a shell of its former self. Long gone are the days of reclusive Dr. Frankensteins making artificial feline Siamese twins. Modern-day animal labs are overseen by vets and vet techs in addition to teams of compassionate students, fully aware of the ramifications of their work. All academic labs are overseen by internal animal care and use committees (IACUCs) that ensure the mitigation of undue pain and stress. The best institutions (including our very own UConn) are voluntarily AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) certified, ensuring an additional layer of protection and oversight.

I recently had the unique opportunity to travel to Capitol Hill with the American Society for Pharmacology and Experimental Therapeutics (ASPET) to advocate for animal research. I had the pleasure of meeting with top staff members from Connecticut's Senators and Representatives. To my surprise, I found that even the healthcare staffers knew very little about animal research, so I used my time with them as an opportunity to simply tell them about animal research rather than just blindly asking them to push for budget increases. What I found was that every one of them was receptive and supportive. I applaud our state's commitment to furthering science with the intent to improve public health. However, the most important thing I took away from my time in Washington was that there is a glaring disconnect between scientists and non-scientists, and I want to change that. I wish the science community would stop talking down to non-scientists, widening that gap. I want people to sit down and have productive conversations about science and society.

What I want from you is not to think about issues like animal research in terms of right or wrong or left or right; I want you to look at them from all sides and in the context of a global society. But at the end of the day, I want you to answer one question: would you want to be operated on by a surgeon who had never performed a surgery before?

The DEA, Scheduling, and Cannabis: A Call for Consistency

Laura Erwin *LSU Health Sciences Center*

Recently, in response to two different petitions to reschedule cannabis, the DEA requested the Department of Health and Human Services (HHS) to conduct a rigorous scientific and medical evaluation. The evaluation was carried out by the US Food and Drug Administration (FDA), which determined that cannabis should remain a Schedule I compound. As someone who regularly works with controlled substances, including delta-9-tetrahydrocannabinol (THC), I find the DEA's conclusions to keep cannabis a Schedule I drug perplexing.

Cannabis, aka marijuana, is a complex alkaloid mixture derived from the *Cannabis sativa* plant. The most abundant cannabinoids found in the plant are delta-9 tetrahydrocannabinol (THC), cannabidiol, and cannabinol; however, the main psychoactive component is THC. While today we think of cannabis as an illegal substance, in the 1600's cannabis was widely used by the Puritans of North America in rope, sails, clothing, and as medicine sold openly in pharmacies. However, Dr. James Munch, expert witness for the Federal Bureau of Narcotics, convinced Congress that cannabis was linked to insanity, rape, and even bigamy. To illustrate his point, Munch included 69 "authenticated case reports" of crimes committed by those who'd smoked "the devil's weed." Though almost all of these case reports have been thoroughly debunked today, Munch's testimony was strong enough at the time to help pass the 1937 Marijuana Tax Act, which made the transfer of cannabis illegal throughout the US. In addition, the propaganda film "Reefer Madness" changed the way our country perceived cannabis and this sentiment continued to linger throughout the decades. In 1970, the Controlled Substance Act classified cannabis as having high abuse potential and no medical use. However, only five short years later in 1975, the FDA established the Compassionate Use Program for medical marijuana. This program allowed medical marijuana for the treatment of glaucoma, multiple sclerosis, and cancer. However, due to an overload in patient demand and pushback from the Bush administration, it was later terminated. It is curious though, that if marijuana once had an accepted medical use, where did that use go?

From the current evaluation, the HHS determined that cannabis would remain a Schedule I compound largely for three reasons: the chemistry of cannabis was not reproducible in terms of creating a standardized dose, it had a high potential for abuse, and it had no accepted medicinal purposes. While it does remain true that no two samples of cannabis leaves will have the exact same chemical makeup since it is a natural plant, it could still be moved to a Schedule II if the drug was considered to have accepted medical use. In the FDA's evaluation, they used extremely complex evaluation criteria to narrow down peer-reviewed published studies on cannabis from 566 abstracts to only 11 publications. Then, from these 11 publications the FDA, yet again, decided that these 11 still did not meet their criteria. So, somehow between the years of 1974—2013, not a single published paper was able to meet the FDA's golden standard. However, if you review the results of these papers, which examined the effects of cannabis on either neuropathic pain, spasticity related to Multiple Sclerosis (MS), appetite stimulation in human immunodeficiency virus (HIV) patients, glaucoma, or asthma, you will find that 9 of those 11 papers found that cannabis helped alleviate symptoms or mitigate pain.

In addition, though the FDA does seem to be sure cannabis has no accepted medicinal benefit, two drugs that the agency has approved are nabilone (brand name Cesamet®) and dronabinol (brand name Marinol®). Nabilone is a Schedule II drug marketed by Valeant Pharmaceuticals International and dronabinol is a Schedule III drug marketed by Insys Therapeutics; however, both are synthetic THC derivatives. So, how is it that cannabis, whose major psychoactive component is delta-9-THC has no accepted medical use, yet nabilone and marinol, whose major psychoactive component is also delta-9-THC, does? Isn't it also interesting that Insys Therapeutics donated $500,000 to Arizonans for Responsible Drug Policy,

a group who opposes cannabis legalization in the state of Arizona? While Insys Therapeutics has stated the company opposed the legislation in order to "protect the children", it doesn't take a detective to notice the correlation between cannabis legalization and pharmaceutical sales. In fact, since states began legalizing cannabis, the average Insys January opening stock has decreased from 23.69 in 2016 to 9.97 in 2018. Regardless of economics, the fact remains the same—all three of the drugs are THC derivatives and yet only one has no medicinal purpose and is labeled a Schedule I compound.

In limiting cannabis alone to this classification, the FDA creates its own catch 22. A Schedule I classification increases the regulatory burden on researchers due to the cost of licensing, mandatory DEA inspections, storage requirements, and extended wait time to receive approval on supply. The Schedule I classification of cannabis closes the door on research possibilities to only those investigators that possess a license, effectively shutting out all others. Therefore, while the FDA maintains there are zero publications to date which meet their criteria for proving safety and efficacy of cannabis, keeping it a Schedule I substance actually prohibits much research from being conducted in the first place which could move it to Schedule II or III.

Though the original prohibition on cannabis in the United States may have been instigated by Dr. James Munch and a little propaganda film named Reefer Madness, today's issues regarding cannabis reform lie squarely with the inconsistency in the scheduling and evaluation process of controlled substances by the DEA, FDA, and HHS. While pharmaceutical companies are continually looking to expand their market of Schedule II or III medically approved synthetic-THC derivatives, when will non-pharmaceutically owned THC also prove its medicinal capabilities? I guess only time will tell – or, according to the FDA's Compassionate Use Program, maybe a time machine.

Visit ASPET's Redesigned Advocacy Webpage

Check out the newly re-vamped advocacy section of the ASPET website. The new layout is easier to navigate, lists recent news items chronologically, and highlights accomplishments of the Public Affairs department.

Additionally, you can access the new online application process for the Washington Fellows Program in the Advocacy section of the website.

Visit www.aspet.org/advocacy to check it out.

Education News

Terri Clister Discusses Her Celgene Internship and Pursuing a Career in Industry

As the Pharmacology Industry Internships for PhD Students (PIIPS) program completes its second year, Catherine Fry, PhD, Director of Education at ASPET, interviewed Terri Clister, PhD, on her experience as a PIIPS intern at Celgene. Having recently received her PhD from Johns Hopkins University, Dr. Clister is now a postdoctoral researcher at Celgene.

CF: What was your motivation for pursuing an industry internship?

TC: I knew I didn't want to be a PI in an academic lab or to have a teaching-focused career, so industry was a strong interest of mine. My mentor, Dr. Jin Zhang, was also really supportive and actually suggested this opportunity for me. I was about 80% sure I wanted a career in industry before the internship, and now I am 100% sure. We already had discussions about my interest in industry, so she knew about my career goals and was really helpful in pursuing this opportunity.

CF: How did you choose Celgene for your internship?

TC: When I applied to be in the program, there was a list of all the companies that we had a potential partnership with, and I had to rank my top three. I was ultimately given a choice between two, and I set up some informational interviews to help choose between them. When I talked to them, I tried to get a feel for the science and their priorities to see if it was a good fit. I also tried to get a sense of the company culture and who they collaborate with. The project Celgene had pitched for an intern was really interesting to me. I also talked with some friends who have industry positions, and they recommended Celgene since it's a larger company and it can be harder to get a foot in the door.

CF: Now that you are working as a postdoc at Celgene, what has the transition been like from academic to industry research?

TC: I'm actually working with the same group that I did as an intern, which has been really ideal. I already know everyone, and I can jump back into it. We've been characterizing a mouse model that was developed a few years ago to make sure that it's a model we want to pursue. The postdoc position is for two years, so I feel like I can come in being productive right from the start. I feel fortunate that Celgene does hire interns into postdoc positions, since not every company does that. I think I am probably more independent than I even would have been in an academic postdoc – my manager has a lot on her plate and depends on me to work mainly on my own. There is still an expectation to publish, although I have to think a little more about what might become proprietary. I feel like the work I'm doing here is much more translational and I am closer to the science that will be used in the clinic, which is really rewarding.

CF: If you could go back in time and give yourself some advice at that start of your internship, what would it be?

TC: I think I would have adjusted my expectations a little. There was a part of me that thought I could still go back to my academic lab, maybe on the weekends, and do a few experiments. But that never happened—I jumped fully into the internship. I think I would have

more cleanly tied up some loose ends before starting the internship so when I came back to wrap things up in my academic lab, it would have been more smooth. I did find that the experience of the internship made me a lot more motivated to finish and graduate, since I was certain about what I wanted to do next.

CF: Do you have any advice for other graduate students who are interested in industry internships?

TC: Some companies have their own internship programs, which is always a good place to start. Before I became involved in PIIPS, I tried cold-contacting some companies. I was looking at smaller companies that I thought might be interested in cheap labor, but I heard from at least one that they felt their time was more important than their money. So it may have been better to target larger companies that had the time and resources to spend on interns. When I was actually in the internship, I made a point to ask other people I ran into how they ended up at Celgene, what their jobs were like, and what they enjoyed about it. A lot of them had been in industry for a few years and could also talk about how Celgene compared to other companies. That was really helpful in gauging what possible careers might look like and what things to think about for industry jobs. I was an interesting case because I was pretty certain I wanted to go into industry before I started, but I still think it's a really valuable experience if you're not sure. It's just as useful to figure out what's not a good fit, and an internship is a pretty low-risk way to do that.

CF: What's next for you?

TC: I've only been in my postdoc role with Celgene for a few weeks, so I am looking forward to learning more during my time here. I do plan to stay in industry for at least 5, or maybe 10 years. I'm really enjoying the work that I do.

We thank Terri for taking the time to talk with us about her internship and her current job at Celgene. For more information on PIIPS, see https://bit.ly/2DprtX4.

Individual Summer Undergraduate Research Fellowship (SURF) Program

Applications Due February 1, 2019 for Summer 2019 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 awards for individuals 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 pharmacology-related 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.

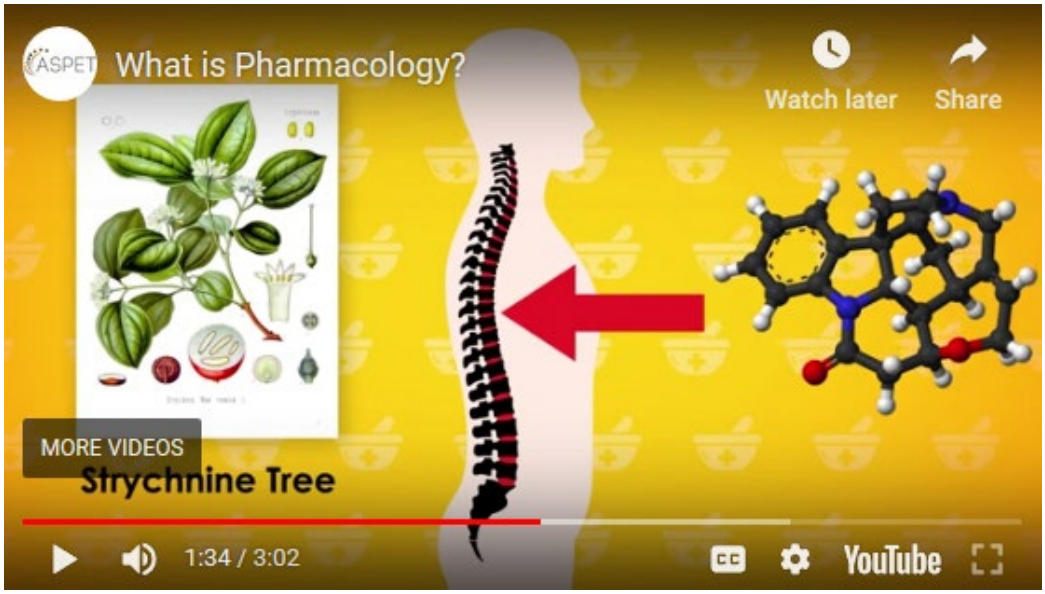
Program Overview

- 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 $2,800 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.

Spread the Word: What is Pharmacology?

Part of ASPET's Strategic Plan focuses on increasing public awareness of pharmacology as a discipline. To meet this particular goal, ASPET participates in many outreach opportunities both at national conferences and online using our social media platforms. One of the most basic questions we get from high school students, college students, and the general public is "What is pharmacology?" It is very often confused with "pharmacy." To clear up this confusion and to answer that common question, ASPET created a very simple to follow video entitled "What is Pharmacology?" in December of 2016.



The video provides a brief history of pharmacology, how it impacts many other scientific fields and medical discoveries, and where pharmacology is heading in the future. Since then, we have had over 29,000 views on YouTube. Have you watched it? The video is found online at https://www.youtube.com/watch?v=PQ2m-nrf2z8&t=3s.

ASPET has been promoting this important video over the last two years, and we have noticed that the video is beginning to make an impact. When you search using the phrase "What is Pharmacology," our video is one of the first to appear in the results. Some university pharmacology departments use our video on their web sites. This summer we received a request to use the video in a setting we did not foresee. On November 3, 2018 on the campus of Oklahoma State University in Oklahoma City, Kevin M. Jones, owner of Bear Claw Interpreting & Consulting, hosted a six- hour continuing education workshop titled "ASL Pharmacopeia: An interpreters guide to the world of prescription pharmaceuticals." The workshop focused on the broad field of pharmacology and provided participants with an introductory lesson on pharmacokinetics and pharmacodynamics as well as an overview of more than 30 different drug classes, the common drugs in each class, and guidance on the American Sign Language (ASL) interpretation of some of the key principals learned during the workshop. ASPET's "What is pharmacology?" video was shown at the workshop as an introduction to the topic.

"The participants seemed to really enjoy the video, and the video primed the participants for the remainder of the day."
-Kevin M. Jones

You can help spread the word about pharmacology. Share this video on your department webpage, in your classroom lectures and workshops, and in your own outreach efforts. Together as a Society, we can educate the general public and the broader health science community about what we do.

Health Professions Week 2018: Thanks to Our ASPET Member Volunteers

ASPET participated in Health Professions Week (HPW), November 5-9, 2018. The free, virtual outreach event for high school and college students attracted more than 11,300 registrants interested in learning about careers in health professions.

ASPET focused on pharmacology as it joined 19 other professional societies in educating students about different career paths in the health professions.

Thanks to ASPET members, we expanded our involvement this year by guest hosting the official HPW Instagram account. Dubbed the ASPET Instagram Takeover for HPW 2018, our social media posts featured ASPET members sharing—via short videos under one minute—their professional advice from the perspective of young scientists. The Instagram event took place one week prior to the HPW kickoff.

To watch the videos and read our posts, please visit: https://www.instagram.com/HealthProfWeek.

ASPET thanks these members for participating in the HPW Instagram event:

- Stephanie M. Davis
- Rebecca Fleeman
- Bettiné E. Gibbs
- Chiagoziem A. Otuechere
- Yadira Pérez-Páramo

ASPET members also volunteered during two days of HPW 2018 Virtual Fairs, reaching high school and college students. ASPET members answered questions about college coursework to prepare for pharmacology graduate degrees, career opportunities in the field, ways to get involved in research, and how pharmacologists interact with other professions. We thank the following members for volunteering to answer questions in the virtual ASPET booth:

- Stephanie M. Davis
- Peter Gannett
- Margaret Gnegy
- Rae Matsumoto
- Jeff Paul
- Patricia Rose

Journals News

Plan S: A Boon or a Threat to Global Science?

Submitted by Eddie Morgan, ASPET President and Mary Vore, Chair, Board of Publications Trustees

As you know from the presentations at the Annual Meeting, revenue from the ASPET journals represents 73% of ASPET annual income and is therefore essential for the society to function. The journals also provide an indispensable service to the pharmacology community through expert, fair and timely reviewing, to ensure that the research we publish is rigorous, reproducible and highly valued. A recent initiative from Europe called Plan S would mandate that scientists whose research is funded by any one of at least 15 national funding bodies must publish that research in a totally open access journal. The Howard Hughes Medical Institute and the Wellcome Trust have also signed on to Plan S. As such, we think that Plan S represents a potentially dire threat to ASPET and our journals, especially if that initiative takes hold in the United States.

Open Access (OA) principles state that scholarly research literature should be openly available to the public without restriction. In 2013, the White House issued an executive order that federal funding agencies must provide free public access to research that they fund. In the biological sciences, this is done via mandated deposition of accepted articles in PubMed Central (PMC). ASPET deposits in PMC the final version of all articles that cite such funding as a service to authors. In response to concerns from ASPET and other publishers, the government currently allows authors and publishers to embargo the release of articles on PMC until one year after acceptance. This retains the incentive for libraries to subscribe to the journals to allow their institutions access to the latest research. Because some funders require their grantees to publish under a Creative Commons License that allows for reuse of all or any part of the article with attribution only, ASPET provides a “Gold” OA option for each of our journals. ASPET journals are thus considered “hybrid journals,” and as such, are not compliant with Plan S. However, since 2003, ASPET has made the manuscript version of all articles in *DMD, JPET,* and *Molecular Pharmacology* freely accessible from the time of acceptance. In partnership with the British Pharmacology Society and Wiley, ASPET also created a wholly OA journal, *Pharmacology Research & Perspectives*. It is interesting to note that 85% of current journals do not meet the requirements of Plan S.

The principle of OA publishing for all scientific articles may seem highly desirable on the surface. Informed members of the public and scientists from small institutions or developing countries would have immediate access to articles they currently have to buy for a significant fee. Researchers would be free to legally distribute PDFs of their published papers to anyone, or just post them on their lab or institution website. What’s not to like? Consider the following. Society publishers like ASPET would have to rely solely on OA fees to offset their costs, because libraries would no longer need to purchase subscriptions. Under this model, ASPET journal income would be a fraction of what it is currently, and we would have to consider potentially dramatic cuts to society functions and services, including our annual meeting. Although dues would need to rise substantially, this would only compensate for a small amount of the lost revenue. This would affect just about every scientific society in the US that relies on their journals to help support their programs. The societies provide crucial support for science, such as networking opportunities, professional development, and venues for our trainees to gain experience and confidence in presenting themselves and their research. In this context, we contend that the current arrangement that makes federally funded articles available to the public one year after acceptance adequately satisfies the open access ideal, and that implementation of Plan S requirements in the United

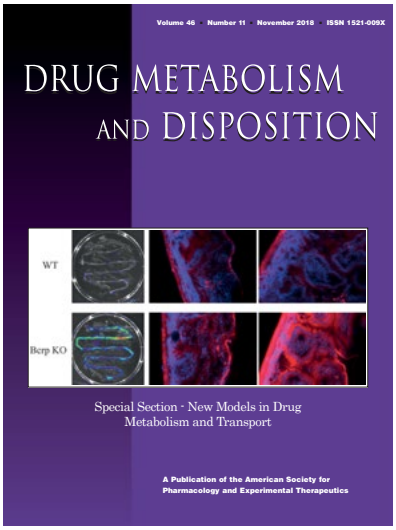
States is not only unnecessary but is also a bad idea because of the great harm it would do to the fabric of science and the development of young scientists.

It is to be emphasized that the ultimate requirements and implementation of Plan S are not yet determined, and although its advocates have talked with the White House Office of Science and Technology Policy (OSTP), there is no suggestion as yet whether or not OSTP might seriously consider adopting it. ASPET is working through the Board of Publications Trustees and our Science Policy Committee (SPC), and together with FASEB and IUPHAR, to develop our position and appropriate strategies to advocate for it should the need arise. In the meantime, we ask you to consider the impact Plan S would have on science, the scientific research community globally and on ASPET. We will be sure to keep you informed as Plan S evolves.

At press time, Plan S guidelines were published. We will address them in a future issue.

DMD Special Section: Emerging Models of Drug Metabolism, Transporters, and Toxicity

The *Drug Metabolism and Disposition* November issue features 24 commentaries, minireviews, and original research articles on novel models of drug metabolism and disposition. Dr. Aarti Sawant-Basak and Dr. R. Scott Obach were the guest editors for the special section.



The content covers novel static or micro-flow based models of the intestine, liver, eye, and kidney. Static intestinal systems like mucosal scrapings and cryopreserved intestinal enterocytes, as well as novel bioengineered or chemically engineered intestinal models derived from primary human tissue, iPSCs, enteroids, and crypts are included. Experts have reviewed hepatic systems like cryopermeabilized Metmax hepatocytes and longer term, hepatocyte coculture system from HμREL, yielding in vivo-like primary and secondary drug metabolite profiles. Minireviews also discuss applications in laboratory animals and humanized mice models of CYP450, UGT, and oatp1a4 as well as in vitro and in vivo models of drug metabolism derived from genetic, chromosomal, and tissue engineering techniques. Additional liver models, including micropattern hepatocyte coculture, 3D liver spheroids, and microflow systems, applicable to the study of drug disposition and toxicology, have also been reviewed. Ocular disposition models including corneal permeability models are included, as is commentary on in vitro and in vivo models of drug metabolism derived from breakthrough genetic, chromosomal, and tissue engineering techniques.

The special section went online on October 17 and is available at https://bit.ly/2OKckqA. The special section content is freely accessible through January 15, 2019.

Call for Papers – *JPET* Special Section on the Opiate Crisis: Novel Therapeutics Directions for Opioid Use Disorder and Pain Beyond Opioids

The Journal of Pharmacology and Experimental Therapeutics invites submission of manuscripts that present original research pertaining to the pharmacodynamic, pharmacokinetic, translational pharmacology, and phase 2/3 clinical trials of emerging therapeutic modalities, including (but not limited to) small molecules, antibodies, oligonucleotides, vaccines, and viral or gene-based therapies. Manuscripts describing efforts to apply novel in vitro, in vivo, or modeling approaches to characterizing the pharmacodynamics/pharmacokinetic properties of these novel therapeutic modalities are highly encouraged. Research papers pertaining to translational medicine or the efficacy and safety of novel therapeutics in phase 2/3 trials are also highly encouraged.

Review articles addressing any aspects of the pharmacodynamics, pharmacokinetic, preclinical models, or translational medicine paradigms addressing the aforementioned therapeutic modalities will be considered as well; proposals for such articles should be sent to the guest editors: Gerard Marek (gerard.marek@astellas.com), Kathryn Cunningham (kcunning@utmb.edu), and Kurt Rasmussen (kurt.rasmussen@nih.gov) for approval prior to submission.

The submission deadline is February 1, 2019. The special section is planned for publication in the *JPET* October 2019 issue.

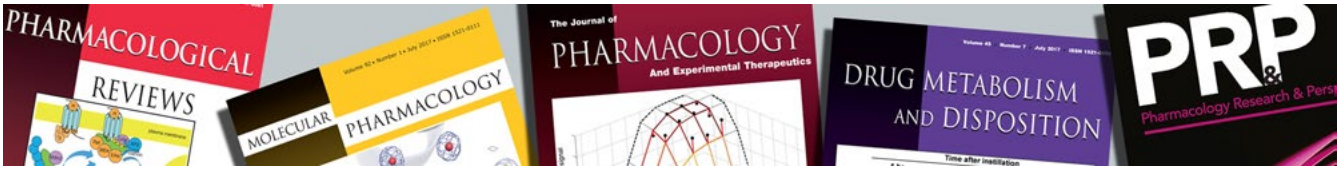
Call for Papers – *DMD* Special Section on Pharmacokinetic and Drug Metabolism Properties of Novel Therapeutics Modalities

Drug Metabolism and Disposition welcomes submission of manuscripts that present original research pertaining to the pharmacokinetic, pharmacodynamic, metabolic, and/or distribution properties of emerging therapeutic modalities, including (but not limited to) fusion proteins, bispecific antibodies, oligonucleotides, proteolysis targeting chimeras, CAR-T cells, and viral or gene-based therapies. Manuscripts describing efforts to apply novel in vitro, bioanalytical, or modeling approaches to characterizing the ADME properties of these novel therapeutic modalities are highly encouraged. Research papers pertaining to the ADME properties of peptides and peptidomimetics, antibody-drug conjugates, or nanoparticle therapeutics may also be considered.

Review articles addressing any aspects of the pharmacokinetic, metabolic, or distribution properties of the aforementioned therapeutic modalities will be considered as well; proposals for such articles should be sent to the guest editors, Rob Foti (rfoti@amgen.com) or Brooke Rock (brooke@amgen.com), for approval prior to submission.

The submission deadline is February 1, 2019. The special section is planned for publication in the August 2019 issue of *Drug Metabolism and Disposition*.

Joint Virtual Issues



ASPET has posted its first joint virtual issues, which are topic-focused collections of papers published in *Pharmacological Reviews*, *Drug Metabolism and Disposition*, *The Journal of Pharmacology and Experimental Therapeutics*, *Molecular Pharmacology*, and *Pharmacology Research & Perspectives*. The articles were selected by the journals' editors, and all are freely accessible.

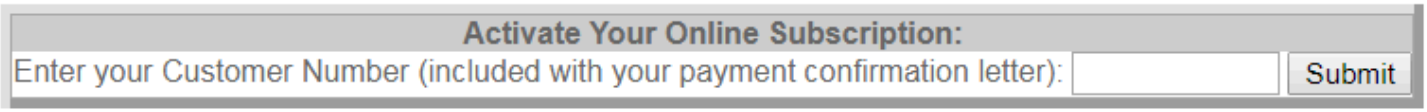
The first joint virtual issue, titled Pain Pharmacology Advances, includes 43 articles. Its table of contents is on the ASPET website at https://bit.ly/2pN8LAR. Article titles are linked to the full text of each research or review paper.

Quoting from the issue's introduction, "The innovative research in this virtual issue highlights a diverse array of nociceptive mechanisms, models, and novel interventional strategies that are particularly timely in light of the safety and societal issues associated with opioid dependence and abuse."

The second joint virtual issue, Diabetes Pharmacology Advances, is available at https://bit.ly/2JbA5SI. Its content is a "representative selection of outstanding peer-reviewed original research and topical reviews on type-2 diabetes mellitus (T2DM) and related topics." The collection of 45 papers, as further noted in the introduction, "should be of considerable interest to all investigators working to better understand T2DM and develop new therapeutics interventions."

In addition to the links above, the joint virtual issues can be accessed from a new link on the menu bar at the top of each journal's web pages and from the menu on the ASPET website under "journals" at www.aspet.org.

Access Is a Member Benefit



All ASPET members get access to the Society's journals as a member benefit. If you have not yet taken advantage of your member subscription, all you have to do is activate it by creating a user name and password. These can be the same credentials you use for the members-only section of the ASPET website or anything you choose. Go to https://bit.ly/2ilt4i2 and enter your ASPET member number and follow the simple instructions on the page that comes next. Don't know your member number? No problem—send an email to membership@aspet.org. ASPET staff members will be happy to help you.

This member benefit will be even more valuable at the end of the year when free access to the journals is modified.

Since its earliest years of online publishing, ASPET has provided free access 12 months after publication to all articles published after 1997. In 2001, the Board of Publications Trustees created free subscriptions for all ASPET members. In 2005, the Fast Forward (manuscript) version of articles, which are posted online within days of acceptance, have been freely accessible to all. Almost 20 years of free content has accumulated.

As anyone might assume, this has had an effect on subscriptions, pay-per-view purchases, and document delivery sales. To maintain the financial viability of the Society's publishing program, the Board of Publications Trustees approved a recommendation to make the copyedited and fully formatted version of articles freely accessible for a rolling 5-year window that begins 12 months after publication. As articles age out of the 5-year window, they will go back under access control. This change will take effect at the end of December 2018.

Fast Forward articles will continue to be made freely accessible immediately upon acceptance for publication. They will remain freely accessible after the formatted version goes online, just as they do now. Fast Forward articles receive a large number of hits, so we are confident that they are meeting the needs of those who cannot subscribe or join ASPET.

In addition, ASPET participates in a program called Research4Life that provides free access to all content in the journals (back to 1909) to people in developing countries. ASPET joined Research4Life in 2014 and will remain in the program.

Take advantage of this ASPET member benefit and activate your member subscription today.

Please note: The journals are on a different website than the Society's main website. You must log into one of the journals to access articles. Once you are logged in, you can go to any of the four wholly owned ASPET journals. If you have any problems with your subscription, you can send an email message to subscriptions@aspet.org, send feedback from the link in the footer of every journal web page, or call ASPET's content licensing and subscriptions manager Chris Keene at 301-634-7782.

Molecular Pharmacology Highlighted Trainee Authors

Congratulations to Kathryn (Kadee) Luderman of the National Institute of Neurological Disorders and Stroke, NIH, and Michal Lisnyansky with the Sacker Faculty of Medicine, Tel Aviv University, for being selected as the two most recent Highlighted Trainee Authors. Their work appears in the October and December issues, respectively, of the journal. Read about their areas of research, current projects, and the anticipated impact of their work at https://bit.ly/2yX1YeH.

The *Molecular Pharmacology* Highlighted Trainee Author program showcases the work of a young researcher selected from each issue of the journal. Dr. Adriano Marchese, a member of the journal's Editorial and Advisory Board, manages the selection process. Trainee authors may be nominated by a corresponding author or self-nominated.

Michal Lisnyansky

Kathryn (Kadee) Luderman

Membership News

Renew your 2019 Membership

Thank you for your support this year. We look forward to renewing your 2019 ASPET membership. We hope you continue to get involved and make a positive impact on the Society and pharmacology community. Your support is invaluable to our mission of being the professional home for educators, students, researchers, healthcare practitioners, and other professionals working to advance pharmacology research.

Renew today by visiting www.aspet.org/renew.

New Members

ASPET welcomes our newest members!

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Nicola Carter, Pacific Univ, OR
Gang Chen, Univ of Kentucky
Dawn L. Duval, Colorado State Univ
Holly A. Feser Stessman, Creighton Univ, NE
Debra A. Hoppensteadt Moorman, Loyola Univ, IL
Keiko Hosohata, Osaka Univ of Pharmaceutical Sciences, Japan
Uzoma Ikonne, A.T.Still Univ, AZ
Elisha R. Injeti, Cedarville Univ Sch of Pharmacy, OH
Karunya K. Kandimalla, Univ of Minnesota
Hye Jung Kim, Gyeongsang Natl Univ, Republic of Korea
Priyanka R. Kulkarni, Amgen Inc., MA
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Brian J. Murphy, Bristol-Myers Squibb, PA
Ulhas Naik, Thomas Jefferson Univ, PA
Hoa Q. Nguyen, Shire, MA
Maureen T. O'Brien, Charles River Laboratories, MD
Anshul Pandya, Univ of Alaska Fairbanks
Olga Pol, Institut de Recerca. Hospital de Sant Pau, Spain
Michael Rieder, Univ of Western Ontario, Canada
Brooke Rock, Amgen Inc. Lib, CA
Jason A. Sprowl, Univ at Buffalo, NY
Rajeev Taliyan, Birla Inst of Tech and Sci Pilani, India
Tal Teitz, Creighton Univ, NE
Peter J. Tonge, Stony Brook Univ, NY
Steven Trasino, Hunter Coll, NY
Maryam Vasefi, Lamar Univ, TX
Jennifer T. Wolstenholme, Virginia Commonwealth Univ
Shetuan Zhang, Queen's Univ, Canada

POSTDOCTORAL MEMBERS

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Ramon Ayon, Univ of Arizona
Tapan Behl, Chitkara Univ, India
Lillian J. Brady, Vanderbilt Univ, TN
Simone Brixius-Anderko, Univ of Michigan, MI
Sean M. Collins, Univ of Cincinnati, OH

Lindsay C. Czuba, Univ of Washington, WA
Lindsey Kuiper, Wake Forest Baptist Med Ctr, NC
Chiagoziem A. Otuechere, Redeemer's Univ, Nigeria
Aboubacar Alassane Oumar, Univ of Sciences, Mali
Fengrui Yang, Johns Hopkins Hospital, MD

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Patrick McGee, LA
Olayinka O. Ogunleye, Lagos State Univ Coll of Med, Nigeria
Dinesh S. Senevirathna, Sri Lanka

GRADUATE STUDENTS

Carla Abrahamian, LMU Munich, Lebanon
Ahmed Alarabi, Univ of Texas, El Paso
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Mohammadamin Asadirad, California Northstate Univ
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Miryam M. Pando, Univ of Texas Hlth Sci Ctr, San Antonio
Shravan K. Paswan, CSIR-National Botanical Research Institute, India
Ashley C. Payne, Florida A & M Univ
Dhandevi Persand, NYIT Coll of Osteopathic Med, NY
Akila Ram, Utah State Univ
Bello-Omenesa Z. Ramatu, Univ of Putra Malaysia
Larry Rodriguezc, Univ of Southern California
Dianicha Santana, Univ of IL of Hlth Sci
Karan B. Shah, SMT NHL Municipal Med Coll, India
Dauda Sheriff, Chicago State Univ, IL
Aaminah Siddiqui, Chicago State Univ, IL
Emily Taylor, Baylor Univ, TX
Mavis A. Tenkorang, Univ of North Texas Hlth Sci Ctr
Kimberly C. Thibeault, Vanderbilt Univ, TN
Kaitlyn K. Thompson, Stony Brook Univ, NY
Keomany Vatthanaphone, KY
Pritt Verma, CSIR-National Botanical Res Inst, India
Nicholas Warren, Dartmouth Coll, NH

UNDERGRADUATE STUDENTS

Haidar Ahmed, Univ of Texas, El Paso
Timothy H. Amin, Rutgers Univ, NJ
Ruth O. Anyaeche, Fisk Univ, TN
Joseph Artemiou, Gettysburg Coll, NJ
Jaya Banerjee Chatterjee, Rutgers Univ, NJ
Sierra Boyd, Michigan State Univ
Thomas Hong, Rutgers Univ, NJ
Bryce S. Jurkouich, Rutgers Univ, NJ
Danielle Konan, Univ of Notre Dame, TN
Jordan M. Lee, Rutgers Univ, NJ
Alina Lou, Rutgers Univ, NJ
Charlotte A. Love, Rutgers Univ, NJ
Caroline G. Madigan, Univ of Pittsburgh, PA
Callum Malcolm, Rutgers Univ, NJ
Larshe D. Moore, Clark Atlanta Univ, PA
Anjeli V. Nandwani, Univ of Florida
Tyler Natof, Univ of Illinois, Urbana Champaign
Nina Park, Drexel Univ, PA
Tracy Peng, Rutgers Univ, NJ
Sakina A. Plumber, Rutgers Univ, NJ
Alexa S. Podolsky, Rutgers Univ, NJ
Evan L. Reeder, Univ of Cincinnati, OH

Humam Shahare, Univ of Arkansas, Little Rock
Farhan Shahid, Shifa Tameer-e-Millat Univ, Pakistan
Hye Min Shin, Rutgers Univ, NJ
Ashten M. Stambersky, Alma College, MI
Alexandra R. Tribo, Univ of North Carolina, Chapel Hill
Nicole Tryon, Rutgers Univ, NJ
John Vusich, Alma College, MI
Rachel Watson, Univ of Wisconsin, Madison
Rachel Winner, Rutgers Univ, NJ
Eden Zewdie, Univ of Wisconsin, Madison
Melanie Zhang, Rutgers Univ, NJ
Shane Zhang, Rutgers Univ, NJ

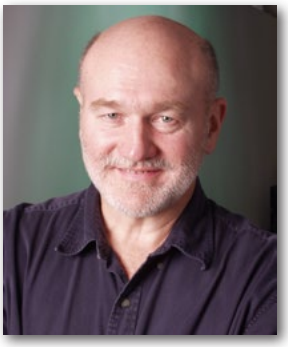
In Sympathy

ASPET notes with sympathy the passing of the following members.

Ernest Hodgson
Lawrence J. Fischer
Lowell E. Hokin
Robert J. McIsaac
David A. Reinke

Members in the News

Achievements, Awards, Promotions, and Scientific Breakthroughs



Peter G. Wells, PharmD

University of Toronto

Peter G. Wells, PharmD, is a professor in the Division of Biomolecular Sciences in the Faculty of Pharmacy and the Department of Pharmacology & Toxicology in the Faculty of Medicine, University of Toronto. Dr. Wells recently received the 2018 Gabriel L. Plaa Award of Distinction from the Society of Toxicology of Canada (STC), for his outstanding and sustained contributions to the science of toxicology in Canada.

Dr. Wells' laboratory focuses on the toxicology of reactive intermediates, particularly involving the roles of oxidative stress and DNA damage and repair in congenital defects, neurodevelopmental disorders, and neurodegeneration. Dr. Wells has given over 125 invited presentations, including symposium talks at annual meetings of the Society of Toxicology, ASPET, Teratology Society (USA), Int. Society for the Study of Xenobiotics, STC, Int. Union for Pharmacology (IUPHAR) and Int. Union for Toxicology (IUTOX) (2007 keynote lecture; 2019).

He has supervised 24 PhD and 14 MSc students, 7 postdoctoral fellows, and over 115 undergraduate research students, and he has over 140 peer-reviewed publications.

Dr. Wells has been a member of ASPET since 1984 and is a member of the **Divisions for Toxicology**, **Drug Metabolism and Disposition**, **Molecular Pharmacology**, **Neuropharmacology**, and **Translational and Clinical Pharmacology**.

Wolfgang Löscher, DVM

University of Veterinary Medicine Hannover, Germany

Wolfgang Löscher, DVM, professor and director of the Department of Pharmacology, Toxicology, and Pharmacy at the University of Veterinary Medicine Hannover, as well as head of the Center for Systems Neuroscience in Hannover, Germany, received the 2018 Lifetime Accelerator Award of the U.S. Epilepsy Foundation for his contributions to the field of epilepsy research, including the development of new medications and the development of the first available animal model of refractory seizures, which was used to characterize mechanisms involved in drug resistance. Dr. Löscher's group recently published a new mechanism of drug extrusion at the blood–brain barrier in *PNAS*. His research interests are in the pharmacology of antiepileptic drugs, the mechanisms of pharmaco-resistance in epilepsy, and the pathophysiology of temporal lobe epilepsy with the aim to find new targets for treatment. He has over 600 refereed publications and has obtained several other awards for this research, including the American Epilepsy Society's Epilepsy Research Award for Basic Science Research in 2006, and the Ambassador for Epilepsy Award of the ILAE and IBE in 2011, and the European Epileptology Award of the ILAE/CEA in 2014.

Dr. Löscher has been a member of ASPET since 2000 and is a member of the **Divisions for Neuropharmacology and Behavioral Pharmacology.**

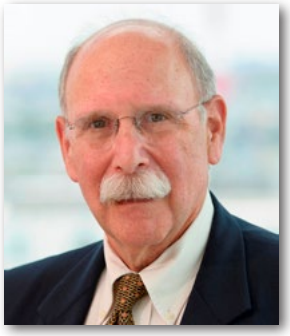
Richard Okita, PhD

National Institute of General Medical Sciences

Richard Okita, PhD is a program director in the Pharmacology, Physiology, and Biological Chemistry Division of the National Institute of General Medical Sciences (NIGMS). Dr. Okita will receive a Medal of Merit Award from the American Society of Clinical Pharmacology and Therapeutics (ASCPT) at their annual meeting in March 2019.

Dr. Okita has managed the institute's T32 predoctoral training grants in the pharmacological sciences and postdoctoral training awards in clinical pharmacology. In addition to training awards, he also managed various research and conference awards, F31 and F32 fellowship awards, and K99/R00 Pathway to Independence awards.

He has been a member of ASPET since 1990 and is a member of the **Divisions for Drug Metabolism and Disposition**, **Drug Discovery and Development**, **Molecular Pharmacology**, and **Translational and Clinical Pharmacology**.



Gavril W. Pasternak, MD, PhD

Memorial Sloan Kettering Cancer Center

Gavril W. Pasternak, MD, PhD, is the Anne Burnett Tandy Chair in Neurology at the Memorial Sloan Kettering Cancer Center, and he is also the Laboratory Head in the Molecular Pharmacology Program within the Sloan Kettering Institute. Dr. Pasternak is the proud recipient of the 2019 Frederick W.L. Kerr Basic Science Research Award of the American Pain Society. Dr. Pasternak also received the 2018 PhRMA Foundation Award in Excellence in Pharmacology/Toxicology.

His research has focused on opioid receptors and their mechanisms of action, resulting in over 400 publications and 14 patents. He has served on numerous editorial boards and served on the Board of Scientific Counselors of the National Institute on Drug Abuse, which awarded him their Senior Scientist Award and MERIT Awards. He is an elected member of the Johns Hopkins Society of Scholars, and he is also a fellow of both the American Academy of Neurology and the American Neurological Association.

Dr. Pasternak has been a member of ASPET since 1981, and is a member of the **Divisions for Neuropharmacology** and **Molecular Pharmacology**.

Sarah L. Withey, PhD

McLean Hospital/Harvard Medical School

Sarah L. Withey, PhD was recently awarded an Alkermes Pathways Research Award for her project entitled "Extended-release naltrexone: effects on relapse-related behavior and neural circuitry in laboratory animals." The program offers support for early career investigators committed to advancing research in substance use disorders.

Dr. Withey is currently an instructor in Dr. Jack Bergman's laboratory at McLean Hospital and is examining the effects of long-term exposure to pharmacotherapies used in the treatment of drug abuse.

Dr. Withey has been a member of ASPET since 2015 and is a member of the **Division for Behavioral Pharmacology.**

Paul Jenkins, PhD

University of Michigan Medical School

Paul Jenkins, PhD is an assistant professor of pharmacology and psychiatry at the University of Michigan Medical School. Dr. Jenkins is the proud recipient of the 2018 One Mind Rising Star Bipolar Disorder Translational Research Award (2018-2021).

Dr. Jenkins received his undergraduate degree and a doctorate in pharmacology from the University of Michigan. He continued his training as a postdoctoral fellow at the Howard Hughes Medical Institute at Duke University. His current research concentrates on

the cellular and molecular underpinnings of complex psychiatric diseases like bipolar disorder.

He has been a member of ASPET since 2008 and is a member of the **Divisions for Neuropharmacology** and **Molecular Pharmacology**.

Fernando B. de Moura, PhD

McLean Hospital/Harvard Medical School

Fernando B. de Moura, PhD recently received The Livingston Award from the Department of Psychiatry at Harvard Medical School. Dr. de Moura completed his PhD in pharmacology at the University of Texas Health Science Center at San Antonio, and is currently a postdoctoral fellow with Drs. Jack Bergman and Stephen Kohut at McLean Hospital.

His research focuses on elucidating pharmacological mechanisms associated with abuse-related behaviors in order to identify novel targets for candidate medications.

Dr. de Moura has been a member of ASPET since 2014. He is a member of the **Divisons for Behavioral Pharmacology** and **Neuropharmacology.**

Kenneth L. Byron, PhD

Loyola University, Chicago

Kenneth L. Byron, PhD, has been appointed to the position of interim chair in the Department of Molecular Pharmacology and Therapeutics at Loyola University Chicago.

For the past 25 years, Dr. Byron has directed an extramurally funded research program at Loyola, focusing on calcium signaling and regulation of ion channels in vascular and airway smooth muscle. He is listed as the inventor on multiple US patents related to this research. Dr. Byron is also actively involved in a variety of scientific organizations and societies, serves on the editorial boards of several scientific journals, and has served on numerous NIH, VA Merit, AHA, and state scientific review groups since 1994.

Dr. Byron has been a member of ASPET since 2004 and is a member of the **Divisions of Cardiovascular Pharmacology** and **Molecular Pharmacology.**

Karen Houseknecht, PhD

University of New England, Biddeford

Karen L. Houseknecht, PhD, professor of pharmacology at the University of New England, Biddeford, has been appointed associate provost for research and scholarship. In this role, Dr. Houseknecht will lead research strategy and research compliance efforts across all academic programs at UNE. She has served as the interim dean for the UNE College of Pharmacy since June 2017, and she also serves as professor of pharmacology in the UNE College of Osteopathic Medicine. Prior to joining the University of New England in 2009 as a founding faculty member in the College of Pharmacy, Dr. Houseknecht served as associate research fellow at Pfizer Global Research and Development in Groton, CT; visiting professor of clinical physiology at the Karolinska Institute in Stockholm, Sweden; and assistant professor of endocrinology in the Department of Animal Sciences at Purdue University.

Dr. Houseknecht's research focuses on the pathophysiology of obesity and diabetes. Her work is devoted to her unwavering passion around the discovery and development of novel therapeutics for the treatment of metabolic disease and mood disorders, with a specific focus on patient safety.

Dr. Houseknecht has been a member of ASPET since 2017 and is a member of the **Divisions for Molecular Pharmacology, Drug Discovery and Development, Drug Metabolism and Disposition, Neuropharmacology, Pharmacology Education,** and **Toxicology.**

Division News

2019 Division Elections

The 2019 election includes nominees for ASPET Council (president-elect, secretary/treasurer-elect, and councilor), as well as Division officers: Division for Behavioral Pharmacology (BEH), Division for Cardiovascular Pharmacology (CVP), Division for Drug Metabolism and Disposition (DMDD), Division for Molecular Pharmacology (MP), Division for Pharmacology Education (DPE), and Division for Toxicology (TOX). The election will open on January 7, 2019 and eligible voting members will receive an email with instructions.

Division for Behavioral Pharmacology

Nominee for Chair-Elect

William E. Fantegrossi, PhD
Associate Professor, Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences College of Medicine

Nominees for Secretary/Treasurer-Elect

Kevin S. Murnane, PhD
Assistant Professor of Pharmaceutical Sciences, Mercer University

Peter J. Winsauer, PhD
L. Allen Barker Professor of Pharmacology, Louisiana State University Health Sciences Center

Division for Cardiovascular Pharmacology

Nominees for Chair-Elect

Fadi T. Khasawneh, PhD
Associate Professor and Chair, Department of Pharmaceutical Sciences, School of Pharmacy, The University of Texas, El Paso

Hemal H. Patel, PhD
Professor and Vice Chair for Research, Department of Anesthesiology, University of California, San Diego

Nominees for Secretary/Treasurer-Elect

Anastasios Lymperopoulos, PhD
Associate Professor of Pharmacology and Pharmaceutical Sciences, Nova Southeastern University

Michael Tranter, PhD
Assistant Professor, Department of Internal Medicine, Division of Cardiovascular Health and Disease, University of Cincinnati

Division for Drug Metabolism and Disposition

Nominees for Chair-Elect

Robert S. Foti, PhD
Principal Scientist, Pharmacokinetics and Drug Metabolism, Amgen Inc.

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

Nominees for Secretary Treasurer-Elect

Aarti Sawant-Basak, PhD
Associate Director, Clinical Pharmacology, Early Clinical Development, Pfizer

Yurong Lai, PhD
Director of Drug Metabolism, Gilead Sciences, Inc.

Division for Molecular Pharmacology

Nominees for Chair-Elect

J. Silvio Gutkind, PhD
Professor, Department of Pharmacology, Associate Director of Basic Science, University of California, San Diego Moores Cancer Center

JoAnn Trejo, PhD
Professor and Vice Chair of Pharmacology, University of California, San Diego

Nominees for Secretary/Treasurer-Elect

Kirill Martemyanov, PhD
Professor and Chair, The Scripps Research Institute

Manoj A. Puthenveedu, PhD
Associate Professor, Department of Pharmacology, University of Michigan

Division for Pharmacology Education

Nominees for Chair-Elect

Katharina Brandl, RPh, PhD, FAPE
Assistant Professor, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego

Helmut B. Gottlieb, PhD
Professor, Department of Pharmaceutical Sciences, University of the Incarnate Word Feik School of Pharmacy

Nominee for Secretary/Treasurer-Elect

Gagani Athauda, MD
Associate Professor, Department of Cellular Biology and Pharmacology, Florida International University

Division for Toxicology

Nominees for Chair-Elect

Qin M. Chen, PhD
Professor of Pharmacology, University of Arizona College of Medicine

Kenneth E. McMartin, PhD
Professor of Pharmacology, Toxicology & Neuroscience at Louisiana State University Health Sciences Center

Nominee for Secretary/Treasurer-Elect

Brendan D. Stamper, PhD
Associate Professor, Pacific University School of Pharmacy

Division Awards Update

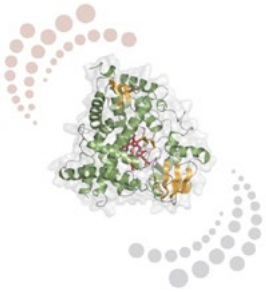
The Division for Behavioral Pharmacology is pleased to recognize Dr. James H. Woods' service to pharmacology by naming the division's early career award in his honor as the: **JH Woods Early Career Award in Behavioral Pharmacology**. The inaugural awardee will be announced in January 2019.

Also, the Division for Drug Metabolism and Disposition is pleased to recognize Dr. Richard Okita's service to pharmacology by naming the division's early career award in his honor as the: **Richard Okita Early Career Award in Drug Metabolism and Disposition**. The awardee will be announced in January 2019. An event to celebrate is being planned for Tuesday, April 9 during the ASPET Annual Meeting at EB 2019.

Dr. James H. Woods

Dr. Richard Okita

ASPET will announce all scientific achievement and division awardees in January 2019.



Division for Drug Metabolism and Disposition

Member Spotlight

Bettie Sue Masters: An Inspirational Journey through CYP450 Reductase, Scientific Collaborations, and Women in STEM

Submitted by Michael J. Espiritu and Aarti Sawant-Basak

Bettie Sue Masters, PhD, received her BS with double majors in biology and chemistry in 1959 from Roanoke College where she graduated as salutatorian. Although she was initially accepted into the College of William and Mary, she decided to pursue her degrees at Roanoke College where she received a science scholarship, due to being refused a science scholarship for being a woman at W&M. She then went on to graduate from Duke University with a PhD in biochemistry in 1963, under the guidance of Dr. Henry Kamin.

Following her PhD, Dr. Masters completed prestigious postdoctoral fellowships, first with the American Cancer Society followed by an American Heart Association Advanced Research Fellowship and an Established Investigatorship and joined the University of Texas Southwestern Medical School as an Assistant Professor. Dr. Masters spent 14 years at the University of Texas Southwestern Medical School, after which she was selected to serve as the chair of the Department of Biochemistry at the Medical College of Wisconsin at the age of 45, where she served as department chair for eight years.

She was awarded the first Robert A. Welch Foundation Endowed Chair at the University of Texas Health Science Center at San Antonio, from which she retired as Professor Emeritus in 2016.

During Dr. Masters' long and successful career she has published over 325 journal and book articles, which are fundamental to our understanding of the expression and purification techniques of cytochrome P450 reductase in microsomal fractions as well as the role of this flavoprotein during catalysis of P450-mediated reactions.

This work also led her laboratory into the study of the properties and mechanisms of the three genetically encoded nitric oxide synthases, which share the common property with cytochrome P450 reductase of requiring both FAD and FMN in the catalysis of their respective activities.

In addition to her continued contributions to the fields of Biochemistry and Drug Metabolism, she has been an active member of several societies, including ASPET, where her membership began in 1975. She has served as a scientific advisory board member for the *Drug Metabolism and Disposition* journal and previously served on the Board of Publication Trustees. She has consistently published in ASPET journals and in 2000 received the Bernard B. Brodie award in Drug Metabolism. In this article she has shared some of her valuable insights from her long and highly productive career:

For our readers, can you summarize your career in the field of drug metabolism?

BM: My career began at Duke as a graduate student in the Department of Biochemistry, where I now serve as an adjunct professor. After retiring in 2016 from the University of Texas System, where I served on the faculties of two institutions (University of Texas Southwestern Medical School for 14 years and University of Texas Health Science Center in San Antonio for over 25 years with an interim chairmanship at the Medical College of Wisconsin for 8 years), I have come full circle to my professional origins. It just happens that both daughters and their families live here with my three grandchildren—lucky me! When I began my research at Duke, Charles Williams, a graduate student in Dr. Henry Kamin's laboratory, had completed his dissertation, which determined that NADPH-cytochrome c reductase was found in the microsomal fractions of cell lysates. I continued his research after he left for a postdoctoral fellowship in Sheffield, England. This was an exciting time as his dissertation research and the contributions of others in the field, such as Jim Gillette, Ron Estabrook and the Japanese groups, led by Ryo Sato and Tsuneo Omura, provided evidence for the role of reductase in cytochrome P450 activities. During my graduate studies, I performed the first homogeneous purifications of cytochrome c reductase. This led to the production of antibodies for this enzyme, which I and others demonstrated could inhibit drug metabolism, as well as steroid metabolism, identifying it definitively as the cytochrome P450 reductase. This naturally put me on the road to investigating drug metabolism further. I have had the great pleasure of working with a young faculty member in the Department of Biochemistry at the Medical College of Wisconsin, Dr. Jung-Ja Kim, with whom I collaborated to produce the first crystal structure of the rat reductase in 1996, followed by the structure of the human reductase in 2011. In the 1970s I had the opportunity to work with another talented visiting scientist, Dr. Yukio Yasukochi, who developed a bio-specific affinity chromatography method for reductase, a technique that continues to be used to this day, not only for cytochrome P450 reductase purification but for nitric oxide synthase purification. This technique led to our most cited work to date and has resulted in over 1400 citations.

In addition to your contributions to your field, you have been highly involved in ASPET activities. Can you briefly describe your ASPET/DMD journey and comment on the most rewarding aspects of being involved with the society?

BM: Although I am a biochemist, my involvement with ASPET was a natural outcome. I officially joined ASPET in 1975 but have attended most of the Microsome and Drug Oxidation meetings since 1968. I am proud to say that I recently joined in celebrating the 50th anniversary of these meetings at which Tsuneo Omura (one of the co-discoverers and purifiers of cytochrome P450 in 1962) and I were the only two people who had also been in attendance at the inaugural meeting in 1968. In 2002, I was honored to receive the Bernard B. Brodie Award in Drug Metabolism. Previously, I have served on the Board of Publications Trustees of ASPET and recently, I have served on the Brodie Award Committee and currently I still serve on the Scientific Advisory Board of the journal, *Drug Metabolism and Disposition*. I would say the most rewarding aspect of being involved with ASPET is meeting with people who have similar interests. What many young people don't often realize is how important it is to attend and present their research at these meetings. One of the best ways to become noticed and be remembered within your field is making sure that you continually share your research with others and benefit from having scientific conversations with your peers.

Historically many STEM fields have been male dominated. What was it like entering into the field of drug metabolism as a woman in the early 60s?

BM: Regrettably, I have to offer some criticism here. Historically, ASPET has not recognized many female scientists with its awards. I was saddened to learn that I was one of the few women being recognized in the centennial publication in 2008, despite being surrounded by so many competent and accomplished female scientists. I continue to be disheartened at the lack of female platform speakers, despite approximately half of the current trainees in the field being women. This is not to say that things are not changing, however. I have noticed a rise in female leadership in ASPET and the Drug Metabolism Division in recent years and am hopeful that this trend will continue.

You have had a very long and prosperous career. What do you feel is the most valuable thing you have learned over the years?

BM: My main theme has always been collaboration and sharing. I have never fooled myself to believe I know everything. One of the greatest things I have learned is to learn from other people's expertise and scientific findings. This is not only beneficial for pushing the field forward but can often result in life-long friendships. I firmly believe that the world would be a better place if more collaboration could occur. I also believe it is important to collaborate with purpose and not just for monetary gain. Focusing on monetary goals can have a detrimental impact on true advancement of science and, if we truly want to create new drugs, we need to have the proper focus for the right reasons.

What emerging research topics in the field of drug metabolism and disposition are you most excited about?

BM: I would say that I am most excited about the new multidisciplinary studies and collaborations that have been developing lately. I am excited about the melding of fields such as chemistry, immunology and metabolism, including cell signaling. I am excited about new discoveries in proteomics and signaling at the molecular level and using these discoveries as a means to maintain human health and improve therapeutic modalities. Pharmacogenomics is definitely an area to watch as well. The future for drug metabolism means broadening our horizons and I believe that is happening.

As scientists many of us are inspired by our mentors or others who have come before us and made significant contributions to our field, such as yourself. Who did you find most inspirational as a young scientist and what about their work inspired you the most?

BM: When I was a child, I did not know who I was or what I wanted to be. The first person to really inspire me to pursue science was my high school science teacher, who happened to point out my analytical qualities. Neither of my parents attended college, so they did not have much advice on the subject; however, this teacher guided me to enter the Westinghouse Science Talent Search (the precursor of the Intel and now the Regeneron Science Talent Searches), which resulted in my obtaining a science scholarship to attend college. Once in college I had several professors provide me with invaluable guidance toward career choices and, without their advice, I would not have continued on to graduate school. Of special mention is my PhD mentor, Henry Kamin. Dr. Kamin was a true renaissance man. He not only provided me with the *guidance* necessary to navigate my scientific career but with *opportunities* to learn unique, state-of-the-art skills and to present my research around the world. In addition to developing my scientific expertise, he also helped me acquire a true appreciation of music, history and art. It was really the kind of education that is priceless! If I were to choose a career to follow today, I would make exactly the same choices.

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Chapter News

ASPET Welcomes Canadian Chapter

ASPET is pleased to announce our newest chapter—the **Canadian Society of Pharmacology and Therapeutics (CSPT)**.

CSPT is a not-for-profit organization that strives to be the Canadian voice fostering the application of educational and research excellence to drug discovery and therapeutic choice. They bring together a multidisciplinary group of members with broad interests in optimally safe and effective drug therapy. Their membership includes both basic and clinical researchers in government, academia, industry, and consulting across Canada.

The CSPT was founded in 2008 through the merger of the Pharmacological Society of Canada (PSC) and The Canadian Society of Clinical Pharmacology (CSPS). Prior to the merger, the PSC and CSPS operated as separate societies for over 25 years. CSPT is the official Canadian representative for IUPHAR, the International Union of Basic and Clinical Pharmacology.

We look forward to partnering with this new chapter to increase scientific communications across our borders; to broaden public awareness of pharmacology; and to share in being a positive force for the discipline of pharmacology.

Learn more about the CSPT Chapter at https://bit.ly/2zbxnlv.

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2018 Mid-Atlantic Pharmacology Society Annual Meeting in Review

Submitted by Bradford D. Fischer, PhD

MAPS 2018 meeting attendees.

The Mid-Atlantic Pharmacology Society (MAPS) held its 2018 Annual Meeting on September 27th at University of Pennsylvania's Pennovation Center in Philadelphia, PA. As in years past the meeting highlighted recent pharmacological advances through a diverse and interactive 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, *Opioids and Analgesia*, and featured recent advances into the mechanisms of opioid analgesic action and withdrawal, molecular mechanisms that underpin the pain-relieving properties of opioids, and new insights into the measurement of pain sensation. The keynote address by Gregory Scherrer, PharmD, PhD (Stanford University School of Medicine) shed light on the neural mechanisms that underlie the sensory and affective dimensions of pain experience, as well as how opioids interfere with these mechanisms to provide pain relief. Podium

presentations, by researchers at the cutting edge from the mid-Atlantic area, fueled discussions on the use of buprenorphine for the treatment of neonatal abstinence syndrome (Walter Kraft, MD, Thomas Jefferson University), the assessment of pain sensation using sub-second behavioral mapping and statistical modeling (Ishmail Abdus-Saboor, PhD, University of Pennsylvania), and the importance of the mTOR pathway in kappa opioid-induced behavioral aversion (Lee-Yuan Liu-Chan, PhD, Temple University).

The biotech roundtable discussion featured representatives from local biotech companies at various stages of development. The session was moderated by R. Kyle Palmer, PhD (Opertech Bio and MAPS Councilor), and participants included Renee Stewart, PhD (CSO, LeVolta Pharmaceuticals), Neha Saxena, PhD (Director of Product Development, PolyAurum), and Taciana Pereira (Director of Bioengineering, Allevi). Questions from meeting attendees probed into biotech operations, investor targeting phases, and career turning points.

The annual George B. Koelle Award was presented to Paul McGonigle, PhD (Drexel University), who emulates the outstanding qualities of Dr. Koelle, including "profound commitment to teaching, fondness for encouraging students, excellence in research, and strong devotion to the science of pharmacology". Congratulations to Dr. McGonigle! Continuing the commitment to foster trainee development, MAPS selected invited trainee talks by graduate students Andre Toussaint (Temple University) and Karan Muchhala (Virginia Commonwealth University). Poster topics covered broad areas of pharmacology. Poster awards were given to undergraduate students Demetrius Lee (Temple University) and Hannah Work, Joseph Iovine, Nakoa Webber, and Taylor Douglas (Rowan University); graduate students Matthew Hoffman (Temple University School of Medicine) and Michael Ippolito (Thomas Jefferson University); and post-doctoral fellow Shivon Robinson, PhD (University of Pennsylvania). Congratulations to all the trainees!

Thank you to all our sponsors, attendees, and presenters 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 photos and more at @MAPS_ASPET on Twitter!

See you next year!

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