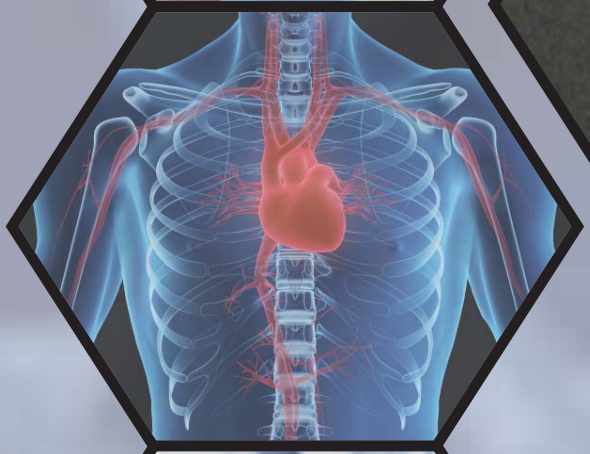
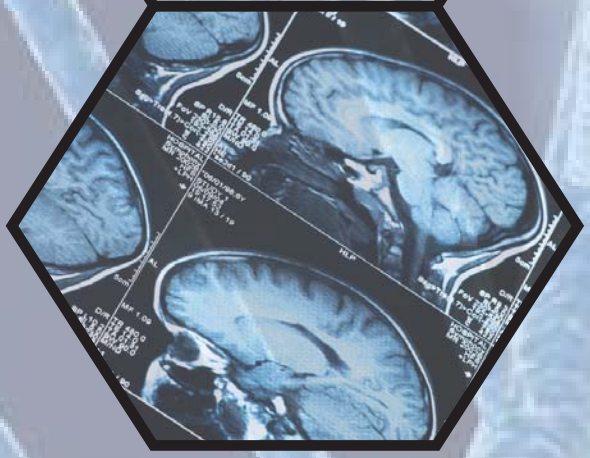
aspet The Pharmacologist
Vol. 55
Number 2
2013
June





End of an era

ASPET Executive Officer Christine K. Carrico retiring

In this issue:

Contents

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

The Pharmacologist (ISSN 0031-7004) is published quarterly in March, June, September, and December by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995. Annual subsciption rates: $20.00 for ASPET members; $45.00 for U.S. nonmembers and institutions; $70.00 for nonmembers and institutions outside the U.S. Single copy: $20.00.

Periodicals postage paid at Bethesda, MD. GST number for Canadian subscribers: BN:13489 2330 RT.

ASPET assumes no responsibility for the statements and opinions advanced by contributors to *The Pharmacologist*.

Deadlines for submission of material for publication: Issue 1, February 15; Issue 2, May 8; Issue 3, August 6; and Issue 4, November 5.

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

President's Corner

Comings and Goings

Dear ASPET Members:

It has been my privilege to serve as your president during the past year. We just completed one of the most successful ASPET Annual Meetings at Experimental Biology 2013 in Boston. Despite the challenges of the tragic events that preceded the meeting in Boston, we had a record attendance and a fabulous program highlighted by the 4th GPCR Colloquium. We were pleased that the British Pharmacological Society joined us, which brought a new international dimension to the meeting and also provided a convenient venue to announce the launching by the two Societies with John Wiley & Sons of an open access, online-only, peer-reviewed journal entitled *Pharmacology Research & Perspectives* (*PR&P*). This exciting new journal will publish original research and reviews in pharmacology, clinical pharmacology, therapeutics, education, and related research areas. The Editor-in-Chief is Michael J. Curtis and the Deputy Editor is Darrell Abernethy. The journal expects to publish its first issue in the autumn of 2013. As mentioned at the Annual Business Meeting, we have adopted a new accelerated symposium review process that we anticipate will increase the timeliness of our program. I hope you will join us in San Diego next year (April 26 – 30), where we plan to host the Chinese Pharmacological Society.

As I reflect on the events during my tenure as ASPET President, the most prominent and disconcerting was a telephone call earlier in the year with our Executive Officer, Christie Carrico, where she declared her intention to retire. Despite my impassioned plea and those of numerous former ASPET Presidents, Christie was firm in her decision. It is sobering to remember that ASPET has had only four Executive Officers in its entire 105-year history. Christie has been our Executive Officer for the last 16 years. During that time, not only has she ensured the daily activities in the ASPET office function flawlessly, overseeing all of ASPET's operations, programs, and initiatives, including our publications, award ceremonies, and Council and committee meetings, but she created the divisional architecture that we now enjoy, expanded the ASPET staff, and helped place ASPET on sound financial grounds. Countless presidents have been chaperoned by Christie, and all are grateful to have enjoyed her wisdom. The Society has been truly blessed having Christie as our Executive Officer. While it will be impossible to replace Christie, a search committee has been formed, comprised of myself, Lynn Wecker, Rick Neubig, Jim Barrett, Annette Fleckenstein, and Brian Cox, and we already have a short list of candidates we expect to interview. We are hopeful a new Executive Officer will be identified and will join us by September. We all wish Christie a wonderful retirement and great enjoyment as she begins a new adventure!

As was mentioned at the Annual Meeting, our Member-Get-A-Member Program and social media programs have been wonderful developments, as has our new ASPET Career Center, which Suzie Thompson thoughtfully developed. We have also launched an effort to enhance our Awards program. I encourage all of you to visit the ASPET website and investigate these innovative vehicles for helping our members. I also want to congratulate our newly elected officers: President-elect Annette E. Fleckenstein, our Secretary/Treasurer-elect Paul A. Insel, and Councilor John D. Schuetz. I am sure you will join me in welcoming our new President Rick Neubig, who is currently a Professor in the Department of Pharmacology, Co-director of the Center for Chemical Genomics, and Director of the Center for the Discovery of New Medicines at the University of Michigan. In addition to becoming ASPET President, Rick will assume the Chair of Pharmacology at Michigan State University. Rick is considered one of the pioneers in the investigation of the biophysics of adrenergic receptors, in GPCRs, and in a set of proteins that directly regulate G protein signaling (RGS molecules). Rick and I have been working together to ensure the comprehensive self-appraisal process that has been undertaken by McKinley Advisors will help position the Society for our younger membership and the next decade of growth.

I wish to thank everyone who helped make this presidency so enjoyable, especially our Past President Lynn Wecker and the extremely talented staff at the ASPET office.

Pharmacologically yours,

John S. Lazo

Farewell Message from the Executive Officer

Christine K. Carrico, Ph.D., ASPET Executive Officer (1997 – 2013)

Christie then (1998) and now (2009).

Very few people, I think, are lucky enough to actually have their dream job and love the work they do for sixteen years. I have been one such person. It has been a pleasure and a privilege to work for ASPET. I have worked with seventeen presidents, beginning with Sue Duckles and ending with Rick Neubig. Along the way, I have had the privilege of getting to know and be a colleague, and I hope friend, to many, many wonderful men and women who served as President and officers of ASPET.

When I came to ASPET there were four full-time and two part-time staff. We now total 14 full-time and one part-time staff, all but one of which have come in the past 15 years. A couple of weeks after I came to ASPET in August, I was told that our four journals were going to go online with HighWire Press, one a month, starting in September. In early September I was contacted by HighWire and told that all I had to do was enter the author and subscription information online in HTML! A quick trip to Borders to get *HTML for Dummies* and we were set to go! That fall, the Board of Publications Trustees decided to move publishing from Williams and Wilkins to in-house which would necessitate hiring someone to oversee the publications enterprise. The first person I hired was Richard Dodenhoff to be Journals Director. After our part-time public affairs staff person moved full-time to the Nutrition Society, it became clear that ASPET need a full-time public affairs staff person. On Tony Mazzaschi's recommendation, I interviewed Jim Bernstein and he became my second hire. Both Rich and Jim have been with ASPET almost as long as I have, and are valued colleagues and advisors. More recently, I was lucky to be able to hire as part of the senior staff Suzie Thompson (twice!) as Director of Marketing and Matthew Hilliker as Chief Financial Officer.

The past sixteen years have been a period of tremendous growth for ASPET, which is probably one reason why I have loved the job so much. No day was ever a repeat of the one before, and there was always something exciting just around the next bend. To my mind, the best decision Council ever made was to create and empower the Divisions. This happened at my first Council meeting after I joined ASPET, and one of my first tasks was to "make this happen." At times it has been like trying to raise 10 children with differing skills and interests (and attention spans!), but like a proud parent, I can say that they are mostly strong and independent and a vital part of ASPET.

I also came in just as concrete planning was to begin for the 2002 International Congress of Pharmacology for which ASPET had won the bid as host a decade earlier. Working with an international organization like IUPHAR was a challenge, but due to a close working relationship with Tom Burks, and then Sue Duckles, we brought it off. Unfortunately, due to the timing of the Congress only a few months after 9/11, attendance was not what we had hoped (or budgeted) for, and that was both an emotional and financial disappointment for those of us who had worked so hard to bring it to fruition. I also was lucky to be able to work closely with Bill Dewey on the planning and execution of the ASPET Centennial celebration. Fairly early in my tenure, Ken Harden, then chair of the Board of Publications Trustees, expressed an interest in a new journal tailored more for leisure reading than the existing ASPET quartet. Thus was born *Molecular Interventions* which was an exciting and fun adventure, but which, sadly, never made it to break even stage and publication was ceased 10 years later.

Christie and the centennial cake at the ASPET centennial celebration at EB 2008 in San Diego.

Sue Duckles (left), Christie, William Fleming (second from right), and Thomas Burks (right).

I would like to take this opportunity to thank the leaders of ASPET with whom I have worked over the years, and especially John Lazo who took on the Presidency having no idea that he would have to run a search committee. And I would especially like to thank the staff of ASPET (past and present) who have always made me look good.

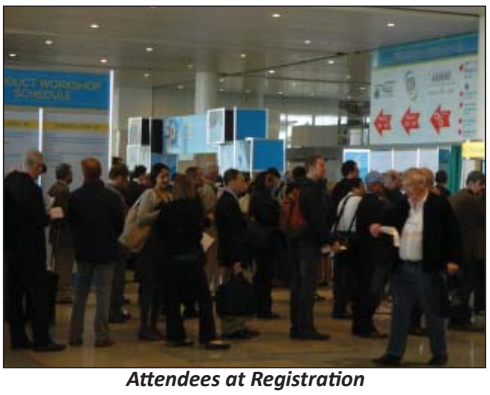
Christie K. Carrico

Experimental Biology 2013 in Review

On April 20 – 24, 2013, ASPET met jointly with the British Pharmacological Society as part of ***Experimental Biology*** in Boston, MA. Despite the heightened security situation in Boston earlier that week, EB 2013 had record attendance with over 14,500 conference attendees. The meeting had a stellar scientific program and provided a great mix of important symposia and fun networking events.

Boston Strong sign outside of the Convention Center

Boston Convention & Exhibition Center



Attendees at Registration

The ASPET Business Meeting took place on Saturday, April 20. President John Lazo delivered a welcome message and presented attendees with an update on the Society and the different initiatives and programs we are currently working on. There were also updates on public affairs activities, finances, publications, and other business. The members in attendance voted to pass a By-laws change in which we will no longer require a sponsor for new Regular, Affiliate, and Postdoctoral membership applications. Student membership applications will need sponsorship from either their mentor or department chair. This was passed and will now go out to the larger membership for final approval. It was also announced that ASPET has recently joined partnerships with the British Pharmacological Society and John Wiley & Sons, Ltd. to launch a new open access journal called P*harmacology Research & Perspectives*. President Lazo also presented our current Executive Officer, Christine Carrico, Ph.D. with some gifts in appreciation of her dedicated and invaluable service of over 16 years. Dr. Carrico will be retiring from ASPET later this summer. And last but not least, ASPET's awards were presented to this year's highly regarded winners.

Crowded attendance at the ASPET 2013 Business Meeting

President John Lazo delivers a report on ASPET's activities.

President John Lazo and incoming President Rick Neubig thank Christie Carrico for her services as ASPET's Executive Officer.

Incoming President Rick Neubig thanks President John Lazo for his services.

Recipients of ASPET's 2013 Awards

ASPET Graduate Student Travel Award Winners for 2013

ASPET Washington Fellows for 2013

ASPET Young Scientist Travel Award Winners for 2013

Summer Undergraduate Research Fellowship Award Winners for 2013

The PhRMA Foundation Award in Excellence in Pharmacology/Toxicology is presented to Dr. William Campbell.

PhRMA Foundation Postdoctoral Fellowship winners Drs. Byron Roberts (second from left), Taryn James (center), and Adam Walker (second from right)

PhRMA Foundation Predoctoral Fellowship winner Gilbert Kim

PhRMA Foundation Research Starter Grant winners Drs. Michy Kelly and Phillip Kopf

Following the ASPET Business Meeting, members kicked off the start of the 2013 Annual Meeting with an opening reception. The opening reception also served as the launch party for ASPET's newest journal, *Pharmacology Research & Perspectives*.







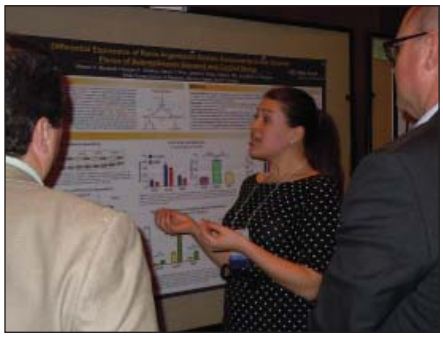
The exhibit hall was buzzing this year with lots of activity everywhere. The ASPET booth had many visitors from members and non-members alike. We sold lots of T-shirts, ASPET plush donkeys, and other items. We also signed up 46 new members! Also at the booth, we had Council Members and ASPET Journal Editors available for a "Meet & Greet" with members.

Exhibit Hall at EB 2013

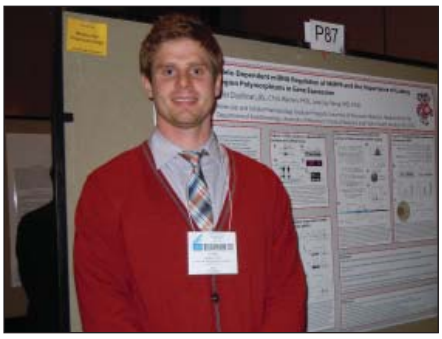
ASPET Booth in the Exhibit Hall

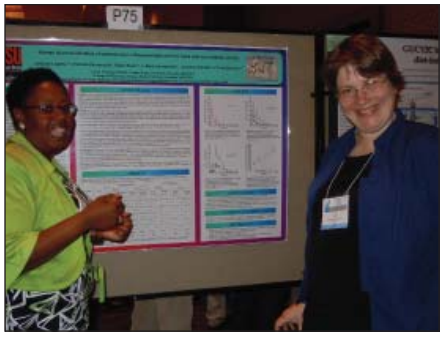
"Meet & Greet" with Past-President Lynn Wecker and Incoming President Rick Neubig

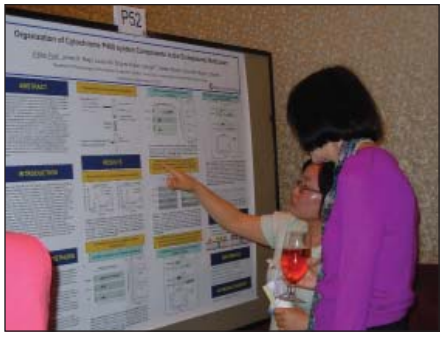
The Student/Postdoc Best Abstract Competition gave students and young scientists a chance to present their work and mingle with fellow ASPET members. Each of the ASPET divisions plus the British Pharmacological Society held their competitions simultaneously.

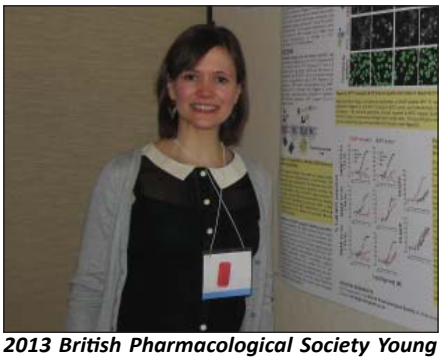









2013 Dolores C. Shockley Best Abstract Award winner Antentor Hinton, Jr., Baylor College of Medicine



2013 British Pharmacological Society Young Scientist Best Abstract Award winner Laura Kilpatrick, University of Nottingham

Following the poster competition, ASPET and BPS students and postdocs let their hair down at the Student/Postdoc Mixer. Young members enjoyed drinks, dessert, and some karaoke singing with the D.J.!



The WIP into Shape Networking Walk took place on Tuesday, April 23. ASPET members gathered for a walk around Boston.


After an exciting meeting, ASPET held a closing reception on Wednesday, April 24, where members ate, drank, and had their caricatures drawn.






EB
Experimental Biology

Save the Date!

Join us at the Joint Annual Meeting of ASPET and the Chinese Pharmacological Society at Experimental Biology 2014

San Diego, CA

April 26 - 30, 2014

aspet

CHINESE PHARMACOLOGICAL SOCIETY

Call for Award Nominations

John J. Abel Award

Deadline for submissions is September 15, 2013.

The John J. Abel Award in Pharmacology, named after the founder of ASPET and supported by Pfizer, was established to stimulate fundamental research in pharmacology and experimental therapeutics by young investigators. The annual Award, sponsored by Pfizer, Inc., consists of $5,000, a plaque, hotel and economy airfare for the winner and spouse to the award ceremony at the annual meeting of ASPET. The winner will be invited to give a lecture at the annual meeting.

Nominees for this award shall not have passed his/her **forty-fifth birthday by September 15 (nomination deadline) of the year in which s/he is nominated**. The candidate need not be a member of the Society; however, the nomination must be made by an ASPET member. No member may nominate more than one candidate a year and no candidate may be nominated for more than one major ASPET award in any given year.

The Award shall be made for original, outstanding research in the field of pharmacology and/or experimental therapeutics. Independence of thought, originality of approach, clarity and excellence of data presentation are important criteria. Candidates shall not be judged in comparison with the work of more mature and experienced investigators. Quality rather than the number of contributions shall be emphasized. It shall be the responsibility of the sponsor to make clear the contribution of the candidate to any jointly authored reprints and manuscripts and the originality and independence of the candidate's research. Selection will be made by the ASPET Awards Committee, appointed by the President of ASPET.

Nominations must be submitted electronically to **awards@aspet.org** and shall consist of:

1. Letter of nomination with a summary that describes the importance of the candidate's work.
2. Brief biographical sketch of the candidate.
3. Candidate's curriculum vitae and bibliography.
4. Six published articles or manuscripts accepted for publication that are a representation of the candidate's work (provided as PDFs or as hyperlinks to the article). **Submit each manuscript as a separate attachment.**

Nominations for this award must be received no later than 5:00 p.m. (EDT) on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the John J. Abel Award in Pharmacology

1947	George Sayers	1969	Ronald Kuntzman	1991	Terry D. Reisine
1948	J. Garrott Allen	1970	Solomon H. Snyder	1992	Frank J. Gonzalez
1949	Mark Nickerson	1971	Thomas R. Tephly	1993	Susan G. Amara
1950	George B. Koelle	1972	Pedro Cuatrecasas	1994	Brian Kobilka
1951	Walter F. Riker, Jr.	1973	Colin F. Chignell	1995	Thomas M. Michel
1952	David F. Marsh	1974	Philip Needleman	1996	John D. Scott
1953	Herbert L. Borison	1975	Alfred G. Gilman	1997	David J. Mangelsdorf
1954	Eva K. Killam	1976	Alan P. Poland	1998	Masashi Yanigasawa
1955	Theodore M. Brody	1977	Jerry R. Mitchell	1999	Donald P. McDonnell
1956	Fred W. Schueler	1978	Robert J. Lefkowitz	2000	William C. Sessa
1957	Dixon M. Woodbury	1979	Joseph T. Coyle	2002	Steven A. Kliewer
1958	H. George Mandel	1980	Salvatore J. Enna	2003	David S. Bredt
1959	Parkhurst A. Shore	1981	Sydney D. Nelson	2004	David P. Siderovski
1960	Jack L. Strominger	1982	Theodore A. Slotkin	2005	Randy Hall
1961	Don W. Esplin	1983	Richard J. Miller	2006	Christopher M. Counter
1962	John P. Long	1984	F. Peter Guengerich	2007	Michael D. Ehlers
1963	Steven E. Mayer	1985	P. Michael Conn	2008	Katarina Akassoglou
1964	James R. Fouts	1986	Gordon M. Ringold	2009	John J. Tesmer
1965	Eugene Braunwald	1987	Lee E. Limbird	2010	Russell DeBose-Boyd
1966	Lewis S. Schanker	1988	Robert R. Ruffolo, Jr.	2011	Laura M. Bohn
1967	Frank S. LaBella	1989	Kenneth P. Minneman	2012	Jin Zhang
1968	Richard J. Wurtman	1990	Alan R. Saltiel	2013	Arthur Christopoulos

Julius Axelrod Award in Pharmacology

Deadline for submissions is September 15, 2013.

The Julius Axelrod Award in Pharmacology was established to honor the memory of the eminent American pharmacologist who shaped the fields of neuroscience, drug metabolism and biochemistry and who served as a mentor for numerous eminent pharmacologists around the world. The Julius Axelrod Award is presented annually for significant contributions to understanding the biochemical mechanisms underlying the pharmacological actions of drugs and for contributions to mentoring other pharmacologists.

The award consists of an honorarium of $2,500, a medal, hotel, and economy airfare for the winner and spouse to the annual meeting. The formal presentation of this award and medal will be made at the annual meeting of ASPET. The recipient will be invited by the President of the Society to deliver the Julius Axelrod Lecture and organize the Julius Axelrod Symposium at the annual meeting a year hence. The recipient will also be invited by the Catecholamine Club to give a less formal presentation at its annual dinner meeting the year of the award.

There are no restrictions on nominees for this award. However, a nomination must be made by a member of the American Society for Pharmacology and Experimental Therapeutics (ASPET) or the Catecholamine Club. No member may nominate more than one candidate in a year and no candidate may be nominated for more than one major ASPET award in any given year. The award shall be made on the basis of originality and uniqueness of accomplishments throughout a long career distinguished by sustained, significant contributions to research and mentoring in pharmacology. Selection of the recipient will be made by the Axelrod Award Committee, appointed by the President of ASPET and comprised of members of ASPET and the Catecholamine Club.

Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Letter of nomination describing the research and mentoring contributions to pharmacology of the candidate that make him/her eligible for this Award, listing major contributions. Up to two additional letters of support would be welcome (need not be from ASPET members).
2. Brief biographical sketch of the candidate.
3. List of individuals mentored by the individual. Up to two letters from former trainees describing the quality of their training with the nominee and its impact on their careers would be welcome (need not be from ASPET members).
4. Candidate's curriculum vitae and bibliography.

Receipt date for nominations for the Julius Axelrod Award will be will be 5:00 p.m. (EDT) on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the Julius Axelrod Award

1991	Ullrich Trendelenberg
1992	Arvid Carlsson
1993	Norman Weiner
1994	Robert Furchgott
1995	Irvin Kopin
1998	Sidney Spector
1999	Solomon Snyder
2000	Erminio Costa
2001	Toshi Nagatsu
2002	Salomon Langer
2003	Richard Weinshilboum
2004	Richard Palmiter
2005	Marc Caron
2006	Susan Amara
Award taken over by ASPET	
2007	Tong H. Joh
2008	Randy D. Blakely
2009	Palmer W. Taylor
2010	Brian Kobilka
2011	Elaine Sanders-Bush
2012	Gavril W. Pasternak
2013	Lee E. Limbird

Pharmacia-ASPET Award for Experimental Therapeutics

Deadline for submissions is September 15, 2013.

The Pharmacia-ASPET Award in Experimental Therapeutics is given annually to recognize and stimulate outstanding research in pharmacology and experimental therapeutics—basic laboratory or clinical research that has had, or potentially will have, a major impact on the pharmacological treatment of disease. The award is supported in perpetuity by a gift from Pharmacia (now Pfizer).

The winner will receive a $2,500 honorarium, a plaque, hotel and economy airfare for the winner and spouse to the award ceremony at the ASPET annual meeting.

There are no restrictions on nominees for this award. The candidate need not be a member of the Society; however, the nomination must be made by an ASPET member. No member may nominate more than one candidate a year and no candidate may be nominated for more than one major ASPET award in any given year. The Award shall be made on the basis of published reprints, manuscripts ready for publication, and a two-page summary. Selection will be made by the ASPET Awards Committee, appointed by the President of ASPET.

Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Letter of nomination with a two-page summary that details the importance of the candidate's work.
2. Brief biographical sketch of the candidate.
3. Candidate's curriculum vitae and bibliography.
4. Six articles published or ready for publication by the candidate that have direct bearing on the Award (provided as PDFs or as hyperlinks to the article). **Submit each manuscript PDF as a separate attachment.**

Nominations for this award must be received no later than 5:00 p.m. (EDT) on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the ASPET Award for Experimental Therapeutics

1969	John A. Oates
1970	Joseph R. Bertino
1971	Elliot S. Vesell
1972	Francois M. Abboud
1973	Dean T. Mason
1974	Leon I. Goldberg
1975	Mackenzie Walser
1976	Louis Lasagna
1977	Allan H. Conney
1978	Attallah Kappas
1979	Sydney Spector
1980	Sanford M. Rosenthal
1981	David G. Shand
1982	William H. Prusoff
1983	Marcus M. Reidenberg
1984	Sir James Black
1985	Louis Lemberger
1986	Alan C. Sartorelli
1987	Albrecht Fleckenstein
1988	Jean-Francois Borel
1989	Benedict R. Lucchesi
1990	Albert Sjoerdsma
1991	Theophile Godfraind
1992	James W. Fisher
1993	V. Craig Jordan
1994	Susan Band Horwitz
1995	Henry I. Yamamura
1996	Robert F. Furchgott
1997	Michael M. Gottesman
1998	Phil Skolnick
1999	Yung-Chi Cheng
2000	Salomon Z. Langer
2001	George Breese
	Became Pharmacia-ASPET Award in Experimental Therapeutics
2002	Darryle D. Schoepp
2003	William C. De Groat
2004	Philip Needleman
2005	Donald P. McDonnell
2006	John C. Lee
2007	P. Jeffrey Conn
2008	Jerry J. Buccafusco
2009	Kenneth A. Jacobson
2010	Garret A. FitzGerald
2011	Jan Balzarini
2012	Angela H. Brodie
2013	Richard R. Neubig

Robert R. Ruffolo Career Achievement Award in Pharmacology

Deadline for submissions is September 15, 2013.

The Robert R. Ruffolo Career Achievement Award in Pharmacology has been established in recognition of the contributions made to drug discovery and development by Dr. Ruffolo.

The award consists of a $2,500 honorarium, a commemorative medal, complimentary registration to the annual meeting, hotel, and economy airfare for the winner and his/her spouse to the award ceremony at the annual meeting.

There are no restrictions on nominees for this award. However, the nomination must be made by a member of the American Society for Pharmacology and Experimental Therapeutics (ASPET). No member may nominate more than one candidate in a year and no candidate may be nominated for more than one major ASPET award in any given year.

The Award is presented annually to recognize the scientific achievements of scientists who are at the height of their careers (typically mid- to late-career) and who have made significant contributions to any area of pharmacology. The award shall be made on the basis of the originality and impact of the nominee's accomplishments in pharmacology. Selection of the recipient will be made by the ASPET Awards Committee, appointed by the President of ASPET.

Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Letter of nomination with a summary that describes the importance of the candidate's work and his/her seminal discovery.
2. Brief biographical sketch of the candidate.
3. Candidate's curriculum vitae and bibliography.
4. Six published articles or manuscripts accepted for publication that are a representation of the candidate's work (provided as PDFs or as hyperlinks to the article), including early seminal discoveries. **Submit each manuscript PDF as a separate attachment.**

Receipt date for nominations for the Robert Ruffolo Award will be 5:00 p.m. (EDT) on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipient of the Robert R. Ruffolo Career Achievement Award

2012 Robert J. Lefkowitz

2013 Pancras C. Wong

Bernard B. Brodie Award in Drug Metabolism

Division for Drug Metabolism

Deadline for submissions is September 15, 2013.

The B. B. Brodie Award in Drug Metabolism has been established to honor the fundamental contributions of Bernard B. Brodie in the field of drug metabolism and disposition. The Award is presented biennially in even years to recognize outstanding original research contributions in drug metabolism and disposition, particularly those having a major impact on future research in the field. The B. B. Brodie Award is sponsored by the Division for Drug Metabolism, and funds to support the award come from members' contributions.

The award consists of a $2,000 honorarium, a commemorative medal, hotel, and economy airfare to the award ceremony at the annual meeting. A lecture, delivered by the awardee at the annual meeting, describing appropriate research accomplishments and their future direction, will be published in *Drug Metabolism and Disposition*.

There are no restrictions on institutional affiliation, and a candidate need not be a member of the Society. The only restriction for the Award is that supporting research accomplishments must not be used to win any other major award. Only one nominator is necessary, although more are acceptable, and the nominators need not be members of ASPET. Selection of an awardee will be made biennially by the B.B. Brodie Award Committee, appointed by the President of ASPET with input from the Division for Drug Metabolism.

Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Nominating letter and no more than five supporting letters detailing accomplishments of the nominee.
2. List of, and comments on, the outstanding papers.
3. Brief biographical sketch of the candidate.
4. Candidate's curriculum vitae and bibliography.

Receipt date for nominations for the Bernard B. Brodie Award will be 5:00 p.m. on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the Bernard B. Brodie Award in Drug Metabolism

1978	James R. Gillette
1980	Minor J. Coon
1982	Donald M. Jerina
1984	Gilbert J. Mannering
1986	Daniel W. Nebert
1988	Wayne M. Levin
1990	Daniel M. Ziegler
1992	F. Peter Guengerich
1994	Paul R. Ortiz de Montellano
1996	Anthony Y.H. Lu
1997	Ronald W. Estabrook
1999	Marion W. Anders
2000	Bettie Sue Masters
2002	Eric F. Johnson
2004	Thomas L. Poulos
2006	Frank J. Gonzalez
2008	Curtis D. Klaassen
2010	James Halpert
2012	Yuichi Sugiyama

P.B. Dews Lifetime Achievement Award for Research in Behavioral Pharmacology

Division for Behavioral Pharmacology

Deadline for submissions is September 15, 2013.

ASPET's Division of Behavioral Pharmacology sponsors the P. B. Dews Award for Research in Behavioral Pharmacology to recognize outstanding lifetime achievements in research, teaching and professional service in the field of Behavioral Pharmacology and to honor Peter Dews for his seminal contributions to the development of behavioral pharmacology as a discipline. The biennial award is supported by an endowment made possible by contributions from Aventis, Centre de Recherche Pierre Fabre, Eli Lilly, Harvard University, International Life Sciences Institute Caffeine Committee, Merck (San Diego), Pepsi Cola Company, Pfizer Central Research and Pfizer Global Research and Development, Pharmacia, Wyeth Research, and ASPET members.

The Award consists of $1,000, a plaque, and partial travel expenses to the award ceremony at the ASPET Annual Meeting. The recipient will be invited by the Chair of the Division of Behavioral Pharmacology to deliver a special lecture on this occasion. The lecture will be published subsequently in an appropriate ASPET-sponsored publication.

There are no restrictions on nominees for this award. Nominations may be made by members of ASPET or of any relevant scientific society. Selection will be made by the P.B. Dews Award Committee, appointed by the President of ASPET with input from the Division for Behavioral Pharmacology.

Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Description of the candidate's major contributions, including scientific, teaching and professional achievements.
2. Candidate's curriculum vitae and bibliography.
3. List of the candidate's trainees.
4. Five major publications (provided as PDFs or as hyperlinks to the article). **Submit each manuscript PDF as a separate attachment.**
5. Brief biographical sketch of the candidate.

Receipt date for nominations for the P. B. Dews Award will be 5:00 p.m. on **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the P.B. Dews Lifetime Achievement Award for Research in Behavioral Pharmacology

2002	William H. Morse	2006	Leonard Cook	2010	Donald E. McMillan
2004	Joseph V. Brady	2008	Charles R. Schuster	2012	James E. Barrett

Goodman and Gilman Award in Receptor Pharmacology

Deadline for submissions is September 15, 2013.

The Louis S. Goodman and Alfred Gilman Award in Drug Receptor Pharmacology, contributed by GlaxoSmithKline, was established to recognize and stimulate outstanding research in pharmacology of biological receptors. Such research might provide a better understanding of the mechanisms of biological processes and potentially provide the basis for the discovery of drugs useful in the treatment of diseases.

The award is presented biennially in even years and consists of an honorarium of $2,500, a plaque, hotel, and economy airfare for the winner and spouse to the award ceremony at the ASPET annual meeting.

There are no restrictions on the nominees for this award; however, nominations must be made by a member of ASPET. No member may nominate more than one candidate a year, and no candidate may be nominated for more than one major ASPET award in any given year. The award is to be made on the basis of the research contributions described in published work or submitted manuscripts and a summary of those contributions described in the letter of the individual who nominates the candidate. Selection will be made by the ASPET Awards Committee, appointed by the President of ASPET.

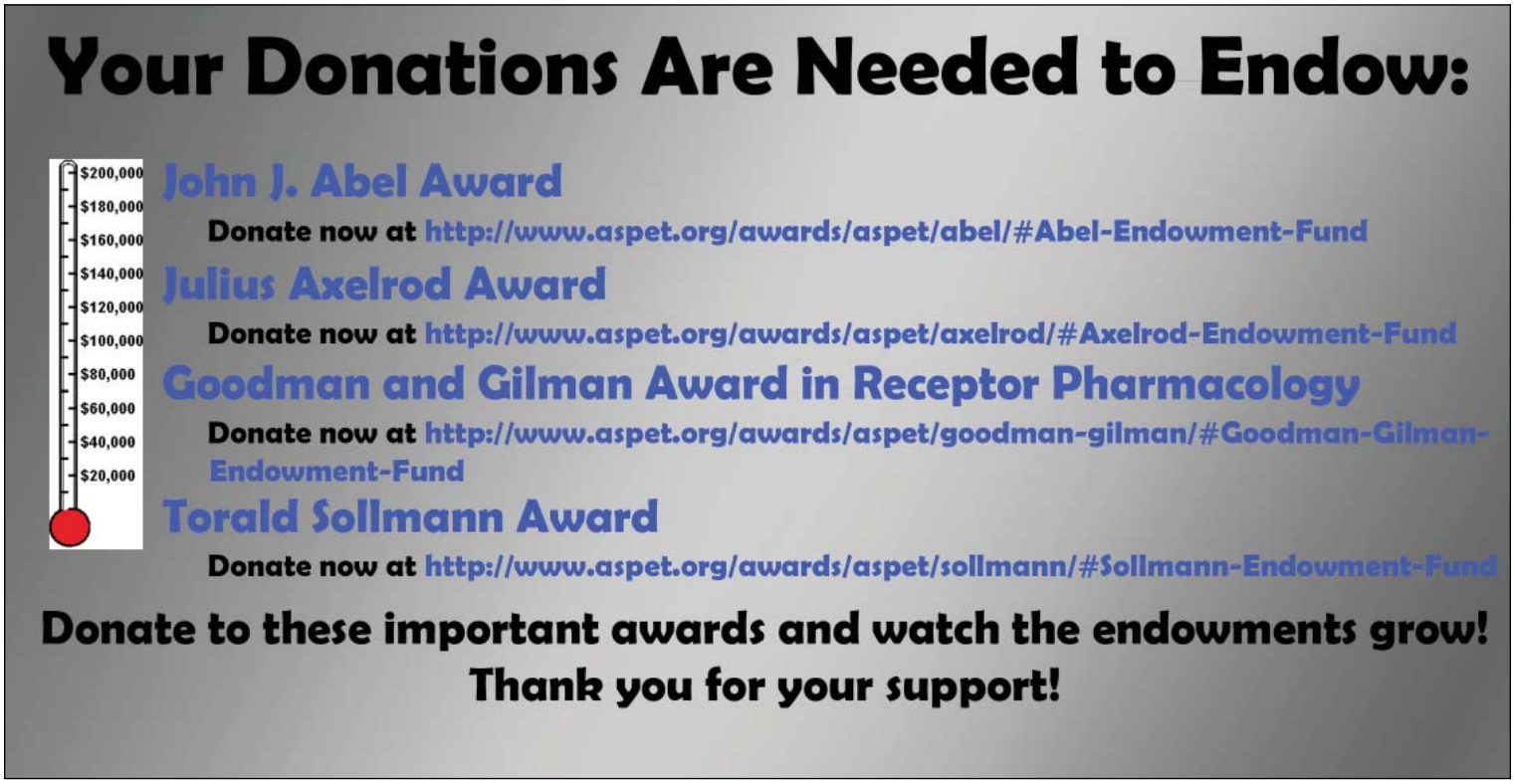
Nominations shall be submitted **electronically** to **awards@aspet.org** and shall consist of:

1. Summary that details the importance of the candidate's work.
2. Six articles published or ready for publication that have direct bearing on the award. (provided as PDFs or as hyperlinks to the article). **Submit each manuscript PDF as a separate attachment.**
3. Brief biographical sketch of the candidate.
4. Candidate's curriculum vitae and bibliography.

Receipt date for nominations for the Goodman and Gilman Award in Receptor Pharmacology will be **September 15, 2013** for an award to be presented at Experimental Biology 2014 in San Diego, CA.

Recipients of the Goodman and Gilman Award in Receptor Pharmacology

1980	Solomon H. Snyder	1990	Alfred G. Gilman	2000	Melanie Cobb	2010	Alan R. Saltiel
1982	Pedro Cuatrecasas	1992	Paul Greengard	2002	William B. Pratt	2012	V. Craig Jordan
1984	Robert F. Furchgott	1994	Jean-Pierre Changeux	2004	Lee E. Limbird		
1986	Robert J. Lefkowitz	1996	Elliott M. Ross	2006	Anthony R. Means		
1988	Ronald M. Evans	1998	David Garbers	2008	Craig C. Malbon		



Paul M. Vanhoutte Distinguished Lectureship in Vascular Pharmacology

Division for Cardiovascular Pharmacology

Deadline for submissions is September 15, 2013.

The Paul M. Vanhoutte Award in Vascular Pharmacology was established to honor Dr. Vanhoutte's lifelong scientific contributions to our better understanding and appreciation of the importance of endothelial cells and vascular smooth muscle function in health and disease and for his mentoring of countless prominent endothelial and vascular biologists and pharmacologists.

The Paul M. Vanhoutte Award is a biennial award, consisting an honorarium of $1,000, a custom-designed crystal bowl depicting the named Lectureship, and up to $2,000 travel expenses including registration to the annual spring ASPET meeting. A recipient will be selected and invited to deliver a state-of-the-art lecture on recent advances in vascular biology and pharmacology at the spring ASPET meeting (Division's programming session). The presentation of his/her research should be of broad interest and contribute to the growth of the Cardiovascular Pharmacology Division.

There are no restrictions on institutional affiliation, nationality, or age of the candidate but the recipient must be an active member of the ASPET before receiving the award nomination. Nominations must be made by a member of the ASPET, and no member may nominate more than one candidate per year. Final selection of the recipient will be made by the Award Committee of the Division for Cardiovascular Pharmacology.

Nominations should consist of not more than five letters from nominators describing the contributions to vascular biology and pharmacology of the candidate that make him/her eligible for this Award and listing of his/her major contributions, together with a complete curriculum vitae. To ensure consideration, all information must be submitted electronically to: **awards@aspet.org** no later than **September 15, 2013**.

Recipients of the Paul M. Vanhoutte Distinguished Lectureship in Vascular Pharmacology

2008	Donald D. Heistad	2010	William B. Campbell	2012	Richard A. Cohen

FEATURE ARTICLE

Hitchings and Elion: Perfect Together

by Stanley Scheindlin, D.Sc.

Figure 1. ***Dr. George Hitchings and Gertrude Elion*** *(Courtesy of the Federation of American Societies for Experimental Biology)*

The year 2013 marks 25 years since Gertrude Belle Elion (1918 - 1999) and George Herbert Hitchings (1905 - 1998), along with Sir James Black of the U.K., shared the 1988 Nobel Prize in Physiology or Medicine. On this silver anniversary, this article celebrates the achievements of these two gifted scientists, and recalls some interesting aspects of their life stories.

Some may have felt it strange that the prize was awarded to these individuals. To begin with, Hitchings and Elion were employees of a pharmaceutical firm — a class of people rarely recognized by the Nobel Committee, which tends to favor academic researchers. Also, awardees who share a prize generally have worked in laboratories distant from each other; whereas these two were members of the same team, working for the same firm. In addition, Gertrude Elion did not possess a doctorate degree; her graduate education having stopped at the Master's level. Finally, her relationship with Hitchings had begun as employee/supervisor, though it now was a relationship of colleagues.

Background and Early Life

The family backgrounds of Hitchings and Elion could hardly have been more different. On his mother's side, Hitchings' ancestors came from Scotland, arriving in the Colonies about 1735. His father's forebears migrated from London and North Ireland to New Hampshire. As loyalists to the Crown, they moved to Canada during the Revolution. Hitchings' grandfather Andrew, returned to the U.S. in 1869, moving his family to Eureka, CA. Located in northern California, amid extensive stands of the world's tallest trees, Eureka played a leading role in the lumber trade as well as the building of wooden ships. Hitchings' grandfather and father were skilled craftsmen in shipbuilding, his father becoming a marine architect and master builder. His maternal grandfather, also a shipbuilder, moved his family from Maine in 1875, settling in Eureka. George was born in Hoquiam, Washington, where his mother's father, Peter Matthews, had established a shipyard. Upon Matthews' death, the senior Hitchings took over the business.

By contrast, Elion's parents both stemmed from rabbinic Jewish families in the eastern European areas which were part of Russia before the Great War. Their stories were typical of many Jewish immigrants of that time. Her father, Robert Elion, came to the U.S. at age 12, and put himself through dental school by working nights in a drug store. Her mother sailed to this country alone at the age of 14, joining her older sisters in New York. She worked in a needle-trade shop before marrying. Robert Elion was, for a time, a successful entrepreneur and was able to move his family out of the Lower East Side to the more spacious and airy Bronx. However, the stock market crash of October 1929 left him bankrupt, and he spent much of the rest of his life working to repay his creditors.

Having attended the New York public schools, Gertrude was naturally exposed to ethnic diversity in her classes. George, due to numerous family relocations, attended grade school in Berkeley and San Diego, CA, and in Bellingham and Seattle, WA. He noted the significance of his attendance at Franklin High School in Seattle. The school's heterogeneous student body included upper class kids and minorities: blacks, Filipinos, Japanese, and Chinese. Here, he became comfortable in dealing with people from different cultural backgrounds, which may have explained his readiness to hire diverse people for his future research team.

Despite their different backgrounds, both Hitchings and Elion were drawn to careers in medical research by similar traumatic events in their youth. George Hitchings' father, George Herbert, Sr., died after a prolonged illness when George was but twelve years old. The impression made by his father's suffering and early death led Hitchings to enter college as a premedical student. But the enthusiasm of the chemistry department faculty and students proved infectious, and by the end of his freshman year, he became a chemistry major.

In Elion's case, it was her *zayde* (grandpop). In 1921, when Gertrude was three years old, her grandfather came over from Russia. Learned in Talmudic studies, he was a watchmaker by trade, but now his eyesight was poor and he could no longer work. He would take his little red-haired Trudy to the park and tell her stories. For 13 years they enjoyed a loving relationship, but then her *zayde* died, slowly and painfully, from stomach cancer. It was then that Gertrude decided that fighting cancer was her calling.

Hitchings did his Ph.D. work under a fellowship grant in biological chemistry at Harvard Medical School. His dissertation was on the development of analytic methods for the purine bases.

Elion, because of her father's bankruptcy, attended Hunter College, a tuition free institution supported by New York City. She chose to major in chemistry rather than biology to avoid having to dissect animals. Although graduating Phi Beta Kappa, with highest honors in 1937, she could get no fellowship or assistantship at any of the 15 graduate schools where she applied.

For the next seven years, she worked at various marginal and temporary jobs, such as being a substitute school teacher and testing food products for a grocery chain. One prospective employer told her "You're qualified, but we've never had a woman in the lab before, and we think you'd be a distracting influence." During these years, she saved enough money for one year's graduate school at NYU, obtaining her Master of Science degree in 1941.

Hitchings earned his doctorate in 1933 in the midst of the Great Depression. That year was sweetened for him by his marriage to Beverly Reimer. Like Elion, Hitchings went through a period of impermanence. But his temporary jobs were at Harvard's C.P. Huntington Labs in cancer research, Harvard School of Public Health in nutrition research, and Western Reserve Dept. of Medicine in electrolyte research.

The lives of Hitchings and Elion intersected at the Wellcome Research Laboratories in Tuckahoe, NY, the research arm of Burroughs Wellcome & Co. *(1) – (3)*.

History of Burroughs Wellcome

Burroughs Wellcome (B-W) was a unique pharmaceutical company. Established in London in 1880, its founders were two American pharmacists, Silas M. Burroughs and Henry S. Wellcome. Burroughs was Wyeth's agent in Britain. He noticed that while U.S. drug manufacturers were adopting the new technology of producing compressed tablets, in England most medicines were still being compounded by mortar and pestle. Realizing that there was money to be made by importing compressed tablets and marketing them in England, and Europe, he invited his friend Wellcome to join him as a partner. The new firm proved successful and profitable from the start.

Following the death of its founders, ownership of B-W passed to the Wellcome Foundation, Ltd., a charitable trust which they had established. All profits were used to support medical research in universities and teaching hospitals around the world. Not until 1992 did the Foundation's trustees make B-W a public corporation, and in 1995, it merged with Glaxo to form Glaxo Wellcome. In the early 1940s, the company's U.S. laboratory was housed in a converted rubber factory in Tuckahoe, about eight miles north of New York City *(4)*.

Hitchings and Elion at B-W

Wellcome Research Laboratories hired Hitchings in 1942 as the head and sole member of the biochemistry department. His budget was small, but he was given full freedom to develop his own program of research.

Elion had never even heard of Burroughs Wellcome until one day in 1944 her father, the dentist, received a sample of analgesic tablets (probably Empirin compound) from them. She got on the telephone and asked whether they had any research openings. The following Saturday, she traveled to Tuckahoe, was interviewed by Dr. Hitchings, and was hired at $50 per week. She was then 26 years of age.

Hitchings was impressed by Elion's capabilities. He found her an intelligent, hard-working, and ambitious young woman. He was generous in showing his appreciation, encouraging her to write scientific papers and to publish her findings once patent applications had been filed. In time, he made her his first assistant, and as Hitchings was promoted within the company, Elion stepped up to the position he had left. Ultimately, she became head of the Department of Experimental Therapy. In this capacity she elucidated the mode of action of acyclovir, work which she later described in her Nobel address *(1)*.

Early Discoveries: Anti-infectives

In the 1940s, the sulfonamides, the first anti-infective "wonder drugs," were very new; yet, as early as 1940, it had been noted that sulfanilamide was inactivated in the presence of pus, tissue, or yeast extract. Donald Woods at Oxford showed that *p*-aminobenzoic acid (PABA), present in all the above, strongly antagonized sulfanilamide. He proposed that the sulfonamide acted as an antimetabolite of PABA because of the structural similarity of the two compounds.

George Hitchings saw possibilities in the antimetabolite hypothesis. His thesis having been on the purine bases found in the nucleic acids, he was aware that the rate of nucleic acid synthesis in bacteria, viruses, or neoplasms was more rapid than that of the surrounding host tissues. He therefore initiated a program of synthesizing derivatives of purine and pyrimidine bases as potential antagonists *(5)(6)*.

Sneader, the historian of drug development, calls Hitchings' approach "somewhat inspired," as Watson and Crick's elucidation of the role of DNA was still a decade in the future. A typical biochemistry textbook of 1943 *(7)* recognizes that nucleoproteins, composed of protein and nucleic acid, are essential constituents of both animal and plant cell nuclei. The sugar components ribose and deoxyribose, as well as the purine and pyrimidine components, had all been characterized. However, there is no mention of DNA or RNA and no hint of their importance.

Hitchings, with Gertrude Elion, Elvira Falco, Peter Russell, and M.B. Sherwood, prepared numerous potential antimetabolites of the purine and pyrimidine components of nucleic acid. This work would bear fruit several years later.

One of the major scientific events of the 1940s was the isolation of a new vitamin, folic acid, and the discovery that some of the vitamin's analogs acted as antifolates. A compound's antifolic action could be demonstrated by its inhibition of the bacterium *Lactobacillus casei*. The mode of action was shown to be inhibition of dihydrofolate reductase (DHFR), the enzyme which enables folic acid to be utilized in the

formation of thymine, which is then incorporated into DNA. Another key finding was that the degree of DHFR inhibition by antimetabolites varied with the species from which the enzyme was derived.

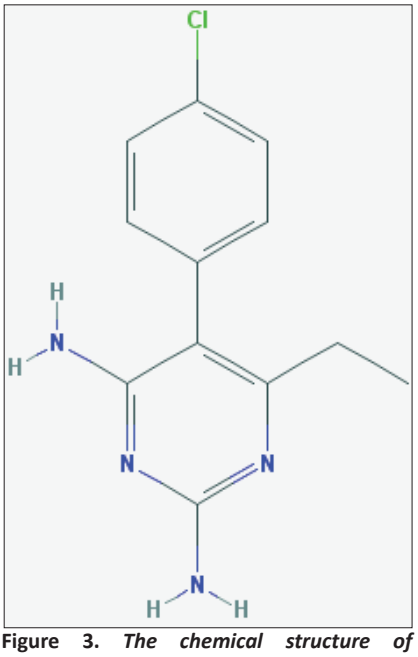


Figure 3. ***The chemical structure of pyrimethamine.*** *(Courtesy of the National Library of Medicine)*

In 1948, Hitchings and colleagues showed that many 2,4-diaminopyrimidines were folate antagonists and inhibited the growth of *L. casei*. Substituted benzyl derivatives of 2,4-diaminopyrimidines exhibited species variation against DHFR. A compound, later named trimethoprim, was 50,000 times as potent against bacterial DHFR as against the human enzyme. For therapeutic use, trimethoprim was combined with a long-acting sulfonamide, sulfamethoxazole. The combination product, known as Co-trimoxazole, was marketed by B-W and remains a much-prescribed anti-infective to this day.

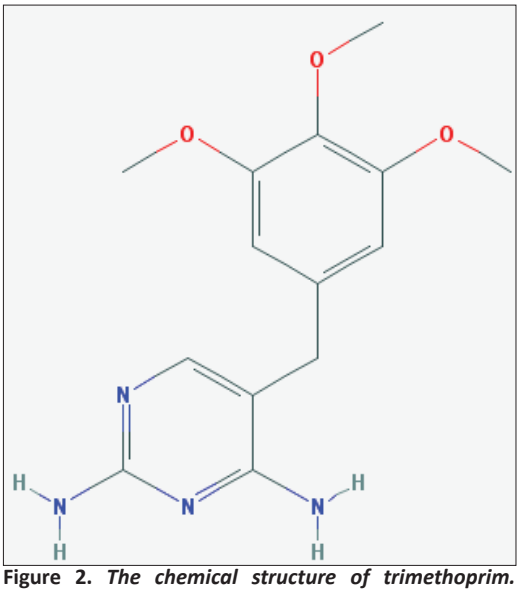


Figure 2. ***The chemical structure of trimethoprim.*** *(Courtesy of the National Library of Medicine)*

The antifolate research at B-W also led to the discovery of an antimalarial drug, pyrimethamine (DaraprimR). In 1949, Hitchings and his assistants picked up on a structural similarity between one of their antifolate compounds and the antimalarial proguanil. Finding that this compound showed antimalarial activity, they synthesized a large number of derivatives. In 1951, they produced pyrimethamine. After evaluation at the Wellcome Laboratories of Tropical Medicine in London, Daraprim was introduced for both chemoprophylaxis and treatment of malaria, as well as treatment of the protozoal disease toxoplasmosis *(5)(6)*.

Discovery of 6-Mercaptopurine

In 1948, Hitchings began to divide the responsibilities in his department. In view of the expertise she had developed in purine metabolism, Elion was assigned to purines.

At this time, the only promising drugs against the dread acute myeloid leukemia (AML) in children were the folate antagonists aminopterin and the less toxic methotrexate which superceded it. Patients were kept alive eight to nine months on average, and one in 100 might be cured. More potent cytotoxics were sought among the inhibitors of the growth of *L. casei*. One of Hitchings' purine antimetabolites, 2,6-diaminopurine, was evaluated in vitro and clinically, but proved inferior to aminopterin and methotrexate. However, in 1952, Elion took a look at 6-mercaptopurine (6-MP), which she had made in 1951 merely as an intermediate for further synthesis. Its action against *L. casei* was outstanding. In its clinical trial at Memorial Hospital it was found to be the safest and most effective antileukemic discovered up to that time. The average remission induced by 6-MP lasted about one year *(5)*.

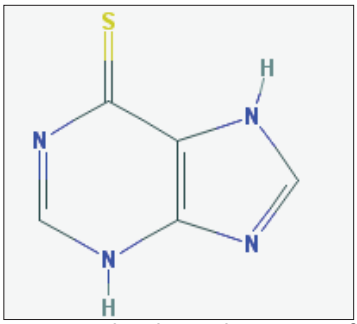


Figure 4. ***The chemical structure of 6-mercaptopurine (6-MP).*** *(Courtesy of the National Library of Medicine)*

Combined therapy with 6-MP and cortisone produced more and longer-lasting remissions than either drug singly. By the late 1950s, the mean survival rate for children with AML was more than one-and-a-half years; for those untreated it was less than three months.

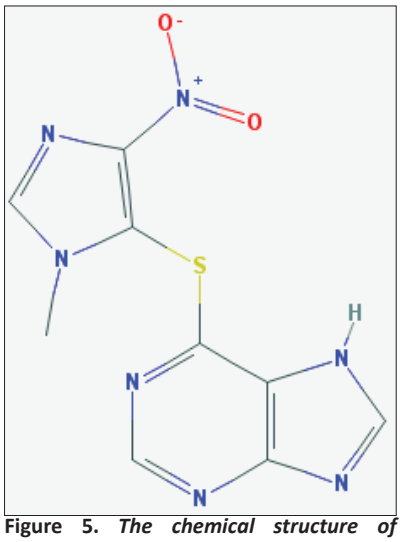


Figure 5. ***The chemical structure of azathioprine.*** *(Courtesy of the National Library of Medicine)*

In a 1986 publication, Elion summarized the then 30-year history of 6-MP. In this article, she made a point of the rapidity with which the compound went from its first synthesis to becoming an accepted antileukemic drug for human patients. Elion synthesized 6-MP in 1951, and by late 1953 it was approved. While she remarks on this, she makes no attempt to explain it.

Certainly the rapid development process was largely owing to the zeal of the scientists involved — Elion herself, the people at Sloan-Kettering who performed animal testing, Fred Philips who conducted short-term toxicology tests in several species, and Burchenal who tested 6-MP in sick children. But it was also due to the fact that 6-MP was developed in the 1950s when only safety testing was required for FDA approval of a new compound. After the thalidomide disaster of 1962 *(9)* and passage of the Drug Amendments of 1962, effectiveness had to be demonstrated, and more rigorous safety testing was required as well, all extending the development time for a new drug.

Azathioprine, Allopurinol, and Acyclovir

One disadvantage of 6-MP was its partial oxidation by the enzyme xanthine oxidase. Efforts at B-W to circumvent this led to the synthesis of a prodrug azathioprine (Imuran R.). This compound produced the desired sustained release of 6-MP but was a failure in the clinic.

Meanwhile, Medawar in London and Dameshek and Schwartz at Tufts in Boston were seeking drugs to suppress the immune response, theorizing that such would make it possible to do bone marrow transplantation in patients with leukemia, aplastic anemia, or radiation damage. 6-MP showed some promise as an immune system suppressant in rabbits and dogs.

Following up on these developments, Hitchings set up a screening program from which, in 1961, azathioprine emerged as the most effective compound. It soon became a useful immunosuppressant in transplant surgery. Its primacy was reduced after 1978, when the antifungal antibiotic Cyclosporin A came into use for this purpose.

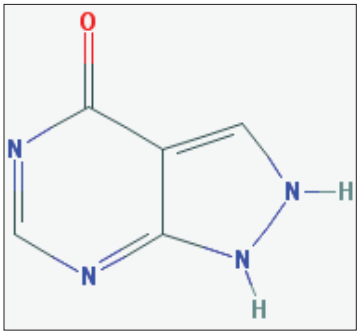


Figure 6. ***The chemical structure of allopurinol.*** *(Courtesy of the National Library of Medicine)*

Of the several hundred 6-MP analogues prepared at Tuckahoe in the search for a superior antileukemic, two dozen were effective in mice but none were as effective in humans as 6-MP. A new strategy was then adopted: to find an inhibitor of xanthine oxidase to be used in conjunction with 6-MP. Among the many purine analogues already synthesized at B-W, several pyrazolopyrimidines had been found back in 1957 to be xanthine oxidase inhibitors. Hitchings and Elion selected 4-hydroxy pyrazolopyrimidine for further study. This compound had no cytotoxic activity but inhibited xanthine oxidase *in vitro* and *in vivo*. In patients, it was very safe and permitted the dosage of 6-MP to be reduced, but the dose reduction did not confer any therapeutic advantage.

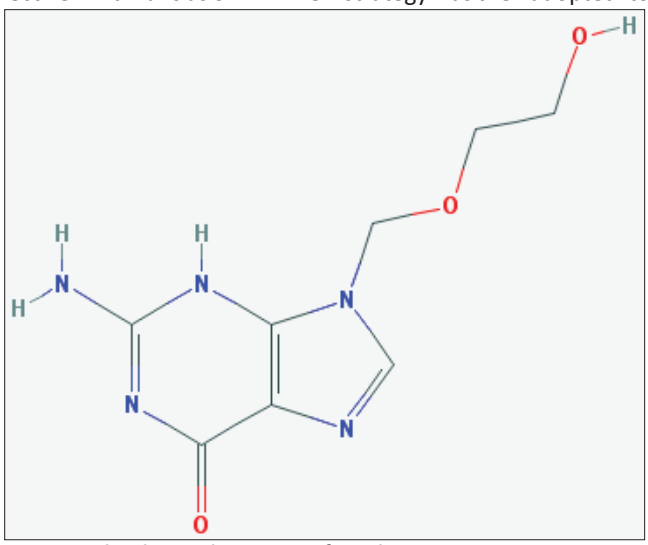


Figure 7. ***The chemical structure of acyclovir.*** *(Courtesy of the National Library of Medicine)*

However, by inhibiting xanthine oxidase, this compound reduced the amount of uric acid in the blood. This was found helpful clinically for patients with gout. It was marketed by B-W for this purpose in 1966 under the name Zyloprim R (allopurinol). Remarkably, allopurinol was the first new gout therapy since the alkaloid colchicine (from the meadow saffron plant) was first recommended by a Byzantine physician in the sixth century.

In 1975, Elion and her colleagues reported that the arabinosides of guanine and 2,6-diaminopurne were active against DNA viruses. The Wellcome team having previously found that the intact sugar ring was not essential for binding to enzymes, a search for antivirals was conducted among acyclic analogues. In 1977, acyclovir (Zovirax R) was reported to have excellent activity against the herpes virus. Acyclovir is now used topically to treat cold sores, orally for palliation of genital herpes, and for infections in immuno-compromised patients *(5)(6)*.

Careers in Retirement

In 1968, when B-W outgrew its Tuckahoe facilities, Hitchings oversaw the relocation to the Research Triangle area of North Carolina and established good relationships with the three universities there.

He retired as Vice President and became Scientist Emeritus in 1976. Among other activities this gave him time to care for his wife Beverly, who suffered from collagen disease which required a constant routine of medication. Despite this handicap, George and Beverly traveled nearly 400,000 miles, for pleasure and on lecture tours before her death in December 1985.

Philanthropy was Hitchings' other major focus. He became Director, then President, of the nonprofit B-W Fund, which supports biomedical research. In 1983, he founded what is now called the Greater Triangle Community Foundation to serve the needs of the Triangle area. He also was active in volunteer civic activities such as United Way, American Red Cross, Foundation for Better Health of Durham, and the Royal Society of Medicine Foundation, a British provider of continuing medical education.

In his Nobel biography, Hitchings states that, at his baptism, his father held him up and dedicated his life to the service of mankind. He felt proud that, to some extent, he had fulfilled his father's hopes *(1)*.

In contrast to Hitchings' happy family life with Beverly and their daughter and son, Gertrude Elion never married. Before she joined B-W, she was engaged to a gifted young man who was struck down by bacterial endocarditis before penicillin became available. For a time, every young man she met did not measure up to her lost lover. Then, as her work absorbed her more and more, the idea of marriage faded. Her social life centered around Dr. Hitchings' family, her other colleagues, her brother Herbert, and especially her nieces and nephews.

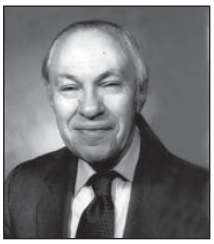
At the Nobel ceremonies in Stockholm, she was accompanied by her nieces and nephews along with their spouses and children, four of whom were under the age of five. She insisted that the children be allowed to attend the formal banquet, telling the official in charge, "Put them at a separate table where they can see their parents and their parents can see them, and they'll be fine." The children lived up to her expectation, charming the press and hotel staff alike *(3)*.

Elion retired in 1983, staying on as Scientist Emeritus and Consultant. Retirement gave her more time to indulge her desire to travel and her love of music, especially opera. Winning the Nobel Prize brought her many additional honors, including an honorary doctorate and the National Medal of Science, presented to her in 1991 by President George H.W. Bush. Despite these honors, her most cherished memorabilia were letters she received from grateful patients and from parents of children whose lives had been saved by the medicines she discovered. She was quoted as saying "What greater joy can you have than to know what an impact your work has had on peoples' lives?" In this, she echoes the feeling expressed above by Hitchings.

Elion and Hitchings' achievement was twofold. They discovered new drug therapies for malaria, leukemia, organ transplantation, herpes, gout, and bacterial infection. They were also pioneers in rational drug design. Both scientifically and in their human values they were indeed "perfect together."

References

1. George H. Hitchings-Autobiography. Nobelprize.org Accessed 15 Nov 2012.
2. Gertrude B. Elion-Autobiography. Nobelprize.org. Accessed 28 Nov 2012.
3. McGrayne, S.B. *Nobel Prize Women in Science: Their Lives, Struggles, and Momentous Discoveries, 2nd ed*. 1993. The National Academies Press, Washington, DC.
4. Bailey, P. The birth and growth of Burroughs Wellcome & Co. http://www.wellcome.ac.uk/About-us/History/WTX051562.htm
5. Sneader, W. *Drug discovery: the evolution of modern medicines*. Chichester, UK: John Wiley & Sons, 1985.
6. Sneader, W. *Drug discovery a history*. Chichester, UK: John Wiley & Sons, Ltd., 2005.
7. Harrow, B. *Textbook of Biochemistry, 3d ed*. Philadelphia: W.B. Saunders Co., 1943.
8. Elion, G.B. Historical background of 6-mercaptopurine. *Tox. Ind. Health* **2:**1-9, 1986.
9. Scheindlin, S. The courage of one's convictions: The due diligence of Frsnces Oldham Kelsey at the FDA. *Mol. Interv.* **11:**3-9, 2011.



Stanley Scheindlin, D.Sc., held a B.S. in pharmacy from Temple University and graduate degrees in pharmaceutical chemistry from Philadelphia College of Pharmacy and Science (now University of Sciences in Philadelphia). His academic research dealt with plant constituents and chemical interactions of vitamins. In his pharmaceutical industry career, he handled new drug formulation developments, and later regulatory affairs, presiding over the filing of about 100 generic new drug applications and two innovative drug applications. Dr. Scheindlin passed away on May 10, 2013.

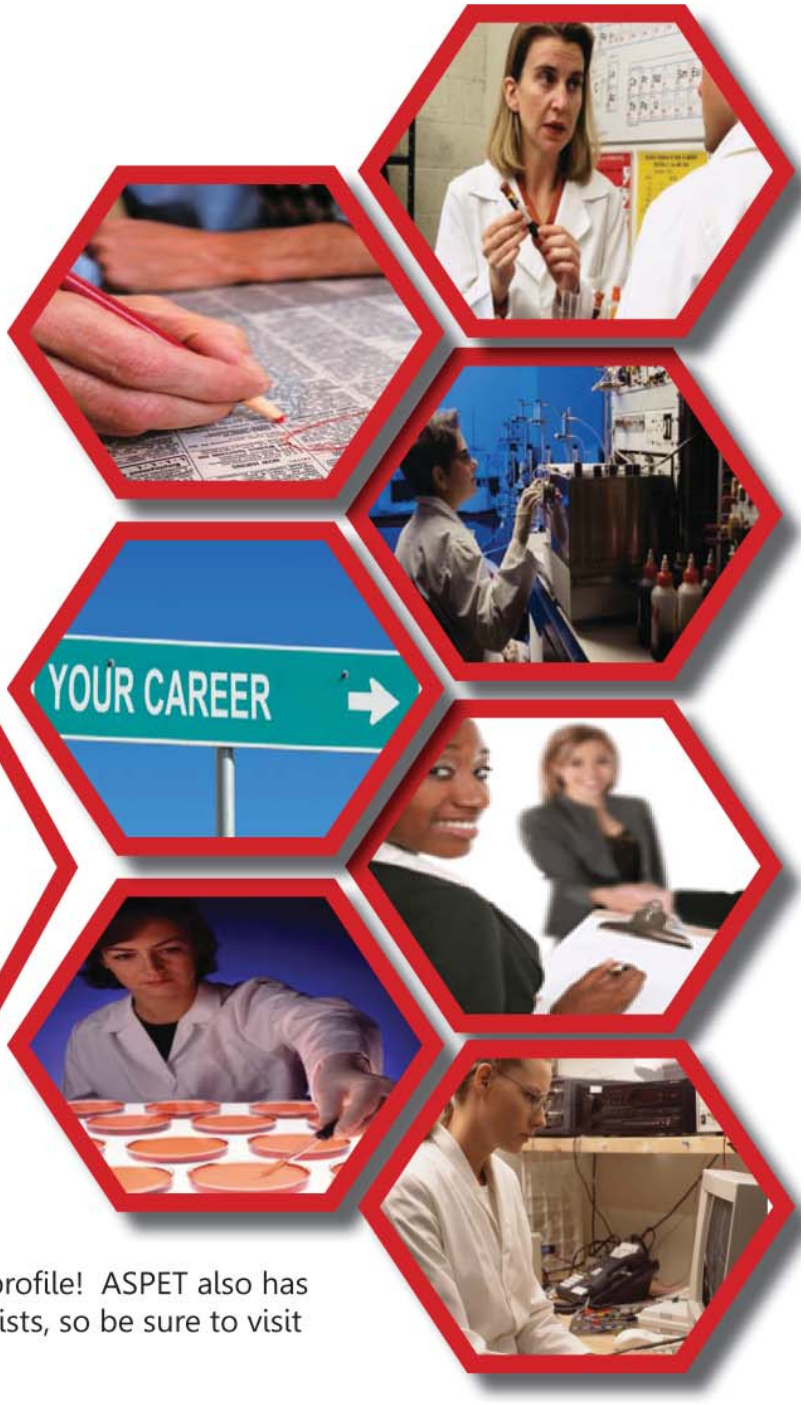
ASPET Career Center

Are you looking for a new job?

Want to make your *CV* available to relevant employers who are looking for candidates just like you?

Register on the ASPET Career Center today to connect with the best jobs!

- Free & confidential resume posting
- Quickly and easily find relevant jobs using key words
- Sign up for automatic email notification of new jobs that match your criteria
- As part of the National Healthcare Career Network, you not only have access to jobs posted to the ASPET Career Center, but to jobs posted by over 250 other professional associations like *SFN* & *AAPS*!



It is FREE to register on our site and create your profile! ASPET also has extensive resources for early career pharmacologists, so be sure to visit our website at www.aspet.org.

Register today at: http://careers.aspet.org/

aspet

Career Center

by Suzie Thompson

The ASPET Career Center has a brand new look!

In keeping with our commitment to helping you make the most of your job search, ASPET is pleased to inform you of the exciting new changes to our Career Center.

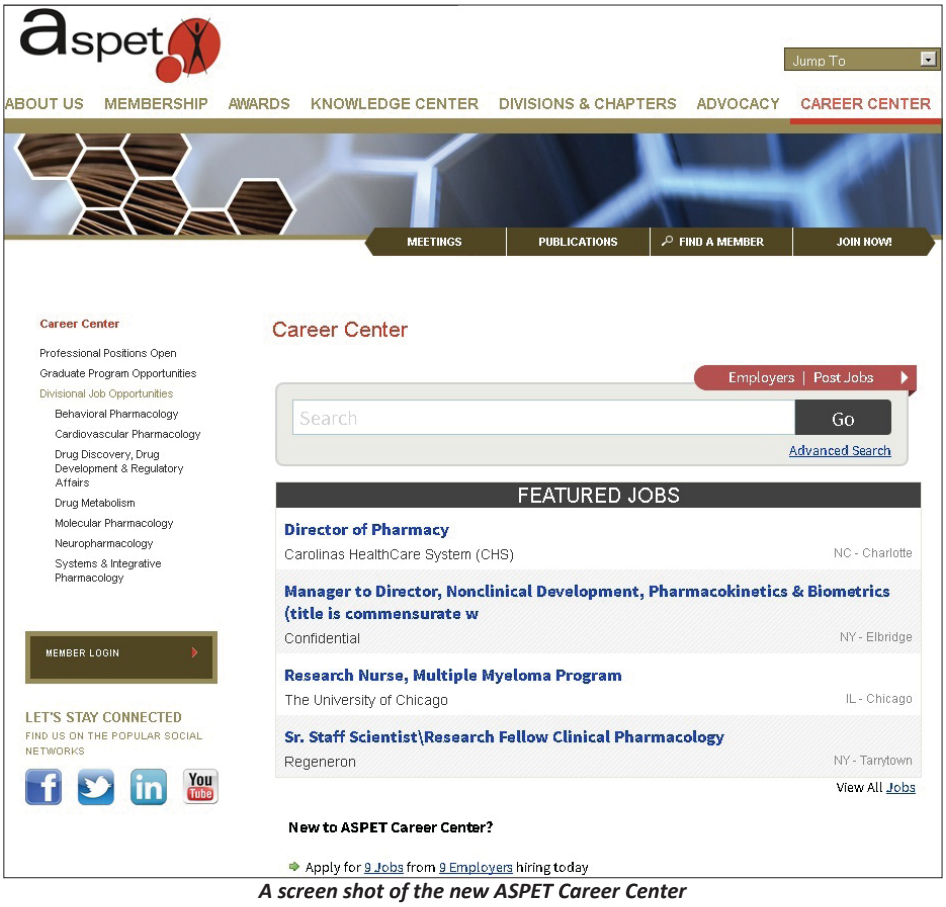
Our May 29 release consisted of a more optimal mobile viewing experience, newly formatted job seeker pages, simplified navigation, and prominent placement of valuable content. Here is a brief overview of the enhancements we have implemented to offer a more cohesive look and improve the job seeker experience.

- **Upgraded Job Seeker Detail Pages**
  A contemporary layout and better organized content gives candidates an immediate snapshot of ASPET's entire suite of career services. Career resources, Society news, and fresh content are embedded within every job seeker page to make it easier to find the information you need.

- **New Career Center Landing Page**
  In keeping with industry standards, the main job seeker page will function as the initial starting point of the ASPET Career Center. All job seeker components will now have better placement within the new landing page and eliminate the number of clicks that you need to take in order to access important information.

- **Responsive Design Elements**
  By incorporating Responsive Design elements into the newly upgraded job seeker pages, the ASPET Career Center enhances your viewing experience by automatically shifting and resizing the career center pages based on the type and orientation of the mobile device that you are using.

The new Career Center enhancements are designed to make your experience better than ever! We will continue to work hard to bring you the most comprehensive employment resource for pharmacology professionals. Check out the latest enhancements by visiting **http://careers.aspet.org/** today!



A screen shot of the new ASPET Career Center

New Editorial Board Members

DMD, *JPET*, and *Molecular Pharmacology* added new members to their editorial boards since the last issue of *The Pharmacologist*. We welcome the following people:

Drug Metabolism and Disposition *Editorial Board*

Su Zheng, Ph.D., Zhejiang University
Min Huang, Ph.D., Sun Yat-sen University

Molecular Pharmacology *Editorial and Advisory Board*

Cecilia B. Bouzat, Ph.D., INIBIBB-UNS/CONICET
Nigel W. Bunnet, Ph.D., Monash University
Hong-Zhuan Chen, Shanghai Jiaotong University School of Medicine
Susan P.C. Cole, Ph.D., Queen's University and PARTEQ Innovations
Adrianne D. Cox, Ph.D., University of North Carolina at Chapel Hill
Niels Decher, Dr. phil. nat., Philipps-Universität Marburg
Jian Ding, Ph.D., Shanghai Institute of Materia Medica
Liwu Fu, Ph.D., Sun Yat-sen University
Alasdair J. Gibb, Ph.D., University College London
Grace L. Guo, Ph.D., Rutgers University
Masatoshi Hagiwara, M.D., Ph.D., Kyoto University
Ellen J. Hess, Ph.D., Emory University School of Medicine
Hidenori Ichijo, D.D.S., Ph.D., Univeristy of Tokyo
Robin A.J. Lester, Ph.D., University of Alabama at Birmingham
Zijian Li, Ph.D., Peking University Third Hospital
Timothy W. Lovenberg, Ph.D., Johnson & Johnson Pharmaceutical Research and Development, LLC
Kenneth P. Machie, M.D., University of Indiana
Daniel S. McGehee, Ph.D., University of Chicago
Andrew B. Tobin, D. Phil., University of Leicester
JoAnn Trejo, Ph.D., University of California, San Diego
Lixia Yue, Ph.D., University of Connecticut Health Center
Michael Xi Zhu, Ph.D., University of Texas Health Science Center at Houston

JPET *Editorial Board*

Chunxiang (Kevin) Zhang, M.D., Ph.D., Rush University

The Board of Publication Trustees appreciates the commitment of these researchers to ASPET's journals and is grateful for their service.

New Member Benefit

The $75 manuscript submission fee for *DMD, JPET*, and *Molecular Pharmacology* is now waived for ASPET members. To qualify for the fee waiver, at least one author listed on a manuscript must be an ASPET member in good standing. If the author is in a dues-paying category of membership, then the author's membership dues must be current.

Because articles published in *Pharmacological Reviews* are invited, that journal does not have a manuscript submission fee.

The fee waiver was implemented on the evening of May 2.

Open-Access Option Coming

Within the next few months, ASPET will offer an author-pays open-access option for articles published in *DMD*, *JPET*, and *Molecular Pharmacology*. ASPET has made the manuscript version of all articles in these journals freely accessible upon acceptance since April 2005. For some funding agencies, this is no longer sufficient.

Under the new open access option, the final, formatted version of the article will be freely accessible immediately (versus an embargo period of 6 or 12 months), and the authors will retain copyright.

Articles will be published under a Creative Commons License. These licenses allow others to "distribute, remix, tweak, and build upon" a work as long as credit is given to the original authors. ASPET's authors may choose between a Creative Commons Attribution-Noncommercial (CC-BY-NC) license for $2,000 and a CC-BY license for $3,000. The latter allows for commercial reuse of a work and is required by some funding agencies. For more information about Creative Commons Licenses, see **http://creativecommons.org/licenses**. The open access fees are in addition to page charges.

Articles published under the open-access option will also be deposited with PubMed Central and will be available there without an embargo.

The Board of Publications Trustees made this move to meet the increasingly stringent requirements of funding agencies such as the Wellcome Trust and the Research Councils UK. Both organizations provide funds specifically for open-access fees so that researchers do not have to pay the fees from research grants.

The open-access program will take a couple of months to implement. Look for updates at the website for each journal, on Facebook and Twitter, and in email messages sent to all ASPET members.

PR&P Launches at Annual Meeting

Pharmacology Research & Perspectives (PR&P) was officially launched at ASPET's 2013 Annual Meeting in Boston, on Saturday, April 20. The new journal, co-published by ASPET, the British Pharmacological Society, and Wiley, is now open for submissions. The first issue is to appear in September, but articles may be published as early as June.

PR&P will publish original research, reviews, and perspectives in all areas of preclinical and clinical pharmacology, therapeutics, education, and related research areas. As an open-access journal, all content in *PR&P* will be made freely available immediately upon publication to read, download, and share. Articles will be published under a Creative Commons license that meets the requirements of funders such as the Wellcome Trust and the Research Councils UK.

The journal's Editor-in-Chief is **Michael J. Curtis, Ph.D.**, King's College, London. The journal's Deputy Editor is **Darrell R. Abernethy, M.D., Ph.D.**, Johns Hopkins University School of Medicine. Dr. Curtis and Dr. Abernethy are assembling the journal's Editorial Board.

PR&P is utilizing cascading reviews from the other journals published by ASPET and the BPS. Cascading reviews allow scientifically rigorous articles that do not meet the priority objectives of the other journals to be referred to *PR&P* for publication. This saves authors time and effort. The authors of a referred manuscript must opt in to have the paper considered by the new journal. *PR&P* also welcomes *de novo* submissions.

The journal charges publications fees. For manuscripts submitted directly to *PR&P*, the fee is $2,500. ASPET and BPS members who submit directly to the journal receive a 10% discount. The fee for referred manuscripts is $2,000, a 20% discount.

To read more about *PR&P*, submit a manuscript, or sign up for content alerts, go to **http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2052-1707**.

Written Testimony of the American Society for Pharmacology and Experimental Therapeutics Submitted to House and Senate Appropriations Subcommittees on Labor, Health and Human Services, Education & Related Agencies

Fiscal Year 2014 Appropriations for the National Institutes of Health

The American Society for Pharmacology and Experimental Therapeutics (ASPET) is pleased to submit written testimony in support of the National Institutes of Health (NIH) FY 2014 budget. ASPET recommends a budget of at least $32 billion for the NIH in FY 2014.

Sustained growth for the NIH should be an urgent national priority. Research funded by the NIH improves public health, stimulates our economy, and improves global competitiveness. Several years of flat funding and mandatory budget cuts required by sequestration in the current fiscal year prevents and delays advances in medical research, jeopardizes potential cures, and eliminates jobs. Additionally, the nation will lose a generation of young scientists who see no prospects for careers in biomedical research, creating a "brain drain" as many graduate students, post-doctoral researchers, and early career scientists leave the research enterprise or look for employment in foreign countries.

The 5% sequestration cut further diminishes NIH's research capacity that has already fallen 20% since 2003 as a result of flat funding and inflation. With sequestration, NIH's purchasing power will be reduced by nearly 25% since 2003. Continued erosion of NIH's research capacity will accelerate further the diminishment of American leadership and innovation in biomedical research. Without a commitment to sustained funding for the NIH, the nation's biomedical research capacity will erode further.

A $32 billion budget for the NIH in FY 2014 is a start to help restore NIH's biomedical research capacity. Currently, the NIH only can fund one in six grant applications, the lowest rate in the agency's history. Furthermore, the number of research project grants funded by NIH has declined every year since 2004.

A budget of at least $32 billion in FY 2014 will help the agency manage its research portfolio effectively without having to withhold funding for existing grants to researchers throughout the country. Scientific research takes time. Only through steady, sustained, and predictable funding increases can NIH continue to fund the highest quality biomedical research to help improve the health of all Americans and continue to make significant economic impact in many communities across the country.

There is no substitute for a steady, sustained federal investment in biomedical research. Industry, venture capital, and private philanthropy can supplement research but cannot replace the investment in basic, fundamental biomedical research provided by NIH. Industry and venture capital both face their own economic challenges and venture capital investment in biomedicine has declined since 2007. Neither the private sector nor industry will be able to fill a void for NIH funded basic biomedical research. Much of industry support is applied research that builds upon the discoveries generated from NIH-funded projects. The majority of the investment in basic biomedical research that NIH provides is broad and long-term providing a continuous development platform for industry, which would not typically invest in research that may be of higher risk and require several years to fully mature. In addition to this long term view, NIH also has mechanisms in place to rapidly build upon key technologies and discoveries that have the ability to have significant impact on the health and well being of our citizens. Further, industry research is focused on developing drugs that are protected by patents and often does not make their data publicly available.

Many of the basic science initiatives supported by NIH have led to totally unexpected discoveries and insight that have transformed our mechanistic understanding of and our ability to treat a wide range of diseases.

Diminished Support for NIH Will Negatively Impact Human Health

Continued diminishment of funding for NIH will mean a loss of scientific opportunities to discover new therapeutic targets. Without a steady, sustained federal investment in fundamental biomedical research, scientific progress will be slower and potentially helpful therapies or cures will not be developed. For example, more research is needed on Parkinson's disease to help identify the causes of the disease and help develop better therapies; discovery of gene variations in age-related macular degeneration could result in new screening tests and preventive therapies; more basic research is needed to focus on new molecular targets to improve treatment for Alzheimer's disease; and diminished support for NIH will prevent new and ongoing investigations into rare diseases that FDA estimates almost 90% are serious or life-threatening.

Historically, our past investment in basic biological research has led to many innovative medicines. The National Research Council reported that of the 21 drugs with the highest therapeutic impact, only five were developed without input from the public sector. The significant past investment in the NIH has provided major gains in our knowledge of the human genome, resulting in the promise of pharmacogenomics and a reduction in adverse drug reactions that currently represent a major worldwide health concern. Several completed human genome sequence analyses have pinpointed disease-causing variants that have led to improved therapy and cures but further advances and improvements in technology will be delayed or obstructed with inadequate NIH funding.

Investing in NIH Helps America Compete Economically

A $32 billion budget in FY 2013 will also help the NIH train the next generation of scientists and provide a platform for broader workforce development that is so critical to our nation's growth. Many individuals trained in the sciences via NIH support become educators in high schools and colleges. These individuals also enter into other aspects of technology development and evaluation in the public and private sectors to further enrich the community and accelerate economic development.

This investment will help to create jobs and promote economic growth. Limiting or cutting the NIH budget will mean forfeiting future discoveries and jobs to other countries.

The U.S. share of global research and development investment from 1999 – 2009 is now only 31%, a decline of 18%. In contrast, other nations continue to invest aggressively in science. China has grown its science portfolio with annual increases to the research and development budget averaging over 23% annually since 2000, including a 26% increase in 2012. Russia plans to increase support for research by 65% over the next five years. And while Great Britain two years ago also imposed strict austerity measures to address that nation's debt problems, that nation had the foresight to keep its strategic investments in science at current levels. The European Union, despite great economic distress and the severe debt problems of its member nations, has proposed to increase spending on research and innovation by 45% between 2014 and 2020.

NIH research funding catalyzes private sector growth. More than 83% of NIH funding is awarded to over 3,000 universities, medical schools, teaching hospitals, and other research institutions in every state. One national study by an economic consulting firm found that federal (and state) funded research at the nation's medical schools and hospitals supported almost 300,000 jobs and added nearly $45 billion to the U.S. economy. NIH funding also provides the most significant scientific innovations of the pharmaceutical and biotechnology industries.

Conclusion

ASPET appreciates the many competing and important spending decisions the Subcommittee must make. The nation's deficit and debt problems are great. However, NIH and the biomedical research enterprise face a critical moment. The agency's contribution to the nation's economic and physical well being should make it one of the nation's top priorities. With enhanced and sustained funding, NIH can begin to reverse its decline and help meet its potential to address many of the more promising scientific opportunities that currently challenge medicine. A budget of at least $32 billion in FY 2014 will allow the agency to begin moving forward to full program capacity, exploiting more scientific opportunities for investigation, and increasing investigators' chances of discoveries that prevent, diagnose, and treat disease. NIH should be restored to its role as a national treasure, one that attracts and retains the best and brightest to biomedical research and provides hope to millions of individuals afflicted with illness and disease.

2014 ASPET Washington Fellows Program

Applications are now being accepted for the 2014 ASPET Washington Fellows Program. The deadline to apply is September 1, 2013.

ASPET Washington Fellows on Capitol Hill

The Washington Fellows Program was created in 2013 with the goal to develop early career scientists interested in science policy to learn about and become more engaged in public policy issues. Washington Fellows develop an understanding of how public policy decisions made in Washington help shape and impact science policy, such as funding for the National Institutes of Health and other science agencies. Fellows come to Washington and learn how to advocate effectively on Capitol Hill and in their home districts. This program will help Fellows develop the skills and insights to become future leaders in science.

The inaugural 2013 Washington Fellows have completed their Capitol Hill meetings with their respective Congressional Delegations. Fellows were on Capitol Hill in March and early April during the ongoing discussions involving sequestration, a particularly busy and hectic time for all involved. Each of the Fellows made a persuasive case for providing adequate funding for NIH. Of particular note was the interest Congressional offices had concerning the future career prospects. The 2013 ASPET Fellows are all graduate students and post-doctoral trainees. Hearing directly from young investigators – the future scientists of America – that they are considering leaving biomedical research or considering leaving the country to have an opportunity to pursue their chosen career path made an impression upon many in Capitol Hill that the "brain drain" is a critical problem.

Although their advocacy in Washington may be behind them, the 2013 ASPET Washington Fellows' work is not done! Fellows are currently involved in developing a survey of ASPET's graduate students and postdoctoral trainees about their career prospects and expectations and writing op-ed pieces for their local news outlets.

Application Information

The 2014 ASPET Washington Fellows Program is open to any graduate student, postdoctoral trainee, or researcher no more than four years past the completion of his/her postdoctoral training. Fellows serve one-year terms. Applicants must be members of ASPET in good standing and have a strong interest in science and its intersection with public policy. Fellows will be selected by the ASPET Science Policy Committee. We anticipate up to 10 Washington Fellows Program participants in 2014.

All applications must contain the following information and be submitted by September 1, 2013 as a single combined PDF:

- A letter (no more than two pages) from the applicant stating their interest in public policy and why they are interested in the Washington Fellows Program
- A curriculum vitae
- A letter of support from the candidate's mentor and/or department chair supporting the application

Additional information is available on the ASPET's home page: **www.aspet.org**.

Final NIH FY 2013 Budget Figures Show Significant Decline in Funding

NIH released complete information on their operating plan for FY 2013. The agency reports that the total funding line decreases by 5.5%. Research Project Grants decline by 6.1%, including reductions of 4.9% for noncompeting awards and 8.6% for competing awards. The number of competing awards is down by 8.5% from FY2012. As a result of the sequestration, the NIH budget for FY 2013 falls to $29.15 billion.

It will surprise no one that the budget and appropriations process now underway for FY 2014 is going to be difficult in the weeks and months ahead. Here is why: the Budget Control Act of 2011 (BCA) created a trigger for sequestration to happen when Congress failed to agree on a deficit reduction plan. The BCA also imposed strict spending caps for ten years on discretionary spending. As a result, if Congress spends more money than the budget caps in any given year, across-the-board spending cuts would be triggered to bring the spending level below the overall spending cap. The FY 2014 spending cap level for discretionary funds is approximately the same as the sequestered FY 2013 level. Assuming the appropriators keep spending at or under the spending cap level for FY 2014, there will be no new across-the-board spending cuts. That would be good news but does not necessarily allow for growth in the NIH budget either. Of course, notwithstanding FY 2013's historic cut to its budget, NIH does enjoy bipartisan support. So it is possible that the agency could be one of the winners in FY 2014 and receive an increase (meaning other programs would have to be cut to remain at or below the spending caps).

Most Members of Congress are aware of the impact that sequestration and spending caps have on future budget decisions for NIH. And some Members of Congress are trying to rally support for increases for the NIH. A Senate letter of support organized by Senators Robert Casey (D-PA) and Richard Burr (R-NC) obtained 43 Democrat and nine Republican signatures. The letter requests Appropriation Committee leadership to "maintain a strong commitment to funding for the National Institutes of Health…" The letter notes investment in NIH is declining, resulting in "promising, talented young researchers being discouraged from the field of biomedical research and some investigators deciding to abandon scientific research altogether or to conduct their research outside the United States."

Similarly, a House letter of support organized by Reps. David McKinley (R-WV) and Ed Markey (D-MA) gathered 168 signatures. The House letter specifically requests that NIH receives at least $32 billion for FY 2014, a level consistent with ASPET's written testimony (see page 102) in support of NIH funding. The letter makes mention of the loss of aspiring scientists "being forced into other careers" and notes the $32 billion budget request is the "minimum level of funding needed to reflect the rising costs associated with biomedical research and to help mitigate the impacts of sequestration."

ASPET also joined hundreds of other healthcare, education, and other stakeholders in a letter urging Congressional Appropriations leadership to "provide the largest possible fiscal year 2014 302(b) allocation to the Labor, HHS Education and Related Agencies Appropriations Subcommittee." The Labor/HHS subcommittee funds the NIH. In Congressional parlance, the 302(b) allocation refers to the amount that each subcommittee receives from the full Appropriations Committee. The "302(b)" allocation establishes a cap on that subcommittee's spending bill. The subcommittees do not determine the level of funding for each bill; they only determine how that money is spent among the agencies and programs under the subcommittee's jurisdiction. The higher the 302(b) allocation, the greater the opportunity there is to increase funding for specific programs under that subcommittee's jurisdiction.

Beyond normal procedural matters, the FY 2014 spending bills will almost certainly get caught up in what has become business-as-usual Washington melodrama. Another fight to raise the debt ceiling may be around the corner later this summer or fall. Remember, it was the Budget Control Act of 2011 that raised the debt ceiling limit but would ultimately trigger the sequestration to take effect and put the spending caps in place. This year, Congressional Republicans may be more likely to seek tax reforms instead of significant spending cuts in any agreement to raise the debt ceiling. All this will be played out during the summer and most likely through the fall too.

Appropriators have indicated they plan to move through FY 2014 spending bills even without a budget agreement. It is not known when or even if the Labor/HHS Subcommittee will be able to "markup" or consider its bill that includes funding for the NIH.

The one certain thing we know is that biomedical scientists need to continue to contact their Representatives and Senators to remind them how critical their support is to help begin to restore sustained funding for the NIH.

Draft Legislation Threatens Peer Review

In late April, the Chairman of the House Science, Space and Technology Committee, Lamar Smith (R-TX) introduced the "High Quality Research Act," that mandates public certification by the Director of the National Science Foundation that every NSF grant meets the following requirements:

- The research is in the interests of the U.S. and advances national health, prosperity or welfare, and secures the national defense by promoting science;
- The science is of the finest quality, ground breaking, and answers important questions; and
- The research is not duplicative of other research projects funded by NSF or other federal agencies.

The legislation also requires the Office of Science and Technology Policy to prepare a report on how other federal science agencies can implement these requirements.

The Ranking Member of the House Science Committee, Eddie Bernice Johnson (D-TX), responded to both the proposed legislation and Rep. Smith's expressed interest in reviewing NSF's mission and peer review process. In a strongly worded letter to Rep. Smith, Johnson says that the proposed legislation, "is a first step on a path that would destroy the merit-based review process at NSF and intrudes political pressure into what is widely viewed as the most effective and creative process for awarding research funds in the world." Johnson further states that "interventions in grant awards by political figures with agendas, biases, and no expertise is the antithesis of the peer review process…."

Privacy Tips for Facebook: A Starter Guide to Protecting Your Profile and Presence

For those of you who have been avoiding social media, particularly Facebook, out of fear that it takes away your sense of privacy online, we wanted to take the time to review a couple of features for you and ease your fears. We briefly touched upon the issue of privacy in our "How To" Tips for Facebook document, **http://www.aspet.org/uploadedFiles/Knowledge_Center/Social_Media_Resources/How-Tos-for-Facebook.pdf**. We aim to get into much more detail here.

Starting off with one of the most basic features, most social networks, including Facebook, give you the option of posting a picture of yourself for a main profile picture. It is highly recommended that you post a picture of yourself for your main profile picture and have elements in the "about [me]" section of your profile that describe who you are and what you do. This serves as a way for other people to be able to verify that you are who the Facebook profile says you are. Beyond your profile picture, you can post as many or as few pictures as you like. After all, you don't have to show the world every aspect of your life.

Facebook recently made major privacy changes, making your privacy settings easier to find and tweak. They have added several shortcuts to the privacy settings, but before taking you through the shortcuts, let's go through the privacy functions and settings in detail. You can get to the privacy settings by clicking on the "gears" at the far right of the blue bar atop the page and clicking on "Privacy Settings."

The left navigation menu on the privacy settings screen.

A view of the full Privacy Settings and Tools menu on Facebook.

Privacy Settings and Tools

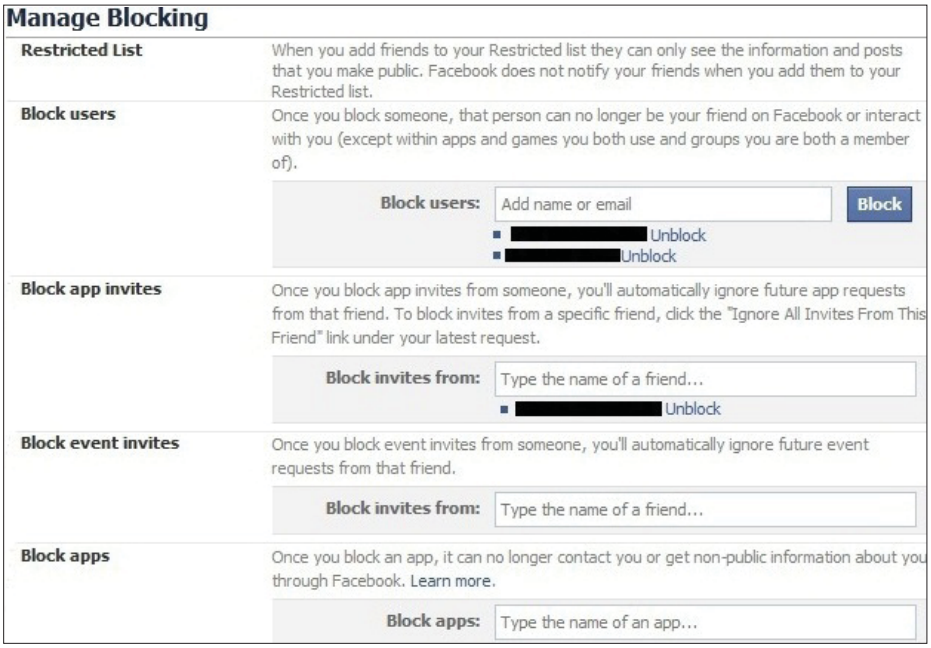
On the expanded Facebook privacy settings page, you are first asked, "Who can see my stuff?" Per the first question in this subsection, this involves your posts. You can allow certain categories of people to see your Facebook posts by setting it to Public (everyone), Friends (only the Facebook friends you're connected to), only you, or certain lists of which you are a part. The second item of this subsection allows you to see and review all posts and things you're "tagged" in by going to your User Activity Log. (We'll address "tagging" in greater detail below in the "Timeline and Tagging Settings" section.) The User Activity Log basically allows you to view all that you have done on Facebook and all that has been done by others who have involved you in certain activities on the site. In addition to limiting who can view your future content, the final question of this subsection asks you, "Limit the audience for posts you've shared with friends of friends or Public?" This basically allows you to control who can see previous posts you have put up on your Facebook timeline.

The next subsection of the Facebook privacy settings page greets you with the question, "Who can look me up?" This feature allows you to control who can search for you by email address, phone number, or name on your timeline. Putting your phone number on your profile may be a bit of a risky move, as that's just one more piece of information that you would have to safeguard. You could, however, change these settings so that your contact information can only be viewed by your Facebook friends. Next, Facebook asks you, "Do you want other search engines to link to your timeline?" Leaving this feature in the "off" position limits the information in your profile to being found only on Facebook and not via search engine queries. Making your Facebook timeline searchable in search engines just puts more of your information at the fingertips of random Web users.

Timeline and Tagging Settings

One clever interactive feature on Facebook that has been around for a while is "tagging." You can "tag" pictures and posts of people and places on the social network, and other people can "tag" you. Being "tagged" simply means that someone is pointing you out in a picture or status update. If you have ever wanted to look over or delete old posts or pictures in which someone has "tagged" you, you can click on the link to your "Activity Log" (a grey rectangular box towards the top of your timeline page). Additional information about tagging is covered below in the "Timeline and Tagging Settings" and "Notifications Settings" sections.

Take a look at what you can tweak on Facebook's Timeline and Tagging Settings menu.



If you want to hide your profile from certain people, have been bombarded by app or event invites from Facebook friends, and want to avoid certain applications, here is where you block them.

Here's where you can decide what you want Facebook to notify you about and how you want Facebook to notify you.

Timeline and Tagging Settings (continued)

To access your "Timeline and Tagging Settings" settings, go to the menu on the left of your screen and click on "Timeline and Tagging." The question, "Who can add things to my timeline?" allows you to tweak who can post items to your timeline. Your options for who can post items to your timeline are either "friends" or "only me." In this subsection, you can also set your "tagging" settings so that Facebook will require you to review any post or picture in which you are tagged before that item gets posted to your timeline. So, have fun with the site and let your Facebook friends post on your timeline! After all, you have the option to review content in which your friends tag you.

Now, take a look at "Who can see things on my timeline?" where you can review what others see on your timeline by viewing it as your friends see it when they look you up on Facebook. To do this, click on the "View As" link next to "Review what other people see on your timeline." You can also select who can see posts on your timeline in which you have been tagged by other people, and select who can see content that others have posted on your timeline.

If you're wondering "How can I manage tags people add and tagging suggestions," Facebook also gives you the option of reviewing tags people add to your posts before the tags actually show up on your Facebook posts. If you are of the judicious sort and want to see what your friends just tagged you in, this may be an option for you to consider. Also, when you're tagged in a post, Facebook asks, "Who do you want to add to the audience if they aren't already in it?" Here, you can change the list of who can view posts you are tagged in by allowing only certain friends or groups of people to see these posts. In wrapping up the "Timeline and Tagging Settings," Facebook asks you, "Who sees tag suggestions when photos that look like you are uploaded?" In order to keep complete control over your Facebook presence, your best option would be to set this feature to "no one."

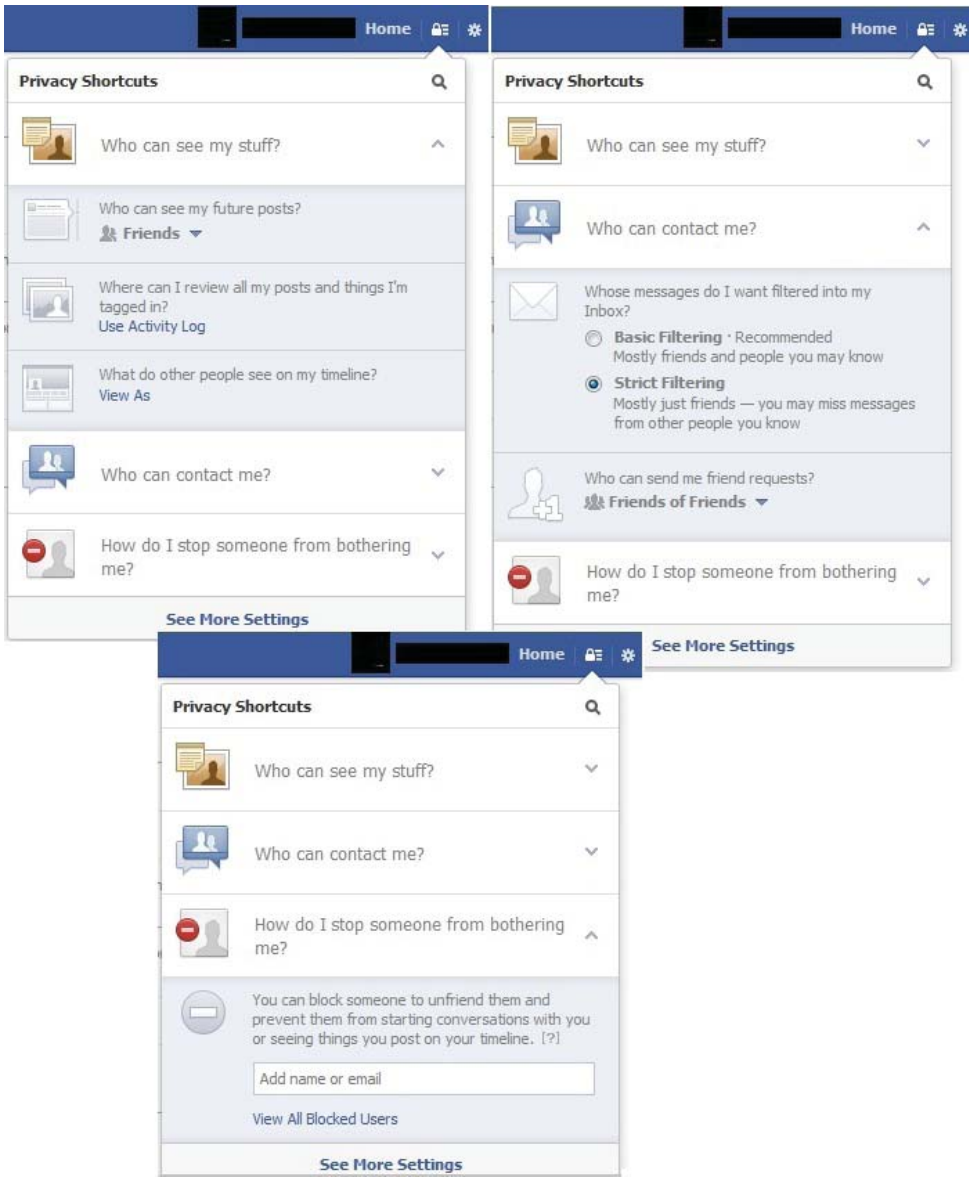
Blocking

The next item you should click on in the left-hand navigational menu of the user profile settings screen is "Blocking." Here, you can block a user from viewing your timeline. Facebook also gives you the option of blocking app and event invites from certain people. If you don't want to block all application invitations from friends but are tired of seeing requests for certain apps, you also have the ability to block individual applications.

Notifications Settings

Let's now go to the "Notifications" screen (to the left). Three of the top four items here are pretty straight forward. You can decide what notifications you receive from Facebook on Facebook, via email, or via text message. You can also learn how to control push notifications from your smart phone through a link on the "Notifications" page. (A push notification is an automatic notification sent to your phone by a particular application.) Furthermore, you can control how Facebook notifies you about activities involving you, close friends, pages you manage, and Facebook groups you have joined. Facebook can also notify you when you have been "tagged" by certain groups of people in a status update or picture.

View your Facebook apps, or lack thereof, on the App Settings screen.



Screenshots of all components of Facebook's privacy shortcut menus.

App Settings

The "App Settings" screen allows you to keep track of what applications you have given Facebook permission to access information on your timeline. One of the safest things you can do on Facebook is keep this in the "off" position, thereby disallowing Facebook and third-party applications from mining any information about you from your timeline. Yet, no one could fault you for adding an element of fun and intrigue to your Facebook experience by allowing access to apps.

Privacy Shortcut Menu

Now that you have a handle on the detailed privacy settings, let's take a look at the privacy shortcut menu. Find the "lock" icon in the upper right-hand corner of the blue bar atop of all Facebook pages. Click on the icon to see three questions. The items under the first question, "Who can see my stuff?" can also be found under the "Privacy Settings and Tools" and "Timeline and Tagging Settings" menus. The next category, "Who can contact me?" is a way to control spam that you could potentially receive on your timeline or in your Facebook inbox. Selecting "Basic Filtering" will allow messages from friends and people you may know, whereas "Strict Filtering" keeps a tighter lid on spam controls but potentially allows you to miss messages from people who want to be your Facebook friends but aren't connected with you yet. The last item on the shortcut menu is "How do I stop someone from bothering me?" This provides a quicker way of blocking another Facebook user than going to the "Manage Blocking" settings. The full privacy settings screen can be accessed from the shortcut menu by clicking on "See More Settings" at the bottom of the menu.

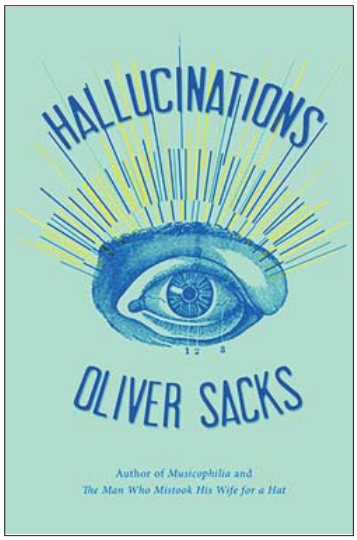
From a general standpoint, you should be vigilant about your online persona. This includes what you post on social media and information you put into your social media profiles. A main rule of thumb is to not post anything visible to the general public online that could come back to haunt you. Think of the security questions that you might be prompted to answer when you forget your password to certain online accounts or websites. If you, for example, post on your Facebook profile the name of the street you grew up on, the name of your pet, or where you attended elementary school, you have essentially just given an online intruder access to some of the items you may have used as answers to security questions in your other online accounts.

One last tip, and this one cannot be overstated: When you are done with Facebook, whether you are on a public, shared, work, or personal computer, remember to sign out so that no one else can mess around with your information on Facebook. Social media can be a safe haven, but you have to put forth the effort to make it happen. So, first and foremost, make an effort to protect yourself on Facebook, and then head on over to ASPET's Facebook page at **https://www.facebook.com/ASPETpage** and "like" us. After you click the "Like" button, move your mouse away and then hover over the "Like" button once more without clicking anything. In the menu that pops up, click on "Show in News Feed." This will ensure that you receive the latest ASPET updates on policy issues, events, and more.

Book Review

by Christine K. Carrico, Ph.D.

Hallucinations



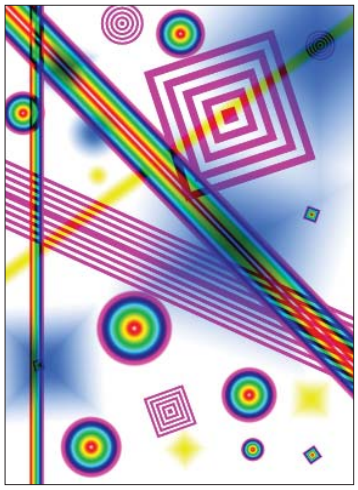
I am a big fan of Oliver Sacks and have read most of his books. I reviewed two of these for *Molecular Interventions*. In *Island of the Color Blind* (*Mol Interv* October 2004 4:296-297; doi:10.1124/mi.4.5.9) I was particularly taken by the richness of his writing and descriptions. *Uncle Tungsten* (*Mol Interv* April 2002 2:110-111; doi:10.1124/mi.2.2.110) gave a face to chemistry and brought it to life. So when I saw that he had a new book out on such a fascinating topic as *Hallucinations*, I couldn't wait to get my hands on it and read it. Sadly, I found this book to be a major disappointment and not at all in the same league as his other books that I have read. Hallucinations is essentially a litany of hallucinations. Each chapter describes the hallucinations associated with a different condition, although because of the overlap of types of hallucinations, the description of visual hallucination associated with sensory deprivation could pretty much substitute for the description of one in epilepsy. Unfortunately, there is little discussion of what causes the hallucinations, or even in many cases where they arise in the brain. Perhaps this isn't known, but that is not obvious.

The book starts with Charles Bonnet Syndrome and the hallucinations experienced by those who have suffered visual deprivation. These are interesting to read since they frequently contain elaborate people and places, and are usually friendly, pleasant, or inspiring, or perhaps the novelty of reading descriptions of hallucinations has not yet worn off. This chapter is followed by the hallucinations suffered by those with other sensory deprivation. Chapters on hallucinatory smells (complex and often putrid smells) and auditory hallucinations (voices and music involving multiple areas of the brain) follow.

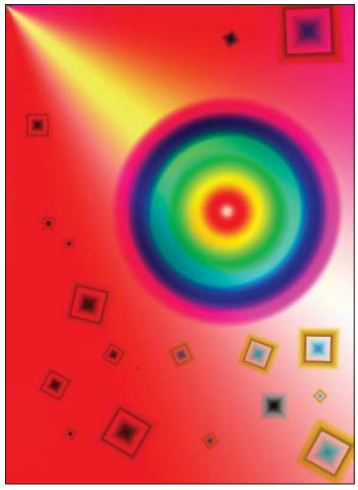
Sacks then moves to the hallucinations suffered by people with diseases or conditions such as Parkinson's, epilepsy, and visual migraine. He covers virtually every type of hallucination from phantom limbs, to drug-induced visions, to PTSD. Unfortunately, in reading this book, you lose track of just what condition is being discussed. Some of the patients described (and there are many) are Sacks' own, although more often than not, he quotes from other sources.

I found interesting the initial similarity between the hallucinations suffered in epilepsy and migraine. Both types appear suddenly, last their course, and then disappear. Both types usually precede the actual attack. Both show a slow movement of the symptoms and the electrical disturbances in the brain that underlie the hallucinations. The actual type of hallucination differs, however, being much more complex in epilepsy evoking images, color, people, and voices. Hippocrates called epilepsy the "Sacred disease – a disorder of divine inspiration." Visual migraine hallucinations are generally geometric patterns and auras.

Hypnogogic hallucinations, those images that appear during the "unique state of consciousness between wakefulness and sleep," were interesting because virtually everyone has experienced this type of quasi-hallucination at one time or another. Not quite dreams, but not quite reality either.



An illustrious group of people are mentioned for the hallucinations they have experienced and written about. Literature seems to have benefited from these experiences. Lewis Carroll suffered from migraines, and there is speculation that the hallucinations he experiences during these attacked greatly influenced his writing in *Alice in Wonderland*. Charles Dickens writes of hallucinations as only one who has experienced them can in *Great Expectations* and *A Christmas Carol*. Other luminaries include Aldous Huxley, William Taylor Coleridge, Baudelaire, Edgar Allen Poe, and Linnaeus. Sacks, himself, offers an extraordinarily honest and vivid description of his own hallucinatory experiences suffered during his neurology residency when he experimented liberally with cannabis, LSD, amphetamines, chloral hydrate, morning glory seeds, and ultimately morphine. I am just glad he was never ***my*** doctor during that time.



A chapter or two of this book is a fascinating read because of the detailed descriptions of the hallucinations. A whole book is a bit much.

Interviews with ASPET Members

Our members come from a diverse array of backgrounds, pharmacological interests, and career levels. "In the Spotlight: Interviews with ASPET members" picks three ASPET members from each category of membership (Regular, Postdoc, and Student) to interview for each issue of The Pharmacologist*. Get to know your fellow members:*

JONATHAN L. KATZ, Ph.D.
National Institute on Drug Abuse/National Institutes of Health - Regular ASPET Member

Who or what have been your greatest influences in your work?

I have benefitted throughout my career from the good counsel of several people that I consider mentors for life. I am not sure that they think of themselves as having that role, and I am equally unsure if they would have signed on had they known. But I don't think that anyone ever outgrows the need for mentoring, and so I have continued to go to them as often as I can for advice and guidance.

My doctoral thesis advisor, J.E. Barrett, has probably had the most profound effect on my career. I learned so many things from him that it is difficult to sum them up, or even begin to list them. But of the many things I learned from him, probably the most indispensable was to carefully pick projects. Your time is your most precious commodity, and it has to be invested wisely. The best investments of your time are with projects that pay off no matter what the outcome. This is especially important for those in the early stages of their careers.

When I was in Jim's lab, he was doing the earliest of the experiments that were recently described in his P.B. Dews Award address (*The Pharmacologist*, **55:**35-42). New and interesting influences on the behavioral effects of drugs were being discovered with a dizzying frequency, and behavioral pharmacology was evolving before our eyes. What was so compelling about these discoveries was that knowledge of the pharmacology and neuropharmacological mechanisms of many of these drugs was no doubt important but insufficient for a full understanding of their behavioral effects. What was needed was an appreciation of reciprocal influences of the drugs and the behavioral history of the organism. Those histories and drug effects were dynamically interrelated – combinations of experiences of the organism that could result in long-lasting changes in the effects of drugs.

Another mentor who is of immeasurable value to me is J.H. Woods. I sat in on the pharmacology course at Harvard Medical School, but Jim really taught me pharmacology and how to apply pharmacological principles to the analysis of the behavioral effects of drugs. Lessons I learned from Jim, with some additional help from a couple of dozen morphine-dependent rhesus monkeys, are ones that I still apply daily to good effect. And it is always fun and profitable to send Jim a graph or two showing some recent results and follow it up with a phone call that starts with the graphs and often ends up somewhere completely unanticipated. Above all he revels in the joy of scientific discovery.

Among the greatest influences on my work were P.B. Dews, W.H. Morse, R.T. Kelleher, as well as their seminal papers in behavioral pharmacology. The paper by Dews, published in *JPET* in 1955, found that the schedule of reinforcement that maintained a readily repeated behavior could play a critical role in determining the effects of pentobarbital. In that study, there was a range of doses over which pentobarbital increased response rates under one schedule and decreased those rates under another schedule. Some of us take that effect for granted today, and others don't appreciate its significance. But it remains a thought-provoking outcome – a "depressant" drug had diametrically opposed effects depending on the schedule of reinforcement. Neither traditional pharmacological nor psychological principles were of use for interpreting these results. A bit later, Kelleher and Morse published a paper in *Ergebnisse der Physiologie* (1968) that put the growing number of like findings within a context related to precedents in physiological pharmacology (e.g. Langer and Trendelenburg, 1964). The principles still apply today. Arrangements of behavioral consequences and stimuli surrounding those events are used often to study other "things," but those stimuli and arrangements constitute a schedule of reinforcement that can be an important determining influence on behavioral and pharmacological outcomes. To paraphrase Dews: this does not mean that environmental influences on the behavioral effects of drugs are the only subject for behavioral pharmacology, but he who ignores these influences does so at his peril.

Tell us about your most favorite experiment/study with which you have been involved.

Working as a bench scientist is probably the best job on earth – getting paid to do what you love, and I have been fortunate to have worked with some great students in my lab over the years. Picking a single favorite experiment or study is like Sophie's Choice, but I would, if pressed, have to pick our current research on sigma receptors. We recently published a paper showing that active self-administration of cocaine triggers reinforcing effects of sigma-receptor agonists that are not active as reinforcers in subjects without this cocaine experience. Once induced, the reinforcing effects of sigma-receptor agonists remain with the subjects for life and, unlike the inducer cocaine, are independent of dopamine systems. Because cocaine also has agonist actions at sigma receptors, in addition to its actions at the dopamine transporter, this induction of σR-mediated reinforcement may be involved in the pernicious nature of stimulant abuse and its intractability when treated by medicines targeting dopamine systems alone. It is like a metastasis of reinforcement mechanisms. Further, the targeting of sigma receptors or the dopamine transporter singly does not affect cocaine self administration, but the dual targeting of these proteins produces a decrease in cocaine self administration, without effects on other behaviors. As is evident from the above, all of this follows from the ground-breaking work of those that influenced me.

What advice would you offer to aspiring pharmacologists?
I would advise aspiring pharmacologists to collaborate and embrace the changes in science as they unfold. At the same time, think through your experimental questions and use the most appropriate techniques. It is tempting to be seduced by all of the new technical advances that proliferate in science today, but what is most important is to use the techniques that best answer the questions.

For those that aspire to careers studying the behavioral effects of drugs or behavioral neuroscience, I will refer them to a 14th century friar, William of Ockham, who did not invent the Law of Parsimony but used it so effectively he got into trouble with the Church. For our purposes, the Law of Parsimony, or Ockham's razor as it is known, states that the hypothesis with the fewest assumptions is preferred over the more complex hypothesis. Start with the simplest explanations and add complexity only as necessary. And be careful when you construct your "explanations." Most of us would deny being Cartesian dualists, but as Bennett and Hacker (2003) have so ably documented, many of us simply use the brain, or one of its substructures, in the way René Descartes explained things with the concept of mind. Nonsense is just that, regardless of whether it is cloaked in *au courant* nomenclature.

How has membership in ASPET benefitted you and your career?
ASPET is a great community of scientists, and the Annual Meeting is the one I always want to attend. The Program Committee does a fantastic job, and I think that the 2013 meeting, despite the unfortunate events surrounding it, may have been the best yet. Pharmacology is a great subject matter in part because it facilitates interdisciplinary science. And interdisciplinary science is a great opportunity for learning new things.

What do you see in store for the future of pharmacology? How do you see the science advancing?
The technical advances that are here now and those that are on the horizon were implausible when I was in graduate school. There is so much potential for advances that it is truly impossible to know what the life sciences will look like in a few decades. What is clear is that the most profound advances will employ multidisciplinary approaches to the questions being asked. But what is equally clear is that when you combine disciplines you can't compromise one for the other. Any multidisciplinary research is only as strong as its weakest component.

REMY L. BRIM, Ph.D.
United States Senate, Office of Senator Elizabeth Warren - ASPET Postdoc Member

What sparked your interest in pharmacology?
When I was in college at Michigan State, I had the opportunity to spend an afternoon with Dr. Stephanie Watts in the Pharmacology Department and caught her enthusiasm! I was a microbiology major and had a great undergraduate experience in that discipline, but my afternoon with Dr. Watts stuck with me. When I knew I wanted to pursue a discipline that was more directly translational for my Ph.D., pharmacology seemed like a great fit.

Tell us about your most favorite experiment/study with which you have been involved.
My thesis project focused on the development of a biological drug product to treat cocaine toxicity. The final set of experiments aimed to determine how our enzyme was eliminated. We didn't know how it was eliminated, just that it was eliminated quickly. I performed immunohistochemistry to see if we could visualize it. I wasn't expecting to see anything, since we assumed it was eliminated completely by proteolysis, so I still remember how shocked I was looking at my slides and seeing the protein in the kidneys. We never would have guessed it was eliminated through renal filtration! I think that's the best part about science, being constantly surprised, and having the opportunity to be the first person to learn something no one else has known before.

What got you interested in health and science policy?
During my graduate work, I was lucky enough to work with collaborators in industry and at other academic institutions to move our enzyme toward clinical trials. I found that I enjoyed acting as a liaison between these groups and being a part of a multi-disciplinary team working toward the same goal more than performing the science directly. This was all happening at the same time as the health care reform debates, and taken all together, I knew I wanted to find a career that would allow me to stay engaged in science, drug development, and technology, while impacting public policy.

How did you transition from bench science into policy?
I moved to Washington, DC for a postdoc in clinical bioethics at the NIH, because it would give me the opportunity to explore regulatory and policy issues in clinical research and health care delivery. It also allowed me to develop my research, writing, and communication skills outside of the lab. The most transformative opportunity was my fellowship with Congresswoman Allyson Schwartz. I fell in love with the congressional work, was able to learn about the delivery side of health policy, and gain the skills necessary for a career on Capitol Hill.

How do you use your pharmacology background in your career?
Having a background in pharmacology is a fantastic base for any career. Pharmacology is such a collaborative and diverse discipline that you learn early on how to reach out to your peers, be fearless diving into new subject areas, and think outside the box. Having those skills and experiences are invaluable in any job. In my current position, I focus on issues surrounding Medicare and Medicaid, Affordable Care

Act implementation, the health care workforce, FDA, NIH, and all other health-related policy topics. I have to be ready to collaborate, learn new areas, and see things from multiple perspectives on a daily basis! I know that my training in pharmacology contributes to my success.

What do you find most challenging about your work?
Every day is something new, different, and unexpected, but that's also what makes my job so fun. I get to meet extraordinary people, learn about new science and technology, and be involved in transforming the health care system during a very exciting time. Working for the Senator, who is such a smart and passionate advocate, is incredibly rewarding, and although it's the most challenging work I've ever done, it doesn't feel like work!

Outside of science and health policy, what are your other interests?
I'm very active, whether it's biking, running, yoga, or something I've never done before. I also enjoy cooking, which probably stems from my love of experiments! Washington is a great city, and just exploring and taking advantage of what it has to offer is a hobby in itself!

Do you have any suggestions for ASPET regarding anything in the organization in which you would like to see improvement?
I think ASPET is a great resource for students and early career scientists, but I don't think that its members always use it to its full potential. ASPET could do more to educate its members about career development, both the young and senior members. The Mentoring Committee is taking great first steps in launching initiatives that empower students to shape their careers and inform mentors about how to help their students. Careers outside academia used to be considered "alternative careers," but now the academic track is really turning into the "alternative" to everything else. We need to make sure that students and early career scientists are equipped with the skills they need to enter the non-academic job market.

TASHA N. BLATT, B.E.
University of North Carolina at Chapel Hill - ASPET Graduate Student Member

What sparked your interest in pharmacology?
I graduated from Vanderbilt in 2005 with an engineering degree and ended up at the MLSCN site working with David Weaver and Jeff Conn. Though my initial work involved instrumentation management and robotic programming, I slowly began to work more with assay development and screening optimization. When we started to identify novel compounds, the rush of discovery was exhilarating, and I knew I wanted to work with pathway activation and drug interactions.

What drew you to the University of North Carolina at Chapel Hill?
I wanted a change of scenery, but not an extreme change. I had applied for jobs in the RTP area before obtaining my bachelor's degree and was very interested in all of the Triangle universities. The IBMS program (precursor to the current umbrella program) at UNC allowed for me to explore all of the possibilities of pharmacology in other departments.

How would the people in your program describe you?
That would depend on how well the mice and instrumentation are cooperating. Most people would describe me as focused and ambitious, because my project is in a field that is relatively new to our lab as well as quite challenging. Others know me as "the little baker" (see below).

What do you like to do for fun?
Cook! As a way to attack science-related stress (or celebrate major experiments), I bake various types of sweet treats for the lab (and nearby occupants). I also enjoy soccer, watching sports, reading, and spending time with my husband.

How are you hoping that membership in ASPET will benefit your career and interest in pharmacology?
I am hoping to network with other labs and put faces to the literature that I have been reading for the past six years. Though I am still not 100% set on a specific career path, having a group of like-minded scientists to connect with is invaluable to better understand what I want out of my degree.

What are your career goals or aspirations in pharmacology?
I love teaching. Not just classroom knowledge with test regurgitation, but hands-on learning at the bench. I get great satisfaction from passing a skill on to a new student and seeing them succeed with it. Though I may not be the type to run my own academic lab, I believe that I can impact future scientists by sharing my passion for teaching and learning. Of course, nothing quite beats the the thrill of being the first person to characterize a specific drug or pathway.

ASPET

Early Career Pharmacologists

Resources Available for Undergraduates, Graduate Students, and Postdoctoral Fellows

* Awards & Fellowships
* Information on Graduate Studies in Pharmacology
* Graduate Programs
* Career Resources
* Discussion Forums
* Social Networking Resources:
    - ~ Facebook
    - ~ LinkedIn
    - ~ Twitter
* ASPET Membership Information

Find us at:
http://www.aspet.org/knowledge/early-career/

We welcome your feedback! Is there something you'd like to see on our Early Career Pharmacologists page? Email us at gaxelrod@aspet.org.

aspet

Members in the News

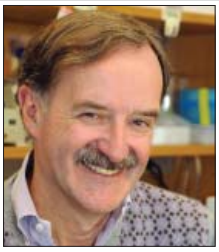
James E. Barrett

Drexel University recently appointed **James E. Barrett, Ph.D.**, founding director of the Clinical and Translational Research Institute. The Clinical and Translational Research Institute is a new University-wide initiative housed in the Drexel University College of Medicine. According to a mass email from the Drexel University College of Medicine sent in late April, the objective of the institute is to "promote and support outstanding research and academic programs that lead to innovative science, advanced therapeutic applications and, ultimately, improved clinical care." Dr. Barrett currently serves as professor and chair of the Department of Pharmacology and Physiology at Drexel and director of the university's Drug Discovery and Development Program. A past president of ASPET, he also currently serves as the chair of ASPET's Board of Publication Trustees and president of the Association of Medical School Pharmacology Chairs.

William B. Campbell

At the ASPET Annual Meeting at EB 2013, held in Boston, MA from April 20 – 24, **William B. Campbell, Ph.D.**, Professor and Chairman of Pharmacology and Toxicology at Medical College of Wisconsin, was presented with the 2013 PhRMA Foundation Award in Excellence. This award from the PhRMA Foundation recognizes past early career grantees who have gone on to lead distinguished careers in science or academia. In 1976-77, his first year as a faculty member at the University of Texas Health Science Center (currently known as Southwestern Medical Center) in Dallas, he received a two-year starter grant from PhRMA which he used to purchase lab supplies. Dr. Campbell's initial grant from PhRMA helped him provide data for an independent research article and led to key findings that resulted in his first grant from NIH and an NIH Research Career Development Award.
http://phrma.org/phrma-foundation-2013-award-in-excellence-blog

Garret FitzGerald



The Institut de France recently announced **Garret FitzGerald M.D., F.R.S.**, Chair of the Perelman School of Medicine's Pharmacology Department at University of Pennsylvania, as one of the winners of the 2013 Grand Prix Scientifique of the Lefoulon-Delalande Foundation. The Grand Prix Scientifique is considered to be the highest honor in cardiovascular research. Dr. FitzGerald received the award on June 5, 2013 at a presentation with the Institut de France and the French Academy of Sciences. FitzGerald, who is known for his work on aspirin, shares the prize with Carlo Patrono, M.D., for their development of low-dose aspirin which helps stave off cardiovascular disease. **http://online.wsj.com/article/PR-CO-20130416-909557.html**

Alfred Gilman

Alfred Gilman, M.D., Ph.D., was recently elected as an inaugural Fellow of the American Association for Cancer Research (AACR). The AACR Academy elects as Fellows people who have made significant scientific contributions and great progress in the fight against cancer. Gilman, who currently holds the title of professor emeritus at the University of Texas Southwestern Medical Center, won the 1994 Nobel Prize in Physiology or Medicine for his role in identifying G proteins and exploring how they interact with cells in order to gain a better understanding of many diseases including cancer. ASPET's biennial Goodman and Gilman Award in Receptor Pharmacology was named in part to honor Dr. Gilman's research contributions in pharmacology of biological receptors. Read more online at the *Hartford Courant*:
http://www.courant.com/community/new-haven/hcrs-72887hc-new-haven-20130326,0,1237094.story.

Robert J. Lefkowitz, Brian K. Kobilka, and Christian Felder

Left to right: Kobilka, Lefkowitz, and Felder

In a *Genetic Engineering & Biotechnology News* article, 2012 Nobel Laureate in Chemistry **Robert J. Lefkowitz, M.D.** (Duke University Medical Center), is quoted about biased agonism in GPCRs. Dr. Lefkowitz talks about his collaboration with **Brian K. Kobilka, M.D.**, (Stanford University School of Medicine) with whom he shared the Nobel Prize. The article, "Exploring GPCRs as Therapeutic Targets," also extensively quotes **Christian Felder, Ph.D.** (Eli Lilly and Company).
http://www.genengnews.com/gen-articles/exploring-gpcrs-as-therapeutic-targets/4830/

Juan Lertora

On March 6, 2013, **Juan Lertora, M.D., Ph.D.**, Director of the Clinical Pharmacology Program at NIH Clinical Center and Adjunct Professor of Medicine at Duke University, received the 2013 PhRMA Foundation Award in Excellence in Clinical Pharmacology at the annual meeting for the American Society for Clinical Pharmacology and Therapeutics (ASCPT) in Indianapolis, IN. This award honors former PhRMA Foundation grant recipients for outstanding career achievements. Prior to his time at NIH, Dr. Lertora was awarded a three-year PhRMA Foundation (known at the time as PMA Foundation) Faculty Development Award in Clinical Pharmacology while teaching pharmacology at Northwestern University. He later received a PMA Foundation Clinical Pharmacology Unit Award as an Associate Professor of Medicine and Pharmacology and Section Head of Clinical Pharmacology at the Tulane University School of Medicine. Dr. Lertora has been recognized previously for his educational work. He received the NIH Clinical Center Director's Award for Teaching and Training in 2008. Two years later, he was honored with the Ruth L. Kirschstein Mentoring Award from the National Institutes of Health for encouraging the continuation of mentoring activities, and establishing mentoring as a core value at NIH. The press release from the PhRMA Foundation can be viewed at:
http://www.phrmafoundation.org/download/PhRMA%20Foundation%202013%20Award%20in%20Excellence_Juan%20Lertora.pdf

Sidhartha D. Ray, Rick G. Schnellmann, and F. Peter Guengerich

Left to right: Ray, Schnellmann, and Guengerich

The Society of Toxicology (SOT) recently honored a trio of ASPET members at the SOT Annual Meeting and ToxExpo for their important achievements. SOT's Annual Meeting was held March 10 – 14, in San Antonio, TX.

Sidhartha D. Ray, Ph.D., Professor and Chair of the Department of Pharmaceutical Sciences at Manchester University (Fort Wayne, IN), received the 2013 Undergraduate Educator Award for "his outstanding contributions to the teaching of undergraduate students in toxicology and toxicology-related areas."

Rick G. Schnellmann, Ph.D., Professor and Chair of the Department of Drug Discovery and Biomedical Sciences at the Medical University of South Carolina (Charleston, SC), received the 2013 SOT Education Award for "his distinguished teaching and training of toxicologists and for his significant contributions to education in the broad field of toxicology."

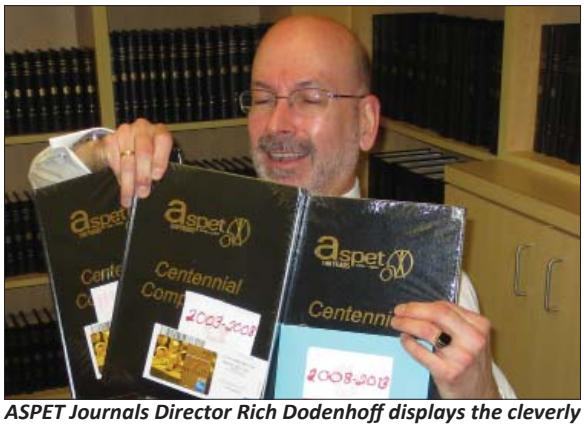
F. Peter Guengerich, Ph.D., Stanford Moore Professor of Biochemistry at the Vanderbilt University School of Medicine (Nashville, TN), received the 2013 SOT Merit Award for "recognition of his distinguished contributions to toxicology throughout his entire career."

For further details, please visit **http://www.eurekalert.org/pub_releases/2013-02/sot-sot021513.php.**

Staff News

Rich Dodenhoff

At ASPET's April 3, 2013 staff meeting, Journals Director **Rich Dodenhoff** was honored for his 15 years of service at ASPET.



ASPET Journals Director Rich Dodenhoff displays the cleverly disguised gifts he received for his 15 years of service at ASPET.

Matthew Hilliker

Matthew Hilliker, who joined ASPET in July 2012 as Director of Accounting, Membership & Subscriber Services, has been promoted to Chief Financial Officer. His duties remain the same, including managing ASPET's accounting operations and being responsible all financial activities of ASPET to ensure compliance with generally accepted accounting principles and government regulations. Additionally, Matt supervises and works with the Membership and Subscriber Services team.

Danielle Jordan

Danielle Jordan, ASPET's Awards Coordinator, has taken on the additional role of Meetings Manager. Danielle joined ASPET in June 2011. She is the primary point of contact for all issues related to ASPET Awards and the ASPET Annual Meeting. Danielle is working diligently on planning and organizing the ASPET Annual Meeting at Experimental Biology 2014 in San Diego, CA.

Keep in Touch...

Have you moved?
Changed your email address?
Changed jobs?

Keep us informed of changes to your contact information so you don't miss out on any important ASPET News!

Email us at membership@aspet.org

New ASPET Members

Regular Members

Ramachandran Balasubramanian, NIH
Aygul Balcioglu, Massachusetts General Hospital
Cecilia Bouzat, Instituto de Investigaciones Bioquimicas, Argentina
Ishfaq A. Bukhari, Shifa College of Medicine, Pakistan
Nigel W. Bunnett, Monash Inst of Pharmaceuticals Science, Australia
Michael F. Callahan, Univ of Missouri
Marian Castro, Univ of Santiago de Compostela, Spain
Zhongjian Chen, Guangdong Academy of Agricultural Sciences, China
Linda M. Console-Bram, Temple Univ School of Medicine
Daniel R. Deaver, Alkermes, Inc.
Ryan A. Dick, MyoKardia
Lir-Wan Fan, Univ of Mississippi Med Ctr
Carrie R. Ferrario, Univ of Michigan Medical School
John H. Griffin, The Scripps Research Institute
Michelle L. Halls, Monash Univ - Inst of Pharm Sci, Australia
Atsushi Hashimoto, Virginia Commonwealth Univ
Manish Issar, Western Univ of Health Sciences
W. K. Ajith Karunarathne, Washington Univ School of Medicine
Kathleen M. Knights, Flinders Univ School of Medicine, Australia
Alan Kopin, Tufts Univ Medical Center
Sukhwinder S. Lakhman, D'Youville College , DYC School of Pharmacy
David Y. Lee, Harvard Medical School/Mclean Hospital
Sang Haak Lee, St. Paul's Hospital, The Catholic Univ of Korea, South Korea
Lenard M. Lichtenberger, Univ of Texas Health Science Center at Houston
John Malysz, Univ South Carolina, South Carolina College of Pharmacy
Diane W. Morel, Philadelphia College of Pharmacy
Evangelia Papadimitriou, Univ of Patras, Greece
Elizabeth A. Rondini, Wayne State Univ
Linda M. Rorick-Kehn, Eli Lilly and Co.
Abu J. Sadeque, Arena Pharmaceuticals Inc.
Vincent S. Setola, West Virginia Univ
Barbara S. Slusher, Johns Hopkins Univ Brain Science Institute
Thomas E. Taylor-Clark, Univ of South Florida
Gabor Tigyi, Univ of Tennessee
Prakash Srinivasan Timiri Shanmugam, LSUHSC, SHreveport
Chandra Tucker, Univ of Colorado-Denver
Charles R. Wolf, Univ of Dundee, United Kingdom
Naunihal T. Zaveri, Lake Erie College of Osteopathic Medicine
Hong Zhou, Peking Univ, China

Affiliate Members

Kathleen G. Barrett, Wayne State Univ
Lucindo J. Quintans, Univ of Iowa

Postdoctoral Members

Shashi Bhushan, Emory Univ
Samuel Buxton, Iowa State Univ
Kei Hang Katie Chan, Univ of California, Los Angeles
Jesmond Dalli, Harvard Medical School Brigham and Women's Hospital
Ayesha Elias, St. Jude Children's Research Hospital
Xiang Li, Virginia Commonwealth Univ
Margaret Sperow, Temple Univ

Graduate Student Members

Nadia Ayala-Lopez, Michigan State Univ
Catherine M. Bell, Virginia Commonwealth Univ
Brandon M. Brown, Univ of California, Davis
Yi Cai, Long Island Univ
Tom De Bruyn, K. U. Leuven, Belgium
Ahmed M. Elharram, Queen's Univ, Canada
Chantell S. Evans, Univ of Wisconsin-Madison
Emily R. Garnett, Univ of Wisconsin-Madison
William M. Johnson, Case Western Reserve Univ
Faraz Kazmi, XenoTech LLC
Ayokulehin M. Kosoko, Univ of Ibadan College of Medicine, Nigeria
Lalitha Kurada, Univ of North Dakota
Yao Li, Univ of Vermont
Kassondra M. Meyer, Univ of Wisconsin-Madison
Robert C. Moot, Emory Univ
Sanket N. Patel, St. John's Univ
Christopher Racine, Marshall Univ
Janet O. Sangodele, Univ of Ibadan, Nigeria
Abdul Naveed Shaik, Massachusetts College of Pharmacy and Health Sciences
Anish Stephen, Sri Ramachandra Medical College & Research Institute, India
Marcus W. Stepp, Univ of Louisville
Andrew R. Stothert, Univ of South Florida
Rajiv H. Tikamdas, Univ of Florida - Coll of Pharmacy
Brendan J. Tunstall, American Univ
Brigitte C. Vanle, Univ of Iowa
Cody J. Wenthur, Vanderbilt Univ

Undergraduate Student Members

Natalie M. Arabian, Univ of Southern California
Linda O. Iheme, Univ of Benin School of Dentistry, Nigeria
Sana Khan, Manipal College of Medical Sciences, Nepal
Hyun Chung Kim, Rutgers Univ
Saad Salman, Manahil Coaching Acad, Pakistan
Rosa Y. Torres, Michigan State Univ
Zachary T. Wilson, Univ of Arizona

In Sympathy

ASPET Notes with Sympathy the Passing of the Following Members:

Desmond R. H. Gourley

Harry R. Keiser

Obituaries

Desmond R. H. Gourley (1922 – 2012), Pharmacology Education Pioneer

Des Gourley passed away on December 4, 2012 shortly after his 90th birthday. In addition to his contributions on the evolving concept of drug receptors, specifically insulin receptors in skeletal muscle, he was among the first to advocate supplementing classical pharmacology lecture/laboratory teaching with case-based clinical problem solving. As a well-known raconteur, in his retirement he was in demand to provide humorous human interest stories for regional public radio as well as presentations of his photos of flowers as objects d'art. Des was also an ardent genealogist. Before the days of the Internet, he traveled to many family home sites, traced his family back several generations, and published his work in genealogy journals.

Des was born in Thunder Bay, Ontario, Canada and served in the Canadian Officers Training Corps from 1942 – 1945. After receiving a BS in biochemistry from the University of Toronto, he studied with C.L. Gemmill and was awarded a Ph.D. in pharmacology in 1945 from the University of Toronto. After a brief stint in the Department of Zoology at the University of Toronto, he joined the faculty of the University of Virginia. From 1965 – 1968, he chaired the Department of Pharmacology at UVA. From 1973 – 1988, he established the Department of Pharmacology at Eastern Virginia Medical School (EVMS) as its founding Professor and Chair.

At UVA, he studied the role of insulin in skeletal muscle function and was on the leading edge of research into the biochemical mechanisms of opioid tolerance and dependence. He was well known for his work on the emerging concept of drug receptors including the isolation and characterization of membrane drug receptors. During a sabbatical at the Physiologisches Institut der Universitat, Freiburg, Germany, he compiled a book, *Interactions of Drugs with Cells* (Charles C. Thomas, pub., 1971). The slim volume is indicative of how little was known about drug receptors at that time. A very important contribution to insulin action field was Des's demonstration that insulin increased K+ uptake into liver, which resulted in establishing liver as an insulin sensitive organ. Others had argued that liver was insulin insensitive since insulin did not increase glucose transport.

A true passion of Des's was teaching. He was in demand as a lecturer and honored with many teaching awards. Des was a pioneer in identifying the emerging use of recreational and dependence producing drugs in the early 1970s and designed a lecture course for area schools and educators in Virginia. This resulted in a book entitled *Educational Perspectives on the Drug Crisis*, published by Jarmen Press in 1971. His contributions to the teaching of pharmacology, now known as pharmacotherapeutics, are still evident today. As early as 1966, he encouraged the inclusion of clinical material when teaching pharmacology. In 1983, as a founding member of the Committee on Knowledge Objectives in an Ideal Pharmacology Curriculum, Association for Medical School Pharmacology, he was on the forefront of the movement to establish written knowledge objectives to guide medical students. At EVMS, he initiated case-based clinical problem solving as an integral part of the pharmacology curriculum, which was rapidly adopted by other disciplines. He further developed this concept of Patient Oriented Problem Solving (POPS) under the sponsorship of the Upjohn Company for distribution to all medical schools. This concept of case based clinical problem solving is now widely employed in most medical, pharmacy and other allied health programs.

Des was a mentor, before the word was coined, a valued colleague and friend with a smile and cheerful word for all. Des is survived by his wife, Marjorie Curl Gourley, five sons Robyn, Alan, David, Bruce, and Donald, their wives, numerous grandchildren, and great-grandchildren.

prepared by Tom Westfall, Joe Lamer, and Pat Williams

John C. "Jack" McGiff, M.D. (1927 – 2013), Past Recipient of ASPET's Otto Krayer Award in Pharmacology

John Charles "Jack" McGiff passed away on February 2, 2013 at his home in Patchogue, NY. Dr. McGiff was a distinguished pharmacologist, medical scientist, teacher, chairman, and an articulate spokesman for pharmacology. He was Professor and Chairman Emeritus at New York Medical College (Valhalla, NY), had been a member of the American Society of Pharmacology and Experimental Therapeutics (ASPET) since 1966, a member of the American Society of Clinical Pharmacology and Therapeutics since 1975, a recipient of the Otto Krayer Award from ASPET in 1997, a member of the Association of Medical School Pharmacology Chairpersons, a member of the British Pharmacological Society since 1975, and Chairman of the Eicosanoid Research Association in 1970.

Jack McGiff received his B.S. degree from Georgetown University and an M.D. from the Columbia University College of Physicians and Surgeons. He interned at Cincinnati General Hospital and entered medical residency at the University of Virginia, which was interrupted by military service. After attending the U.S. Naval School of Aviation Medicine (Pensacola, FL), Dr. McGiff served in Korea and Japan with the Marine Air Groups 11 and 12 as senior medical officer and flight surgeon. On discharge, he returned to Columbia University as a research fellow of the American Heart Association (AHA). He completed his clinical training at the Pennsylvania Hospital and in 1962 was appointed to a joint faculty position in the Departments of Medicine and Pharmacology at the University of Pennsylvania. Dr. McGiff received an established investigatorship from the AHA (1964 – 1969) and in 1966 was awarded a grant from the National Institutes of Health (NIH), which he still held at the time of his passing.

From 1966 to 1971, Dr. McGiff served as Chief of Cardiology at St. Louis University. In 1971, he joined the Department of Pharmacology at the Medical College of Wisconsin and was made a Burroughs Wellcome Fund Scholar in Clinical Pharmacology. In 1974, he was invited by Sir John Vane to join the Wellcome Research Laboratories (England) as a visiting scientist, where he remained until 1976, when he was appointed Chair of Pharmacology at the University of Tennessee. Dr. McGiff had been Chairman of Pharmacology at New York Medical College from 1979 – 2010. He was married to Sara Leighton Babb (Sally) (deceased) and they had five children: John, Katharine (deceased), Sara, Jeremiah, and Elizabeth.

Dr. McGiff served on three study sections of NIH, concluding with service as Chairman of the Cardiovascular Renal Study Section (1994 – 1996). He was appointed to the NIH Arteriosclerosis, Hypertension and Lipid Metabolism Advisory Committee for a four-year period and served as a delegate in scientific exchange programs sponsored by NIH with Italy, Poland and the Soviet Union (1978 – 1984).

Over the past 20 years, Dr. McGiff had worked mainly in the area of the biochemistry, physiology, and clinical pharmacology of novel arachidonate metabolites generated by cytochrome P450 monooxygenases that serve critical mechanisms involved in circulatory and renal physiology and impact on the clinical management of hypertension, congestive heart failure, renal disease, and hepatic cirrhosis. His most recent research involved altered release of cytochrome P-450 metabolites of arachidonic acid in renovascular disease and demonstrating that red cells participate in the regulation of the circulation by producing and releasing epoxyeicosatrienoic acid.

Through the years, Dr. McGiff received several other awards that bear mentioning: the Outstanding Research Award from the Wisconsin Heart Association (1975); The Medal of Achievement, Copernicus Academy of Medicine, Krakow, Poland (1984); the CIBA Award for Hypertension Research from the AHA Council for High Blood Pressure Research (1986); the MERIT Award from NHLBI (1990 – 2000); the Richard Bright Award from the American Society of Hypertension (1997); the Lifetime Achievement Award in Hypertension from the Council for High Blood Pressure Research, AHA (2004); the Western Returned Scholars Association Lifetime Achievement Award, Beijing, China (2009).

He has also received honorary doctorates from the Copernicus Academy of Medicine in Krakow, Poland (1987) and Fu Jen University in Taiwan (2001).

prepared by James W. Fisher, Ph.D.

Division News

Behavioral Pharmacology Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Leonard L. Howell, Ph.D.**, Professor at the Emory University Yerkes National Primate Research Center's Division of Neuropharmacology & Neurologic Diseases, will serve as the Program Committee liaison for the Behavioral Pharmacology Division.

News

Behavioral Pharmacology Division Best Abstract Awards Competition

The competition at Experimental Biology 2013 included 10 postdoctoral fellows, 17 graduate students, and five undergraduate students. First place winners of the postdoctoral and graduate student competitions received $300, a certificate and ribbon, and a two-year appointment to the BPD Executive Committee. Second place winners received $200 and a certificate and ribbon. The winner of the undergraduate competition received $150 and a certificate and ribbon. The second place winner received $50 and a certificate and ribbon.

Postdoctoral Winners
First place – **Brian Kangas**, McLean Hospital, Harvard Medical School
Second place – **Dan Manvich**, Emory University

Graduate Student Winners
First place – **Harshini Neelakantan**, Temple University School of Medicine
Second place – **Clayton Bauer**, Virginia Commonwealth University School of Pharmacy

Undergraduate Student Winners
First place – **Jonathan Bauer-Erickson**, University of Arkansas for Medical Sciences
Second place – **Maria Briscione**, American University

From left to right: Leonard Howell, Chair; Harshini Neelakantan; Maria Briscione; Daniel Manvich; Brian Kangas; Clayton Bauer; and Paul Czoty, Secretary/Treasurer

Ray Fuller Lecture at Experimental Biology 2014

Jeff Witkin, Senior Research Advisor for Psychiatric Drug Discovery at Eli Lilly and Company, and Chair-Elect of the BPD, has been selected as the Ray Fuller Lecturer at EB 2014. His lecture will focus on treatment resistant depression and will be followed by a full symposium on the topic.

Cardiovascular Pharmacology Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Nancy L. Kanagy, Ph.D.**, Professor in the Department of Cell Biology & Physiology at the University of New Mexico Health Science Center, will serve as the Program Committee liaison for the Cardiovascular Pharmacology Division.

News

Cardiovascular Pharmacology Division Best Abstract Awards Competition

Postdoctoral Winners
First place – **Amy Arnold**, Vanderbilt University
Second place – **Susan Austin**, Mayo Clinic
Runner Up – **Styliani Goulopoulou**, Georgia Health Sciences University
Runner Up – **Wuqiang Zhu**, Indiana University School of Medicine

Graduate Student Winners
First place – **Alex Morrison-Nozik**, SUNY-Buffalo
Second place – **Asif Pathan**, University of Arkansas for Medical Sciences
Third place – **Miyoun Hong**, New York University School of Medicine
Fourth place – **Robert Helsley**, University of Kentucky
Runner Up – **Farnaz Bakhshi**, University of Illinois-Chicago
Runner Up – **Louise See Hoe**, Griffith University
Runner Up – **Paulo Pires**, Michigan State University
Honorable Mention – **Cameron McCarthy**, Georgia Health Sciences University

Front row (left to right): Amy Arnold, Louise See Hoe, Miyoun Hong, Farnaz Bakhshi, Asif Pathan
Back row (left to right): Cameron McCarthy, Styliani Goulopoulou, Alex Morrison-Nozik, Robert Helsley, Susan Austin

Lucchesi Lecture in Cardiac Pharmacology

Dr. Benedict Lucchesi gave the Lucchesi Lecture in Cardiac Pharmacology on his pioneering research entitled, "Reperfusion injury: Can it be prevented?" The Benedict R. Lucchesi Award in Cardiac Pharmacology was established to honor Dr. Lucchesi's lifelong scientific contributions to our better understanding and appreciation of the pharmacological treatment and prevention of cardiovascular disease and for his mentoring of countless prominent cardiovascular pharmacologists in translational approaches.

Drug Discovery and Development Division

Division Program Committee Liaision for 2013 – 2014

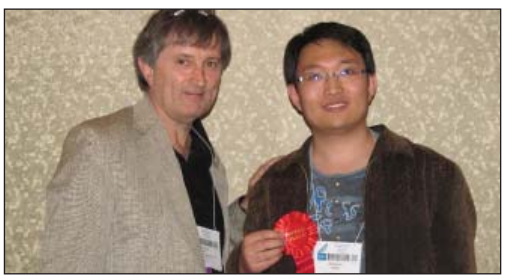
From July 1, 2013 – June 30, 2014, **Robert J. Leadley, Jr., Ph.D.**, Assistant Dean of Sciences at Schoolcraft College, will serve as the Program Committee liaison for the Drug Discovery and Development Division.

News

Drug Discovery and Development Division Best Abstract Awards Competition

Postdoctoral and Graduate Student Winners
First Place – **Jason Conley**, Purdue University
Second Place – **Zhiqiang Meng**, Harvard Medical School-New England Primate Research Center

Best Abstract Competition winner Jason Conley with Drug Discovery and Development Division Chair Kenneth Tew.



Second place winner Zhiquiang Meng with Drug Discovery and Development Division Chair Kenneth Tew.

Drug Metabolism Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Jeffrey P. Jones, Ph.D.**, Professor in the Department of Chemistry at Washington State University, will serve as the Program Committee liaison for the Drug Metabolism Division.

News

Summary of Experimental Biology 2013 Activities

Despite the uncertainty with investigations into the bombing at the Boston Marathon, the EB 2013 meeting was quite successful. The Drug Metabolism Division sponsored numerous activities including:

Drug Metabolism Division Best Abstract Awards Competition

Of the numerous high-quality posters that were presented at the competition on Sunday evening, the Drug Metabolism Division presented awards for the graduate student and postdoctoral categories.

Postdoctoral Winners

First place – **Lindsay Avery**, Johns Hopkins University School of Medicine, *Compartmental distribution and antiviral effect of efavirenz metabolites*

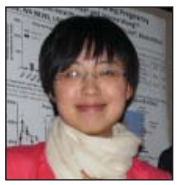
Second place – **Cara Nelson**, University of Washington, *Cellular retinoic acid binding proteins (CRABPs) channel retinoic acid to CYP26A1*

Third place – **Jin Kyung Lee,** University of Illinois-Chicago, *Induction of cytochrome P450 (CYP) 2E1 expression by placental lactogen*

Graduate Student Winners

First place – **Nora Lee**, University of Washington, *The organic cation transporter 3 (OCT3) facilitates fetal disposition of metformin during pregnancy*

Second place – **Lai Peng**, University of Kansas Medical Center, *Long noncoding RNAs and transcription of cytochrome P450s in mouse liver during maturation*



Third place – **Xian Pan**, University of Illinois-Chicago, *Induction of CYP2D6 expression during pregnancy is associated with an increased activity of hepatocyte nuclear factor 4a*

Drug Metabolism Early Career Achievement Award

This award is presented biennially to an investigator who is within 15 years of their terminal degree. As the recipient of the award for 2013, **Dr. Nina Isoherranen** presented her research entitled, *The biochemistry and clinical significance of CYP26 enzymes in regulating retinoic acid homeostatsis*.

Gillette Award Winners

Hamsell Alvarez accepts his James Gillette Award.

The James Gillette Best Paper Awards are presented annually for the best papers published in the ASPET journal, *Drug Metabolism and Disposition*. Two awards were presented in the areas of (a) drug metabolism and (b) drug transport and pharmacokinetics.

Dr. Hamsell Alvarez accepted the award in Drug Transport and Pharmacokinetics and presented their paper entitled, *Effects of PEGylation and Immune Complex Formation on the Pharmacokinetics and Biodistribution of Recombinant Interleukin 10 in Mice*.

Shigeyuki Uno accepts his James Gillette Award.

The Gillette Award winner in the drug metabolism category was **Dr. Shigeyuki Uno**. He presented his paper entitled, V*itamin D receptor activation enhances Benzo[a]pyrene metabolism via CYP1A1 expression in macrophages*.

Symposia

In addition to the Drug Metabolism Division Platform Session, the Division was the primary sponsor of two symposia. The first symposium focused on "Correlating Structure and Function of Drug Metabolizing Enzymes: An Ongoing Challenge." The session opened with an excellent overview of existing crystallographic structures of cytochrome P450 enzymes involved in xenobiotic metabolism. Given by **Dr. Eric Johnson** (Scripps Research Institute), this presentation emphasized the role of distinct active site cavities and interactions in respective protein/ligand relationships and presented exciting opportunities for more rapid structures of CYP2D6 using soaking methods. This was followed by a prospective look at emerging capabilities using protein NMR to examine the interactions between cytochrome P450 enzymes and cytochrome b5, NADPH-cytochrome P450 reductase, and ligands. The human steroidogenic CYP17A1 was the cytochrome P450 example presented in this talk by **Dr. Emily Scott** (University of Kansas). Attendees then learned from **Dr. Lianhong Xu** (Gilead Sciences) how structure, function, and medicinal chemistry approaches were employed to design the selective CYP3A4 inhibitor cobicistat. This novel pharmacoenhancer is now used in patients to extend the half-life of HIV drugs metabolized by CYP3A4. Finally, **Mr. Patrick Connick** (Louisiana State University Health Sciences Center – New Orleans) shared his work using bioluminescence resonance energy transfer to probe the physical interactions between cytochromes P450 enzymes in a membrane environment. This research, selected from the abstracts, focused specifically on CYP1A2 and CYP2B4.

The "Epigenetic Control of Drug Metabolism and Transport" symposium was sponsored by the Divisions for Drug Metabolism; Drug Discovery and Development; Integrative Systems, Translational and Clinical Pharmacology; Molecular Pharmacology; and Toxicology. Epigenetics is a rapidly evolving area, and there is also increasing evidence that drug-metabolizing enzymes and transporters are regulated by epigenetic factors including histone modification, DNA methylation, and noncoding RNAs. Four speakers, **Drs. Magnus Ingelman-Sundberg** (Karolinska Institution), **Xiaobo Zhong** (University of Connecticut), **Oliver Hankinson** (UCLA), and **Aiming Yu** (SUNY-Buffalo), presented their new findings on epigenetic mechanisms underlying variable drug metabolism and transport, consequent influence on pharmacological and toxicological effects, and implications for individualized medication. In addition, one abstract related to epigenetic mechanism was invited to give a 20-minute oral presentation, which was given by **Lai Peng** from University of Connecticut. Approximately 150 scientists and students attended this symposium on Sunday afternoon, April 21, 2013, and the audience joined good discussion on this hot topic.

Integrative Systems, Translational and Clinical Pharmacology Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Jeffrey Paul, Ph.D.**, Executive Director of Global Clinical Pharmacology and Exploratory Development at Astellas, will serve as the Program Committee liaison for the Integrative Systems, Translational and Clinical Pharmacology Division.

News

Integrative Systems, Translational and Clinical Pharmacology Division Best Abstract Awards Competition

Postdoctoral Winners

First Place – **Ross Corriden**, University of California, San Diego

Second Place – **Jieru Lin**, Thomas Jefferson University

Photo Not Available

Runner Up – **LeeCole Legette**, Oregon State University

Graduate Student Winners

First Place – **Naeem Patil**, University of Arkansas for Medical Sciences

Photo Not Available

Second Place – **Jacqueline Reilly**, University of Iowa

Photo Not Available

Third Place – **Garrett Ainslie**, University of North Carolina-Chapel Hill

Jeffrey Paul (far left) and Hamid Akbarali (far right) with those who were honorable mentions (from left to right) – Vaidehi Jatin Thanawala, Allyson Marshall, Melissa Geyer, Nisha Nanaware-Kharade, Aravind Gade, Mohamed Ghonim. Not pictured: Lola Yen

Molecular Pharmacology Division

Division Program Committee Liaision for 2013 - 2014

From July 1, 2013 – June 30, 2014, **Randy A. Hall, Ph.D.**, Professor in the Department of Pharmacology at the Emory University School of Medicine, will serve as the Program Committee liaison for the Molecular Pharmacology Division.

News

Molecular Pharmacology Division Best Abstract Awards Competition

Postdoctoral Winners
First Place – **Jamie Doyle**, Tufts Medical Center
Runner Up – **Jennie Conroy**, National Institute of Neurological Disorders and Stroke / NIH
Runner Up – **Vanessa Wehbi**, Univ of Pittsburgh School of Medicine

Graduate Student Winners
First Place – **Tyler Duellman**, University of Wisconsin-Madison
Finalist – **Mourad Ali**, University of Georgia
Finalist – **Pui Yee Chan**, University of Rochester
Finalist – **Jillian Rourke**, Dalhousie University
Finalist – **Chuu-Yun Wong**, Creighton University School of Medicine

Postdoctoral winners from left to right: first place Jamie Doyle (won $500 and a two-year appointment on the Molecular Pharmacology Division Executive Committee), runners up Vanessa Wehbi and Jennie Conroy ($250 each).

Graduate student winners from left to right: finalists Mourad Ali and Jillian Rourke ($150 each), first place Tyler Duellman (won $300 and a two-year appointment on the Molecular Pharmacology Division Executive Committee), and finalists Pui Yee Chan and Chuu-Yun Wong ($150 each).

Neuropharmacology Division

Division Program Committee Liaision for 2013 - 2014

From July 1, 2013 – June 30, 2014, **Michael W. Wood, Ph.D.**, Director of Licensing and Collaboration at AstraZeneca Pharmaceuticals LP, will serve as the Program Committee liaison for the Neuropharmacology Pharmacology Division.

News

Neuropharmacology Division Best Abstract Awards Competition

As usual, the judges had a very tough time selecting our 2013 winners from a group of outstanding students and postdoctoral fellows.

Postdoctoral Winners

First place – **Christopher Cottingham**, University of Alabama-Birmingham, C*ross-talk between beta and alpha2 adrenergic receptors in sympathetic neurons relies on protein kinase A and spinophilin*

Second place – **Nicole Northrop**, University of Toledo, *Increased plasma ammonia concentration contributes to methamphetamine-induced blood-brain-barrier damage*

Third place – **Harriet Schellekens**, University College Cork, *Dimerization of G-protein coupled receptors (GPCRs) in appetite regulation and food reward*

Graduate Student Winners

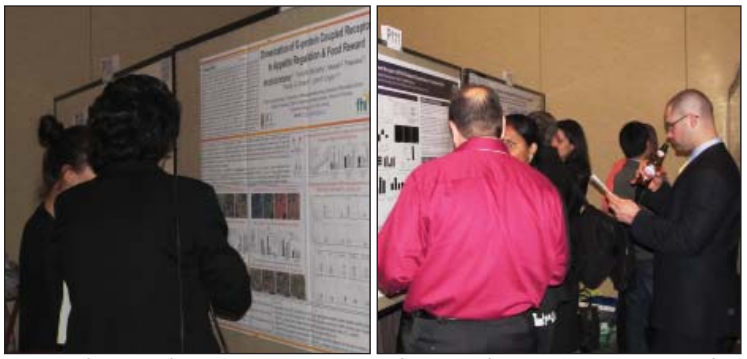
First place – **Loc Thang**, Michigan State University, *Macrophage (Mf) depletion reduced vascular oxidative stress, restored alpha-2 adrenergic autoreceptor (a2AR) function and attenuated blood pressure development in deoxycorticosterone acetate (DOCA)-salt hypersensitive rats*

Second place – **Edward Siuda**, from Washington University in St. Louis, *Optogenic and pharmacological activation of beta-adrenergic receptor signaling in the basolateral amygdala promotes anxiety and aversive behavior*

Third place (tie) – **Erin Bobeck**, Washington State University, *Blockade of extracellular regulated kinase1/2 (ERK1/2) alters antinociception and tolerance to DAMGO, but not to fentanyl*

Third place (tie) – **Brendan Harmon**, Northeastern University, *Intranasal delivery of pGDNF nanoparticles provides neuroprotection in the rat 6-hydroxydopamine model of Parkinson's disease*

Left to right: Dr. Nicole Northrop (secnd place, postdoctoral award), Brendan Harmon (third place, student), Dr. Harriett Schellenkens (third place, postdoctoral), Dr. Lynette Daws (Chair, Neuropharmacology Division), Edward Siuda (second place, student), Erin Bobeck (third place, student) and Dr. Eric Barker (Secretary/Treasurer, Neuropharmacology Division). All winners received a cash prize. First place winners for each category were honored with membership to the Division's Executive Committee.



Neuropharmacology Division Posters at the Best Abstract Competition at the ASPET Annual Meeting at EB 2013

Executive Committee Member News

The Neuropharmacology Division had a very successful meeting in Boston 2013. At the Executive Committee meeting, we welcomed our new Members-at-Large, **Dr. Charles Nichols**, **Dennis Paul**, and **Misty Smith**. In addition we welcomed our new Postdoctoral Fellow representatives, **Drs. Vikas Dukande** and **Christopher Cottingham**, as well as new student representative **Mr. Loc Thang**.

We also gave thanks to our outgoing Executive Committee members, **Dr. Peggy Gnegy** (Immediate Past-Chair), **Dr. Linda Dykstra** (Immediate Past-Secretary/Treasurer), **Dr. Lynn Wecker** (ASPET Council Liason), **Dr. Spring Farrell** (Postdoctoral Representative) and **Mr. Jason Kehrl** (Student Representative). All made tremendous contributions to our division for which we are very grateful.

With **Dr. Laura Bohn** and **Dr. Lakshmi Devi** beginning their term as Chair and Secretary/Treasurer, respectively, on July 1, 2013, we will be holding elections for Chair-Elect and Secretary/Treasurer-Elect later this year.

Highlights from Boston

Our own **Lakshmi Devi** from Mount Sinai School of Medicine was the keynote speaker for the "Postdoctoral Scientist Award Finalist" symposium. Dr. Devi gave a timely and excellent presentation titled, "How to do big science on a modest budget: Lessons from deorphanizing a G protein-coupled receptor," which was inspiring for investigators across the board.

Division member, **Dr. Arthur Christopoulous**, from Monash University, Melbourne, Australia, and recipient of this year's J.J.Abel Award, gave an outstanding lecture titled, "Reciprocal relationships: The yin and yang of GPCR allostery." The turnout at this lecture was standing room only, with many spilling out into the hallway to hear the elegant work of Dr. Christopoulous.

The Neuropharmacology Division co-sponsored the 4th GPCR Colloquium at the end of the ASPET meeting which was co-organized by our own Laura Bohn. The two-day colloquium was kicked off by Nobel Laureate **Robert Lefkowitz**, who presented the Sir James Black Lecture. The Colloquium featured the latest in developments in GPCR structure and function and included a reception and poster session. It was extremely well attended, with more than 600 participants at the opening.

This year, the Neuropharmacology Division joined with the Behavioral Pharmacology Division in a joint mixer. Winners of the Neuropharmacology Best Student and Best Postdoctoral Fellow Competition were announced, and as always, a good time was had by all.

Members of the Neuropharmacology and Behavioral Pharmacology Divisions at their joint mixer at EB 2013

Humphrey Rang of the British Pharmacological Society presents the Sir James Black Lecture Award to Robert Lefkowitz.

Future Events

Mark your calendars. This year, the Neuropharmacology Division will be hosting a mixer at the Society for Neuroscience meeting to be held on Monday, November 11, 2013.

This social event is for faculty, students, alumni, and others with an interest in Neuropharmacology and related disciplines. Our goal is to provide an exciting networking opportunity for neuropharmacologists attending the Society for Neuroscience's annual meeting to socialize with like-minded researchers. We hope that you will join us to meet those who are making neuropharmacology an exciting field. Light refreshments and libations will be provided, and there will be no charge or registration for SfN annual meeting participants. Keep an eye out for more details closer to the event.

We are also creating a new travel award to allow junior trainees (postdoctoral fellows and students) to attend neuropharmacology-related meetings. Details on how to apply will be posted on the Division's website in the coming months: **http://www.aspet.org/Neuropharmacology/Home/**.

Annual Meeting Programming for 2014

Programming is shaping up nicely for the Neuropharmacology Division for the ASPET Annual Meeting at EB 2014. The shortened time frame for submissions of proposals is working well, with many exciting ideas coming forward. The ASPET programming committee will finalize symposia this June for the 2014 meeting in San Diego. Stay tuned for details.

Getting Involved

We would love to hear from our membership. What can we do better? What would you like to see on our website? We are always looking for ways to improve, so all ideas or comments are most welcome. Please send them to **Laura Bohn** (**LBohn@scripps.edu**) or **Lynette Daws** (**daws@uthscsa.edu**).

Pharmacology Education Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Senthil Kumar Rajasekaran, Ph.D.**, Associate Professor at Oakland University's William Beaumont School of Medicine, will serve as the Program Committee liaison for the Pharmacology Education Division.

Awards at EB 2013

Robert Theobald congratulates Kelly Karpa, Ph.D. on membership to the Academy of Pharmacology Educators.

A. Laurel Gorman, Ph.D. receives her Pharmacology Education Travel Award from Division Executive Committee Member Robert J. Theobald, Ph.D.

Michelle M. Duffourc, Ph.D. receives her Pharmacology Education Travel Award from Division Executive Committee Member Robert J. Theobald, Ph.D.

Robert Theobald presents Kim Eberle-Wang, Ph.D. with a special award to recognize her contributions in creating awareness in Pharmacology among high school students.

Toxicology Division

Division Program Committee Liaision for 2013 – 2014

From July 1, 2013 – June 30, 2014, **Jack A. Hinson, Ph.D.**, Distinguished Professor in the Division of Pharmacology & Toxicology at the University of Arkansas for Medical Sciences, will serve as the Program Committee liaison for the Toxicology Division.

News

Toxicology Division Best Abstract Awards Competition

Postdoctoral Winner

First Place – **Prasad Krishnan**, Pennsylvania State University

Graduate Student Winners

First Place – **Jessica Morgan**, University of Tennessee Health Science Center

Second Place – **Hridgandh Donde**, University of Louisville

Chapter News

Great Lakes Chapter

SAVE THE DATE! 26th Annual Scientific Meeting: Updated Program

Friday, June 14, 2013
The Searle Conference Center
Rush University Medical Center, Chicago, IL
1725 W. Harrison St.
Professional Building
Chicago, IL

To register for the meeting, ASPET Members should login to the Members Only section of the website: **https://www.aspet.org/login.aspx**. Nonmembers should visit **https://www.aspet.org/cvweb_aspet/cgi-bin/eventsdll.dll/EventInfo?sessionaltcd=GLC2013** to register.

Visit **http://www.aspet.org/GLCMeeting/** for more information.

2013 Annual Meeting Program

8:30 – 10:30 a.m. Registration (The Searle Conference Center, Professional Building, 5th Floor); Continental Breakfast (Main Lounge); Poster Session (Main Lounge)

8:30 – 12:00 p.m. Vendor Exhibits (Main Lounge)

10:45 – 11:45 a.m. **Young Investigator Symposium** (542 Brainard Room)

10:45 – 11:00 a.m. *MicroRNA-30c regulates EMT, drug resistance and breast tumor invasion*
Jessica Bockhorn, Postdoctoral Fellow, University of Chicago

11:00 – 11:15 a.m. *Reprogramming of the ovarian cancer microenvironment by miRNA*
Fred Kohlhapp, Postdoctoral Fellow, Northwestern University

11:15 – 11:30 a.m. *Micro-RNA-mediated downregulation of Kv channels in pulmonary arterial hypertension*
Nichole Pohl, Postdoctoral Fellow, University of Illinois at Chicago

11:30 – 11:45 a.m. *Inhibition of microRNA-200a promotes endothelial cell proliferation in pulmonary arterial hypertension*
Cristina Bardita, M.D., Graduate Student, Rush University

12:00 – 1:00 p.m. Lunch (Fenger-Sippy Room); Lunch and Learn Career Workshop (Fenger-Sippy Room)

1:00 – 4:15 p.m. **Symposium: Functional microRNA in disease: Novel opportunities for pharmacology** (542 Brainard Room)

1:00 – 1:15 p.m. Welcome and Opening Remarks by **Alejandro Mayer**, Midwestern University, President, GLC-ASPET, and Symposium Chairs **Eric Blomme**, AbbVie, and **Maria Barbolina**, UIC

1:15 – 1:45 p.m. *Regulating the microRNA machinery*
Zain Paroo, University of Illinois at Chicago

1:55 – 2:25 p.m. *MicroRNAs as biomarkers of safety and efficacy in drug discovery and development*
Jonathan Maher, Abbott Laboratories

2:35 – 3:05 p.m. *MicroRNA roles in tumorigenesis and chemotherapy resistance*
Gianpiero Di Leva, The Ohio State University

3:15 – 4:15 p.m. **Keynote Address:** *MicroRNAs in cardiovascular disease: Current progress and challenges*
Chunxiang (Kevin) Zhang, Rush University

4:30 – 5:00 p.m. **Business Meeting and Awards Presentation**
Election Results: **Alejandro Mayer**, GLC ASPET President
Awards: Presented by Poster Competition Coordinators
Ricardo Monzon, Xavier University and
Saverio Gentile, Loyola University Medical Center

Mid-Atlantic Pharmacology Society

Save the Date: Mid-Atlantic Pharmacology Society 2013 Meeting: October 7, 2013

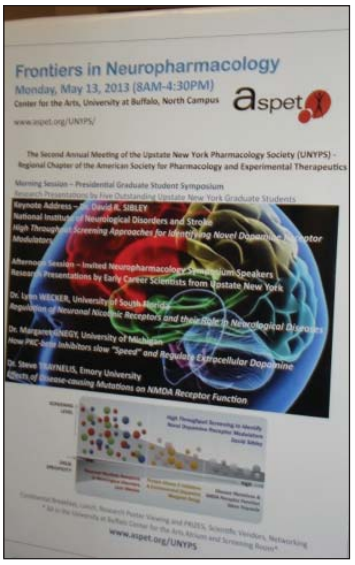
The Mid-Atlantic Pharmacology Society is pleased to announce its annual meeting: "G-protein Coupled Receptors: Current thoughts and new directions." The 2013 meeting will be Monday, October 7, 2013 at the Science and Technology Center at the University of the Sciences in Philadelphia, PA. The University of the Sciences will be our host for the meeting. **Lakshmi Devi, Ph.D.**, from the Icahn School of Medicine, Mount Sinai, will give the keynote presentation. Other invited speakers with confirmed presentations include: **Lawrence (Skip) Brass, M.D., Ph.D.**, from the University of Pennsylvania; **J. Silvio Gutkind, Ph.D.**, from the National Institutes of Health; **Madhu Chintala, Ph.D.**, from Merck; **Mary Abood, Ph.D.**, from Temple University; and **Athan Kuliopoulos, M.D., Ph.D.**, from Tufts University.

The day will begin with poster presentations by undergraduate and graduate students, postdoctoral fellows, and research associates. Two trainees will be invited to give 10-minute oral presentations during the symposium. The day will end with an awards ceremony and networking reception.

Online registration and a complete schedule will be available on the MAPS/ASPET website, **http://www.aspet.org/MAPS/**, in early June. Please join us! For additional information, contact **Diane Morel** at **d.morel@usciences.edu**.

Upstate New York Pharmacology Society

Summary from the 2nd Annual Scientific Meeting



The Upstate New York Pharmacology Society (UNYPS) Chapter of ASPET held its 2nd Annual Scientific Meeting on May 13, 2013, at the University at Buffalo Center for the Performing Arts in Buffalo, NY. The theme of the meeting was entitled **Frontiers in Neuropharmacology** with principal addresses by the Keynote Speaker **David R. Sibley, Ph.D.**, and by special invited investigators under the Frontiers of Neuropharmacology theme: **Lynn Wecker, Ph.D.**, **Margaret Gnegy, Ph.D.**, and **Steve Traynelis, Ph.D.**

Over 100 pharmacologists attended, including principal investigators, principal scientists, postdoctoral fellows, graduate and undergraduate students from the University of Toronto, Albany College of Pharmacy and Health Sciences, the University of Rochester, Roswell Park Cancer Institute, D'Youville College, Albany Molecular Research Institute, EMD Millipore, Invitrogen Life Technologies, Bio-Rad, and the University at Buffalo Schools of Pharmacy, Arts and Sciences, Medicine and Biomedical Sciences, and Office of Research and Economic Development.

Selected graduate students delivered oral presentations of their research in the opening Presidential Graduate Student Symposium. The meeting ended with distribution of awards to student presenters and the best poster presenters as judged by a diverse panel of judges and with the announcement of the future president-elect, **Gregory G. Tall, Ph.D.**, of the University of Rochester.

Frontiers in Neuropharmacology UNYPS 2013 Program:

8:00 – 9:00 a.m.	Registration and Continental Breakfast – Center for the Arts Atrium
8:00 a.m. – 1:00 p.m.	Poster Sessions (3) – Center for the Arts Atrium. Thirty posters were presented, including 18 doctoral students, seven master's students, and five undergraduate students.
8:00 a.m. – 1:00 p.m.	Vendor Exhibits – Center for the Arts Atrium
9:00 – 9:15 a.m.	Welcome and Opening Remarks **Peter Bradford**, University at Buffalo, Meeting Organizer, UNYPS Secretary-Treasurer – Center for the Arts Screening Room
9:15 – 10:15 a.m.	**Graduate Student Symposium** – Moderator **Kim Bernosky-Smith**, D'Youville College
9:15 – 9:30 a.m.	*Identification and characterization of pharmacological chaperones of the dopamine transporter* **Pieter Beerepoot**, University of Toronto
9:30 – 9:45 a.m.	*Ric-8A deletion as tumor suppressor of oncogenic G-protein alpha subunit alleles* **Bharti Patel**, University of Rochester
9:45 – 10:00 a.m.	*Effects of imidazoline I2 receptor agonist 2-BFI on the development of tolerance and physiological/behavioral dependence to morphine in rats* **David Thorn**, University at Buffalo
10:00 – 10:15 a.m.	*Characterization of neuronal activation responses to social stimulation in a genetic model of reduced NMDA receptor function* **Catharine Mielnik**, University of Toronto
10:15 – 11:00 a.m.	Poster Review, Coffee break, fruits and muffins, Center for the Arts Atrium
11:00 a.m. – Noon	**Keynote Address:** *High throughput screening approaches for identifying novel dopamine receptor modulator* **David R. Sibley**, National Institute of Neurological Disorders and Stroke, NIH

Noon – 1:00 p.m.	Lunch, Poster Review, and Vendor Exhibits – Center for the Arts Atrium
1:00 – 3:00 p.m.	**Frontiers in Neuropharmacology Symposium** – Moderator **Suzanne Laychock**, University at Buffalo – Center for the Arts Screening Room
1:00 – 1:40 p.m.	*Regulation of neuronal nicotinic receptors and their role in neurological disorders* **Lynn Wecker**, University of South Florida
1:40 – 2:20 p.m.	*How protein kinase C beta inhibitors slow "speed" and regulate extracellular dopamine* **Margaret Gnegy**, University of Michigan
2:20 – 3:00 p.m.	*Effects of potential disease-causing mutations on NMDA receptor function* **Steve Traynelis**, Emory University
3:00 – 3:30 p.m.	Concluding Remarks, Business Meeting, and Awards Presentation Election Results: **Gregory Tall**, University of Rochester, elected President-Elect; Awards: **Peter Bradford**, Judging Coordinator

A panel of twelve judges previewed all abstracts and posters and teams of judges interviewed all poster presenters. Awards and cash prizes were given to the following top-ranked posters:

Ph.D. Graduate Students

Hannah Stoveken, Pharmacology and Physiology, University of Rochester, *Biochemical reconstitution of adhesion GPCR GPR56 activation of heterotrimeric G proteins*
Meaghan Paganelli, Neuroscience Program, University at Buffalo, *Molecular mechanisms of local anesthetic inhibition of NMDA receptors*
Vincent Lam, Pharmacology and Toxicology, University of Toronto, *Development of a new homogenous assay for quantitative measurement of surface expression of membrane proteins*
Shannon Clough, Neuroscience Program, University at Buffalo, *Methamphetamine-induced conditioned place preference in C3H/HeN mice is observed during the day (ZT 6-8) but not at night (ZT 19-21)*

Master's Students

Taylor Warren, Pharmacology and Toxicology, University at Buffalo, *Pre-exposure of the urotensin II receptor to ligand differentially reduces the response to subsequent additions of urotensin II or urotensin II-related peptide*
Katie Evely, Pharmacology and Toxicology, University at Buffalo, *Characterization of MT1 melatonin receptor-expressing neurons in the medial habenula, habenula commissure and periaqueductal grey of the C3H/HeN mouse brain*

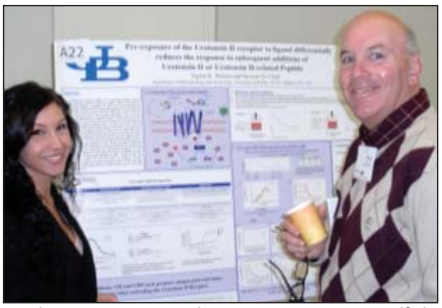
Undergraduate Students

Danielle Precourt, Pharmacology and Toxicology, University at Buffalo, *Melatonin modulation of novel object recognition*
Jason Ma, Pharmacology and Toxicology, University at Buffalo, *MT1 melatonin receptor role in methamphetamine-induced locomotor sensitization in C57BL/6 mice*

Photo Gallery from the ASPET Upstate New York Pharmacology Society Meeting

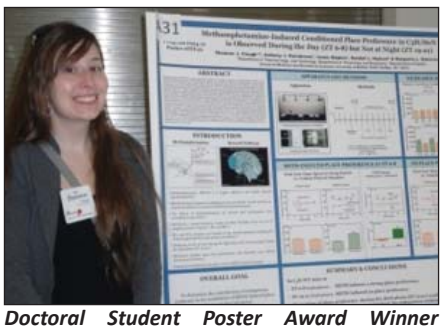
Suzanne Laychock, current UNYPS President-elect

UNYPS ASPET Symposium organizer Peter Bradford welcomes participants



Taylor Warren with University at Buffalo Associate V.P. for Research Ken Tramposch

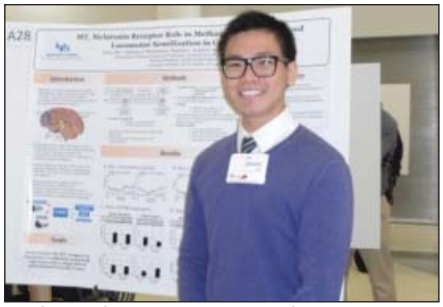
Symposium speaker Steve Traynelis with Paul Kammermeier of University of Rochester



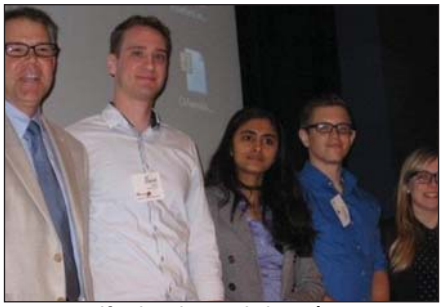
Doctoral Student Poster Award Winner Shannon Clough of University at Buffalo

Undergraduate Poster Award Winner Danielle Precourt of University at Buffalo

UNYPS ASPET Keynote Speaker David R. Sibley of NINDS

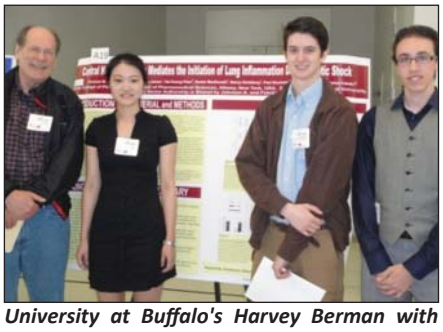


Undergraduate Poster Award Winner Jason Ma of University at Buffalo



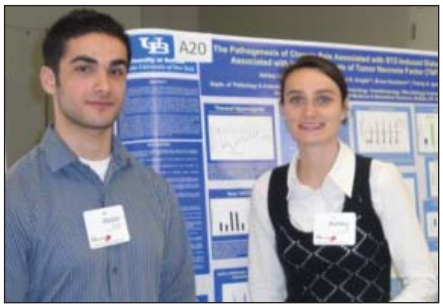
Peter Bradford with David Thorn (University at Buffalo), Bharti Patel (University of Rochester), Pieter Beerepoot (University of Toronto), and Catharine Mielnik (University of Toronto)

Lynn Wecker, David Sibley, Peggy Gnegy, Margarita Dubocovich, and Pablo Paez

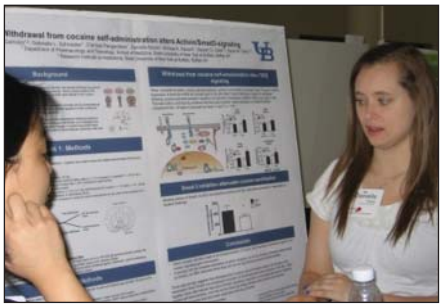


University at Buffalo's Harvey Berman with Albany College of Pharmacy's Jianya Peng, Hunter MacDonald, and Vincenzo Russo

Alissa Verone of the Roswell Park Cancer Institute explains her research.



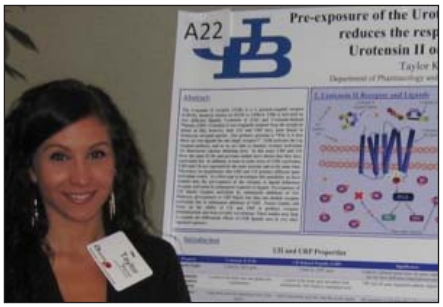
Abdel Alnaji and Ashley Re, graduate student researchers from University at Buffalo



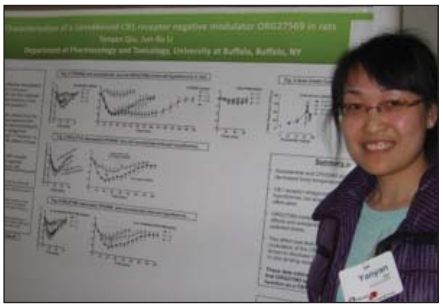
Danielle Adank, undergraduate research presenter from University at Buffalo

Graduate Symposium speaker Catharine Mielnik of University of Toronto

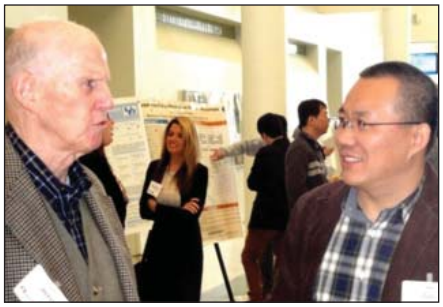
Jianya Peng of the Albany College of Pharmacy and Health Sciences



Master's Student Award Winner Taylor Warren of University at Buffalo



Yanyan Qiu of the University at Buffalo Department of Pharmacology and Toxicology



Jerry Winter and Jun-Xu Li, ASPET members from University at Buffalo

UNYPS Councilor Kim Bernosky-Smith of D'Youville College

UNYPS Graduate and Undergraduate Student Research Award Winners

Membership Information

Definitions of Categories of ASPET Membership

Regular Members: Any doctoral level investigator who has conducted and is the primary author on at least one publication of an original study in the area of pharmacology published in a peer-reviewed journal is eligible for membership in ASPET. Exceptions may be made for someone who does not meet the degree requirement but who has made major research contributions to pharmacology. Regular members must be nominated by one (1) Regular or Retired ASPET member.

Postdoctoral Members: Any qualified person who has received their Ph.D. or equivalent degree in pharmacology or a related field within the past five years is eligible for Postdoctoral membership. Postdoctoral members will receive the same benefits as Regular members, including the right to vote in ASPET elections. Individuals may remain in the Postdoctoral membership category for a maximum of five (5) years from the date of receipt of their PhD (or equivalent) degree after which time they must upgrade to Regular Membership. Applicants for Postdoctoral membership must be sponsored by one (1) Regular or Retired ASPET member.

Affiliate Members: An investigator who does not meet the requirements for Regular membership because of the lack of a degree or lack of publication is eligible to apply for Affiliate membership. Affiliate members receive all the same member benefits as Regular members except that they may not vote in ASPET elections. Affiliate members must be nominated by one (1) Regular or Retired ASPET member.

Student Members: Individuals who are enrolled in undergraduate, graduate, or professional degree programs are eligible for Student membership in ASPET. Student members receive all the same benefits as Regular members except that they may not vote in ASPET elections. Student members must be nominated by one (1) Regular or Affiliate ASPET member. Upon completion of their research doctoral degree, student members must upgrade to Postdoctoral Membership.

Sponsors should send an email or letter addressing the applicant's qualifications for ASPET membership directly to the ASPET office (membership@aspet.org).

Regular Member Benefits (Dues $150):

- Reduced page charges for corresponding authors to publish in ASPET journals – pay $50/page instead of $90/page and save enough with one four-page article to pay your annual ASPET dues!
- No submission fee to submit your paper to ASPET journals (*The Journal of Pharmacology and Experimental Therapeutics*, *Drug Metabolism and Disposition*, and *Molecular Pharmacology*)
- Free full-text access to all four online ASPET journals, including all back issues
- Free subscription to *The Pharmacologist* (online)
- Reduced registration fees for ASPET meetings
- Sponsorship of papers at the ASPET meeting
- Free listing in the FASEB Directory
- Membership in multiple ASPET Divisions for no additional dues

Postdoctoral Members (Dues $70) have all the benefits of Regular members, and may receive:

- Best abstract awards and travel awards for young scientists at the ASPET meeting

Affiliate Members (Dues $150) have all the benefits of Regular members except they may:

- Sponsor candidates for Student membership only
- Not sponsor a paper for a non-member at a Society meeting
- Not vote in Society elections
- Not hold an elected office in the Society

Student Members (Dues $30) have all the benefits of Regular members except they:

- Pay no dues their first year
- Pay only $30 annual dues thereafter. Undergraduate Student members pay no dues and get their first graduate year free
- Must have their papers at Society meetings sponsored by a member
- May not vote in Society elections nor hold an elected office in the Society

Application Instructions

Submit the completed Application for Membership form or use the online application form on the ASPET web site at **www.aspet.org/membership/apply**. Submit a current *curriculum vitae* including bibliography for Regular, Affiliate, Postdoc, and Graduate Student Membership.

Sponsor Statements: Submit a statement of qualifications of the applicant from one Regular/Retired/Postdoctoral Member of ASPET for Regular Membership, Postdoctoral Membership, Affiliate Membership and Student Membership (Affiliate Members may also sponsor student applicants). In addition to the statement certifying that the applicant is qualified for ASPET membership, sponsors should provide their own current address, phone, fax, and email. It is the responsibility of the applicant to insure that these documents are submitted to the ASPET office.

American Society for Pharmacology and Experimental Therapeutics
9650 Rockville Pike, Bethesda, MD 20814-3995 USA
Phone: 301-634-7060 ♦ Fax: 301-634-7061 ♦ www.aspet.org

Membership Application

Please Complete All Sections:

Section 1: Application Details

Application for:

- ❑ **Regular Membership**
- ❑ **Affiliate Membership**
- ❑ **Graduate Student – Expected Date of Graduation:** _____
- ❑ **Undergraduate Student - Year:** ❑ **Fr** ❑**Soph** ❑**Jr** ❑**Sr**

Section 2: Source

How did you hear about ASPET:

- ❑ **Meeting** _____
- ❑ **ASPET Journal** _____
- ❑ **Mentor** _____
- ❑ **Other** _____

Section 3: Personal Information

Name:

Institution:

Address:

Telephone:

Fax:

Email:

Section 4: Optional Demographics (Not Required)

Date of Birth: _____

Sex: ❑ Female ❑ Male

Ethnicity:

- ❑ Asian
- ❑ Black or African American
- ❑ American Indian or Alaskan Native
- ❑ Hispanic or Latino
- ❑ Native Hawaiian or Pacific Islander
- ❑ White
- ❑ Other: _____

The information in this section will be used by ASPET to collate statistics and will be kept private. Completion of this section is voluntary.

Section 5: Sponsor (Must be an ASPET Member)

Name and email of your sponsor:

Please have one sponsor send us a brief letter or e-mail outlining your qualifications for Membership in ASPET to the Membership Department at membership@aspet.org.

Section 6: Division Selection

Divisions: *Division membership is a benefit of ASPET membership and there is no additional charge to belong to a division. It is highly recommended that you join a division so that you may take full advantage of Society participation. Joining a division allows you to participate in creating the scientific program for the annual meeting, network with people in your field at mixers and divisional programs, and receive special notices and newsletters about items and activities of interest in your field. Be sure to pick a division!*

Indicate primary (1) and as many secondary (X) divisions to which you wish to belong:

___Division for Behavioral Pharmacology
___Division for Cardiovascular Pharmacology
___Division for Drug Discovery & Development
___Division for Drug Metabolism
___Division for Integrative Systems, Translational & Clinical Pharmacology
___Division for Molecular Pharmacology
___Division for Neuropharmacology
___Division for Pharmacology Education
___Division for Toxicology

Section 7: Curriculum Vitae

Regular, Affiliate, and Graduate Student applicants: Please send your *Curriculum Vitae* (including bibliography) by email to the Membership Department at membership@aspet.org.

Undergraduate Student Applicants Only:

Current Education :

Expected Degree & Date: School: City/State/Country: Major Field:

Applications are reviewed on a rolling basis. Please DO NOT submit payment with your application.
Upon membership approval, you will be sent a dues statement and welcome package.
Student Membership is FREE for the first year.

Call or e-mail the ASPET Membership Department for additional information: 301-634-7060 / membership@aspet.org.

Appendix

Abstracts presented at the 2013 Upstate New York Pharmacology Society Meeting

FRONTIERS OF NEUROPHARMACOLOGY KEYNOTE ADDRESS

A1. High throughput screening approaches for identifying novel dopamine receptor modulators

David R. Sibley; Molecular Neuropharmacology Section, National Institute of Neurological Disorders and Stroke, NIH

We have recently used high throughput screening approaches to identify novel modulators of various dopamine receptor (DAR) subtypes. We are particularly interested in identifying allosteric ligands, as these have the potential to be more highly selective than currently available therapeutic agents, which are orthosteric in nature. There are various ways in which G protein coupled receptors can be modulated by allosteric ligands, which include affinity and efficacy modulation as well as the possibility for allosteric agonism. Allosteric agents also offer the possibility for large therapeutic windows, the potential for partial antagonism and as well as less or no desensitization for allosteric agonists. As part of our probe discovery program, we screened ~400,000 compounds using an assay that can detect ligands with agonist (allosteric or orthosteric), potentiator (allosteric), or antagonist (allosteric or orthosteric) activities. A wide range of compounds were detected and evaluated and one scaffold with a unique pharmacological profile at the D_2 and D_3 receptors is reported here. Using a beta-arrestin recruitment assay to compare activity at all DAR subtypes, we identified a ligand, MLS3508 (compound 3508), that selectively activates the D2R but not other DAR subtypes. Compound 3508 is an antagonist at the D_3R for beta-arrestin recruitment and has no activity at the D_4R or D1-like DARs (D_1R and D_5R). Compound MLS3508 exhibits full agonist activity with EC50 values ranging from 100 nM – 1 μM in three different functional assays for the D_2R: beta-arrestin recruitment, Ca^{2+} mobilization, and inhibition of cAMP accumulation. Using a Go BRET activation assay, we found that MLS3508 is a full agonist at the D_2R but displays weak partial (<10%) agonist activity at the D_3R. Interestingly, MLS3508 is a full antagonist with no agonist activity on D_2R-linked or D_3R-linked GIRK channel activation, indicating that it is a biased agonist. This is most striking for the D_2R, at which MLS3508 is a full agonist at all the other pathways evaluated. Consistent with our studies in heterologous cells, application of MLS3508 elicited no response in D_2R-activated, whole cell GIRK-mediated currents measured in dopaminergic neurons in mouse midbrain slices, while it effectively blocked the response elicited by the full agonist quinpirole. Molecular modeling studies suggest subtle differences in MLS3508 binding poses to the D_2R and D_3R that may underlie its functional properties. In summary, MLS3508 is a full and selective agonist at both G-protein-linked and beta-arrestin-mediated D_2R signaling pathways; however, it is an antagonist for D_2R GIRK activation, indicating biased agonism. In contrast, because of its lack of agonist efficacy, MLS3508 functions as a potent D_3R antagonist. This is the first compound identified that can selectivity stimulate the D_2 DAR, with no D_3 DAR stimulation, or can selectively block the D_3 DAR, with no D_2 DAR blockade.

FRONTIERS OF NEUROPHARMACOLOGY INVITED SPEAKERS

A2. Regulation of neuronal nicotinic receptors and their role in neurological disorders

Lynn Wecker; Psychiatry and Behavioral Neuroscience, U.South Florida Morsani College of Medicine, Tampa, FL 33613

Nearly 15 years ago, studies indicated that the surface expression of α4β2 neuronal nicotinic receptors and their recovery from inactivation was altered by inhibitors of both cyclic AMP-dependent protein kinase (PKA) and protein kinase C (PKC). However, it was unknown whether these effects were mediated by direct phosphorylation of the receptor itself or post-translational modification of another protein involved in receptor expression or function. Thus, studies determined whether α4 subunits isolated from α4β2 receptors were phosphorylated, and if so, which kinases and amino acids were involved.

Using a multitude of approaches, results indicated that: both rat and human α4 subunits are phosphorylated by PKA and PKC; multiple phosphorylation sites reside on both serine and threonine residues within the major M3/M4 cytoplasmic domain of the protein; PKA and PKC phosphorylate both common and unique sites within the major (M3/M4) intracellular domain of the subunit; and PKA phosphorylates serines 362 and 467, whereas PKC phosphorylates serine 550 and to a lesser extent serine 362. Further, in the basal state, α4 subunits from mature pentamers (in the plasma membrane) are phosphorylated to a greater extent than immature forms of the subunit, and stimulation of PKA enhances the phosphorylation of both free and immature subunits on serine residues 467 and 362, but does not affect phosphorylation in the mature state, whereas stimulation of PKC enhances phosphorylation of subunits at all stages of maturation on several amino acid residues with serine 550 phosphorylated in the immature and mature, but not the free state.

Sustained exposure to nicotine appears to activate PKC, leading to the phosphorylation of immature α4 subunits, enhancing receptor subunit assembly and receptor maturation, resulting in an up regulation of α4β2 receptors. Because nicotine-induced up regulation of these receptors appears to mediate tolerance and addiction to nicotine, PKC may represent a potential target for modulating the effects of nicotine on the brain. Further, considering that α4β2 neuronal nicotinic receptors have been implicated to have a functional role in several neuropsychiatric disorders including addiction, depression, epilepsy, schizophrenia and Parkinson's disease, understanding the role of PKC in modulating receptor function is critical. (These studies were supported in part by a grant from the National Institute of Drug Abuse of the National Institutes of Health under award number R01DA14010.)

A3. How protein kinase C beta inhibitors slow "speed" and regulate extracellular dopamine

Margaret Gnegy; Departments of Neuroscience and Pharmacology, University of Michigan, Ann Arbor, MI 48109

Reinforcing properties of amphetamines depend on the level of extracellular dopamine (DA), which is regulated by DA release, the dopamine transporter (DAT) and dopamine D2-like autoreceptors. We find that protein kinase C (PKC), especially PKCβ, significantly affects both DAT and DA autoreceptor activity in ways that would enhance extracellular DA. Inhibition or deletion of PKCβ, which complexes with DAT, reduces amphetamine-stimulated DA efflux and amphetamine-stimulated locomotor and rewarded behaviors. In addition to enhancing DA efflux through the DAT, PKCβ regulates communication between DAT and D2 receptors. It is well known that D2 receptor activation will increase surface DAT, but we find that DAT itself, acting through PKCβ, regulates D2 trafficking. In heterologous N2A neuroblastoma cells, we found that DAT and PKCβ suppress D2R surface localization as compared to D2R-vector cells. This regulation depends on PKCβ substrate sites in both DAT and D2Rs. Further, we find that PKCβ regulates DA autoreceptor function by reducing dopamine autoreceptor-mediated inhibition of exocytosis. We posit that inhibition of PKCβ would reduce the concentration of extracellular DA in response to amphetamine by reducing outward transport and by enhancing dopamine autoreceptor function. Inhibition of PKCβ could serve a therapeutic function.

A4. Effects of potential disease-causing mutations on NMDA receptor function

Stephen F. Traynelis and Hongjie Yuan; Department of Pharmacology, Emory University, Atlanta, GA 30322

NMDA receptors are ligand-gated ion channels that mediate a slow, Ca^{2+}-permeable component of excitatory synaptic transmission. These receptors are involved in many normal brain functions, including development, learning, and memory. In addition, aberrant NMDA receptor activation has been proposed to be involved in numerous neuropathological conditions such as Alzheimer's disease, Parkinson's disease, schizophrenia, treatment-resistant depression, stroke-induced damage, and

epilepsy. We have begun to investigate whether mutations within the various NMDA receptor subunits from patients with neurological conditions can alter channel function in ways that could be meaningful for the clinical symptoms of patients. In collaboration with the Undiagnosed Disease Program at NIH, we have studied a number of NMDA receptor mutations identified in patients with neurological complications that included developmental delay and seizures. We describe here one GluN2A mutation that enhances NMDA receptor function in a young patient showing signs of neurodegeneration as well as intractable seizures. The effects of this mutation are consistent with it contributing to the clinical symptoms observed for this patient.

FRONTIERS IN NEUROPHARMACOLOGY PRESIDENTIAL GRADUATE STUDENT SYMPOSIUM ORAL PRESENTATIONS

A5. Identification and characterization of pharmacological chaperones of the dopamine transporter

Pieter Beerepoot, A. Ramsey, and A. Salahpour; Department of Pharmacology & Toxicology, University of Toronto, Toronto, ON, M5S 1A8

Hereditary DAT deficiency syndrome is a recently discovered rare pediatric condition that is caused by loss-of-function mutations in the DAT. The disorder is characterized by parkinsonism-dystonia and raised CSF dopamine metabolites. When expressed *in vitro*, the DAT missense mutations reduce or eliminate dopamine uptake as well as preventing DAT protein maturation. We propose that the mutations result in ER retention of an otherwise functional DAT, which could potentially be rescued by using pharmacological chaperones. Compounds that increased surface expression of WT DAT and mutant DAT (G585A and D600A) HEK-293 cells were identified using a β-lactamase-reporter assay, after which effects on DAT protein and function were assessed using western blotting and a dopamine uptake assay respectively. Heterozygous DAT-knockout (DAT-HET, basal DAT levels 50% of DAT in WT mice) mice were treated daily with a putative pharmacological chaperone for a period of two weeks followed by a 1-day washout. Locomotor response to an amphetamine challenge was measured after which animals were sacrificed. DAT protein levels were assessed by performing western blotting on striatal tissue lysates. We tested a number of known DAT ligands and have identified compounds that can promote maturation of both WT and mutant DAT *in vitro*, although DAT deficiency syndrome relevant mutations have so far not been tested. Subsequently, we examined the effect of a putative pharmacological chaperone *in vivo* and our data show that subchronic (2-week) treatment can increase striatal DAT protein in DAT-HET mice. Our data suggest that it is possible to increase DAT protein and function using a pharmacological chaperoning approach. Pharmacological chaperones for DAT could be used as a potential treatment to rescue DAT function in DAT deficiency syndrome.

***A6. Ric-8A* deletion as tumor suppressor of oncogenic G-protein alpha subunit alleles**

Bharti Patel and Gregory G. Tall; Department of Pharmacology and Physiology, University of Rochester, Rochester, NY 14642

Constitutively-active, GTPase defective G protein alpha (Gα) subunit mutants are implicated to cause a variety of disease. For instance, *GNAQ/11-Q209L* mutants were recently found in 83% of human ocular melanomas (OM). There are no therapeutics that specifically target disease-driving mutant G proteins. Ric-8A and Ric-8B proteins are the molecular chaperones specifically required for Gα folding during protein biosynthesis. We hypothesize that blocking Ric-8 function will be a useful therapy to attenuate the abundance of mutant, disease-causing G proteins. To address this, we generated a *Ric-8A* conditional knockout mouse to study the effect of *Ric-8A* gene deletion on suppression of *GNAQ/11-Q209L*-driven established mouse model of the disease. *Ric-8A*-targeted embryonic stem cell lines from KOMP were used to generate a *Ric-8A* chimeric mouse with a knockout-first *Ric-8A* Neo allele. Flp-recombinase breeders were used to convert the null-Neo allele to a conditional *Floxed*-allele. Homofloxed Ric-8A mouse embryonic fibroblasts (MEFs) were isolated and stably transduced with a lentivirus that express Cre recombinase. Cre-mediated recombination excised Ric-8A exon-5, as expected and resulted in production of a *Ric-8A* truncated protein that does not function to fold G-proteins. Using MEFs isolated from *Ric-8A* homofloxed embryos we demonstrate that Cre-mediated recombination successfully induced a Ric-8A knockout at the genetic and protein levels. Significant decreases in levels of endogenous Gαi/o and Gαq/11 family of Gα subunits were observed in Ric-8A knockout MEFs. These results confirm the expected phenotype of reduced functional Gα abundance in *Ric-8A* absence. We generated a *Ric-8A* conditional knockout mouse and showed Ric-8A-knockout dependent decrease in Gα subunit abundance. Our *Ric-8A* conditional knockout mouse will be used to investigate the efficacy of *Ric-8A*-gene deletion suppression of oncogenic G protein allele-driven disease in established mouse models. The proposed work will establish the tenability of Ric-8A as a drug target for diseases caused by mutant G proteins.

A7. Effects of imidazoline I2 receptor agonist 2-BFI on the development of tolerance and physiological and behavioral dependence to morphine in rats

David A Thorn and Jun-Xu Li; Department of Pharmacology and Toxicology, University at Buffalo, Buffalo NY 14214-3000

Pain is a significant health care challenge and current pharmacotherapy cannot meet increasing clinical needs. Opioids are the drugs of choice for many painful conditions, particularly moderate to severe pain. Accumulating evidence indicates that imidazoline I2 receptor agonists enhance the antinociceptive effects of opioids and therefore may be suitable for combination therapy with opioids for pain treatment. However, little is known of the effects of I2 receptor agonists on the untoward effects of opioids, such as the development of tolerance and physical dependence. In this study, two groups of rats (n=9/group) were trained to lever press for sucrose (10%) under a FR10 schedule. Using a cumulative dosing procedure, the rate-suppressing effects of the μ opioid receptor agonist morphine, the imidazoline I2 receptor agonist 2-BFI and the μ opioid receptor antagonist naltrexone were examined each week in rats treated with either (20 mg/kg, s.c.) morphine or (10 mg/kg) 2-BFI plus (20 mg/kg) morphine per day for 3 weeks. Chronic morphine administration induced significant tolerance to the rate-suppressing effects of morphine as demonstrated by a greater than 6-fold increase in the ED50 value, while the chronic administration of 2-BFI plus morphine resulted in a less than 4-fold shift of the morphine ED50 value. In addition, chronic administration of morphine resulted in the development of physical dependence, as evidenced by a marked increase in the sensitivity to the rate-suppressing effects of naltrexone as well as significant body weight loss following the naltrexone test session. Rats treated with daily 2-BFI plus morphine exhibited significantly less naltrexone-induced body weight loss and sensitization to the rate-suppressing effects. Taken together, these results indicate that 2-BFI attenuated the development of tolerance and physical dependence to morphine and further support the therapeutic potential of combining I2 receptor agonists and opioids of pain treatment.

A8. Characterization of neuronal activation responses to social stimulation in a genetic model of reduced NMDA receptor function

Catharine A. Mielnik[1*], Marija Milenkovic[1], Caroline Kim[2], Amy J. Ramsey[1]; [1]Pharmacology and Toxicology, University of Toronto, Toronto, ON M5S 1A8; [2]Cell Biology, Duke University, Durham, NC

One of the most devastating and consistently reported symptoms in schizophrenia is the loss of social cognitive skills and there remains a lack of effective treatment for social dysfunction. Therefore, it is imperative to gain a more comprehensive understanding of the neurobiological substrates of social behavior to allow for suitable treatment. The NR1-KD mouse model expresses reduced levels of the NR1-subunit of the NMDA receptor and show deficits in social behavior. The NR1-KD mouse model can have heuristic value in understanding the underlying neurobiology of social interaction deficits that are present in those who suffer from schizophrenia, which can be observed as deficits in species-specific social behavior. We aim to determine which brain regions are selectively activated in response to social stimulation and to determine whether differences in neuronal activation could be observed in mice that display reduced sociability. Sociability was measured with a modified "three-chamber sociability test" where the test mouse was exposed to a novel mouse as social stimulus. The amount of time spent in social investigation over a ten-minute period was determined using videotracking software. Neuronal activation was subsequently quantified by c-fos immunoreactivity one hour after exposure to social stimulus. Clozapine was administered one hour before measurement of sociability in wildtype and NR1-KD mice. Several brain regions showed an increase in activation that was selective for exposure to social stimulus: cingulate cortex, lateral septal nuclei, hypothalamus, and amygdala. NR1-KD mice displayed a reduction in social behavior and activation in the two brain regions quantified, the cingulate cortex and septal nuclei. Reduced sociability was more pronounced in adult NR1-KD mice than in younger mutants. Low dose of clozapine did not significantly alter sociability in wild-type or mutant mice. Our studies highlight the role of the cingulate cortex and septal nuclei in affiliative social behavior. The decrease in neuronal excitability in adult NR1-KD mice likely indicates that activation of these regions is important for the expression of affiliative interaction.

A9. Molecular mechanisms of local anesthetic inhibition on NMDA receptors

Meaghan A. Paganelli and Gabriela K. Popescu; Department of Biochemistry, Neuroscience Program, University at Buffalo, Buffalo, NY 14214

Local anesthetics are widely used in clinical practice to prevent and alleviate pain during surgery. Recently, it has been demonstrated that aside from impeding the generation of action potentials by blocking sodium channels, local anesthetics may also affect *N*-methyl-*D*-aspartate (NMDA) receptor currents, which are critical mediators of synaptic plasticity. Importantly, local anesthetics inhibited NMDA receptor-mediated synaptic transmission in the dorsal horn, a spinal cord region involved in central sensitization. To evaluate local anesthetics' effects on NMDA receptor responses, we recorded single-channel activity form HEK 293 cells transiently transfected with GluN1/GluN2A receptors. Records were obtained in the absence of divalent cations (1 mM EDTA). In these conditions, we observed that bupivacaine, an amide-class local anesthetic, decreased channel open probability in a concentration dependent manner, in which increasing concentrations caused both an increase in the duration of closed events and a subsequent decrease in the duration of open events. Similar potency was observed for both GluN2A and 2B isoforms. Further, we found that in the presence of bupivacaine, but not in its absence, open durations increased with depolarization, an indication of possible voltage-dependent block. However, a mutation that eliminates NMDA receptor voltage-dependent sensitivity to magnesium and zinc, maintained wild type-like sensitivity to bupivacaine. Based on these results we suggest that local anesthetics may act at a different site than divalent cationic pore blockers.

A10. Inhibition of GluN2A-containing NMDA receptors by 2-naphthoic acid

Han Yu and Gabriela K. Popescu; Department of Biochemistry, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY 14214

NMDA receptors (NRs) mediate excitatory synaptic transmission in central nervous system and play important roles in development and synaptic plasticity, but also mediate glutamate neurotoxicity. Recently, 2-naphthoic acid (NPA) and its derivatives have been identified as allosteric, noncompetitive NR inhibitors. The selectivity of NPA derivatives among NR subtypes was mapped structurally to the ligand-binding domain (LBD), and was proposed to be mediated by residues on the S1 segment. The wide range of its selectivity among NRs gives its derivatives great potential in both experimental and clinical applications, so it is important to delineate the kinetic mechanism by which NPA inhibits NR activity. We used whole-cell and cell-attached single-channel patch clamp on HEK293 cells expressing recombinant GluN1/GluN2A. Kinetic modeling was used to investigate the effects of NPA on the channel gating. We found that NPA has 50% inhibitory effect at 1.9 mM. Further, from one-channel current recordings, we found that 4 mM NPA caused a 62% decrease in open probability by decreasing mean open time 2.5-fold and by increasing mean closed time 2-fold. Kinetic modeling suggested that NPA binding stabilizes NR closed states and increases the energy barriers toward open states, causing NRs to dwell longer in pre-open states along the activation pathway. The reaction mechanisms we derived provide quantitative insight into the inhibitory mechanism of NPA, and help anticipate its effects on GluN1/GluN2A receptors during both physiological and pathological activation modalities.

A11. Glycine gating of NR1/NR2A NMDA receptors

Kirstie A. Cummings and Gabriela K. Popescu; Department of Biochemistry, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY 14214

N-Methyl-D-Aspartate receptors (NMDARs) are ligand-gated ion channels that mediate excitatory neurotransmission in the mammalian central nervous system. They are required for normal neuronal function and are a factor in several neuropathies including Alzheimer's disease and schizophrenia. Classical NMDARs require both glycine and glutamate bound for receptor activation. Reaction mechanisms have been developed for several receptor isoforms, however these models assume saturation of glycine sites and a quantitative understanding of glycine-dependent gating kinetics is currently inadequate. We used several patch-clamp configurations including cell-attached, whole-cell, and fast agonist application on outside-out patches to study the mechanism by which glycine gates NMDARs in transiently transfected HEK293 cells. For single channel records, data were idealized with the SKM algorithm in QuB, after filtering digitally at 12 kHz. Modeling with the MIL algorithm (QuB) was done by fitting state models to idealized data. Macroscopic simulations were done in QuB using models acquired following ligand concentration-dependent global fits across several concentrations. We developed ranked kinetic state models with association and dissociation rate constants under several subsaturating glycine concentrations. To test these schemes, we also developed models for two lower-affinity glycine-site agonists, L-serine and 3,3,3-trifluoro-DL-alanine. In all cases, log likelihood calculations indicate that binding occurs at kinetic state C2. We then measured macroscopic responses using fast application of glycine onto outside-out patches and whole-cell perfusion of glutamate under different concentrations of background glycine. Finally, we generated glycine dose-response curves and calculated EC_{50} values. For each condition, experimentally-recorded traces were compared to simulated responses for each candidate model.

These data taken together support a model in which glycine and glutamate bind and activate NMDARs in a sequential manner. Knowledge about how glycine gates NMDARs will contribute to a more comprehensive understanding of the activation of these physiologically and pathologically relevant receptors. (Supported by RO1NS052669 to GKP)

A12. SNARE proteins are essential in the potentiation of NMDA receptors by group II metabotropic glutamate receptors

Jia Cheng, Wenhua Liu, Zhen Yan: Department of Physiology and Biophysics, University at Buffalo, Buffalo, NY 14214

The group II metabotropic glutamate receptor (mGluRII) has emerged as a new drug target for schizophrenia treatment. To understand the potential molecular mechanisms underlying the antipsychotic effects of mGluRII, we examined its impact on NMDA receptors, since NMDAR hypofunction has been implicated in schizophrenia. We previously found that application of APDC, a highly selective mGluRII agonist, caused a potent enhancement of NMDAR-mediated currents in cortical pyramidal neurons. Here we examined whether this effect of mGluRII involves the exocytosis of NMDA receptors mediated by SNARE proteins, such as SNAP-25 (synaptosomal-associated protein of 25 kDa) and Syntaxin 4. We found that the enhancing effect of APDC on NMDAR currents was abolished when SNARE complex was disrupted by delivering Botulinum toxin or SNAP-25 C-terminal blocking peptide into the neurons. Moreover, knockdown of Syntaxin 4 blocked mGluRII potentiation of NMDAR currents. Syntaxin 4 is a postsynaptic component interacting with Rab4, a small Rab GTPase mediating fast recycling from early endosome to the plasma membrane. The effect of APDC on NMDAR currents was abolished by dominant negative Rab4, and occluded by constitutively active Rab4, suggesting the involvement of Rab4-mediated NMDAR exocytosis to the cell membrane. Taken together, these results have revealed the key molecules involved in mGluRII enhancement of NMDA receptor trafficking and function. (Supported by NIH MH84233 and MH85774 to Z.Y.)

A13. Biochemical reconstitution of adhesion GPCR GPR56 activation of heterotrimeric G proteins

Hannah M. Stoveken[1], Brigitta Gehl[2], Lei Xu[2], and Gregory G. Tall[1]; [1]Pharmacology and Physiology, [2]Biomedical Genetics, University of Rochester Medical Center, Rochester, NY 14642

The adhesion G protein-coupled receptor GPR56, regulates cancer progression and cortical neuron migration during brain development. The proximal signaling events downstream of GPR56 and the pharmacological mechanisms of action of its putative ligands remain largely unknown. The extracellular matrix proteins, transglutaminase 2 and collagen III are proposed natural ligands that may regulate GPR56-dependent melanoma progression and cell migration. GPR56 is auto-proteolyzed during biosynthesis to produce an N-terminal fragment (NTF) that remains non-covalently associated with the 7-transmembrane-spanning C-terminal fragment (7TM-CTF). Previous work showed that the NTF inhibited 7TM-CTF signaling outputs in cells. The mechanism of ligand engagement by the NTF and how this may influence GPR56 7TM-CTF G protein coupling is not understood. We have biochemically reconstituted GPR56 activation of G protein heterotrimers. Purified, recombinant G protein heterotrimers (Gi/o, Gq, G13, Gs) were pre-coupled to membranes prepared from GPR56-expressing Sf9 insect cells. The GPR56-influenced [^{35}S]-GTPγS binding kinetics of each G protein heterotrimer were measured. The auto-inhibition of the GPR56 7-TM-CTF by its NTF was investigated by extracting the NTF from isolated membranes with urea prior to measurement of G protein

[^{35}S]-GTPγS binding. GPR56 robustly stimulated G13 GTPγS binding. GPR56 modestly enhanced the kinetics of Gi/Go GTPγS binding, and did not couple to Gq or Gs. Urea-treated GPR56 membranes were substantially more efficacious than untreated membranes towards G13 activation, supporting the inhibitory function of the NTF. Chemically stripping the GPR56 NTF from prepared membranes with urea stabilizes the active conformation of the GPR56 CTF. To prove that the GPR56 NTF suppresses GPR56 signaling during brain development and cancer progression, urea-stripped GPR56 membranes will be reconstituted with purified NTF and a series of designed NTF truncations. GPR56 activation of G13 will be measured to identify the portion(s) of the GPR56 NTF that are sufficient to suppress receptor signaling. (Supported by NIH grant RGM088242A to G.G.T. and NIH grant R01GM098591 to L.X.)

A14. The mechanism of the Ric-8 protein requirement in heterotrimeric G protein biosynthesis

PuiYee Chan and Gregory G. Tall; Pharmacology and Physiology, University of Rochester Medical Center at Rochester, NY 14642

We recently demonstrated that Ric-8 guanine nucleotide exchange factors regulate an early event during heterotrimeric G protein α subunit biosynthesis. Newly made Gα subunits are defective in initial association with an endomembrane in cells that are *Ric-8A*$^{-/-}$. To define the precise molecular events by which Ric-8 mediates Gα biosynthesis, we utilized cell-free translation systems to study potential Ric-8A influence of Gα subunit translation kinetics and protein folding.The kinetics of Gα subunit translation and production of functional, folded protein from mock- and Ric-8A-(immuno)depleted RRL were compared. Gα proteins were examined using a trypsin protection assay of the activated conformation. Resolution of translated Gα proteins by gel filtration chromatography enabled evaluation of intermediate complexes of chaperones and Gα subunits during biosynthesis and folding.

Endogenous Ric-8A was immunodepleted from RRL. Gα subunit translation rates and overall produced protein amounts were equivalent in Ric-8A- and mock-depleted lysates. The function of Ric-8A in Gα biosynthesis was revealed when folded Gα protein levels were quantified. Properly folded Gα subunits can adopt the active GTP-bound conformation, a form resistant to limited trypsinolysis. GDP-AlF4--bound Gα subunits produced in mock-depleted RRL had characteristic resistance to trypsinolysis. However, Gα subunits produced from Ric-8A-depleted RRL were not protected. Add back of recombinant Ric-8A protein to the Ric-8A-depleted RRL markedly enhanced trypsin protection of GDP-AlF_4^--bound Gα subunits. Similar results were obtained in WGE that has no endogenous Ric-8 component. WGE-translated Gαq was resolved by gel filtration and was found to be a high molecular weight aggregate. Ric-8A addition to WGE made Gαq elute as a dimeric complex with Ric-8A that was dissociable with GTPαS, producing functional Gαq-GTPαS monomer.

This is the first report that Ric-8A serves a necessary function as a folding chaperone during biosynthetic folding of Gα subunits. This work has prompted us to identify additional cellular chaperones that may work with Ric-8A during G protein biosynthesis/folding. A Ric-8A-dependent fluorescence-based Gα folding assay has been established and will be presented. (Supported by NIDA Grant T32 DA07232 and RGM 088242A).

A15. Withdrawal from cocaine self-administration alters activin/Smad3-signaling

Amy Gancarz[1,2], Gabrielle Schroeder[2], Clarisse Panganiban[2], Danielle Adank[2], Michael Kausch[2], Stewart D. Clark[1,2], David M. Dietz[1,2]; [1]Research Institute on Addictions, [2]Pharmacology and Toxicology, University at Buffalo, Buffalo, NY

The addicted phenotype is characterized as a long-lasting, chronically relapsing disorder that persists following long periods of abstinence leading the hypothesis that the addicted brain has been functionally "re-wired." Repeated exposure to psychomotor stimulants results in an increase in dendritic spine density in the brain including the nucleus accumbens (NAc) a critical area of the mesolimbic dopamine circuitry mediating drug addiction. These changes are thought to represent alterations in synaptic connectivity that may underlie the life long battle with addiction. Activin receptor signaling is known to regulate the actin cytoskeleton through both direct regulation of actin dynamics, and more indirectly through changes in gene transcription. Here, we examined the role of activin receptor signaling following withdrawal from cocaine-self administration. Following a seven-day withdrawal period from cocaine self-administration, there was a marked increase in the activin receptor II (ActRII) expression at both the mRNA and protein levels in the NAc. Activin receptor activation leads to the phosphorylation of Smad3, which transduce extracellular signals to the nucleus regulating gene transcription. Consistent with the increased expression of activin receptors, we find an increase in phosphorylated Smad3 (p-Smad3), an effect observed seven days but not one day following cocaine self-administration. These data strongly suggests that withdrawal from cocaine self-administration leads to an induction of the transcription factor Smad3 and subsequent activation of Smad-dependent gene expression in the NAc. Taken together, these data indicate that activin/Smad3 signaling is regulated in a time-dependent manner following cocaine self-administration, and may be the molecular bridge between actin dynamics and long-term transcriptional events that have been associated with drug addiction. Grant support: NIAAA training grant T32-AA007583-11

A16. Characterization of a cannabinoid CB1 receptor negative modulator ORG27569 in rats

Yanyan Qiu and Jun-Xu Li; Department of Pharmacology and Toxicology, University at Buffalo, Buffalo, NY 14214

Blockade of the cannabinoid CB1 receptor signaling is implicated in energy homeostasis and the CB1 receptor antagonist Rimonabant® was used clinically for treating obesity. However, its serious side effects (e.g., depression) led to forced withdrawal from the clinic. Recently, a new CB1 receptor modulating site has been described which may achieve functional CB1 receptor antagonism without directly inhibiting CB1 receptor signaling. Such a strategy might be able to retain similar therapeutic potential as orthosteric CB1 receptor antagonists such as Rimonabant® but with better safety profile. However, no in vivo functional studies exist to characterize the pharmacological effects of CB1 receptor modulators. This study examined the effects of a purported CB1 receptor negative modulator ORG27569 on CB1 receptor agonists, CP55940 and anandamide, induced hypothermia in rats.

Different groups of rats were used to evaluate the hypothermic effects induced by ORG27569, CP55940 and anandamide, alone or in combination. Rectal temperature was measured using a Physotemp® rat rectal thermometer. CP55940 (0.1-1 mg•kg(-1)) and anandamide (3.2-32 mg•kg(-1)) dose-dependently and markedly decreased the rectal temperature in rats, with varied duration of action. When studied alone, ORG27569 had no effect on the rectal temperature. However, ORG27569 (3.2 and 10mg•kg(-1)) markedly antagonized CP55940- and anandamide-induced hypothermic effects. ORG27569 attenuates the hypothermic effects induced by CB1 receptor agonists. This effect was likely achieved through negative allosteric modulation of CB1 receptors because ORG27569 does not bind to the orthosteric binding site but has high affinity at a recently described CB1 receptor allosteric modulating site and has been shown to decrease the maximal effects of CB1 receptor agonists in vitro binding assay. These data extend the preliminary observations by confirming that ORG27569 is a CB1 receptor negative modulator and can function as a CB1 receptor antagonist *in vivo*.

A17. The vitamin D3 metabolite 25-hydroxyvitamin D3 (25(OH)D3) inhibits a subset of lung cancer cells independent of CYP27B1 activity

Alissa Verone, Suzanne Shoemaker, Santosh Upadhyay, Pamela Hershberger; Molecular Pharmacology & Cancer Therapeutics Program, Roswell Park Cancer Institute, Buffalo, NY 14263

Epidemiologic data has demonstrated that elevated circulating levels of the vitamin D_3 metabolite, $25(OH)D_3$, are associated with improved overall survival in early stage non-small cell lung cancer (NSCLC) patients. This highlights the clinical importance of vitamin D_3 metabolites in NSCLC. Our laboratory screened a panel of NSCLC cell lines and found that an inverse relationship exists between the vitamin D receptor (VDR) and CYP24 expression, such that two phenotypes exist: $VDR^{high}CYP24A1^{low}$ and $VDR^{low}CYP24A1^{high}$. We predict that VDRhighCYP24A1low cells will display increased sensitivity to vitamin D^3. The precursor metabolite $25(OH)D^3$ and the active metabolite 1α, $25(OH)_2D_3$ both induce VDR target gene transcription and inhibit colony formation. To determine if these results were due to conversion to the active metabolite, cells were exposed to a general CYP enzyme inhibitor, Ketoconazole, in addition to 25(OH)D3. VDR target gene expression remained induced, indicating that lung cancer cells may not require CYP27B1 to promote vitamin D_3 signaling effects. An LC-MS/MS assay was utilized to measure the level of 1α, $25(OH)_2D_3$ production in $VDR_{high}CYP24A1_{low}$ cells, and found to be minimal.

A mouse xenograft experiment was performed to determine if dietary vitamin D_3 had the potential to decrease tumor volume. Mice were administered diets containing 100, 1,000 or 10,000 IU/kg of vitamin D_3. Those mice fed the 10,000 IU/kg diet displayed significantly lower overall tumor volumes, with no toxicity and no change in circulating 1α, 25$(OH)_2D_3$ in the blood. Therefore, $VDR^{high}CYP24A1^{low}$ are a subset of NSCLC cells that display increase sensitivity towards vitamin D_3 treatment, and implies that vitamin D_3 may be useful in an adjuvant therapy setting of NSCLC patients with a $VDR^{high}CYP24A1^{low}$ tumor phenotype.

A18. Central nervous system mediates lung inflammation during septic shock

Vincenzo Russo[1], Jianya Peng[1, 2], Janey James[1], Hai Duong Phan[1], Hunter MacDonald[1], Nancy Gertzberg[1], Paul Neumann[1], Arnold Johnson[1], and Carlos Feleder[1]; [1]Albany College of Pharmacy, Department of Pharmaceutical Sciences, Albany, NY 12208. [2]China Pharmaceutical University, Nanjing, 211198 China.

Septic shock is a systemic inflammatory response due to severe infection, resulting in multiple organ injury. Recently, α7-nicotinic acetylcholine receptors (α7nAChR) have been shown to modulate LPS-induced septic shock, suggesting autonomic nervous system involvement. Additionally, endocannabinoid type 1 (CB1) receptors in the brain are implicated in response to endotoxemia and modulation of the autonomic cholinergic pathway. Our data suggests septic shock is modulated through mechanisms controlled by the brain. Hence, this study tested the hypothesis that brain endocannabinoids and the cholinergic system regulate LPS-induced lung inflammation. Male Sprague-Dawley rats received an intracerebroventricular (ICV) injection of either the CB1 receptor antagonist Rimonabant (250 or 500ng) or vehicle, or a preoptic-anterior hypothalamic area (POA) or nucleus of the solitary tract (NTS) injection of Lidocaine (2%; 1 microL), 5 minutes prior to IV injection of either LPS (1 or 5mg/kg) or saline. Lungs were removed 0.5 h after IV injection of LPS and isolated for assessment of hemodynamics and inflammatory signal biomarkers. In separate studies, permeability to Evan's-blue-labeled BSA was assessed in rat pulmonary microvessel endothelial monolayers (PMEM) grown on transwells, treated with vehicle or LPS (100ng/ml) with or without the α7nAChR-specific agonist PNU-282,987 (100nM) for 4 h. There were increases in (Wet-Dry/Dry) weight ratios and (Wet-Dry/Dry)/pulmonary capillary pressures in the lungs of vehicle/LPS-treated rats, with decreases in both IRAK1 and IκBα levels in lung homogenate. ICV injection of Rimonabant prevented the LPS-induced increased lung weight ratios and decreases in IRAK1 and IκBα. Lidocaine blockade of the POA or NTS prevented the initial lung hemodynamic response to LPS. Lastly, PNU-282,987 prevented the LPS-induced increase in permeability of PMEM. The data indicate that the brain's central endocannabinoids, as well as the cholinergic system, participate in the regulation of the lung response to LPS. (Support: NIH R01 HL059901 to A.J. and NIH R15A1072744 to C.F.)

A19. The pathogenesis of chronic pain associated with STZ-induced diabetic neuropathy is associated with increased levels of tumor necrosis factor in the brain

Ashley Re[1], Abdel-Rahman Alnaji[2], Paul R. Knight[3,4], Bruce Davidson[1,3], Tracey A. Ignatowski[1,5]; [1]Pathology and Anatomical Sciences, [2]Pharmacology and Toxicology, [3]Anesthesiology, [4]Microbiology and Immunology, [5]Neuroscience Program, University at Buffalo, Buffalo, NY 14214

Increases in pro-inflammatory cytokine levels, including tumor necrosis factor-α (TNF), are implicated in neuropathic pain pathogenesis. Inhibition of TNF in the CNS dramatically reduces neuropathic pain, possibly through alteration of autonomic nervous activity. The present goal was to investigate whether an association exists between TNF levels and development of chronic pain during streptozotocin (STZ)-induced diabetes. Male Sprague-Dawley rats were administered STZ (45 mg/kg) to induce diabetes. Rats were tested for pain (thermal hyperalgesia; mechanical allodynia) prior to (baseline) and every other day post-STZ for 60 days. Rat weights were monitored and blood glucose was tested prior to, day-4 post-STZ, and once/week thereafter. On day-61, blood, brain regions, sciatic nerves, and peritoneal macrophages were analyzed for TNF. Adrenergic regulation of lipopolysaccharide-stimulated TNF production by macrophages from control rats (saline), rats with STZ-induced diabetic neuropathy (STZ-DN), and rats injected with STZ, which failed to develop hyperglycemia (non-responders, STZ-NR) was examined. TNF levels were assessed via WEHI bioassay. TNF levels increased in specific brain regions ($p<0.05$) from STZ-DN rats, while no TNF increase occurred in STZ-NRs. Conversely, there was no increase in TNF in serum from STZ-DN animals (day-60 post-STZ), whereas TNF increased in serum from STZ-NR animals ($p<0.05$) confirming NRs received STZ. Macrophages from STZ-DN rats produce more TNF, whereas those from STZ-NRs produce less TNF. We have previously demonstrated that increased brain TNF levels play a critical role in central pain generation. Decreased TNF production by lipopolysaccharide-stimulated macrophages and lack of increased brain TNF in STZ-NR rats may explain lack of neuropathy. Systemic antidepressant and siRNA inhibition of hippocampal TNF studies are ongoing that may identify interactions between adrenergic responses and pro-inflammatory TNF offering a novel approach to treat chronic pain associated with diabetic neuropathy.(Supported by Dept. PAS; UB MDRF Award - A. Re)

A20. Suppression of neurodegeneration in *Drosophila* models of human neurodegenerative disorders

Brittany Casino and Satpal Singh; Department of Pharmacology and Toxicology, University at Buffalo, Buffalo, NY 14214

Our lab has previously identified a mutation *(levy)* that provides a model of Leigh Syndrome (LS) in *Drosophila melanogaster*, as well as a second mutation, *Su(levy)*, which suppresses levy induced neurodegeneration (ND). The *Su(levy)* mutation confers resistance to temperature-induced-paralysis, a phenotypic marker of *levy* in Drosophila. Experiments are underway to identify and characterize which gene the suppressor mutation resides within. Preliminary experiments suggest that ND in the *levy* mutant may be caused by oxidative stress, a feature common to many neurodegenerative disorders such as Parkinson's disease (PD) and Alzheimer's disease (AD). This fact has broadened the suppressor mutation's application to possibly include PD and AD. The pesticide rotenone is known to induce Parkinson's-like symptoms in humans and flies. Using rotenone to create a PD model, our lab is testing whether the suppressor can alleviate the phenotypic symptoms of this model. The suppressor mutation is being genetically combined with AD and PD mutations to further assess its ability to alleviate locomotor symptoms in the fly models of these disorders. Paralysis testing was done in a 38°C water bath. Wild-type and *Su(levy)* flies were exposed to 0 or 500μM concentrations of rotenone. Crosses and rotenone experiments were done at 25°C. The *Su(levy)* mutation made the *levy* flies resistant to paralysis. *Su(levy)* flies were more resistant to paralysis than wild-type. *Su(levy)* protected flies from rotenone toxicity. Experiments suggest that the *Su(levy)* mutation may protect flies from the effect of the pesticide rotenone on locomotion. Suppressor's effects on PD and AD mutants will be measured through longevity, locomotion, and measurement of oxidative stress through ROS assays. If suppressor can alleviate ND in these models, this could provide leads to developing therapeutic approaches toward multiple neurodegenerative disorders. (Supported by NINDS 1R03NS063148-01)

A21. Pre-exposure of the urotensin II receptor to ligand differentially reduces the response to subsequent additions of urotensin II or urotensin II-related peptide

Taylor Warren and Stewart D. Clark; Department of Pharmacology and Toxicology, University at Buffalo, SUNY, Buffalo, NY

The urotensin II receptor (UIIR) is a G protein-coupled receptor (GPCR), formerly known as SENR or GPR14. UIIR is activated by two different ligands, urotensin II (UII) and urotensin-related peptide (URP). Urotensin II was originally isolated from the urophysis gland of fish, however, both UII and URP have been found in numerous tetrapod species. Our primary question is "Why is it that there are two ligands for one single receptor?" UIIR activates the Gq coupled pathway, and so we are able to monitor receptor activation via fluorescent calcium chelating dyes. In this assay URP and UII have the same EC50, and previous studies have shown that they have equivalent Kd. In addition, at least in some areas of UIIR expression, URP and UII are expressed by the same neurons and at the same time. Therefore, we hypothesize that URP and UII produce different post-activation events. As a first step to investigate this possibility we have studied how the pre-exposure of the receptor to ligand influences receptor activation by subsequent exposure to ligand. Pre-exposure of UII blocks receptor activation by subsequent additions of UII. However, pre-exposure to URP blunts but does not abolish receptor activation due to subsequent additions of URP. Future studies will focus on the ability of UII and URP to produce receptor desensitization and beta-arrestin recruitment. These studies may help to explain the differential effects of UIIR ligands seen in vivo after repeated exposure.

A22. Comparative analyses of human estrogen receptor-EF-hand protein complexes: molecular basis for hormone-independent activation

David H. Lee, Bethany K. Asare, Matthew Hudson, Suchitra Singh, Rajendram V. Rajnarayanan; Department of Pharmacology and Toxicology, University at Buffalo, Buffalo, NY 14214

Estrogen Receptor (ER) belongs to the nuclear receptor super family of ligand-triggered transcription factors. ER is present in 70% of breast cancers. It has been shown that calmodulin (CaM), which control calcium mediated signaling pathways, could bind and activate unliganded ER. CaM has four EF-hand motifs that change conformation upon binding Ca2+ ions. Ca2+-CaM complex binds to the target proteins and initiates various signaling cascades. X-ray and NMR studies show CaM forms a compact globular conformation by bending its central helix upon binding its target peptides, which allows CaM to increase its binding affinity for a number of target proteins. S100, a soluble protein that is recently reported to interact with ER has only two EF-hand motifs. S100 protein is overexpressed in several cancers and shares a high degree of sequence homology with calmodulin.

Protein-protein interactions of CaM, S100 with ER alpha were simulated using HADDOCK and HEX. Docking results were analyzed in UCSF Chimera and integrated with data from in vitro proteomics experiments to determine the conformations of ER bound EF-hand protein complexes. Proteomic experiments consisted of chemical crosslinking of the corresponding protein complexes followed by tryptic digestion, analyzing the resulting peptide peaks using FTICR- Mass Spectrometry. Using the fold information and contact regions obtained from the Mass spectrometry, 3D structures of ER-EF hand protein complexes were reconstructed. These structures of ER best represent the conformational state sensed by the specific interacting partner. ER-S100 complex is distinct from CaM. The lack of the connective peptidic region between the EF-hand pairs in S100 attributed to less interaction coverage indicative of only inducing a partial agonist-like conformation. We believe that the ensemble of ER-EF hand protein complexes generated by our integrated proteomics-assisted protein interaction profiling will shed light on the lingering issue of hormone independent activation of ER at the molecular level.

A23. Use of cationic polymers to deliver nucleic acid agents

Sangwon Min[1], Qiuxia Chen[1], Chi-Kuang Chen[2], Chong Cheng[2], Aiming Yu[1]; [1]Department of Pharmaceutical Sciences, SUNY-Buffalo, NY 14214; [2]Department of Chemical and Biological Engineering, SUNY-Buffalo, NY 14214

MicroRNAs (miRNA) are small non-coding RNAs which are involved in gene regulation through different pathways of post-transcriptional modification. Thus, their delivery across the cytoplasmic membrane would influence gene regulation. To investigate the relativity in miRNA expression, we implied cationic polylactides (CPLA) and Lipofectamine 2000 as modes of miRNA expression plasmid delivery. CPLAs are positively charged biodegradable polymers possessing "proton sponge" effect that leads to an increase in delivery efficacy. Visual determination of efficacy in CPLA mediated delivery was obtained through transfecting phrGFP-II reporter plasmid with various plasmid to CPLA weight ratios. Cell viability assay was then applied to obtain optimum delivery weight ratio within low cytotoxic range. With the optimized weight ratio, microRNA-1291 (miR-1291) expression plasmid delivery into two pancreatic tumor cell lines, AsPC-1 and BxPC-3 was conducted. Resultant miR-1291 expression level was quantified via qPCR and its altered target protein expression was determined by Western blot analysis. In comparison to Lipofectamine 2000, CPLA mediated delivery exhibits an equivalent to higher expression of miR-1291 in both cell lines with subsequent decrease in target protein expression. Our results imply CPLA54 as a potent vehicle for miRNA delivery.

A24. Development of a new homogenous assay for quantitative measurement of surface expression of membrane proteins

Vincent Lam[1], S. Angers[2], and A. Salahpour[1]; [1]Pharmacology and Toxicology, University of Toronto, Toronto, ON, M5S 1A8; [2]Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, M5S 1A8

Trafficking of membrane proteins is a dynamic process that is tightly regulated and sometimes defective in human diseases. It is therefore important to develop new tools that would allow simple and quantitative measurement of surface expression of membrane proteins. The objective of this study is to develop and validate a new assay for quantification of cell surface expression of GPCRs.

We have generated β-lactamase fusion constructs and produced stable cell lines for the following GPCRs: β2-AR and GBR1.Cells seeded in a 48-well plate overnight were washed once and the cell impermeable substrate of β-lactamase, nitrocefin added to the wells. A mouse monoclonal anti-HA antibody was used for all ELISA studies. Using the β-lactamase assay we were able to measure isoproterenol induced internalization of β2-AR in a dose and time dependent manner. The results obtained by the β-lactamase assay are quantitatively and qualitatively similar to classical ELISAs. These conditions also yielded a Z'=0.52 in a 96 well plate for the β-lactamase assay. Using the β-lactamase assay we were also able to show that pre-incubation with antagonists (propranolol or alprenolol) were able to dose dependently block agonist mediated internalization of the β2-AR. Lastly in our stable cell lines for GBR1, transfection of increasing amounts of GBR2 led to increased surface expression of GBR1 in a dose dependent manner in both the β-lactamase assay and ELISA. We have validated a novel assay for the quantification of surface expression of membrane proteins that is qualitatively and quantitatively similar to classical ELISA. However this assay has the advantage of being 5-10 times lower in cost and 4-5 times faster than classical ELISA. Moreover, the measured Z' Factor indicates that the β-lactamase assay is adequate and amenable to high throughput screening.

A25. Disrupting the vasculature for enhanced drug delivery and therapeutic efficacy against gliomas

Margaret Folaron[1], Marianne Marcotte[1], Steve Turowski[1], Michael Ciesielski[2], Robert Fenstermaker[2] and Mukund Seshadri[1]; [1]Pharmacology and Therapeutics and [2]NeuroOncology, Roswell Park Cancer Institute, Buffalo, NY, USA 14263

Angiogenesis, or the formation of new blood vessels, is a major hallmark in the progression of most solid tumors including gliomas. Tumor-vascular disrupting agents (tumor-VDAs) are a distinct class of agents that cause disruption of established tumor vasculature, depriving the tumor of nutrients and oxygen and leading to inhibition of tumor growth. Since microvascular proliferation is a critical component of glioma biology, we hypothesized that targeting glioma vasculature using tumor-VDAs could be of potential benefit against gliomas. To test this hypothesis, we examined the activity of the tumor-VDAs alone and in combination with chemotherapeutic agents in multiple experimental glioma models.

As experimental glioma models, subcutaneous and intracranial GL261 and U87 gliomas were established in C57BL6 and athymic nude mice. Animals were treated with VDA (ASA404 or EPC2407), Temozolomide, Irinotecan, Dexamethasone alone or in combination. Magnetic Resonance Imaging (MRI) was performed to assess both short term and long term response of VDA therapy. Treatment with VDA alone results in an early increase in vascular permeability within a few hours of treatment (detected by MRI). VDA treatment enhances the antitumor activity of multiple classes of chemotherapeutic agents against gliomas, exhibited through enhanced long term survival. In addition, combination therapy was well-tolerated and resulted in enhanced inhibition of tumor growth compared to either monotherapy. These results demonstrate the potential of combining tumor-VDAs with chemotherapy against gliomas. MRI offers a useful, noninvasive method of monitoring changes in the glioma microenvironment following VDA treatment. (Supported by the American Brain Tumor Association Translational Grant award (M.S) – In honor of Michael Baldasaro)

A26. Melatonin modulation of novel object recognition

Danielle M Precourt[1], Shannon J. Clough[1,3], Iwona Stepien[1], Randall L. Hudson[2], and Margarita L. Dubocovich[1]; [1]Department of Pharmacology and Toxicology, [2]Department of Physiology and Biophysics, 3Neuroscience Program, School of Medicine and Biomedical Sciences, University at Buffalo SUNY, Buffalo, NY 14214

Melatonin acts on two receptors, termed MT_1 and MT_2, which are expressed in the central nervous system. Action on the MT_2 receptor is shown to inhibit long-term potentiation, a key component in learning and memory. The goal of this study was to assess whether melatonin has an effect on learning and memory. We used a novel object recognition paradigm (NOR) which is based on the theory that rodents are novelty preferring. Therefore when exposed to novel and familiar objects, mice should show a preference for the novel alternatives. We expect that the mice lacking the MT_1 receptor (MT_1KO) will not show an increased preference for novelty. Male C57 mice (wild-type

[WT] or MT_1KO) were evaluated in one of two NOR paradigms. Paradigm 1 involved a 10-minute chamber exposure followed by 3 exposures to the familiar object for 6 minutes each. Paradigm 2 involved a 10-minute chamber exposure on day 1 and a 10 minute exposure to the familiar objects on day 2. Both paradigms utilized a 5 minute novel object test one hour after the familiar object exposure. Interaction with objects was recorded utilizing the LocoScan system (CleverSys, Reston VA). The first paradigm resulted in no preference for the novel (53.03+11.00s, n=4) vs. familiar object (24.73+11.00s, n=4). The second paradigm showed a strong preference for the novel object (66.20+2.10, n=5, p<0.01) over the familiar object (33.80+2.10, n=5) in WT mice. When MT_1KO mice were run in the second paradigm, they showed no preference for the novel object (59.74+8.16, n=7) over the familiar (40.26+8.16, n=7). MT_1KO displayed a deficit in learning and memory compared to WT mice. The learning deficit observed is potentially due to action on the MT_2 receptor in the absence of the MT_1, resulting in an inhibition of long-term potentiation.

A27. MT_1 melatonin receptor role in methamphetamine-induced locomotor sensitization in C57BL/6 mice

Jason Ma[1], Anthony J. Hutchinson[1], Randall L. Hudson[2], and Margarita L. Dubocovich[1]; [1]Pharmacology & Toxicology, [2]Physiology and Biophysics, University at Buffalo, Buffalo, NY 14214

Methamphetamine (METH) and other abused drugs induce sensitization, which may underlie drug abuse related symptoms. Clues to molecular mechanisms between METH and melatonin signaling come from melatonin blocking the inhibitory effect of METH on the phosphorylation of the mammalian target of rapamycin (mTOR; Kongsophul et al., 2008). We investigated the MT_1 receptor in locomotor sensitization and regulation of mTOR after a single METH pretreatment in C57BL/6 mice. Wild-type (WT) and MT1KO mice were pretreated with a single vehicle or METH pretreatment (1.2 mg/kg, i.p.) on Day 1, then challenged with METH (1.2 mg/kg, i.p.) on Day 9. Another group of WT and MT_1KO mice treated with vehicle or METH on Day 1 were decapitated 2½ hours or 8 days later for brain tissue harvest and Western blot analysis. Locomotor sensitization was expressed in METH pretreated WT mice but not in MT_1KO mice. METH treated WT mice expressed total mTOR greater than VEH treated WT mice in caudate putamen and nucleus accumbens (Day 9). MT_1KO mice mTOR levels were not altered. METH treated WT mice also exhibited greater mTOR phosphorylation in the caudate putamen (Day 9) but not the MT_1KO mice. MT_1 receptors mediated the induction of locomotor sensitization to METH in C57BL/6 mice after a single pretreatment. Also, expression of METH-induced locomotor sensitization may involve MT_1 receptor mediated mTOR expression and phosphorylation.

A28. Characterization of MT1 melatonin receptor expressing neurons in the medial habenula, habenula commissure and periaqueductal grey of the C3H/HeN mouse brain

Katherine M. Evely[1], Ekue B. Adamah-Biassi[1], Randall L. Hudson[2], and Margarita L. Dubocovich[1]; [1]Department of Pharmacology and Toxicology, [2]Department of Physiology and Biophysics, School of Medicine and Biomedical Sciences, University at Buffalo, SUNY, Buffalo, New York, 14214

Melatonin (MLT) is rhythmically secreted from the pineal gland and acts on two G protein-coupled receptors, termed MT1 and MT2. Brain tissue from a transgenic mouse line expressing red fluorescence protein (RFP) at the MT_1 receptor promoter provides a method of localizing the receptor. RFP-MT_1 fluorescence and immunoreactivity was localized to the medial habenula (MHb), habenula commissure (HbC) and the midbrain dorsal medial periaqueductal grey (DMPAG) area. The habenula acts as a relay station from forebrain to midbrain. The downstream PAG plays a prominent role in pain transmission (Behbehani, Prog Neurobiol 1995;46:575-605). The goal of our research is to investigate the distribution of the MT_1 receptor in these cholinergic, dopaminergic and glutamatergic neuronal systems. Immunofluorescence co-staining for RFP along with choline acetyl transferase (ChAT), tyrosine hydroxylase (TH) or vesicular glutamate transporter (VGLUT2) is used to investigate the distribution of the MT_1 receptor. Results show RFP-MT_1 expression in the dorsal MHb, clearly separated from ChAT staining in the ventral MHb. TH colocalized with RFP-MT_1 in the HbC, PAG, and the ependymal lining of the aqueduct. VGLUT2 and RFP-MT_1 positive cells are present in dorsal MHb neurons. These results indicate a possible role for the MT_1 receptor in the modulation of glutamatergic and dopaminergic neurotransmission. *(Supported by DA 021870 MLD)*

A29. Melatonin accelerates the re-entrainment rate of multiple spontaneous homecage behavioral rhythms in the C3H/HeN mice

Ekue B. Adamah-Biassi[1], Iwona Stepien[1], Randall L. Hudson[2], and Margarita L. Dubocovich[1]; [1]Department of Pharmacology and Toxicology, [2]Department of Physiology and Biophysics, School of Medicine and Biomedical Sciences, University at Buffalo, SUNY, Buffalo, NY 14214

Activation of MT_1 receptors by melatonin (MLT) accelerates the re-entrainment of circadian rhythms of wheel running activity after an abrupt advance of the dark cycle (Dubocovich et al., 2005). Here, we investigated the effects of melatonin on the re-entrainment rate of multiple spontaneous homecage behaviors after a 6hr advance of the dark onset in C3H/HeN mice. The 15 behaviors assessed include activity (i.e. comedown, jump, hang, walk), exploration (i.e. dig, groom, rearup, sniff, stretch), ingestion (i.e. drink, eat) and resting (i.e. awake, remainlow, rest, twitch). Mice (n=8 per group) were treated for three consecutive days with either vehicle (VEH) (3% ethanol in saline) or MLT (3 mg/kg in VEH, s.c.) at the new dark onset. MLT significantly decreased the number of days (accelerate) necessary for re-entrainment of the spontaneous behaviors including activity (e.g. Walk: VEH, 8.3 ± 0.3d & MLT, 6.2 ± 0.2d, p<0.001), exploration (e.g. Groom: VEH, 8.8 ± 0.7d & MLT, 5.80 ± 0.2d, p<0.01), ingestion (e.g. Eat: VEH, 9.0 ± 0.4d & MLT, 6.6 ± 0.4d, p<0.005) and resting (e.g. RemainLow: VEH, 9.167 ± 0.7d & MLT, 6.8 ± 0.5d, p<0.05). We concluded that MLT acting at MT_1 melatonin receptors accelerates the re-entrainment rate of spontaneous homecage behavioral rhythms. We suggest that MLT or MLT agonists could be useful in the treatment of circadian related disorders including jet lag, circadian sleep and mood disorders. *(Supported by NS 061068)*

A30. Methamphetamine-induced conditioned place preference in C3H/HeN mice is observed during the day (ZT 6-8) but not at night (ZT 19-21)

Shannon J. Clough[1,3], Anthony J. Hutchinson[1], Iwona Stepien[1], Randall L. Hudson[2], and Margarita L. Dubocovich[1]; [1]Department of Pharmacology and Toxicology, [2]Department of Physiology and Biophysics, [3]Neuroscience Program, School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY 14214

Methamphetamine produces reward through its action on the mesolimbic system. Melatonin is synthesized following a circadian rhythm, with low levels during the day (Zeitgeber Time [ZT] 6-8; 12h:12h light-dark cycle, ZT0 = lights on) and high levels at night (ZT19-21) (Reiter, *Mol Cel Endocrinol* 1991; **79:**C153-C158). Melatonin exerts its effects through the MT_1 and MT_2 receptors, which are located in several brain regions including areas of the reward pathway (Uz et al., *Mol Brain Res* 2005, **136:**45-53). At ZT6-8 methamphetamine induces a place preference in C3H/HeN wild-type mice. Deletion of either melatonin receptor blocks this effect, suggesting a role for melatonin in the modulation of methamphetamine-induced reward. The goal of this study was to examine the contributions of endogenous melatonin in the modulation of methamphetamine-induced place preference by comparing preference scores at ZT6-8 and ZT19-21. Male C3H/HeN wild-type mice were subjected to a conditioned place preference test during ZT6-8 and ZT19-21. Animals were conditioned for 6 days with alternating treatments of methamphetamine (1.2mg/kg, ip) and vehicle and tested for place preference 1 day after the last conditioning session. Compartment duration was measured using the LocoScan System (Clever Inc, Reston, VA). A preference score was derived by subtracting the duration spent in the vehicle-paired compartment from the duration spent in the methamphetamine-paired compartment during the post-test. At ZT19-21 mice exhibited a similar preference score regardless of receiving methamphetamine (70.1+37.8s, n=17) or vehicle (23.3+21.5s, n=17). This is in contrast to mice tested at ZT6-8, which displayed a place preference for methamphetamine (226.0+35.5s, n =11, p<0.001) compared to vehicle (-36.3+28.1s, n=12). This time dependent difference suggests the involvement of a mechanism subject to a circadian rhythm, such as melatonin, which may act through inhibition of long-term potentiation (Wang et al., *Eur J. Neuroscience* **22:**22-31, 2005). *(Supported by DA021870 to MLD)*

A31. Shank3 deficiency induces NMDA receptor hypofunction via an actin-dependent mechanism

Lara J. Duffney[1], Jing Wei[1], Katharine R. Smith[2], Josef T. Kittler[2], and Zhen Yan[1]; [1]Physiology & Biophysics, University at Buffalo, [2]Neuroscience, Physiology and Pharmacology, University College London, Gower Street, London, WC1E 6BT, UK

Shank3, which encodes a scaffolding protein at glutamatergic synapses, is a genetic risk factor for autism. In this study, we examined the impact of Shank3 deficiency on the NMDA-type glutamate receptor, a key player in cognition and mental illnesses. We found that knockdown of Shank3 with a small interfering RNA (siRNA) caused a significant

reduction of NMDAR-mediated ionic or synaptic current, as well as the surface expression of NR1 subunits, in cortical cultures. The effect of Shank3 siRNA on NMDAR currents was blocked by an actin stabilizer, and was occluded by an actin destabilizer, suggesting the involvement of actin cytoskeleton. Since actin dynamics is regulated by the GTPase Rac1 and down-stream effector p21-activated kinase (PAK), we further examined Shank3 regulation of NMDARs when Rac1 or PAK was manipulated. We found that the reducing effect of Shank3 siRNA on NMDAR currents was mimicked and occluded by specific inhibitors for Rac1 or PAK, and was blocked by constitutively active Rac1 or PAK. Immunocytochemical data showed a strong reduction of F-actin clusters after Shank3 knockdown, which was occluded by a PAK inhibitor. Inhibiting cofilin, the primary downstream target of PAK and a major actin depolymerizing factor, prevented Shank3 siRNA from reducing NMDAR currents and F-actin clusters. Taken together, these results suggest that Shank3 deficiency induces NMDAR hypofunction by interfering with the Rac1/PAK/cofilin/actin signaling, leading to the loss of NMDAR membrane delivery or stability. It provides a potential mechanism for the role of Shank3 in cognitive deficit in autism.

A32. Affinity and selectivity of luzindole analogues in human and mouse MT1 and MT2 melatonin receptors transiently expressed in mammalian cells

Marina Popovska-Gorevski, Kathleen A. McGowan, and Margarita L. Dubocovich; Department of Pharmacology and Toxicology, University at Buffalo, Buffalo, New York 14214

Melatonin (5-methoxy-N-acetyltryptamine) is released following a circadian rhythm with high levels at night. Melatonin signals through activation of two G-protein coupled receptors, MT_1 and MT_2, which show distinct molecular structures, different chromosomal localizations and select pharmacological characteristics (Dubocovich et. al. Naunyn Schmiedebergs Arch. Pharmacol., 355: 365-375). The goal of this study was to compare the binding affinity and selectivity of luzindole [(2-benzyl N-acetyltryptamine (NAT)] analogues [5-methoxy-NAT; 2-benzyl-N-propionyl-AT (N-0889); p-methoxy-benzyl-NAT (N-0890); 2-p-methyl-benzyl-NAT (N-0891)], 5-hydroxyluzindole, 6-hydroxyluzindole and 5-methoxyluzindole in the human and mouse MT_1 and MT_2 melatonin receptors transiently expressed in COS-7 cells. COS-7 cells were transiently transfected with either human or mouse MT_1 and MT_2 cDNA plasmid. The affinities (Ki) of the various compounds (1 pM to 100 µM) competing for 2-[^{125}I]-iodomelatonin (100 pM) binding for mMT_1 and mMT_2 melatonin receptors were determined and compared with the Ki values for the human receptors. Melatonin competed for 2-[^{125}I]-iodomelatonin binding for the human [Ki (nM) for hMT_1: 0.34 and hMT_2: 0.44] and the mouse [Ki (nM) for mMT_1: 0.80 and mMT_2: 0.33] melatonin receptors with equal affinity. The affinity of luzindole [Ki (nM): 11.23 vs. 368.85], N-0889, N-0890 and N-0891 for hMT_2 receptors was higher than for the mMT_2 receptor. N-0890, N-0891 and 5-methoxyluzindole showed higher selectivity affinity ratios (Ki MT_1/MT_2) for hMT_2 than hMT_1 melatonin receptors, having 56, 91 and 130-fold differences, respectively. In contrast, their selectivity affinity ratios for the mMT_1 and mMT_2 melatonin receptors were identical. These results show differences between the human and the mouse melatonin receptor in terms of the affinities and selectivity ratios of luzindole and its analogues. We conclude that caution is needed when affinities and selectivity ratios are extrapolated to different species. *(Support by NS 061068 to MLD)*