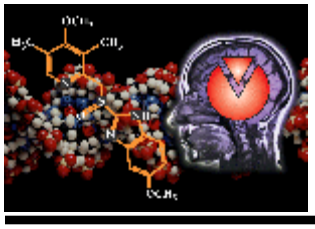


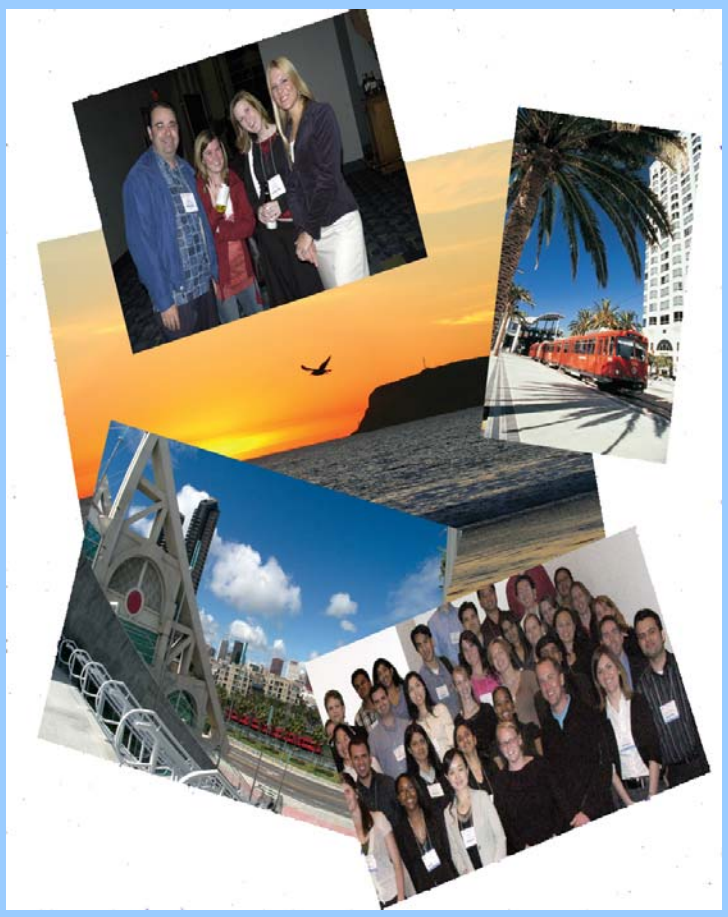
The Pharmacologist

Vol. 49
Number 4
2007
December

Celebrate ASPET's 100th Anniversary!!

aspet 100 YEARS 1908—2008

at Experimental Biology 2008
San Diego, CA, April 5 - 9



Featuring:

Special Centennial Symposia

ASPET Birthday Celebration

ASPET Student Fiesta

Nobel Laureate Reception

Great Giveaways

Details of the celebrations inside this issue!!

Also Inside this Issue:

The PHARMACOLOGIST

News

Features

Announcements

Reminder:
Please pay your 2008 Membership Dues by January 1, 2008. Payments may be made online at www.aspet.org

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

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

YEAR IN REVIEW

As 2008 comes to a close, ASPET would like to thank you for your participation in the Society this year. With the help of member contributions, support and participation, we are pleased to announce the following accomplishments made by ASPET this year:

Journals:
Molecular Interventions received its first Impact Factor 5.6 this year. Thomson Scientific's Journal Citation Reports placed MI within the Biochemistry & Molecular Biology category, where it was ranked in the top 20% of 262 titles.

Awards:
In 2007, we awarded 62 Graduate Student and 20 Young Scientist travel awards to attend the Experimental Biology meeting, all supported by member and corporate donations. In honor of our Centennial year, we will be increasing the number of travel awards for Experimental Biology 2008 in San Diego.

Membership:
Our membership is growing, and 2007 proved to be another successful year in membership recruitment. This year, we have recruited close to 500 new members. Many ASPET members are taking an active role in recruiting their students, colleagues and friends into the Society. We hope to continue this growth and encourage greater interest in ASPET and pharmacology next year.

Centennial Celebration:
We kicked off our 100th Anniversary celebrations in 2007 at Experimental Biology, where we gave out ASPET lapel pins, luggage tags, and *10 Decades of Pharmacology* posters. We also celebrated the founder of ASPET with the Abel Number project, which took on an exciting craze at the meeting. We also published some special Centennial articles in our publications including the significant deciles, a historical perspective in pharmacology and women in ASPET.

It all comes together in 2008 at the Experimental Biology meeting in San Diego (ASPET's official Centennial Meeting). Special Centennial symposia, parties, giveaways and other exciting events are planned for this once-in-a-lifetime meeting. A special thanks to all our members and sponsors who have contributed to the planning of this meeting.

Public Affairs:

This year, ASPET established the ASPET-IOSS (Integrative Organ Systems Sciences) Fund to help support graduate students and post-doctoral researchers seeking training in industry sponsored internships that further training in integrative, whole organ systems pharmacology. The ASPET-IOSS Fund is currently supported by Abbot Laboratories, Merck Research Laboratories, Pfizer, and Wyeth Research.

ASPET has also been actively participating in the The FDA Alliance, a coalition of over 100 organizations dedicated to increasing appropriations for FDA and to supporting FDA's continuing mission as a scientifically-based regulatory agency.

As we head into 2008, we plan to keep providing and improving the valued services you require. Next year will be the most exciting year for ASPET yet as we celebrate our 100th Anniversary. In order to make this a year to remember, we need your participation, support, and input. You can help us by making a contribution to one of the many funds that ASPET sets aside for special awards and events. Making a donation is a great way to demonstrate your commitment to the future of ASPET and to pharmacology. Please take the time to make a donation at http://www.aspet.org/public/membership/membership.html. Thank you for your continued support, and we look forward to making 2008 another successful year for ASPET!!

ASPET gratefully acknowledges the following individuals who have made contributions over and above dues for 2007:

Julius Axelrod Award
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Richard M. Weinshilboum, MD
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Thank you to our Corporate Contributors in 2007

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Paul M. Vanhoutte Award
GlaxoSmithKline
Servier

Because of ASPET's new database conversion this past summer, there have been some anomalies associated with our data. ASPET apologizes to anyone whose name is left off this list because of this.

ASPET Election Now Open

The ASPET election for President-Elect, Secretary/Treasurer-Elect, and Councilor is now open. All Regular and Retired members are eligible to vote. In addition, the following Divisions are holding elections: Division for Behavioral Pharmacology, Division for Drug Metabolism, Division for Molecular Pharmacology, Division for Neuropharmacology, Division for Pharmacology Education, and Division for Toxicology. Those of you with email will receive an email when the election opens and will be reminded of your username and password so that you can login to the Members Only section of the web site and vote. This email will also list the divisions in which you are eligible to vote. If you do not have email, you will be sent a paper copy of the election bulletin and a paper ballot and return envelope. You MUST sign the return envelope and print your name legibly in order for your paper vote to be counted. The divisions in which you are eligible to vote will be listed on your address label.

There are two ways to view the nominee's biographical sketches online. The full election bulletin will be posted in PDF format on the website. You can also click on the name of the nominee on the ballot, and the biographical sketch will appear in a pop-up window.

As required by the by-laws, the election site on the web will be open for a minimum of thirty (30) days from the day of notification. Voting is easy. Just click on the radio button next to the name of the candidate for whom you are voting. When you are finished and have reviewed your choices, click the submit button.

NOMINEES FOR ASPET OFFICE

Candidates for President-Elect

Brian M. Cox

Lynn Wecker

Candidates for Secretary/Treasurer- Elect

L. Charles Murrin

David R. Sibley

Candidates for Councilor

William B. Jeffries

Suzanne G. Laychock

ELECTION 2008

NOMINEES FOR DIVISION OFFICE

DIVISION FOR BEHAVIORAL PHARMACOLOGY

Nominees for Chair-Elect

Michael A. Nader

Galen R. Wenger

Nominees for Secretary/Treasurer-Elect

Emily M. Jutkiewicz

Peter J. Winsauer

DIVISION FOR DRUG METABOLISM

Nominees for Chair-Elect

J. Steven Leeder

Jeffrey C. Stevens

Nominees for Secretary/Treasurer-Elect

Michael H. Court

Yoichi Osawa

DIVISION FOR MOLECULAR PHARMACOLOGY

Nominees for Chair-Elect

Kafait U. Malik

Alan V. Smrcka

Nominees for Secretary/Treasurer-Elect

John R. Hepler

Rennolds S. Ostrom

DIVISION FOR NEUROPHARMACOLOGY

Nominees for Chair-Elect

Margaret E. Gnegy

Roger D. Spealman

Nominees for Secretary/Treasurer-Elect

Linda Dykstra

Kelly M. Standifer

ELECTION 2008

DIVISION FOR PHARMACOLOGY EDUCATION

Nominees for Chair-Elect

George A. Dunaway

Jeffrey S. Fedan

Nominees for Secretary/Treasurer-Elect

Frederick A. Curro

Amy L. Wilson-Delfosse

DIVISION FOR TOXICOLOGY

Nominees for Chair-Elect

Qiang Ma

John D. Schuetz

Nominees for Secretary/Treasurer-Elect

Wayne L. Backes

David E. Moody

PLEASE VOTE AT:
http://www.aspet.org/CVWEB_ASPET/MainLogin.shtml

There will be no elections this year for the following divisions:

Division for Cardiovascular Pharmacology
Division for Clinical Pharmacology, Pharmacogenomics & Translational Medicine
Division for Drug Discovery, Drug Development, and Regulatory Affairs
Division for Systems & Integrative Pharmacology

American Society for Pharmacology and Experimental Therapeutics at Experimental Biology 2008 – San Diego

All rooms listed are in the San Diego Convention Center unless otherwise noted.

LECTURES: 8:00-8:50 AM and 1:15-2:05 PM **POSTERS: 12:00 PM-2:15 PM** **SYMPOSIA: Sunday – Tuesday: 9:00-11:30 AM & 2:30-5:00 PM and Wednesday: 8:00-10:30 AM**

FRIDAY APRIL 4	SUNDAY AM APRIL 6	SUNDAY PM APRIL 6	MONDAY AM APRIL 7	MONDAY PM APRIL 7	TUESDAY AM APRIL 8	TUESDAY PM APRIL 8	WEDNESDAY AM APRIL 9
Day 1 – Colloquium: Recent advances in muscarinic receptor pharmacology & therapeutics **N. Birdsall, R. Eglen** 7:45 AM-7:00 PM Marriott Hall 1	JULIUS AXELROD SYMPOSIUM Celebrating a pioneer pharmacologist & his legacy **L. Eiden** Room 3 **NEU**	BB BRODIE LECTURE **C. Klaassen** Room 5B	RAY FULLER LECTURE Broad spectrum antidepressants: Variations on a monoamine theme **P. Skolnick** Room 2	PB DEWS LECTURE **C. Schuster** Room 2	EPHAR LECTURE Calcium sensors & potassium channels in the vasculature **A. Weston** Room 3	POSTER DISCUSSION Epoxide hydrolases **B. Hammock, J. Imig, C. Omiecinski, C. Morisseau** 12:00-2:15 PM Room TBD	Inflammation: Early disease marker, drug response modifier, therapeutic target **D. Miller, D. Sitar** Room 5B **DDR**, CPTM,TOX,SIP,DM
Day 1 – Third colloquium on regulators of G-protein signaling **M. Koelle, R. Neubig** 1:00 PM-5:30 PM Marriott Hall 2	Drug Discovery Paradigms: Past, Present, Future **R. Ruffolo**	DRUG METABOLISM DIVISION PLATFORM SESSION Biotransformation & drug transport **K. Thummel, T. Kocarek**	RAY FULLER SYMPOSIUM Antidepressants for the new millennium: Circumventing the monoamine synapse **P. Skolnick**	BEHAVIORAL PHARMACOLOGY DIVISION SYMPOSIUM Translational research in behavioral pharmacology **C. France, A. Young**	**ASPET/APS Women's Committees Workshop** Gainfully employed: From launching a job search to navigating negotiations **S. Benyajati, C. Hegg, J. Lameh** 8:00-10:00 AM Room 28A	CLINICAL PHARMACOLOGY, PHARMACOGENOMICS & TRANSLATIONAL MEDICINE DIVISION SYMPOSIUM Drug response predictions: Genotype vs. phenotype **R. Kim** Room 5B **CPTM**	Mitochondria in life & death: From biogenesis to autophagy **R. Schnellmann** Room 5A **TOX**
Day 1 – Behavioral Pharmacology Society Mtg 6:15 PM-9:45 PM Marriott San Diego Ballroom A							
SATURDAY APRIL 5	The G-whizards of GPCR/G-protein signaling **L. Limbird**	Pharmacotherapeutics for drug abuse – The cocaine challenge **A. Young**	The obesity epidemic: Pharmacological challenges **I. Laher**	New concepts in an old system – Renin-angiotensin system **M. Morris, C. Ferrario**	ABC transporters: From drug resistance to drug response **R. Kim**	TOXICOLOGY DIVISION SYMPOSIUM Role of transporters in prevention & exacerbation of toxicity **M. Vore**	A century of development of concepts of ion channel receptors: Past milestones & contemporary development for the next decade **P. Taylor**
Day 2 – Colloquium: Recent advances in muscarinic receptor pharmacology & therapeutics **N. Birdsall, R. Eglen** 7:30 AM-6:00 PM Marriott Hall 1	Room 2 **MP, ASBMB**	Room 5A **BEH**	Room 3 **SIP**	Room 4 **CVP**	Room 2 **CPTM**	Room 5A **TOX**	Room 3 **MP,** BEH,NEU,**ASBMB**
Day 2 – Third Colloquium on regulators of G-protein signaling **M. Koelle, R. Neubig** 7:30 AM-5:30 PM Marriott Hall 2	Cannabinoid CB1 receptor interdependence with other receptor systems as a target for medication development **S. Goldberg** Room 5A **BEH**, DDR,MP,NEU,SIP	Chance favors the prepared mind: A Nobel perspective **J. Fedan** Room 2 **EDU**	P450s: Structure, function, in silico predictions **J. Halpert, E. Johnson** Room 4 **DM**	Development of inhibitors of the soluble epoxide hydrolase **B. Hammock, J. Imig** Room 5B **TOX**	New experimental approaches to the treatment of schizophrenia **P. Conn, C. Tamminga** Room 3 **NEU**	CARDIOVASCULAR PHARMACOLOGY DIV JUNIOR SCIENTISTS' COMPETITION **J. Kermode, J. Shen F. Khasawneh** 2:30-4:15 PM Room 2 **CVP**	Emerging importance of allosteric receptor modulation in drug discovery **C. Murphy, G. Gu** Room 4 **NEU,** SIP,DDR,BEH,MP,CPTM
Day 2 – Behavioral Pharmacology Society Mtg 7:30 AM-5:30 PM Marriott San Diego Ballroom A	Pharmacology education for the next 100 years: Preparing the next generation of pharmacologists **L. Crespo, J. Barnett** Room 5B **EDU**	Regulation of ion channels in cardiovascular disease **S. Sonkusare, N. Rusch** Room 4 **CVP,**MP	The emerging science of drug safety **D. Abernethy, J. Jones** Room 5A **CPTM**, DDR,TOX,BEH,CVP,DM	Neuroplasticity in addiction: Picking up the pieces **P. Kalivas** Room 3 **NEU,**BEH,SIP	Drug metabolism, bioactivation & chemical-induced toxicities: Lessons learned & contemporary issues **T. Monks, K. Thummel** Room 4 **DM,**TOX,CPTM,SIP	PAUL VANHOUTTE DISTINGUISHED AWARD LECTURE Endothelial function in the time of giants **D. Heistad** 4:30-5:30 PM Room 2 **CVP**	The promise & the challenges of pharmacogenetics as a diagnostic tool **J. Leeder** Room 2 **CPTM**, DM,SIP,TOX

SOCIAL EVENTS	CENTENNIAL SYMPOSIA	REGULAR SYMPOSIA	DIVISION SESSIONS	LECTURES

SATURDAY APRIL 5	SUNDAY AM APRIL 6	SUNDAY PM APRIL 6	MONDAY AM APRIL 7	MONDAY PM APRIL 7	TUESDAY AM APRIL 8	TUESDAY PM APRIL 8	WEDNESDAY PM APRIL 9
2008 TEACHING INSTITUTE How to teach graduate students **W. Jeffries** 12:30-3:00 PM Room 5A		G12/13 signaling of cell surface receptors: Molecular insights & disease context **S. Siehler** Room 3 **MP**, CVP,**ASBMB**		SYSTEMS & INTEGRATIVE PHARMACOLOGY DIVISION SYMPOSIUM Ion channel therapy & disease therapy **R. Kass, M. Nelson** Room 5A **SIP**	Integrative urogenital pharmacology: Implications to the treatment of bladder disease **G. Christ, K-E. Andersson** Room 5B **SIP,**DDR	NEUROPHARMACOLOGY DIVISION PROGRAMMING Postdoctoral scientist award finalists **D. Sibley** Room 4 **NEU**	G-proteins and protein kinases **K. Blumer** 2:15-4:35 PM Room 1A **ASBMB**
DIVERSITY COMMITTEE SYMPOSIUM Implications of pharmacogenomics for health disparities **S. Elton, M. Davila-Garcia** 12:30-3:00 PM Room 5B				Growth Regulation **K-L. Guan** 3:30-5:50 PM Room 1A **ASBMB**	DRUG DISCOVERY, DEVELOPMENT & REGULATORY AFFAIRS DIVISION SYMPOSIUM Signal transduction bioinformatics: Integrating pharmacology with signaling molecule discovery **L. Eiden** Room 5A **DDR**	MOLECULAR PHARMACOLOGY DIVISION PROGRAMMING Postdoctoral award finalists **K. Harden** Room 3 **MP**	
GRADUATE STUDENT-POSTDOC COLLOQUIM Learning from the past, training for the future **L. Crespo, T. Smith** 3:15-5:45 PM Room 4						Integration of second messenger signaling **S. Taylor, A. Newton** 3:30-5:50 PM Room 1B **ASBMB**	
ASPET BUSINESS MEETING 6:00-7:30 PM Convention Center Room 6A							
OPENING & AWARDS RECEPTION 7:30 –10:00 PM Convention Center West Pavilion Terrace		GRADUATE STUDENT - POSTDOC BEST ABSTRACT COMPETITION 6:30 – 8:30 PM Marriott Marriott Halls 3 and 4		**ASPET BIRTHDAY PARTY** 7:00-10:00 PM Gas Lamp District "J" Street Between 4th & 5th Ave			

SOCIAL EVENTS	CENTENNIAL SYMPOSIA	REGULAR SYMPOSIA	DIVISION SESSIONS	LECTURES

POSTER PRESENTATIONS 12:00 PM-2:15 PM

Sunday Poster Sessions

Behavioral Pharmacology: Cannabinoids & Other Systems
Drugs of Abuse: Opioid Pharmacology
Drugs of Abuse: Psychomotor Stimulants
Neuropharmacology I
Parkinson's Disease: Mechanism & Mediators
Neuroprotection
Neurotoxicology: Molecular Mechanisms
Hormones & Hormone Receptors
Pharmacology & Women's Health
Drug Discovery
Signal Transduction: Ion Channels
GPCR Structure/Imaging
GPCR Oligomerization
GPCR Ligands & Allosterism
GPCR Desensitization & Internalization
GPCR Interacting Proteins/Signalplex
GPCR Trafficking
Signal Transduction: Cell Surface Receptors
GPCRs in Disease

Monday Poster Sessions

Behavioral Pharmacology: General
Behavioral Pharmacology: Plasticity Processes
Neuropsychiatric Disorders
G Proteins I
G Proteins II
Second Messenger Systems
Signal Transduction: General
Signal Transduction: Kinase/ Phosphatases
Vascular Pharmacology: General
Vascular Pharmacology: Cerebral
Vascular Pharmacology: Coronary
Vascular Pharmacology: Pulmonary
Smooth Muscle Pharmacology
Renal Pharmacology/Toxicology
Pulmonary Pharmacology/Toxicology
DMD: Biotransformation/Chemistry
DMD: Phase I/Phase II Enzymes
DMD: Gene Expression & Regulation
DMD: Pharmacokinetics/ Toxicokinetics

Tuesday Poster Sessions

Neuropharmacology II
Neurotransmission
Neurotransmitter Receptors
Vascular Endothelium
CVP: General
CVP: Protection/Remodelling
DMD: Reactive Metabolites &Toxicity
DMD: Transporters
Gene Expression/Regulation
Genomics/Proteomics/Pharmacogenomics
Clinical Pharmacology/Toxicology
Chemotherapy
Developmental Pharmacology/ Toxicology
GI Inflammation & Toxicology
Immunopharmacology/Toxicology
Mechanisms of Cell Injury

CENTENNIAL UPDATE

The **Experimental Biology 2008 meeting in San Diego, CA, April 5 – 9,** will be the official celebration of ASPET's 100th Anniversary. Be sure to register today for the meeting at www.eb2008.org so that you don't miss out on all the exciting Centennial activities!

Special Centennial Symposia Include:

P450s: Structure, Function, In Silico Predictions
Spkrs: Anthony Lu, Paul Ortiz de Montellano, William Atkins, Eric Johnson, Lovisa Afzelius

Development of Inhibitors of the Soluble Epoxide Hydrolase as a Novel Treatment for Hypertension, Vascular Inflammation and End Organ Damage
Spkrs: Michael Arand, Heather Webb, Bruce Hammock, William Campbell, Darryl Zeldin, John Imig

New Experimental Approaches to the Treatment of Schizophrenia: Moving Beyond Monoamine Antagonists
Spkrs: Carol Tamminga, Darryle Schoepp, Jeffrey Conn, Craig Lindsley

The G-Whizards of GPCR/G-Protein Signaling
Spkrs: Alfred Gilman, Lee Limbird, Robert Lefkowitz, Heidi Hamm

Chance Favors the Prepared Mind: A Nobel Perspective
Spkrs: Alfred Gilman, Louis Ignarro, Ferid Murad

The Obesity Epidemic: Pharmacological Challenges
Spkrs: Matthias Tschop, Francis Kuhajda, Stephen Bloom, Xavier Pi-Sunyer, D. Scott Weigle

Drug Discovery Paradigms: Past, Present, and Future
Spkrs: S.J. Enna, Graeme Milligan, Robert Ruffolo, Brian Zambrowicz

New Concepts in an Old System: Renin-Angiotensin System Blockade as Therapy for General Cardiovascular Disease
Spkrs: Ronald Smith, Genevieve Nguyen, Mark Chappell, Khalid M. Elased, Lisa Cassis, Michael Bader

Pharmacotherapies for Drug Abuse: The Cocaine Challenge
Spkrs: Kenneth Silverman, Jonathan Katz, James Woods, William Woolverton, Maxine Stitzer

ABC Transporters: From Drug Resistance to Drug Response
Spkrs: Erin Schuetz, Alfred Schinkel, Susan Bates, Susan Cole, Richard Kim

Julius Axelrod Symposium: Celebrating a Pioneer Pharmacologist and His Legacy: Creating New Drugs by Revealing Mechanisms of Drug Action in Fundamental Biological Processes
Spkrs: Susan Amara, Marc Caron, Solomon Snyder, Richard Weinshilboum

In addition to the symposia, there will also be several parties you won't want to miss:

Opening Ceremony – Taking place outside on the West Terrace of the Convention Center on Saturday evening, the reception will feature music, food, and plenty of social networking opportunities. This event is free.

Nobel Laureate Reception for Students – Following the Special Centennial symposium, *Chance Favors the Prepared Mind: A Nobel Perspective*, there will be a reception honoring ASPET's Nobel Laureates. This is your chance to speak with some of the brightest minds in pharmacology. The reception will feature appetizers and drinks and is free to students.

CENTENNIAL UPDATE

ASPET Student Fiesta – Following the Student/Post Doc Poster competition, the fiesta themed party will give students the chance to network with each other while enjoying food and drinks. A live Mariachi band will provide music for dancing. This event is free.

ASPET Birthday Party – In celebration of the big 100, this ticketed event is not to be missed. Open to all ASPET members and friends of ASPET, this birthday bash will take place on a private block in the exciting Gaslamp Quarter of San Diego. The street festival will feature dinner, drinks, giveaways, live music, street entertainers, and much more! Tickets may be purchased when you register for the meeting online.

And you won't want to miss out on these exciting Centennial giveaways, exclusively for members who attend the Experimental Biology meeting:

ASPET Centennial Publication – ASPET will be publishing several special Centennial articles including Overview of Nobel Laureates in Pharmacology, Women in ASPET, Executive Officer Interviews, History of ASPET, Centennial Perspectives, etc. All of these articles will be bound together in a commemorative collection that will be given out FREE to all ASPET members who attend the Centennial meeting. This is ONLY available to meeting attendees.

Ten Decades of Pharmacology – Pick up your free poster highlighting 100 years of significant scientific events in pharmacology.

ASPET Lapel Pin – Show your support for ASPET by picking up your free lapel pin.

ASPET Luggage Tags – You can make finding your luggage easy with these durable ASPET luggage tags. These will be available for free at the meeting.

Abel Number Buttons – Figure out your Abel number and pick up your free button at the meeting.

Other giveaways are a surprise, so be sure to attend the meeting so you don't miss out. We will also be raffling off hundreds of dollars of prizes.

And for the first time ever, ASPET will be selling items such as t-shirts, baseball caps, and water bottles with the ASPET logo. These items will be available for a discount at the Experimental Biology meeting.

If you can only attend one meeting in 2008, the ASPET Centennial Meeting at Experimental Biology is the one you can't afford to miss!!

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Stay informed of ASPET Centennial News

Get details and stay on top of all our planned activities.

Be sure to visit our website often:

http://www.aspet.org/public/Centennial/Centennial_home.htm

WE CORDIALLY INVITE YOU TO ATTEND THE ASPET STREET FESTIVAL!!!

Don't miss this exciting, once in a lifetime event, celebrating the 100th anniversary of the American Society for Pharmacology and Experimental Therapeutics.

Date: Monday, April 7th 2008
Time: 7pm – 10pm
Place: "J" Street between 4th and 5th Street
Gaslamp Quarter, San Deigo

The ASPET Street Festival will be taking place on a private block of the Gaslamp Quarter, open only to ASPET members and friends. This ticketed event will feature:

- Large Buffets Catered by Jolt'N Joe's and Red Pearl Restaurants
- Outdoor and Indoor Cocktail Bars
- Live Music by *The Mar Dels* (playing everything from disco to pop music)
- Street Entertainers
- Door Prizes
- Giveaways
- Private Use of the Restaurants on the Block
- Indoor and Outdoor Seating
- Dance Floor
- Billiards and Darts
- Birthday Cake
- Plus much more!

Ticket Prices:
$25 – ASPET Members and Family of ASPET Members
$15 – ASPET Student Members
$35 – Non-ASPET Members

Purchase your tickets when you register to attend the Experimental Biology 2008 Meeting
April 5 – 9, San Diego, CA
www.eb2008.org

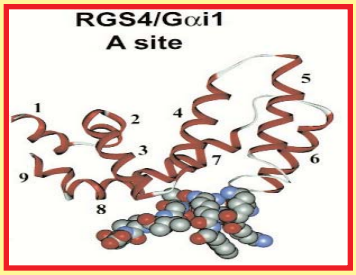
3rd RGS Colloquium

April 4-5, 2008, San Diego, CA

Organized by: Michael Koelle, PhD and Richard R. Neubig, MD, PhD

This is a Satellite Meeting to Experimental Biology 2008

Topics and Speakers include:



RGS Structure/Function

John Tesmer, University of Michigan

Roles of RGS proteins and RGS homology domains in signaling scaffolds

John Sondek, University of North Carolina at Chapel Hill

R7-family RGS proteins

RGS Targeting/Cellular Localization

John R. Hepler, Emory University

RGS proteins as multifunctional scaffolding proteins in cell physiology

Kendall J. Blumer, Washington University School of Medicine

Post-translational modifications regulating RGS protein shuttling

Kirill Martemyanov, University of Minnesota

Macromolecular complexes of RGS9 - master regulators of G protein signaling in retina and striatum

Marilyn G. Farquhar, University of California at San Diego

Roles of RGS-PX1 in endocytosis and G protein signaling

Andrew Tinker, Royal Free & University College Medical School

The molecular basis of the pleiotropic effects of RGSs in the regulation of G-protein gated K+ channels

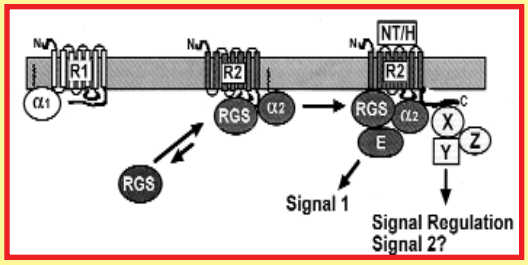
Novel Interactions/Functions

Vladlen Slepak, University of Miami

Structure and function of Gbeta5-R7 complexes: 10th anniversary

Peter Chidiac, University of Western Ontario

Novel regulatory properties of RGS2



Additional speakers will be selected from meeting registrants based on their submitted abstracts

RGS Action In Vivo

John H. Kehrl, National Institute of Allergy and Infectious Diseases

Insights into RGS protein function from the analysis of RGS and Gi alpha knock-out mice

John Traynor, University of Michigan

RGS proteins as a potential drug target for depression

Vanna Zachariou, University of Crete

A role of RGS9, RGS4, and RGSz in addiction and analgesia

Additional Program Information and Registration at:

http://www.aspet.org/public/meetings/meetings.html

We anticipate, but cannot guarantee, being able to provide some funds to assist junior scientists with travel to the meeting. See website for details.

Recent Advances in Muscarinic Receptor Pharmacology and Therapeutics

April 4 - 5, 2008

San Diego Marriott Hotel and Marina, San Diego, CA

Organized by Richard Eglen, Nigel Birdsall, Christian Felder, Allison Fryer and Neil Nathanson

Topics and Speakers Include:

Physical/Biophysical Studies:

Muscarinic receptor structure and function: Mutatis mutandis
Ed Hulme, MRC National Institute for Medical Research

Muscarinic receptor dimers and clustering - single molecule studies on living cells
Nigel Birdsall, MRC National Institute for Medical Research

Novel Aspects of Muscarinic Receptor Pharmacology:

At long last - emerging selective muscarinic receptor pharmacology
Christian Felder, Eli Lilly & Company

Potential for allosteric activators of M_1 and M_4 muscarinic receptors in the treatment of schizophrenia
Carrie Jones, Vanderbilt University

Optimizing inhaled muscarinic receptor antagonist dissociation rates to enhance duration and subtype selectivity
Steven Charlton, Novartis

Muscarinic Receptor Signaling and Phenotypes:

Regulation of muscarinic receptor expression and function
Neil Nathanson, University of Washington

Emerging data from novel muscarinic receptor mutant mouse models
Jurgen Wess, NIDDK/NIH

Subtype-specific functions of mAChRs revealed by the use of knock-out mice
Minoru Matsui, Chiba Institute of Science, Japan

Muscarinic modulation of striatal physiology in health and disease
James Surmeier, Northwestern University

Therapeutic Uses of Muscarinic Drugs:

Muscarinic receptor agonists: a novel treatment for schizophrenia
Anantha Shekhar, Indiana University

Muscarinic antagonists and bladder dysfunction
TBD

Muscarinic antagonists and lung dysfunction
Allison Fryer, Oregon Health & Science University

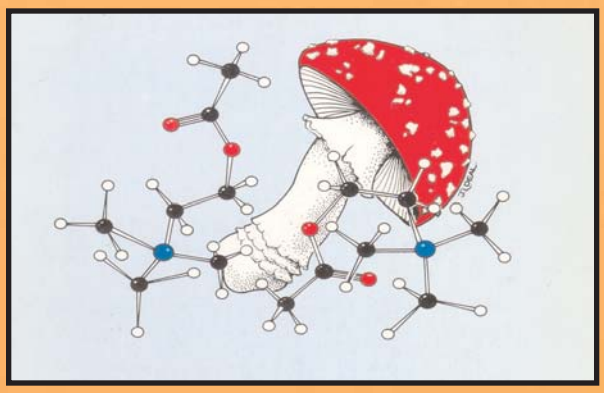
Emerging Areas and Novel Concepts:

Non neuronal muscarinic systems
Sergei Grando, University of California at Irvine

Muscarinic receptors and apoptosis
Andrew Tobin, University of Leicester

Plenary Lecture:

Structure and dynamics of the human beta$_2$ adrenergic receptor
Brian Kobilka, Stanford University



Awards Opportunities

Otto Loewi New Investigator Awards and Lectures:

To recognize and encourage the work of young scientists, the Colloquium will offer prizes to up to three young investigators for scientific studies on muscarinic receptors.

Ruth Levine Award:

To recognize Ruth Levine's outstanding encouragement and promotion of the research of graduate and immediate post-doctoral scientists, three presenters will be selected by the Scientific Committee in advance of the meeting on the basis of their poster abstracts and will be asked to present orally their most important findings. The best presentation, based on both oral presentation and poster, will be awarded the first Ruth Levine Award.

For more information and to apply, visit the meetings section on www.aspet.org

Additional Program Information and Registration at:

http://www.aspet.org/public/meetings/meetings.html

Women in ASPET: A Centennial Perspective

Marlene L. Cohen[1], Holly Brevig[2], Christine Carrico[3], and Lynn Wecker[4]

[1]Vice President, Creative Pharmacology Solutions LLC, Carmel, Indiana; [2]Graduate Student, Department of Pharmacology, University of Michigan Medical School, Ann Arbor, Michigan; [3]Executive Officer, American Society for Pharmacology and Experimental Therapeutics, Bethesda, Maryland 20814; [4]Distinguished Research Professor of Molecular Pharmacology, Physiology, Psychiatry & Behavioral Medicine, University of South Florida College of Medicine, Tampa, Florida

Introduction

As the centennial approaches, the Women's Committee of ASPET was inspired to document, recognize and commemorate the contributions of women to the Society. This retrospective analysis provides a review of the role women played in the leadership, growth and accomplishments of ASPET since its formation in 1908. The information gathered was highly dependent on records from ASPET as documented in editions of *The Pharmacologist*, a documentary of the first 60 years of ASPET (Chen, 1969), the assistance of the ASPET Executive Office, information readily available on the internet, and our collective recollection of events and situations. We hope that this information is both informative and useful as we move into ASPET's next century.

The First 60 Years

ASPET was founded in 1908 by 18 male pharmacologists, including John Jacob Abel, often considered the "Father of Pharmacology." Women did not have a major role in ASPET in the early years, likely more a reflection of the times and the role of women in science than of any conscious decision or philosophy of exclusion by the Society. The growth of the involvement of women in ASPET seems to have paralleled the growth of women in other societies (Lees, 2002) and women in science and medicine in general (Jagsi et al., 2006). Men were clearly more entrenched in ASPET in the early 1900s, consistent with societal gender roles. It was not until the late 1970s that the number of women admitted to ASPET reached a level high enough to exert a significant influence on Society thoughts and activities.

The women elected to ASPET during the first 30 years are listed in Table 1. For those women whose photographs were available, they are shown in Figure 1. To the best of our knowledge, Louise Pearce was the first woman elected to the Society, and from 1915 to 1929, was the only female member of ASPET (Chen, 1969). Louise was not a 'card-carrying' pharmacologist, but rather a physician pathologist who graduated from Stanford University with a bachelor's degree in physiology and from The Johns Hopkins University School of Medicine with an M.D.. She spent most of her career at the Rockefeller Institute for Medical Research in New York and was the first woman to work with its director, Simon Flexner, although she was never granted 'full' membership at that institution. Her involvement with pharmacology resulted from her breakthrough studies with Flexner leading to the development of tryparsamide, an effective therapy for African sleeping sickness. She pursued therapeutic studies with this drug when an outbreak occurred in the Belgian Congo, for which she received the King Leopold II prize along with a check for ten thousand dollars from the Belgian government. Louise also served as part-time president of the Woman's Medical College of Pennsylvania from 1946 to 1951. Louise died in 1959 after a short illness. Additional information may be found at:
http://www.nlm.nih.gov/changingthefaceofmedicine/physicians/biography_248.html.

Table 1. Women members of ASPET prior to 1940

Year	Name
1915	Louise Pearce
1929	Helen Bourquin
1931	Helen Graham
1933	Janet Travell
1934	Gerty Cori
1937	Phoebe Crittenden
1939	Helen Coombs

[1]The information contained in this Table was taken from Chen (1969) based on the assumption that newly elected female members of ASPET have been listed using first names while male members have been listed predominantly by first initials only.

Helen Bourquin, the second female member of ASPET, graduated from Colorado College, and received an M.A. and Ph.D. from the University of Chicago. Although it has been somewhat difficult to trace Helen's career path, she was a member of the Department of Physiology at The University of South Dakota at about the time she was elected to membership in ASPET, and she relocated to the Department of Materia Medica and Therapeutics at the University of Michigan Medical School shortly thereafter. Helen's research focused primarily on diabetes.

Helen Graham, the third woman elected to ASPET membership, received her bachelor's and master's degrees from Bryn Mawr College, and her Ph.D. in chemistry from the University of Chicago. Helen worked in the laboratory of John Jacob Abel at the Johns Hopkins University Medical School while her surgeon husband, Evarts A. Graham, was in the military. When her husband accepted the Chair of the Department of Surgery at the Washington University School of Medicine, Helen joined the faculty as a research assistant in pharmacology. She was elected to ASPET membership the same year she was promoted to assistant professor. Helen gradually rose through the faculty ranks, and almost 30 years later, was promoted to professor in the Department of Pharmacology. Helen's research focused on the physiology and pharmacology of peripheral nerves, as well as histamine. She discovered that mast cells and basophils stored histamine, and she developed methods for measuring histamine in body fluids. Helen was a unique woman who balanced numerous roles and was an inspiration to all who knew her. Helen died in 1971 at the age of 81 on the way to her office. For more information on this truly inspiring individual, please see:
http://beckerexhibits.wustl.edu/women/graham.htm

Janet Travell, the fourth woman in ASPET, graduated Phi Beta Kappa from Wellesley College and received her M.D. in 1926 from Cornell University Medical College where she spent her career. Janet's life was filled with firsts: she was first in her graduating class at Cornell; she was the only female intern on the staff at New York Hospital; and she was the first woman to hold the position of White House physician. Janet achieved the rank of associate professor of pharmacology at Cornell in 1952, and she was a pioneer in elucidating the contribution of muscle trigger points to acute and chronic pain syndromes. She co-authored the textbook "Myofacial Pain and Dysfunction: the Trigger Point Manual" with David Simons. She also wrote her autobiography, published in 1968. Janet succumbed to heart failure at home in 1997. For more information on this outstanding woman, the reader is referred to:
http://www.gwu.edu/gelman/archives/exhibits/travell/
http://www.pain-education.com/100143.php
http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=152828

Gerty Cori, the first American woman to receive the Nobel Prize in Physiology or Medicine, was born and studied in Prague and received her medical degree from the Medical School of the German University of Prague in 1920. During that same year, she married Carl Cori and published her first paper with her husband. The Coris immigrated to the U.S. in 1922 to pursue their research at the New York State Institute for the Study of Malignant Diseases in Buffalo. After they became naturalized citizens in 1931, Carl accepted the position of professor and Chair of the Department of Pharmacology at the Washington University School of Medicine. Because two members of the same family could not simultaneously hold faculty appointments, Gerty became a research fellow in the Department where she spent the next 16 years as a research associate. In 1946, when Carl became Chair of the new Department of Biochemistry, Gerty was finally promoted to professor of pharmacology. The Coris received the Nobel Prize in 1947 for their studies on carbohydrate metabolism and the enzymes that interconvert glycogen to glucose. Gerty suffered from myelofibrosis for nearly 10 years and died in 1957. More information on this outstanding woman is located at:
http://nobelprize.org/nobel_prizes/medicine/laureates/1947/cori-gt-bio.html
http://www.nlm.nih.gov/changingthefaceofmedicine/physicians/biography_69.html
http://beckerexhibits.wustl.edu/mowihsp/bios/cori.htm

The last two women to be elected into ASPET prior to 1940 are Phoebe Crittenden and Helen Coombs. Unfortunately, we could not find out as much about these women as the other five. From her publications, Phoebe Crittenden, who published as P. Jeanette Crittenden, P.J. Crittenden and Phoebe J. Crittenden, was on the faculty of the Department of Physiology and Pharmacology at Northwestern University Medical School in the mid-late 1930s, and at the Merck Institute for Therapeutic Research in New Jersey in the mid-late 1940s. Her research focused on pancreatic secretions, renal excretions, and amino acids. She appears to have accepted a faculty position at Goucher College in the late 1940s or early 1950s, and either discontinued her research or her publishing, as was common in those years for female scientists on the faculty at women's colleges (Appel, 1994). Helen Coombs was a faculty member in the Department of Physiology at New York University and Bellevue Medical College and New York Homeopathic Medical College, which later became

New York Medical College. Helen published many articles on cortical stimulation, seizures and neuronal control of the cardiovascular and respiratory systems.

Louise Pearce
(1915)

Helen Bourquin
(1929)

Helen Graham
(1939)

Janet Travell
(1933)

Gerty Cori
(1934)

No picture available

Phoebe Crittenden
(1937)

Helen Coombs
(1939)

Fig. 1. Women members of ASPET from the inception of the Society until 1940. The number in parentheses is the year the individual was elected to ASPET

Based on the data presented by Chen (1969) and the assumption noted in Table 1, by the end of 1939, of the 265 members of ASPET, women represented 2.6% of the total, and in the 30-year span from 1939 until 1969, the number of female members of ASPET (Table 2) remained fairly constant, representing less than 5% of the total membership.

Table 2. Number of Female members of ASPET from 1908 until 1970

Year	Cumulative Number of ASPET Members[2]	Cumulative Number of Female Members[1]	Female members as a Percent Total
1939	265	7	2.6
1949	512	12	2.3
1959	1014	29	2.9
1969	1804	69	3.8

[1] As in Table 1
[2] Estimated from data in Chen (1969).

The 1970s: An Informal Role for Women in ASPET

ASPET was a highly prominent and desirable society for membership among both male and female pharmacologists, an image that was retained in part through the extensive nomination process and necessary membership voting required before admission to the Society. Membership signified a “coming of age” acceptance into a prestigious group of scientists

recognized for their creativity, innovative research and documented independence. We would imagine that women struggled to achieve recognition for independent research careers during this period.

To ascertain the growth in the number of female members of ASPET from 1970 to the present, we reviewed the new member lists provided by ASPET for 1970, 1980, 1990 and 2000, and with an imperfect assessment of the gender determined by first names, we estimated the number of women in ASPET at the beginning of each decade (Figure 2). Although this estimate has several limitations, including the difficulty of assigning gender to names of foreign scientists as ASPET increased its diversity through the years, data indicate that since 1970, female membership in ASPET increased substantially with a fairly linear trend.

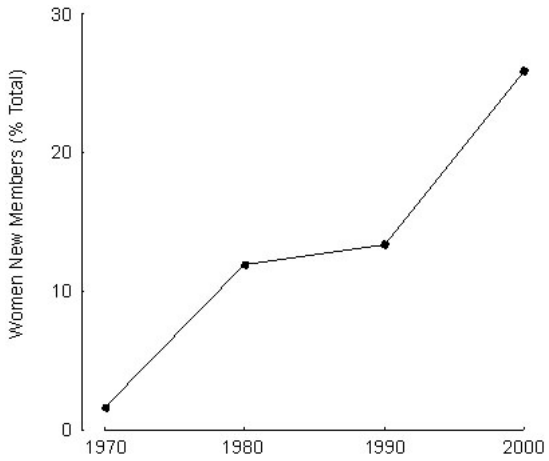


Fig. 2. Growth in the Number of Women in ASPET since 1970

As the number of women in ASPET grew, so did the role of women in influence and leadership of the Society. During the 1970s, women were often influential in rather informal ways, particularly at the fall ASPET meetings, which were attended by both scientists and their families. These meetings provided ample opportunity for women to serve as role models for students and younger female pharmacologists. At breakfast in the hotel, one might find Eva Killam along with one or more of their children, or Elaine Sanders-Bush and her daughter. The informality was particularly useful to young women, as it provided opportunities to mingle, interact and observe the juggling of roles between parenthood and professional life. This type of mentoring opportunity was lost when ASPET eventually moved to only one annual meeting in the spring. To a large extent, these informal interactions and observations shaped collective views of juggling work life issues, in marked contrast to the current need for institutionalized symposia, workshops, corporate divisions and academic departments focused on the topic of mentoring.

The 1980s and Beyond: Women in ASPET Leadership

The ASPET Executive Office

ASPET has had only four Executive Officers in its 100-year history, viz., Ellsworth Cook and Houston Baker followed by two women, Kay Croker and Christine Carrico (Figure 3). Thus, early memories of women in leadership roles in ASPET (other than as wives of prominent men) began with the promotion of Kay Croker from an administrative support role to that of the first female Executive Officer of the Society, a position she held from 1977-1997. This represented an historical move for ASPET, as Kay had served as the administrative assistant to Houston Baker, the previous Executive Officer of the Society.

Although Kay was familiar with society affairs, she recalled the difficulty ASPET had with the decision to promote a woman to this major position in the historically male society. For 20 years until her retirement, Kay served ASPET as it grew in membership and financial independence, and she was instrumental in encouraging the formation of a Women's Subcommittee of ASPET in 1980.

Kay Croker
(1981-1997)

Christine Carrico
(1998 – present)

Fig. 3. Women Executive Officers of ASPET. The numbers in parentheses are the years the individuals serve(d).

Following Kay's retirement in 1997, ASPET was extremely fortunate to recruit Christie as its Executive Officer. Christie was a 'card-carrying' pharmacologist and member of ASPET who served previously as the Executive Director of the Biophysical Society and had considerable experience in management and governmental affairs, and the needs of biomedical scientists. As a consequence, Christie has played a pivotal role in reorganizing the ASPET office, initiating new safeguards and controls, and encouraging leadership to implement new programs and initiatives. Christie helped transition the office to new facilities, supported the formation of a new ASPET journal, consolidated the office staff, and stabilized the financial situation of ASPET during the investment downturn from 2001 to 2004. Christie's strong managerial skills continue to serve ASPET well.

ASPET Officers

Although female membership in the Society increased steadily from 1970, ASPET, like many other scientific societies, was enriched and entrenched with many male colleagues of prominence and stature. Unfortunately, women were not recognized similarly. In spite of the rise in the number of female members of ASPET from 1970 to the present, the first female Councilor, Eva King Killam, was not elected to serve until 1973; the first female Secretary/Treasurer, Ruth Levine, was not elected until 1975, and it was not until 1984 that ASPET elected its first female president, Marjorie Horning. As a matter of note, ASPET has had only five female presidents in its 100-year history (Table 3, Figure 4).

It is interesting that the first two female presidents of ASPET were each married to prominent scientists with whom they worked and collaborated closely. Marjorie Horning obtained a position at the NIH in 1951, where her husband, Evan Horning, had been appointed Chief of the Laboratory of the Chemistry of Natural Products. Marjorie was a prominent biochemist, a recipient of the Garvan Award of the American Chemical Society in 1977, and became a National Honorary Member of Iota Sigma Pi (National Honor Society for Women in Chemistry) in 1985, one of the highest honors bestowed on female chemists.

Similarly, Eva King Killam, ASPET's second female president, was a life-long co-investigator with her husband Keith Killam. In 1953, Eva King moved to the UCLA Medical School, and in 1954, she received the John J. Abel Award for outstanding research in neuropsychopharmacology, the first woman to receive this prestigious ASPET award. After marrying Keith Killam, the couple moved to Stanford University in 1959 where Eva worked as a research associate while Keith joined the faculty of the School of Medicine as an associate professor of pharmacology. The Killams moved to the University of California at Davis in 1968 where Keith founded the Department of Pharmacology, and Eva joined the faculty first as a professor of physiology, and in 1972, as a professor in the Department of Pharmacology. Eva not only served as ASPET President, but was also President of the Western Pharmacology Society and President of the American College of Neuropsychopharmacology. She was well known to all pharmacologists as she served as the editor-in-chief for the *Journal of Pharmacology and Experimental Therapeutics* from 1978-1991.

Sue Duckles was the third female president of ASPET. Sue received a B.A. in Philosophy from the University of California at Berkeley and a Ph.D. in Pharmacology from the University of California at San Francisco. She pursued postdoctoral studies and was an assistant professor at the University of California at Los Angeles before relocating to the Department of Pharmacology at the University of Arizona. In 1985 she moved to the University of California at Irvine where she currently serves as Professor and Vice-Chair of the Department of Pharmacology and Associate Dean. Sue is a cardiovascular pharmacologist and neuroscientist studying the influence of gender and sex steroid hormones on vascular reactivity and mitochondrial function. Sue served as President of the Western Pharmacology Society and as a member of the Board of Directors and Vice President for Science Policy for the Federation of American Societies for Experimental Biology. In 2000 she became founding Chair of the Editorial Board for a new ASPET publication, *Molecular Interventions*. Sue has the distinct honor of serving the international pharmacology community, first as the first female Secretary General for a four-year term, and currently as President of the International Union of Pharmacology (IUPHAR). Sue was the first female recipient of the ASPET Torald Sollman Award in 2007.

Marlene Cohen, elected ASPET President in 2001, received her undergraduate degree in pharmacy from the University of Connecticut and her Ph.D. from the Department of Pharmacology at the University of California San Francisco Medical Center. She completed a postdoctoral fellowship at the Roche Institute of Molecular Biology and joined Eli Lilly and Company Research Laboratories in 1975, from where she retired in 2002. She also served as adjunct Professor of Pharmacology and Toxicology at Indiana University School of Medicine. During her tenure with Eli Lilly, Marlene was the first female promoted to Research Advisor and then to Lilly Research Fellow, a title held by fewer than 10 scientists in the Lilly Research Laboratories in the 1990s. Marlene's research focused on the pharmacology of serotonin receptors, particularly as related to cardiovascular and neuropsychiatric disorders. She received numerous awards throughout her career, and is an ISI highly cited author. Marlene cofounded and is currently Vice-President of Creative Pharmacology Solutions, LLC, providing consulting services on the drug discovery process for chemical and biotechnology companies and on drug-related topics for legal firms.

Elaine Sanders-Bush, the most recent woman ASPET President, received her undergraduate degree from Western Kentucky State College in Bowling Green (now Western Kentucky University) and her Ph.D. in pharmacology from Vanderbilt University. She pursued postdoctoral studies in psychopharmacology at Vanderbilt, where she rose through the academic ranks to Professor and currently serves as Director of the Vanderbilt Brain Institute and Director of the Graduate Program in Neuroscience. Elaine's work has focused on serotonin and serotonin receptors, and she has contributed significantly to our understanding of receptor function and modulation by RNA editing, particularly as related to the action of the antidepressants. Elaine served on the ASPET Board of Publications Trustees and has received numerous awards throughout her career for her contributions in research as well as teaching.

Marjorie Horning
(1984-1985)

Eva King Killam
(1989-1990)

Sue Piper Duckles
(1997-1998)

Marlene L. Cohen
(2001-2002)

Elaine Sanders-Bush
(2006-2007)

Fig. 4 Women Presidents of ASPET. The number in parentheses is the year the individual served.

Women have also served as Secretary/Treasurer of ASPET since 1975 (Figure 5). As Secretary/Treasurer, these women also chaired the ASPET Finance Committee. Interestingly, women have held this position consecutively since 2001.

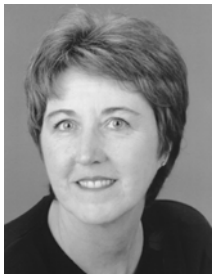

Ruth Levine
(1975-1976)


Marjorie Horning
(1981-1982)


Mary Vore
(1987-1988)


Nancy R. Zahniser
(2001-2002)


Cinda J. Helke
(2003-2004)


Patricia K. Sonsalla
(2005-2006)


Lynn Wecker
(2006-2007)


Annette E. Fleckenstein
(2007-2008)


Susan G. Amara
(2008-2009)

Fig. 5 Women Secretary/Treasurers of ASPET. The year served or to be served is in parentheses.

Women have also held the position of Councilor of ASPET. Council represents the leadership/governing board of ASPET and is charged with administering the affairs of ASPET, including financial, scientific, and publishing activities. Three councilors elected by ASPET members serve to represent members on ASPET Council. Although the number of women elected to this position has remained relatively constant (2 per decade) since 1973 (Table 3, Figure 6), it should be noted that only seven female councilors have been elected during this 32-year period.


Eva King Killam
(1973-1976)


Jean M. Marshall
(1977-1980)


Janice Stickney
(1984-1987)


Paula Stern
(1989-1992)


Sue Piper Duckles
(1992-1995)


Lee E. Limbird
(1995-1998)


Patricia K. Sonsalla
(2002-2005)

Fig. 6 Women Councilors of ASPET. The numbers in parentheses are the years the individual served.

Table 3. Female Officers of ASPET

Position	Name	Years
President	Marjorie Horning	1984-1985
	Eva King Killam	1989-1990
	Sue Piper Duckles	1997-1998
	Marlene L. Cohen	2001-2002
	Elaine Sanders-Bush	2006-2007
Secretary/Treasurer	Ruth Levine	1975-1976
	Marjorie Horning	1981-1982
	Mary Vore	1987-1988
	Nancy R. Zahniser	2001-2002
	Cinda J. Helke	2003-2004
	Patricia K. Sonsalla	2005-2006
	Lynn Wecker	2006-2007
	Annette E. Fleckenstein	2007-2008
	Susan Amara	2008-2009
Councilor	Eva King Killam	1973-1976
	Jean M. Marshall	1977-1980
	Janice Stickney	1984-1987
	Paula Stern	1989-1991
	Sue Piper Duckles	1992-1995
	Lee E. Limbird	1995-1998
	Patricia K. Sonsalla	2002-2005

Committee and Division Chairs

Over the years, Council formed many committees to address specific interests and issues relevant to the Society. In addition to women paving their way on Council, women were integral members of the committee structure and later, the Divisions of ASPET. By the latter half of the 1970s, women began to serve as Committee Chairs, and once the Division structure was initiated in the 1980s, women were frequently elected to chair these Divisions. The female Chairs of ASPET Committees and Divisions, along with their terms served, are listed on Tables 4 and 5, respectively. As with Councilors, although women have served as Chairs, in most cases, women represent only a relatively small fraction of the Committee Chairs over the years based on the long duration that many of the committees have been in existence. Clearly, as women were elected to all these positions, their influence on the Society and their leadership continued to increase.

Table 4. Female Chairs of ASPET Committees

Committee	Name	Years
Affirmative Action in Pharmacology & Experimental Therapeutics: Education and Career Development Subcommittee (1982-1985)[1]	Yvonne Harrison	1985-1987
Awards Committee (1976-1999; 2006-present)	Joanne I. Moore	1985-1986
B. B. Brodie Award Committee (1999-present)	Mary Vore	1999-2000
Committee on the Care & Use of Animals (CCURA) (1985-2002)	Diana Krause	1999-2002
Educational Affairs Committee (prior to 1959-1990)	Ruth R. Levine	1980-1983
	Sue P. Duckles	1992-1993
Committee	**Name**	**Years**
Graduate Recruitment & Education	Rochelle Schwartz-Bloom	1996-1999

Committee (1990-present)	Barbara S. Beckman	2002-2005
	Stephanie W. Watts	2005-2007
Membership Committee (prior to 1959-2001)	Barbara R. Rennick	1976
	Harriet M. Maling	1977
	Mary Vore	1982
	Joanne I. Moore	1983
	Janice L. Stickney	1984
	Mary Vore	1985
	Sue P. Duckles	1988
	Elaine Sanders-Bush	1990
	Marlene L. Cohen	1992
	Lee E. Limbird	1993
	Dolores C. Shockley	1996
	Maria Almira Correia	1999
	Margaret E. Gnegy	2000
	Lorraine Gudas	2003
Minorities Committee/Subcommittee (1985-2005)	Margarita L. Dubocovich	2002-2005
	Yvonne E. Harrison	1985-1990
	Dolores C. Shockley	1990-1994
Nominating Committee (prior to 1959-present)	Marilyn E. Hess	1976
	Joanne I. Moore	1978
	Paula H. Stern	1981
	Doris H. Clouet	1982
	Marlene L. Cohen	1984
	Elaine Sanders-Bush	1993
	Lynn Wecker	1994
	Bettie Sue Masters	1995
	Bettie S. Masters	1995
	Joanne I. Moore	1997
	Joan Heller Brown	1998
	Elaine Sanders-Bush	1999
	Kathryn A. Cunningham	2000
	Suzanne Laychock	2001
	Marlene L. Cohen	2003
	Elaine Sanders-Bush	2008
Preprofessional Education Subcommittee (1980-2001)	Joan M. Lakoski	1991-1997
	Barbara S. Beckman	1999-2002
Program Committee (prior to 1959-present)	Lynn Wecker	1998-2005
Public Information Committee/Subcommittee (1982-2004)	Mary Vore	1985-1986
	Janice L. Stickney	1981-1985
Short Course/Continuing Education Subcommittee (1999-2004)	Rochelle D. Schwartz-Bloom	1999-2003
Teaching and Evaluation Materials Subcommittee (1985-1995)	Patricia B. Williams	1991-1993
Teaching of Pharmacology to Undergraduates & Non-professionals Subcommittee (1974-1980)	Ruth R. Levine	1974-1975
	Ruth R. Levine	1979-1980

[1]The numbers in parentheses denote the years the committee existed.

Table 5. Female Chairs of ASPET Divisions

DIVISION	NAME	YEARS
Behavioral Pharmacology (1999-present)[1]	Linda Dykstra	2004-2005
	Alice M. Young	2005-2007
Cardiovascular Pharmacology (1997-present)	Mariana Morris	2004-2006
	Nancy J. Rusch	2006-2008
	Debra Diz	2008-2010
Developmental Pharmacology Section (1984-1991)	Antonia Vernadakis	1985-1987
Drug Metabolism (1972-present)	Mary Vore	1990-1992
	Bettie Sue Masters	1993-1994
Molecular Pharmacology (1997-present)	Dianne M. Perez	2005-2006
Neuropharmacology (1988-present)	Patricia K. Sonsalla	1997-2000
	Marie Francoise Chesselet	2002-2004
	Kathryn Cunningham	2004-2005
Toxicology (1997-present)	Linda Birnbaum	1999-2000
	Elizabeth Jeffrey	2001-2002

[1]Several of these Divisions were in existence as sections prior to achieving formal Division status; the numbers in parentheses denote the year the Division was founded.

Women in Pharmacology Subcommittee

Based on growth in the number of women in the Society during the 1970s, ASPET formed a new subcommittee in 1980 to provide a forum for the discussion of issues facing women pharmacologists. A similar group created by The American Physiological Society had been highly successful in raising the consciousness of that Society to issues relevant to women. Thus, Women in Pharmacology was established as a subcommittee of the Committee on Education and Professional Affairs, and in 1998 it became a full committee when the parent committee was dissolved as ASPET reviewed committee needs.

Mary Mycek was the founding chair of the Subcommittee, with Floie Vane serving as co-chair (Table 6, Figure 7). Initially, the subcommittee focused on identifying and addressing those issues relevant to the female population of pharmacologists in the Society and raising the awareness of ASPET to issues relevant to women. Importantly, the subcommittee provided a formal mechanism for women to meet each other, in particular during the annual meetings of ASPET. Over the years, the subcommittee initiated symposia, workshops and mixers that focused on mentoring, dual career issues, leadership roles, and the professional advancement of women. More recently, the group has been instrumental in nominating women for ASPET and FASEB Awards.

Mary Mycek Floie Vane

Fig. 7 Founding Chairs of the Women in Pharmacology Subcommittee (SWIP), later Women in Pharmacology (WIP) Committee

Table 6. Chairs of Women In Pharmacology Committee (WIP)

Name	Years
Mary Mycek Floie Vane, co-chair	1980-1983
Paula Stern	1983-1985
Marlene Cohen	1985-1987
Lora Rikans	1987-1994
Terriann Crisp	1994-1995
Suzanne Laychock	1996-1999
Linda Dwoskin	1999-2002
Joan Lakoski	2002-2004
Beth Levant	2004-2005
Laura Nisenbaum	2005-2008

In 1987, the subcommittee, chaired by Marlene Cohen, with encouragement from the Executive Officer, Kay Croker, joined forces with the Women in Physiology, which was chaired by Helen Cooke, to initiate an award for female scientists. For the first three years, the initial awards alternated between physiology and pharmacology and involved a lecture at the annual meeting by the recipient and a plaque provided by the Society. However, the Subcommittee of Women in Pharmacology felt strongly that the recognition of women scientists should be expanded with a significant monetary award and might be broadened to include female scientists from other disciplines.

FASEB was approached with this suggestion, and a FASEB Women's Committee was formed. In December 1989, the FASEB Board approved the opportunity for women to enter discussions that might provide an annual stipend associated with the Award. In a letter from the executive director of FASEB to Kim Bottomly, chair of the FASEB Women's Committee dated December 6, 1989, the committee was "...cautioned that should the award exceed the $10,000 range, it would be important to communicate first with the office. It is the intention of the Board to maintain a 3M Award of $25,000 each year as the major scientific award of the Federation…" Thus, even into the 1990s, there was resistance to equalize and recognize female scientists, and it is to the credit of the dedicated women on this early committee (Kim Bottomly, Chair, Helen Cooke, Linda McManus, Lora Rikens, Phyllis Moser Veillon and Marlene Cohen) that the Excellence in Science Award came into being. Finally, this initial Pharmacology/Physiology Award was expanded to include women from all FASEB societies, and most importantly, Eli Lilly and Company agreed to sponsor the Award with an acceptable $10,000 unrestricted research grant to support the recipient's research. Today, a FASEB committee chooses the recipient of the award annually. This was a significant achievement of the Subcommittee of Women in Pharmacology.

A second achievement by this group occurred in 1998 when the subcommittee became a full committee and began sponsoring formal sessions at the annual meeting. In 1998, the first career session was held entitled "Juggling Life and a Career in Science," and in 1999, the group sponsored a session entitled "It Takes a Village: Mentoring and Retaining Women in Science." In 2000, when ASPET held its annual meeting with the American Society for Biochemistry and Molecular Biology, women from both scientific societies got together at a Women Scientists Networking Session and Reception. The responses to these sessions were so positive that in 2001, the Women in Pharmacology Committee joined forces with the Women in Physiology to jointly program a career session at the annual meeting. These sessions have continued annually since that time (see Table 7) and have proven to be very popular with both men and women due to both the timeliness of the topics discussed and the format, which includes both short talks and breakout sessions.

In addition to these career sessions, the Women in Pharmacology Committee has also sponsored scientific sessions at the annual meetings on numerous topics including the pharmacological treatment of menopause, targeted therapeutics for breast cancer, drug abuse as a gender issue, gender differences in eating disorders, and pharmacogenomics.

Table 7. Joint Sessions at the Annual EB Meetings Sponsored by Women in Pharmacology and Women in Physiology

Topic	Year
How to Get Published in PS and ASPET Journals	2001
How to be a Good Mentor	2002
Presentation Skills	2003
Life After the Ph.D.: Finding a Postdoctoral Fellowship	2004
Managing a Laboratory	2005
Mastering the Juggling Act: Laboratory, Life and Leadership Roles	2006
Being Heard: The Microinequities that Tilt the Playing Field	2007
Gainfully Employed: From Launching a Job Search to Navigating Negotiations	2008

Recognition of Women in ASPET

ASPET has been quite proactive in recognizing the contributions and accomplishments of its members since 1947 with annual or biennial awards supported by a combination of Society funds and corporate or private donations. It is noteworthy that women have received only limited acknowledgement as recipients of these awards over the many years that they have been administered (Table 8, Figure 8).

ASPET initiated the John J. Abel Award in 1947 to recognize young scientists for their original research, independence of thought, originality of ideas, clarity and excellence in data presentation. This award has been presented to 59 scientists since its inception, with three awards to women. Eva King Killam was the first female recipient of this prestigious award in 1954, and 33 years elapsed before the next woman, Lee Limbird, was recognized. Susan Amara was the third woman to receive this award in 1993, over a period of 60 years.

The Pharmacia-ASPET Award has been given annually since 1969 to recognize and stimulate outstanding research in pharmacology and experimental therapeutics that has had, or will have, a major impact on the pharmacological treatment of disease. To date, 38 individuals have received this award, which has been given once to a woman, Susan Horwitz in 1994.

The Epilepsy Research Award was established in 1978 to recognize and stimulate outstanding research leading to better clinical control of epileptic seizures. Since its inception, this award has been presented to 22 researchers, of which one is a woman, Karen Gale.

The Bernard B. Brodie Award was initiated in 1978 to honor scientists working in the field of drug metabolism. It was not until 2000, that a woman, Bettie Sue Masters, was honored with the award.

ASPET initiated the Goodman and Gilman Award in 1980 to recognize outstanding research in the area of biological receptors. Most recently, two women have been honored as recipients of the Goodman and Gillman Award, Melanie Cobb and Lee Limbird.

The Julius Axelrod Award was initiated in 1991 by the Catecholamine Club to recognize significant contributions to understanding the biochemical mechanisms underlying the pharmacological actions of drugs, as well as for mentoring contributions. In 2007, ASPET became affiliated with this Award. One woman, Susan Amara, has received this award since its inception.

The Torald Sollman Award was initiated in 1961 to recognize sustained significant contributions to pharmacology over many years. Finally, in 2007, Sue Duckles became the first female recipient of this award. Sue was well deserving of this honor as she has had a major positive impact on ASPET and pharmacology, both nationally and internationally.

Thus, although women have made considerable progress in receiving recognition by the Society, it is clear that recognition has been sparse, although improving.

Eva King Killam
John J. Abel Award (1954)

Lee E. Limbird
John J. Abel Award (1987)
Goodman & Gilman Award (2004)

Susan G. Amara
John J. Abel Award (1993)
Julius Axelrod Award (1996)

Susan B. Horwitz
Pharmacia-ASPET Award for
Experimental Therapeutics (1994)

Karen N. Gale
Epilepsy Research Award (1995)

Bettie Sue Masters
Bernard B. Brodie Award (2000)

Melanie H. Cobb
Goodman & Gilman Award (2000)

Sue Piper Duckles
Torald Sollmann Award (2007)

Fig. 8. Women recipients of ASPET Awards. The award and year received are in parentheses

Table 8. Female Recipients of ASPET Awards

Award (total # of awardees)	Recipient	Year
John Jacob Abel Award (59)	Eva King Killam	1954
	Lee E. Limbird	1987
	Susan G. Amara	1993
Pharmacia-ASPET Award for Experimental Therapeutics (38)	Susan B. Horwitz	1994
Epilepsy Research Award (22)	Karen N. Gale	1995
Bernard B. Brodie Award (16)	Bettie Sue Masters	2000
Goodman & Gilman Award (14)	Melanie H. Cobb	2000
	Lee E. Limbird	2004
Julius Axelrod Award (14)	Susan G. Amara	2006
Torald Sollman Award (46)	Sue Piper Duckles	2007

The Role of Women in ASPET Journals

ASPET established and has maintained several scientific and informational journals since 1909. To maintain the high standards and quality of these publications, the Board of Publications Trustees was established in 1949 and charged with the responsibility of overseeing the editorships of the Journals and approving decisions regarding new journals,

publishers, subscription rates, etc. During this time, there have been 14 chairs of this Board and none have been women. However, women have been sporadic members of the Board since 1975, as indicated in Table 9, and a woman has served on the Board continuously since 1998.

Table 9: Membership of Women on the Board of Publications Trustees

Name	Years
Jean M. Marshall	1975-1977
Bettie Sue Masters	1983-1987
Marlene L. Cohen	1990-1992
Elaine Sanders-Bush	1998-2004
Lorraine Gudas	2003-2005
Mary Vore	2006-present

The oldest ASPET journal, the *Journal of Pharmacology and Experimental Therapeutics*, was founded in 1909 by John J. Abel and was the first journal to recruit a female editor, Eva King Killam, in 1978. Eva instituted many new initiatives regarding submissions that expanded the prestige of the Journal.

In 1998, Joan Heller Brown accepted the position as Editor of *Molecular Pharmacology* and served in that capacity until 2002. Joan helped guide the Journal through the initial stages of electronic submission and availability.

Of course, Kay Croker, as Executive Director of ASPET, served as Editor of *The Pharmacologist* (the ASPET Newsletter and informational publication) from 1981 to 1997, and the current Executive Officer, Christine Carrico, assumed this position from 2000-2006.

Lastly, in 2001, ASPET took the bold step to start a new Journal, *Molecular Interventions*, under the leadership of Sue Duckles who chaired the Executive Committee charged with oversight of this Journal. Although not officially the editor *of Molecular Interventions*, it was through Sue's leadership that the Journal was conceived and initiated.

The Future

We think it is only fitting that the National Academy of Sciences released their latest report "Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering" in September 2006. While we have 'come a long way,' the report indicates clearly that we still have a long way to go in achieving gender equality in the sciences. Likewise, in ASPET, considerable progress has been made in gender equality, although the effort is by no means complete. We hope that this retrospective review on the role of women in ASPET will provide an historical perspective on women in ASPET and shed light on some of the general issues facing women. Through awareness of this knowledge, further and perhaps more rapid progress in leadership opportunities and advancement of women will transpire in the future. We believe the opportunities for influence and impact are expanding and welcoming for women in science and in ASPET, in particular.

References

Appel, T. A. (1994) Physiology in American Women's Colleges: The Rise and Decline of a female Subculture, *Isis* 85: 26-56.

Jagsi, R., Guancial, E.A., Worobey, C.C., Henault, L.E., Chang, Y., Starr, R., Tarbell, N.J. and Hylek, E.M. (2006) The 'Gender Gap' in Authorship of Academic Medical Literature -- A 35-Year Perspective. *New Engl J Med* 355:281-287.

Lees, M. B. (2002) Participation of Women in Neurochemistry Societies *Neurocheml Research* 27:1259-1267.

Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering, Committee on Maximizing the Potential of Women in Academic Science and Engineering, National Academy of Sciences, National Academy of Engineering, and Institute of Medicine; September 2006

Chen, K.K. (1969) *The American Society For Pharmacology And Experimental Therapeutics, Incorporated: The First Sixty Years 1908-1969*, Judd & Detweiler, Inc., Washington D.C.

You Say You Want an Evolution?
A Role for Scientists in Science Education

Coalition of Scientific Societies[1]

[1]*American Association of Physics Teachers, American Astronomical Society, American Chemical Society, American Institute of Biological Sciences, American Institute of Physics, American Physical Society, American Physiological Society, American Society for Investigative Pathology, American Society for Pharmacology and Experimental Therapeutics, American Society of Human Genetics, Biophysical Society, Consortium of Social Science Associations, Geological Society of America, Federation of American Societies for Experimental Biology, National Academy of Sciences, National Science Teachers Association, Society for Developmental Biology*

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Although evolution is firmly established as one of the most important, integrative, and robust concepts in science, teaching evolutionary science and related subjects (e.g., the origins of the universe, the age of the earth, plate tectonics) has been challenged in school districts across the United States. These challenges—whether introducing religious beliefs as "alternatives" to science, labeling evolution or the big bang as "theory, not fact," or singling out scientific subjects for "critical analysis"—jeopardize science education. Recognizing the harm such actions pose to science education and, ultimately, to the foundation on which scientific advancement is based, 17 scientific societies, representing the physical, chemical, biological, and social sciences and science teachers communities, established an unprecedented coalition to explore opportunities for collective understanding and action. As part of this effort, we engaged a professional research firm to conduct a national survey of approximately 1,000 likely U.S. voters (*1*) that examined attitudes toward science and scientists, views on evolutionary science in the context of education, and means through which the scientific community can effectively bolster support for teaching evolution and related subjects.

Recent studies show that Americans' views on evolutionary science have been relatively stable over the past several decades. Beginning in the 1980s, polls consistently found that between approximately 40% and 50% of the American public accepts human evolution (*2-3*), and 40% to 50% favors a Biblical creationist account of the origins of life (*3*). An analysis by the Pew Research Center shows that Americans' views on evolutionary science vary with the phrasing of the question, however (*3*). For example, when people are asked to choose whether humans developed over millions of years either with or without guidance from God (a Gallup poll question), more select evolution with guidance (38%) than without guidance (13%). A Pew poll question shows a different pattern of results. Respondents were first asked, without reference to a supreme being, if they thought humans evolved or were created in their present form. Those who accepted evolution were then asked if they thought it occurred through natural processes or with guidance. When asked this way, 18% reported that evolution occurred with guidance and 25% accepted that it occurred through natural selection.

We anticipated that acceptance of evolutionary science would also be influenced by the distinction between human and non-human species (Fig. 1). We asked half of the respondents about their views on the evolution of "all living things" and found that 61% accepted that "all living things have evolved over time." Of those, 36% thought all living things "evolved due to natural processes such as natural selection" and 25% thought "a supreme being guided the evolution of living things for the purpose of creating life in the form it exists today." We asked the remaining respondents to consider human evolution and found that 53% accepted that "humans and other living things" evolved. This majority included 32% who accepted that humans and other living things evolved through natural processes and 21% who thought they had evolved with guidance. Compared to other surveys (*3*), we found weaker overall support for creationism: 28% and 31% agreed with statements that "all living things" or "humans and other living things," respectively, were created in their present form. Sixteen percent of respondents who were asked about the evolution of "humans and other living things" and 11% of those asked about the evolution of "all living things" did not know or would not disclose their views.

Although public opinion is often characterized as polarized, there is considerable uncertainty about what to teach in public school science classes, particularly with regard to including certain religious perspectives. Thirty-two percent of

respondents in our study were unsure about teaching creationism and 41% were uncertain about teaching intelligent design. By comparison, 22% expressed uncertainty about teaching evolution. Consistent with other studies (*5*), however, more respondents favored teaching evolution (53%) than creationism (36%) or intelligent design (27%) in public school science classes. These data show that a majority of people favor—and even more may be open to—teaching evolution in science classes.

Why don't more Americans accept evolutionary science? A recent study shows that acceptance is negatively correlated with fundamentalist religious beliefs and politicization of science and positively correlated with genetics literacy (*2*). While we did not examine genetics literacy in particular, we did find a connection between respondents' views on evolution education and their answers to three scientific questions (Fig. S1). Although 69% of survey participants had some college education (27% were college graduates and 14% had attended graduate school), only 23% gave correct responses to all three of the following statements: the continents or land masses on which we live have been moving for millions of years and will continue to move in the future (79% correctly agreed); antibiotics kill viruses as well as bacteria (43% correctly disagreed); the earliest humans lived at the same time as the dinosaurs (53% correctly disagreed). Respondents who answered all three questions correctly were much more likely to respond that humans and other living things evolved (78%) than that they were created in their present form (11%), and more favored teaching evolution (78%) than creationism (27%) or intelligent design (24%). In contrast, respondents who answered fewer than two questions correctly were less likely to accept that life evolved (36%) than to believe it was created in its present form (47%), and they were about as likely to favor teaching evolution (36%) as creationism (38%) and intelligent design (29%).

Studies show that the vast majority of Americans have a strong appreciation for the role of science in health, education, and competitiveness, and they especially value the contribution that scientific research makes to eliminating diseases (*4*). Within this sample, 63% of respondents ranked developing medicines and curing diseases as the most important contributions of science to society. Proponents of teaching evolution (65%), creationism (62%), or intelligent design (63%) were equally likely to view these contributions as science's most important.

People also appear to value the relationship between evolutionary science and medicine. Among a sample of respondents, 61% thought that understanding the contribution that evolution makes to modern medical science, including to understanding and treating diseases such as avian influenza, was a convincing reason to teach evolution in science classes. This finding, together with Americans' consistently strong support of medical research (*4*), suggests that making the connection between evolutionary biology and advancing other areas of medical research (e.g., understanding human gene function or the mechanisms by which antibiotic resistance develops) might be equally compelling. People may also appreciate the contributions that evolutionary science makes to other fields, including agriculture, forensics, and even software engineering, although we did not examine these in this study.

Teaching evolutionary science may also enhance science pedagogy, as it "offers educators a superb opportunity to illuminate the nature of science and to differentiate science from other forms of human endeavor and understanding" (*6*). The tools and techniques that scientists employ to study evolution—gathering evidence from various sources, making logical inferences, establishing and testing competing hypotheses—are the hallmarks of science and necessary for everyday decision-making. Data from this survey suggest that the public values these learning opportunities: a majority of respondents rated learning to draw conclusions from evidence (80%), to think critically (78%), and how science is conducted (63%) as very important purposes of public school science education. Communicating the value of learning science, including evolution, for developing analytical skills that are widely applicable beyond the classroom may strengthen public support for all types of science.

The scientific community—scientists, science teachers, and medical professionals—have a key role in communicating the importance of science education to the public. Sixty-nine percent of respondents had favorable feelings toward scientists and even more viewed medical researchers (72%) and doctors (76%) favorably. While fewer people (59%) rated public school science teachers highly, public school teachers in general were the most widely favored group (79%).

When it comes to scientific issues, the scientific community commands the attention of the public (Fig. 2). Among respondents presented with a list of people who might explain science to the public, 88% expressed interest in hearing from a scientist, and almost as many were interested in hearing from a science teacher (85%) or a doctor or nurse (84%). On the topics of evolution, creationism, and intelligent design, most respondents expressed interest in hearing from scientists (77%), science teachers (76%), and clergy (62%). Fewer people were interested in hearing from Supreme Court Justices on evolution (37%), or from school board members and celebrities either on science (34% and 16%, respectively)

and evolution (30% and 11%, respectively). These data indicate that Americans respect the expertise of science and education professionals and also look to clergy for guidance on scientific issues of potential relevance to religion. The value of encouraging each of these groups—including scientists who hold religious beliefs—to become involved in promoting quality science education cannot be overstated.

In communicating the value of science, scientists must emphasize the outcomes that matter to people—advancing medicine, improving health, fostering critical thinking—and they must do so clearly and understandably. Technical expositions on scientific topics will not get the attention of the public or policy makers who lack relevant expertise. If researchers can not communicate their findings in ways that are comprehensible, meaningful, and relevant to non-scientists, their message to the public—and their effectiveness as spokespeople for science—is lost (*7*). There are ample opportunities for scientists to develop and exercise their communication skills and, whether writing letters to local newspapers, speaking with school boards or community groups, or partnering with educators to design curricula, many scientific and professional societies have trained staff or other resources to help (Table S1).

There is a clear need for scientists to become involved in promoting science education. Challenges to teaching science undermine students' understanding of the scientific method, how scientific consensus develops, and the distinction between scientific and non-scientific explanations of natural phenomena. If our nation is to continue to develop the talent necessary to advance scientific and medical research, we must ensure that high standards in science education are maintained and that efforts to introduce non-science into science classes do not succeed. Failure to reach out effectively to a public that is supportive of science and open to information from the scientific community is not just a missed opportunity; it is a disservice to the scientific enterprise.

References

1. Materials and methods are available as online at http://evolution.faseb.org/sciencecoalition

2. J.D. Miller, E.C. Scott, S. Okamoto, *Science* 313, 765-766 (2006).

3. *Reading the Polls on Evolution and Creationism* (The Pew Research Center for the People and the Press, Washington, DC, 2005; http://peoplepress.org/commentary/display.php3?AnalysisID=118).

4. *America Speaks* (Research!America, Alexandria, VA, 2007; http://www.researchamerica.org/publications/AmericaSpeaks/AmericaSpeaksV8.pdf).

5. *Evolution, Creationism, Intelligent Design* (The Gallup Poll; http://www.galluppoll.com/content/default.aspx?ci=21814).

6. National Academy of Sciences, *Teaching About Evolution and the Nature of Science* (National Academies Press, Washington, DC, 1998).

7. M.C. Nisbet, C. Mooney, *Science* 316, 56 (2007).

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Supporting Online Material

Materials and methods are available as online at http://evolution.faseb.org/sciencecoalition

Figures

Figure 1. Acceptance of evolution. The percentage of respondents who accepted that all living things (left) or humans and other living things (right) evolved due to natural processes (light blue), evolved through guidance by a supreme being (dark blue), were created in their present form (yellow), or who did not know or refused to answer (green).

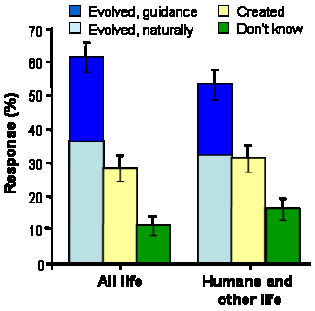


Figure 2. Public interest in spokespeople for science. The percentage of respondents who expressed interest in hearing science (right; yellow) or evolution, creationism, and intelligent design (left; blue) explained by various spokespeople. Respondents were not asked about their interest in hearing from a doctor or nurse about evolution, creationism, or intelligent design or from clergy or a Supreme Court Justice about science.

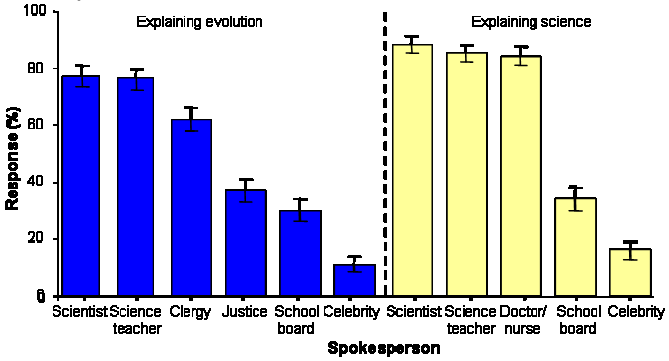


Figure S1. Relationship between scientific literacy and support for teaching evolution. The percentage of respondents who answered zero or one, two, or all three scientific literacy questions correctly who also favored teaching evolution (blue), creationism (yellow) or intelligent design (green) in public school science classes.

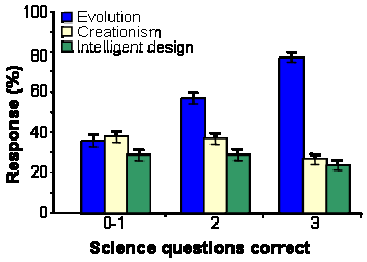


Table S1

Evolution Resources	Web Address
American Association for the Advancement of Science	http://www.aaas.org/news/press_room/evolution/
American Institute of Biological Sciences	http://www.actionbioscience.org/evolution/index.html
American Physiological Society	http://www.the-aps.org/pa/policy/bioissues/evolutionTeach.htm
American Society of Human Genetics	http://www.genednet.org/pages/k12_evolution.shtml
Federation of American Societies for Experimental Biology	www.evolution.faseb.org
Howard Hughes Medical Institute	http://www.hhmi.org/biointeractive/evolution/index.html
National Academies	http://nationalacademies.org/evolution/
National Center for Science Education	http://www.natcenscied.org/
PBS Evolution Website	http://www.pbs.org/wgbh/evolution/
Understanding Evolution (UC Museum of Paleontology)	http://evolution.berkeley.edu/

Journals

Journals Celebrate Centennial

Starting with the December issue of *Pharmacological Reviews*, ASPET's journals will begin publishing a series of articles to celebrate the Society's centennial. The first article contributing to ASPET's 100 birthday celebration is "A Brief History of Great Discoveries in Pharmacology: In Celebration of the Centennial Anniversary of the Founding of ASPET" by Dr. Ronald P. Rubin, Professor and Chair of the Department of Pharmacology and Toxicology, State University of New York-Buffalo School of Medicine and Biomedical Sciences. Structured as a series of essays, Dr. Rubin's history focuses on eminent researchers' discoveries that "had the broadest implication for humankind." This chronicle of pharmacology offers lessons for current and future researchers. Publication of the article is sponsored by ASPET's Centennial Committee.

The Board of Publications Trustees has solicited a number of "Centennial Perspectives" that will appear throughout 2008 in *JPET*, *MolPharm*, and *DMD*. These articles will be short reviews on important topics in pharmacology and therapeutics that explore the development of the topic over the last 100 years and note the related significant research articles published. While they will provide an historical overview of the topic, authors have been encouraged to give their view of future developments in the field. The first Centennial Perspective, slated for the January issue of *DMD*, is entitled **"**The Development of Drug Metabolism Research as Expressed in the Publications of ASPET, Part 1, 1909-1958" by Dr. Patrick Murphy. Dr. Murphy's article was published online in manuscript form last July as a Fast Forward article.

Since its April 2007 issue, *Molecular Interventions* has been publishing "Significant Deciles." These graphically rich ten-year segments of history starting with 1900-1910 present pharmacological discoveries in the context of the technology, culture, and political developments of their time. The series will cover the ten decades since ASPET's founding.

All Centennial Perspectives will be freely available online immediately upon publication. Dr. Rubin's history, the Significant Deciles, and a number of other pieces written in honor of ASPET's centennial will be gathered together in a commemorative collection to be given to ASPET members who attend the Society's annual meeting and centennial celebration in April 2008. The ASPET website provides links to centennial-related articles published in the Society's journals. New links will be added as items are published.

Glitch Provides Bonus to *Pharmacologist* Subscribers

If you received an unexpected copy of the December issue of *JPET*, *MolPharm*, and *DMD*, consider it an early holiday present from ASPET. A glitch in our new database added a number of *Pharmacologist* print subscribers to the December mailing lists for these journals. The problem has been corrected, and we apologize for any confusion caused. No one has complained about receiving the free copies, so we hope they were welcomed and read with enthusiasm!

Public Affairs/ Government Relations

Appropriations Update

At press time, the FY'08 appropriations for most federal agencies remain unresolved. This fall, the President vetoed the Labor/HHS bill that funds the NIH, and the attempt to override the veto failed too. The House and Senate had passed legislation that would have increased the NIH budget by $1.1 billion in FY'08. This projected increase would have reversed several years of flat funding for NIH. The practical effect is that the Labor/HHS bill will be part of a larger omnibus bill, and the NIH increase of $1.1 billion will almost certainly not be realized; by how much is the question. Democratic leadership has said that a potential reduction of approximately $700 million (from the $1.1 billion) might be needed to gain the President's signature. Will the President sign omnibus legislation that cuts domestic programs projected FY'08 budget increases in half? Some House Republicans are calling for stricter spending limits. If the President should fail to sign the omnibus, there would likely be another continuing resolution which would be even more unfavorable for the NIH than events of this past month.

FDA is also caught up in the developing omnibus strategy. House and Senate Agriculture appropriations subcommittee staffs have been meeting to negotiate a final package that both sides can agree upon. What we do know is that FDA's funding level will be no higher than the Senate's proposed increase of $186 million, and could be lower than the House increase of $128 million.

A Continuing Resolution will fund programs through December 14.

ASPET Opposes Farm Bill Amendments

View the ASPET letter to Sen. Tom Harkin (D-IA) asking him to reject two House passed amendments to the Farm Bill that would amend the Animal Welfare Act and prohibit the use of live animals to demonstrate medical devices in sales related contexts and prohibit Class"B" dealer sales of non-purpose bred dogs and cats:
http://www.aspet.org/public/public_affairs/pa_pos_test.html

ASPET Response to NBME Proposed Changes to USMLE

The National Board of Medical Examiners is proposing that the current USMLE exam be replaced with a combined basic science and clinical examination to better integrate basic and clinical components of the examination. In a letter to the NBME, ASPET detailed its opposition to the proposed changes, citing the need for students to demonstrate a fundamental understanding of principles of the basic biomedical sciences and the potential for dilution of emphasis placed on the scientific basis of medicine in medical education: http://www.aspet.org/public/public_affairs/pa_pos_test.html

New Journal on Evolution

A print version of the new journal *Evolution: Education and Outreach* debuted at the National Association of Biology Teachers November conference. The journal will be free online at www.springerlink.com during all of 2008. The journal promotes understanding and teaching of evolutionary theory for a wide audience. Targeting students of all ages including undergraduates, teachers and scientists alike, the journal publishes articles to aid members of these communities in the teaching of evolutionary theory**.**

NIDA Summer Research Training Opportunities

Please see the link below to the National Institute on Drug Abuse (NIDA) news release, announcing the kick off application period for summer research training opportunities at its Intramural Program (IRP) facility in Baltimore, MD. The internship program is part of NIDA's commitment to introducing the science of addiction to some of the best and brightest young scientists in America. View: http://www.nida.nih.gov/newsroom/07/NR11-15.html

NIGMS Anticipates New Round of Proposals for Summer Short Course in Integrative Pharmacology

NIGMS has recognized the importance of training that enables scientists to integrate information from the most basic molecular and cellular systems to the whole organism and to relate such studies to the human condition. The majority of current graduate students receive relatively little training in physiology and integrative pharmacology, and hands-on experience is particularly lacking in the appropriate selection and use of in vivo and intact organ models. Relatively few institutions have sufficient faculty expertise and infrastructure to provide this training. Yet, the need for scientists with training in this area continues to be high in industry, government, and academia, where further attrition of faculty is expected due to retirement trends. In 2004, NIGMS solicited proposals to address this training need, and four programs were funded beginning in summer 2005. It is anticipated that NIGMS will solicit (fall 2007) a new round of proposals to continue the summer short courses from 2009 -2012. http://www.nigms.nih.gov/Training/IOSP.htm

ASPET-IOSS Fund Application Guidelines

The ASPET-IOSS Fund was created to provide support for graduate students and post-doctoral researchers seeking training in integrative whole organ systems sciences. The fund is currently supported by Abbott Laboratories, Merck Research Laboratories, Pfizer and Wyeth Research. The goal is to help augment developing programs (see above) that provide training of students in this field. For application information, visit:
http://www.aspet.org/public/public_affairs/pa_ioss.html

FASEB Releases *Breakthroughs in Bioscience* Article on Asthma

FASEB released "Breathtaking Discoveries: How Basic Research Led to Treatments for Asthma," the latest article in the *Breakthroughs in Bioscience* series. This article describes how fundamental understanding of the immune system, inflammation, and the underlying causes of asthma have resulted in successful treatments for this complex disease. The *Breakthroughs in Bioscience* series is a collection of illustrated articles, published by FASEB, that explain recent developments in basic biomedical research and how they are important to society. FASEB *Breakthroughs* articles are available to all members of FASEB societies, for use in your own teaching and advocacy efforts. They are available in electronic or hardcopy form and cover a range of topics. To obtain a free copy of these publications, visit the *Breakthroughs in Bioscience* Web site:
http://opa.faseb.org/pages/Publications/breakthroughs.htm or contact FASEB's Office of Public Affairs at (301) 634-7650.

FASEB NEWS

For FASEB biweekly news from Capitol Hill: http://opa.faseb.org/

Funding Opportunities

The Pioneer Award application period is from December 16, 2007 to January 16, 2008:
See http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-013.html for application instructions
and http://nihroadmap.nih.gov/pioneer for more information.

New Methodologies for Natural Products Chemistry:
http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-004.html

Notice of Intent to Publish a Request for Applications for Extinction and Pharmacotherapies for Drug:
http://grants.nih.gov/grants/guide/notice-files/NOT-DA-08-005.html

2008 NIH Director's Pioneer Award Program NIH Roadmap Initiatives:
http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-013.html

Division for Neuropharmacology

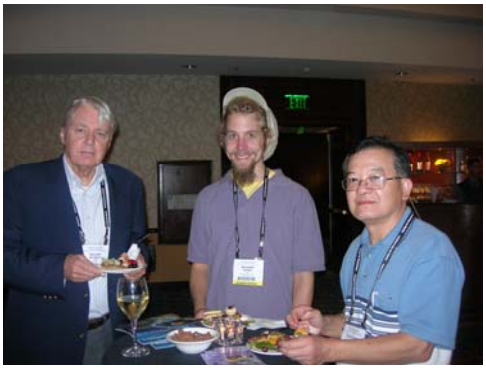
The Division for Neuropharmacology hosted a Social/Mixer at this year's *Society for Neuroscience* meeting in San Diego on November 4, 2007. The well-attended mixer featured light hors d'oeuvres and a cash bar. ASPET members and non-members alike enjoyed an evening of networking and socializing with colleagues and students. The mixer was open to anyone with an interest in neuropharmacology, and it gave younger scientists a chance to meet more established scientists in the field. Non-member attendees were encouraged to apply for membership in ASPET and in the division. As a result of the *Society for Neuroscience* meeting, ASPET signed up 74 new member applications.

Pictures from the Mixer are below:









MEMBERS IN THE NEWS

Peter C. Preusch, PhD has been named chief of the Biophysics Branch of the Division of Cell Biology and Biophysics at the National Institute of General Medical Sciences. Dr. Preusch recently served as acting NIH research training officer while on detail from NIGMS to the NIH Office of Extramural Research. More information regarding Dr. Preusch's appointment may be found at http://tinyurl.com/ypu2ad.

SHARE YOUR NEWS WITH FELLOW ASPET MEMBERS

Send news and photos to sthompson@aspet.org

STAFF NEWS

John Nelson, PhD, Associate Editor of *Molecular Interventions*, successfully ran and completed the 32nd Annual Marine Corps Marathon on October 28, 2007. After training several months, he finished the race in 4 hours and 59 minutes. John received a medal and a finisher's coin.

Christine K. Carrico, PhD, Executive Officer of ASPET, was honored for her 10 years of dedicated service with ASPET at the Council Meeting this fall. Past-President Elaine Sanders-Bush, President Ken Minneman, and President-Elect Joe Beavo presented Christie with a fashionable necklace/memory stick. Many of the successes of ASPET are due to Christie, and ASPET staff are all very appreciative of Christie's support throughout the years.

Nancy J White, ASPET's Meetings Manager, was honored and recognized this year for her outstanding services to ASPET. Nancy has been with ASPET for 10 years and has facilitated and organized many great meetings for ASPET. She was presented with a crystal vase at a staff meeting.

Patricia V. Stoute, Publications Coordinator for ASPET, was also honored and recognized for her dedicated services to ASPET. Pat has been a valued employee for over 12 years and is an asset to the Publications Department. She was also presented with a crystal vase at a staff meeting.

ASPET staff dresses up for Halloween 2007!

ASPET WELCOMES THE FOLLOWING NEW MEMBERS:

Regular Members

Clinton E Canal, PhD, Vanderbilt Univ
David Dime, PhD, Toronto Research Chemicals Inc.
Henrik G Dohlman, PhD, Univ of North Carolina
Patrick Finn, PhD, Genzyme Corp
John A Gruner, PhD, Cephalon, Inc.
W. Keith Jones, PhD, Univ of Cincinnati College of Medicine
David W Koh, PhD, Washington State Univ College of Pharmacy
Gregory M Miller, PhD, Harvard Univ Medical School
Eric C Peterson, PhD, Univ of Arkansas for Medical Sciences
Herve Schaffhauser, PhD, Cephalon Inc.
Aiming Yu, PhD, Univ of Buffalo

Graduate Student Members

Tressa Allington, Univ of Colorado Health Sciences Center
Justin J Anker, Univ of Minnesota
Dorinda D Arch, Univ of Utah
Su-Young Choi, Univ of Illinois-Chicago
Pei-Wen Chu, Univ of Utah
Katherine Cobb, Univ of Arkansas-Monticello
Senthilkumar Damodaran, Univ of Buffalo School of Medicine & Biomedical Sciences
Kennesha L Forbes, Tuskegee Univ
Dan Foster, Univ of Michigan
Laurel Grisanti, Univ of North Dakota
Rainbo Hultman, Duke Univ
Shafi M Kuchay, Univ of Illinois-Chicago
Tuoen Liu, Idaho State Univ College of Pharmacy
Hercules T Maguma, East Carolina Univ Brody School of Medicine
Bruce Mandt, Univ of Colorado Denver - School of Medicine
Anna Nelson, Univ of Colorado-Denver Health Science Center
Ricardo Pena, Univ of Iowa
Richard L Salisbury, Wright State Univ
Cullen Schmid, Ohio State Univ
Julie Stacey, Purdue Univ
Sarah J White, Univ of Arkansas for Medical Sciences

Undergraduate Student Members

Sarah Anoke, Harvard Univ
Ebony Barry, Sacramento City College
Leilani Beasley, Cosumnes River College
Maria Beckford, Univ of Maryland-Baltimore County
Brandon Carter, Dillard Univ

NEW ASPET MEMBERS

Efren Chavez, Univ of Texas-Brownsville
José M Cordero, Univ Puerto Rico-Mayaguez
Shirley A Diaz, Univ of Puerto Rico-Junces
Mary Elhardt, Univ of Houston
Felicia Gibson, Grambling State Univ
José A Herrera, Univ of Texas - Brownsville
Michelle Higgins, Kansas State Univ
Antentor O Hinton, Jr., Winston-Salem State Univ
Oghomwen Igiesuorobo, Chabot College
Jeff Jasper, Univ of Utah
Lauren Kendra, King's College
Kevin Kwan, Univ of Michigan Medical School
Eduardo Llamas, New Mexico State Univ
Elaine E Manzanilla, California State Univ-Sacramento
Kourtney Marshall, University of Maryland-Eastern Shore
Michelle Martensen, Colorado State Univ
Pang Moua, California State Univ-Sacramento
Ridhima Naidu, California State Univ-Sacramento
Ujunwa C Okoye, State Univ of New York - Stony Brook
Kyle Olszewski
Curtis R Powell, Brigham Young University-Idaho
Melissa Simons, Univ of Texas Medical Branch
Robbyn Tanner, Grambling State Univ
Jimmy Tran, Univ of Texas Medical Branch

Recruit An ASPET Member!!

If you know anyone who is not already an ASPET member, but should be, please recommend them for membership.

Applications are reviewed on a rolling basis and may be obtained at

www.aspet.org

ASPET notes with sympathy the passing of the following members:

Alfred H Lawton, MD, PhD, ScD

Andrew J Lonigro, MD

Bill L Martz, MD

Bernard L Mirkin, MD, PhD

FD Sticht, DDS

Maharaj K Ticku, PhD

John Yelnosky, PhD

Great Lakes Chapter - 20th Annual Scientific Meeting, June 08, 2007

Rosalind Franklin University of Medicine and Science, North Chicago, IL

The Great Lakes Chapter of ASPET held its annual meeting on June 08, 2007 at Rosalind Franklin University, North Chicago, IL. The meeting was attended by over 75 pharmacologists from the Chicagoland area and surrounding states of Wisconsin, Indiana and Michigan. The meeting focused on the theme **"Neurobiology of Drug Addiction."** The outstanding panel of speakers for the afternoon Symposium included Dr. Shi-Jiang Li from Medical College of Wisconsin, Milwaukee, who discussed his work on expectation and its modulatory effect on human brain responses to acute cocaine; Dr. Daniel McGehee, from University of Chicago, Chicago, who spoke on nicotinic and opioid receptors controlling mesoaccumbens dopamine release; and Dr. Paul E. Phillips, from University of Washington, Seattle, who discussed his research on subsecond dopamine release during drug abuse. The Keynote address was presented by Dr. Marina E. Wolf, from Rosalind Franklin University of Medicine and Science, who discussed the role of glutamate receptor trafficking in the role of addiction.

Along with this outstanding symposium and keynote address, the meeting featured vendor exhibits, a competitive poster session for students (with awards), a career workshop for students and postdoctoral fellows, and the election of new officers to the Executive Committee of GLC-ASPET.

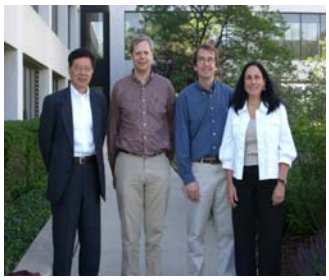
Winners of the Annual Graduate Student and Postdoctoral Poster Research Competition

Graduate Student Awards

1. Alexander Dec, Rosalind Franklin University
2. Mike Kowal, Midwestern University
3. Maud Morshedi, Rosalind Franklin University

Postdoctoral Fellow Awards

1. Stephen Sammut, Rosalind Franklin University
2. Fadi Khasawneh, University of Illinois-Chicago
3. Ruslan Tiniakov, Loyola University



The GLC-ASPET Executive Committee gratefully acknowledges the generous contributions from these Sponsors:

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And these generous Contributors:

Indiana University School of Medicine-Northwest Campus
Loyola University Stritch School of Medicine-Department of Pharmacology
Medical College of Wisconsin-Department of Pharmacology
Midwestern University-Department of Pharmacology
Northwestern University-Feinberg School of Medicine
Rosalind Franklin University-Department of Molecular and Cellular Pharmacology
Dr. Walter Prozialeck

Finally, we would like to thank these vendor exhibitors that participated:

Lonza Walkersville, Inc.
W. Nuhsbaum, Inc.
BD Biosciences, Discovery Labware

Mid-Atlantic Pharmacological Society 2007 Conference – October 8, 2007

Philadelphia College of Pharmacy, University of the Sciences in Philadelphia

The annual Mid-Atlantic Pharmacological Society (MAPS) conference was held on Monday, October 8, 2007, at the Philadelphia College of Pharmacy, University of the Sciences in Philadelphia. The conference was well attended as there were over 130 participants. The theme for this year was Advances in Neurodegeneration Research. The keynote address titled "A Novel RNA-based Method for General Therapies" was delivered by Dr. Sidney Altman, 1989 Nobel Prize winner in Chemistry. John Trojanowski, MD, Ph.D., Director of the Alzheimer's Disease Center, and Co-Director, Center for Neurodegenerative Disease Research, Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA spoke on "Mechanisms of Parkinson's Disease Linked to Pathological Alpha-Synuclein: New Targets for Drug Discovery." Menelas N. Pangalos, Ph.D., Vice President, Neuroscience Research, Wyeth Research, Princeton, NJ, gave an interesting presentation: "Novel Approaches for the Treatment of Alzheimer's Disease – Challenges and Opportunities," that reviewed some of the approaches presently under study by the pharmaceutical industry. Dr. Todd E. Golde, MD, Ph.D., Chair, Professor and Consultant, Department of Neuroscience, Mayo Clinic, Jacksonville, FL, presented "Small Molecule Modulators of Aβ Production and Aggregation as Alzheimer's Disease Therapeutics." The final presentation of the day, by Ruy Tchao, Ph.D., Professor, Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, was on the "Role of Taurine in Macular Degeneration."

There were nearly 40 poster presentations by undergraduate and graduate students as well as postdoctoral associates from a number of colleges and universities. Several prizes were awarded. The meeting concluded with a reception for all attendees.

POSTER AWARD WINNERS

Undergraduate Division

1st Place-Marisa Rosenberg, Temple Medical School (pictured): "Effects of CB1 Receptor Agonism and Antagonism on Extinction Learning in an Appetitively Conditioned Task in Mice"

2nd Place-Jennifer Michener, Temple Medical School: "Interactions Between Norepinephrine and Angiotensin II in Mediating Vasoconstriction in Rat Aorta"

Graduate Student/Research Associate Division

1st Place- Melissa Costell, GlaxoSmithKline (pictured): "Compensatory Role for Sgk2-Mediated Sodium Reabsorption During Salt Deprivation in Sgk1 Knockout Mice."

2nd Place- Jessica Breslow, Temple Medical School: "Immunosuppressive Effect of Morphine on *Acinetobacter baumannii* Infection"

Postdoctoral Division

1st Place- Zhe Ding, Temple Pharmacy School (pictured): "PTX-Insensitive G_Z Transduction Pathway Contributes to Buprenorphine-Induced Supraspinal, but Not Spinal, Antinociception"

2nd Place-Bruce Rasmussen, Temple Pharmacy School: "Effects of Anandamide on Amphetamine-Induced Locomotor Responses"

PICTURES FROM THE MAPS CONFERENCE

Keynote address speaker Dr. Sidney Altman is congratulated by conference host Adeboye Adejare after his presentation on "A novel RNA-based method for general therapies"

Meeting speakers (left to right): Menelas Pangalos, PhD, Wyeth Research; Keynote speaker Sidney Altman, PhD, 1989 Nobel Laureate in chemistry; Conference chairman Adeboye Adejare, PhD, University of the Sciences in Philadelphia/Philadelphia College of Pharmacy; Todd E. Golde MD, PhD, Dept. of Neuroscience, Mayo Clinic (Jacksonville, FL); MAPS president Ronald J. Tallarida, PhD, Temple University School of Medicine; and Ruy Tchao, PhD, University of the Sciences in Philadelphia/Philadelphia College of Pharmacy. [Not pictured: John Q. Trojanowski, MD, PhD, Univ of Pennsylvania]

MAPS Councilor Robert B. Raffa, PhD presenting the 2007 George B. Koelle award lecture plaque to Jeffrey Vaught, PhD, Executive Vice President for Research and Development, Cephalon, Inc.

Marisa Rosenberg, winner, undergraduate division, Temple University School of Pharmacy, presenting her poster to Adeboye Adejare

Winner of the graduate student/research associate award, Melissa Costell, GlaxoSmithKline, receiving her award from MAPS vice president Vincent Aloyo

MAPS vice president Vince Aloyo presenting the postdoctoral poster competition award to Zhe Ding, Temple Pharmacy School

ABSTRACTS FROM THE MAPS MEETING:

Estrogen, Bisphenol A, and the Immune Response: Isolation and Analysis of Macrophages and Cathepsins S and L. Priya Patel*, Theresa Leichner, and Rebecca Roberts. Biochemistry and Molecular Biology, Ursinus College, Collegeville, PA 19426

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects women in a much greater proportion than men. Therefore, there is a possible link between the disease and estrogen (E2), a physiological hormone produced predominantly in women. Even more, an environmental estrogen used in the production of plastics, Bisphenol A (BPA), could also play a role in SLE. These hormones might bind to cellular estrogen receptors, changing pathways and leading to a modified regulation of the immune system. One possible link between estrogen and the immune system is the regulation of cathepsins, proteases that are crucial in the major histocompatibility complex Class II processing and presentation of antigens. Macrophages are white blood cells that present antigens on their surfaces for recognition by other cells to elicit an immune response. These immune cells can be isolated from mice by peritoneal harvesting. We accomplish this by injecting the peritoneal cavities of mice with 3% Brewer's thioglycollate medium and harvesting by washing the cavities after a three day immune response. Splenocytes were isolated from spleens of uninjected, healthy mice. Once isolated, the macrophages and splenocytes were treated with E2 and BPA. Changes in the regulation of cathepsins were determined through western blotting. Cathepsins S and L are the specific proteins studied. In a primary western blot, Cathepsin S was detected in approximately equal levels in untreated, E2-treated (50nM), and BPA-treated (50nM) splenocytes. These results might indicate that the levels of E2 and BPA do not play a role in the regulation of levels of Cathepsin S in these antigen presenting cells. In another primary blot, Cathepsin L appears to be regulated differently in control macrophage samples and those treated with 50nM BPA. Future experiments will focus on obtaining quantifiable western blots to verify regulation of Cathepsins S and L. These results indicate that cathepsins important in antigen processing may be regulated by physiological as well as environmental hormones.

Characterization and Behavioral Effects of Acylated Homoserine Lactones Produced by Extremely Halophilic Archaea. A.T. Panicker* and W. McDonald. * Department of Microbiology, Ursinus College, Collegeville, PA 19426

Quorum sensing is a well-documented phenomenon in bacteria in which small autoinducer molecules, like acylated homoserine lactones (AHLs), are secreted by cells in order to coordinate gene expression and behavior. The phenomenon in archaea has yet to be thoroughly explored and methods of experimentation have not been developed. Through studies of the haloarchaeal strains *Halobacterium* sp. NRC-1, *H. mediterranei, H. hispanica*, *H. coriense*, *N. occultus*, *N magadii*, *H. saccharovorum*, and *H. volcanii*, we have developed a method to improve the isolation, detection, characterization and observance of behavioral effects of AHLs on archaea. After growing the archaea to an optical density of 0.9 (for up to 60 hours) in 250 mL of its specified broth, centrifugation at 8000 rpm for 20 min separated out the cells. The supernatant was then extracted with 200 mL of ethyl acetate and concentrated down to 200 µL by vacuum rotary evaporation. 0.75% AT top agar with 40 µg/mL X-gal and 1:200 concentration of the *A. tumefaciens* KYC55 reporter strain was then poured over AT plates and a well was made in the center to hold 50 µL of each haloarchaeal extract, as well as one plate with an A. tumefaciens KYC6 positive control and negative media (876 medium) control. After 24 hours, *H. hispanica, H. saccharovorum, H. coriense, and H. volcanii* showed distinctive blue rings around the wells showing that the extract triggered the expression of the lacZ gene in KYC55, meaning that AHLs are present within those haloarchaeal extracts. To test behavioral effects of the AHLs in the extracts on colony growth, 10 and 50 µL of either extract or ethyl acetate were spread over plates as test and as a negative control, respectively. After drying, 100 µL of liquid culture at dilutions of 10^{-7} and 10^{-8}M were spread over the plates, testing a total of 8 different plates at different concentrations and dilutions for each strain. *H. mediterranei* showed an increase in mucoid colony development with increased polysaccharide production for both 10 and 50 µL amounts of extract. Further observation of behavioral effects of extracts on haloarchaeal cultures and extracts to characterize haloarchaeal AHLs will allow us to explore the idea of quorum-sensing in archaea.

The Investigation of Synaesthesia as a Continuum and Bidirectional Process in Human Adults. Vicki Mattei* and Joel Bish. Ursinus College, Collegeville, PA 19426

The neurological condition synaesthesia is a rare condition in which there is concurrent atypical triggering of sensory experience. From the Greek words for 'sensation' (aesthesis) and 'together' (syn), synaesthesia is literally two or more sensory experiences occurring together. Although there are a wide variety of forms in which synaesthesia can occur, the form of interest for the current study is Grapheme Color Synaesthesia (GCS), in which a letter or number evokes the sensation of color. One implicit characteristic of this specific condition is the unidirectional nature of graphemes evoking color and not the other way around, with colors evoking letters or numerical properties, however, recent research has made some headway in exploring the possible bidirectional nature of this condition. The presence of bidirectional processing among synaesthetes is one of the investigative aims of the current study, along with synaesthesia as a continuum versus cut and dry presence or absence of the condition. To initially test for the condition, the Test of Genuineness was administered which focuses on color associations with letters and numbers. To test processing aspects of the condition, such as bidirectionality, computer based tasks were employed, which included variations of the Stroop task and other like processing tasks. Thirty-three college-aged adults participated in the study, three of which were confirmed synaesthetes, while the remaining thirty served as the control. The results of this ongoing study indicate that synaesthesia influences cognitive processing in a number of domains.

Co-Localization of BRDU and NEUN for the Purposes of Tracking the Fate of Neural Stem Cells in Spinal Cords of Salamander Tail Regenerates. K.T. Woodard* and Ellen Dawley. Ursinus College Biology Department, Collegeville, PA 19426

Adult Urodeles (salamanders and newts) have the ability to regenerate their tails, including spinal cord; however, other tetrapod vertebrates cannot regenerate their spinal cord, even if they can regenerate their tail. Furthermore, some salamanders have the ability to autotomize their tails for defensive purposes. The ependymal region, which surrounds the spinal cord, provides a stem cell population to replace spinal cord neurons after autotomization or damage. In this study, I examined the time course from stem cell division to mature neuron in red-back salamanders (Plethodon cinereus), a species that autotomizes its tail. I amputated tails and three days later, injected salamanders with BrdU, which becomes incorporated into newly synthesized cells. Regrowth was reamputated at various intervals (2, 4, 6, 8, 10 days post-BrdU injection) and sectioned using cryostat method. I used immunocytochemistry to double label sections with anti-BrdU, to track newborn cells from the ependyma, and anti-NeuN, to tract mature neurons. Some of the new cells radiated out of the ependyma and migrated to their future location in the tail to become differentiated into neurons. Red-backed salamanders showed new neuronal differentiation in 5 to 7 days post-amputation. Future studies to be conducted will include comparison of neural differentiation timeline with a commonly used model organism in spinal cord regeneration, Notophthalmus viridescens.

High Content Characterization of the Sphingosine-1-Phosphate Receptor Family. Carla Valenzuela[1]*, Michael A. Nolan[2] . [1]Univ. of Maryland Baltimore County 21250; [2]Wyeth Research, Cambridge, MA 02140

G protein-coupled receptors (GPCRs) are one of the most successful target classes for drug discovery. For some GPCR targets, a significant challenge is the identification of compounds that act selectively at one member within a family of receptors that share the same ligand. The goal of this study is to determine if the Transfluor high content GPCR internalization assay is a suitable format for determining compound selectivity using the 5 members of the family of sphingosine-1-phosphate (S1P) receptors. The Transfluor system employs a GFP-□-Arrestin fusion protein as a biosensor for GPCR agonist activity by redistributing from even cytoplasmic localization to bright punctae at clathrin-coated pits and vesicles near the plasma membrane. By over-expressing an individual GPCR of interest (in this case $S1PR_{1,\ 2,\ 4,\ or\ 5}$) in Transfluor cells, agonist activity may be quantified by analysis of fluorescent microscopy images. All S1PRs exhibited the expected dose-dependent response to S1P, the nonselective naturally-occurring ligand for this family of receptors. Furthermore, a point mutation in $S1PR_1$ that does not affect ligand binding (H28F) also does not affect the internalization response. Interestingly, the cells expressing $S1PR_4$ showed a small degree of GFP-□-arrestin punctae formation without exogenous S1P, suggesting some level of constitutive activity for this receptor. With the image analysis parameters defined for each receptor, we tested three small molecules previously reported to exhibit selectivity for S1PR family members (dihydro-S1P: $S1PR_4$ selective, Compounds A and B: $S1PR_1$ selective). Each of these agonists did exhibit some degree of selectivity: dihydro-S1P: $S1PR_4$=$S1PR_2$>$S1PR_{1,4,5}$; Compounds A and B: $S1PR_1$>> $S1PR_{4,5}$>>$S1PR_2$. These results demonstrate that the Transfluor high content approach is amenable to determining the selectivity of small molecule agonists for multiple GPCRs within the same family.

Bioanalytical Support for Wyeth's Norepinephrine Reuptake Inhibitor (NRI) Women's Health Discovery Program: An *In Vivo* Blood Brain Barrier Study. Andrew F. Murphy,*[,a] Katherine Laws[b] and Gary Bridson[b]. University of Maryland Baltimore County,[a] Catonsville, MD and Wyeth Research[b], Andover, MA 01810

The Blood Brain Barrier (BBB) has multiple efflux mechanisms that hinder many compounds from diffusing across it. These mechanisms often prevent efficacious delivery of diverse xenobiotics to target tissue within the brain. The therapeutic goal of Wyeth's NRI program is to regulate vasomotor symptoms in menopausal women (VMS). Specifically, the program chemistry targets the hypothalamus that of which is involved in signal vasoconstriction or dilation through a feedback mechanism responsible for temperature regulation. WYE-103231 is a novel chemical entity resulting from the discovery SAR efforts of Wyeth's NRI program. Screening against our efficacy model, a telemetry model measuring rat-tail vein temperatures between light and dark cycles, provides valuable information to the project team. Positive efficacy results are paired with bioanalytical quantitation data to determine if a compound passes the BBB and to what extent. Experimentally, concentrations of WYE-103231 are quantitated from 3 matrices; brain, hypothalamus, and plasma. All are measured at 7-time points post-oral dose of 10 mg/kg in ovariectomized (OVX) female rats. Bioanalytical data is generated utilizing LC/MS/MS; this hyphenated technique is key in the isolation and analysis of the compound from the different tissues and plasma. Our findings indicate that the compound is present in all of the tested tissues. From this study a ratio of tissue to plasma is determined and used for compound ranking.

In Silico Toxicology Tools in DSM: Retrospective Analysis of Clastogenicity Data. Robert L. Kuoch* [1]and Cheryl Mugford[2]. [1]University of Maryland Baltimore County 21250 and [2]Wyeth Research, Collegeville, PA 19426

In silico toxicity prediction tools are software programs containing a large amount of specialized knowledge designed to assist the user to investigate the potential toxicity of a molecule. The software is divided into two categories: qualitative knowledge base programs (Derek, Lhasa, Ltd.) and quantitative structure evaluation systems (MCASE, MultiCASE, Inc). A goal in utilizing these computer tools is to improve lead chemical selection by helping to identify compounds with potential liabilities early in the drug discovery process. The objective of the current research was to evaluate the predictive capacity of MCASE (MultiCASE, Inc.) by conducting a retrospective analysis of over 30 in-house compounds that have been examined in chromosomal aberration and micronucleus assays. This small test set of compounds was processed through six clastogenicity modules of MCASE, each specific for predicting the induction of chromosomal aberrations or micronucleus formation. The MCASE predictions were compared with the in-life findings for each in-house compound. MCASE predictions for the small test set of in-house micronucleus data demonstrated good concordance and specificity;

however, sensitivity and the predictive value for positive compounds were poor. MCASE predictions for the small test set of in-house chromosome aberration data also showed good concordance and specificity. While the software identified one in-life positive compound, sensitivity was poor. The test of in-house compounds has also been examined in Derek (Lhasa, Ltd). Statistical analysis of the comparison of in-life results with the Derek predictions is in progress. The retrospective analysis of in-house compounds will assist in refining the toxic liability predictions generated by MCASE and Derek.

The Pathway of Biosynthesis and Degradation of 2-Arachidonoyl Glycerol in NG108-15 Cells. Samantha McClatchy*[1], Kristen Chevalier[1], WenSheng Lang[2], Gary W. Caldwell[2], Sui-Po Zhang[1] and Christopher Flores[1]. Analgesics Team[1] and Analytical Research Team[2], East Coast Research and Early Development, Johnson & Johnson Pharmaceutical Research and Development, L.L.C., Spring House, Pennsylvania 19477-0776, USA

The molecule 2-arachidonoylglycerol (2-AG) is an endogenous cannabinoid known to play various roles in many biological systems via interactions with CB_1 and CB_2 cannabinoid receptors. However, the pathways of 2-AG biosynthesis and degradation have yet to be fully elucidated. In this study, we investigated pathways of 2-AG synthesis and degradation in NG108-15 cells. The cell homogenate was incubated with calcium to stimulate 2-AG accumulation, which was then analyzed using HPLC/MS. The data showed that the phospholipase C inhibitor U73122 (10 μM) and the diacylglycerol lipase inhibitor orlistat (10 μM) blocked 2-AG accumulation by 40% and 93%, respectively, whereas the monoacylglycerol lipase inhibitors URB602 (100 μM) and methyl arachidonyl fluorophosphonate (100 nM) stimulated 2-AG accumulation by 93% and 257%, respectively. Inhibitors of other lipases, such as 1,2 diacylglycerol kinase, cyclooxygenase and fatty acid amide hydrolase, were also evaluated in this study, but had little or no effect on 2-AG accumulation in the cells. The results demonstrate that, in NG108-15 cells, 1,2 diacylglycerol lipase plays a major role in 2-AG synthesis, whereas monoacylglycerol lipase is involved in the degradation of 2-AG. These in vitro results provide useful insights on approaches that may be used for designing drugs to modulate endogenous 2-AG levels in humans for the treatment of pain and other diseases.

*Currently, SM is a senior student of Gwynedd Mercy College.

Interactions Between Norepinephrine and Angiotensin II in Mediating Vasoconstriction in Rat Aorta. J Michener*, N Lamarre, S Inan and RJ Tallarida. Temple University School of Medicine, Philadelphia, PA 19140

There is an extensive literature dealing with the many pharmacologic actions of both norepinephrine (NE) and angiotensin II (AtII). Interest in these endogenous compounds is widespread and is especially important clinically because the antagonism of these agents represent mechanisms for treating hypertension. Although there has been much reported on each of these compounds, there is an apparent lack of quantitative information on the combined actions of these agents and whether their simultaneous presence is characterized by synergistic, antagonistic or simply additive interactions. Because of recent theoretical advances in modeling drug combinations, that aspect can now be assessed rigorously and was applied to this pair of endogenous vasoconstrictors. In that regard we employed a standard vascular preparation, isolated rat aorta, with intact and minimally disturbed endothelium and adventitia. Our study determined the graded dose-response relation of the individual compounds and a fixed ratio combination of these. The effect obtained was the developed isometric tension which was subsequently normalized to the maximum tension produced by 120 mM KCl. On this normalized scale norepinephrine produced a dose-related effect whose maximum was 107% of the KCl maximum, whereas ATII yielded a much lower maximum, viz., 45%. This pair of dose-effect relations allowed a calculation of the additive (expected) dose-effect curve of a combination consisting of 30% NE and 70% ATII. The dose-effect relation experimentally derived for this combination was found to be virtually identical to the additive (predicted) dose-effect relation, thereby demonstrating that there is no evidence of either synergism or antagonism between these endogenous vasoconstrictors. Interestingly, for effects reached by the individual compounds, NE was found to be more potent than AtII in this preparation. This study was undertaken in order to apply this new method of analysis to this well known pair of agents, and represents the first rigorous quantitative demonstration of this combination. While their individual and combined actions affect numerous systems, this study focused only on the direct vasoconstrictor effects of these agents in rat aorta.

Cocaine and Amphetamine, but not Cannabinoid (WIN 52212-2), Abstinence-Induced Withdrawal/Physical-Dependence is Mediated *Via* A κ-Opioid Receptor-Like Pathway in Planarians: 'Pharmacologic Congruence'. Robert B. Raffa, Gregory W. Stagliano, Geoffrey Ross, Jenay A. Powell, Austin G. Phillips*, Zhe Ding and Scott M. Rawls. Temple University School of Pharmacy, Philadelphia, PA 19140

There is clear evidence for the evolution in complexity of pharmacologic receptor diversification and of receptor-effector signal transduction mechanisms. Pre-mammalian species have less differentiated receptor subtype pharmacology and therefore might share signal transduction pathways to a greater extent than do mammals, a phenomenon that we term 'pharmacologic congruence'. In order to study this evolution of signal transmission, we use planarians, a type of flatworm that is considered to be the lowest species having a centralized nervous system. Planarians are also of relevance because of their relatively sophisticated behavioral repertoire, including learning and memory. We demonstrated previously that planarians display both abstinence-induced and antagonist-precipitated withdrawal signs, indicative of the development of physical dependence. We now report: (1) amphetamine abstinence-induced withdrawal, and (2) attenuation of both cocaine and amphetamine, but not synthetic cannabinoid agonist (WIN 52212-2), abstinence-induced withdrawal by the opioid receptor antagonist naloxone and by the selective κ-opioid receptor subtype antagonist *nor*-BNI (*nor*-Binaltorphimine), but not by the selective μ-opioid or δ-opioid receptor subtype antagonists CTAP (D-Phe-Cys-Tyr-D-Trp-Arg-Thr-Pen-

Thr-NH_2) and naltrindole. These results provide evidence that the withdrawal from cocaine and amphetamine, but not from cannabinoids, in planarians is mediated through a common (κ-opioid receptor-like) pathway.

Effects of CB1 Receptor Agonism and Antagonism on Extinction Learning in an Appetitively Conditioned Task in Mice. Marisa B. Rosenberg*, Sara Jane Ward, and Ellen A. Walker. Temple University School of Pharmacy, Philadelphia, PA 19140

Recent findings suggest that the endocannabinoid system is involved in modulating extinction learning. Typically, researchers have examined how cannabinoid 1 (CB1) agonists and antagonists alter extinction learning by implementing aversive behavioral models such as fear conditioning and water maze procedures. However, little has been studied concerning the role of CB1 receptors in extinction of an appetitively-conditioned task. In the present study, we examined how several extinction behaviors were altered by a CB1 indirect agonist (URB597) or a CB1 antagonist (SR141716) in C57Bl/6 mice. Mice were trained to self-administer a 32% corn oil solution by performing a nose-poke response in an experimental chamber. After learning this behavior, mice were pretreated with either vehicle, URB597, or SR141716 during three subsequent extinction sessions where the corn oil was no longer available. The extinction behaviors examined were: 1) rate to extinguish within a 2 hr session; 2) extinction burst responding; 3) spontaneous recovery, and; 4) food prime-induced reinstatement. The mice pretreated with the indirect CB1 agonist URB597 extinguished at a slower rate than the vehicle control mice. On the next day of testing, spontaneous recovery rates of the URB597-treated and vehicle-treated mice were similar; however the URB597-treated mice again extinguished more slowly. When a food prime was given on the third day, the URB597-treated mice again took longer to extinguish. In contrast, SR141716 pretreatment produced an increase in the rate of extinction compared to vehicle-treated mice. Furthermore, SR141716 treatment attenuated extinction burst responding, spontaneous recovery, and reinstatement behaviors. Others have demonstrated that under aversive conditions, CB1 agonists *facilitate* extinction learning, and CB1 antagonists typically have no effect in these assays. Taken together, these findings suggest an involvement of the endogenous CB system in the extinction of a positively reinforced behavior, and imply that the manner in which this system modulates extinction learning depends greatly on the motivational component (whether aversive or appetitive) of the learned behavior. Supported by grants F32-DA01931 (SJW) and R01-DA014673 (EAW)

Structure Activity Relationship (SAR) Studies of Adamantane-based α-Secretase Inhibitors. Adegoke Adeniji and Adeboye Adejare. Department of Pharmaceutical Sciences, University of the Sciences in Philadelphia, PA 19104

Abnormal processing of amyloid precursor protein (APP) by secretases has been implicated in the pathogenesis of Alzheimer's disease (AD). AD is a neurodegenerative disease characterized by accumulation of amyloid plaques and neurofibrillary tangles which are composed of amyloid α-peptide (Aα) and hyperphosphorylated tau proteins respectively. Several therapeutic targets are currently being pursued to probe the occurrence or halt the progression of the disease. A particularly promising target is α-secretase. The α-secretase complex includes an aspartyl protease that cleaves the product of α or α-secretase processing of APP to produce p3 fragment or Aα40/42 respectively. Overproduction of the Aα peptides particularly Aα42 triggers formation of the characteristic amyloid plaque. Previous work on α-secretase inhibitors conducted in our laboratory identified a novel class of compounds that inhibits this enzyme. In this class, 4-Fluoro-n-(adamantan-2-yl)-benzenesulfonamide (TLR-I-04) inhibited the enzyme with little or no toxic effect at the concentrations tested. Here, we present results of ongoing structure activity relationship studies for this class of adamantane based α-secretase inhibitors. Eight analogues of TLR-I-04 have been synthesized with different substituents on the phenyl ring and are currently being evaluated by in-vitro techniques. α-Secretase inhibitory activity was evaluated using H4 neuroglioma cell line overexpressing wild type APP cultured in Opti-MEM supplemented with 4%FBS and I%Pen/Strep. The cells are treated with the compounds and the media analyzed by sandwich Elisa to determine the level of Aα40 and Aα42. The reduction in the level of Aα peptides relative to vehicle (control) is used as an index of the ability of these compounds to inhibit α-secretase. Toxicity measurement was conducted using a 96-well plate and assessed by the MTT assay. The outcome of this study will help define physicochemical parameters that are critical for the activity of this class of compounds. Preliminary results suggest that Log P and electronic density do not seem to play significant roles in the α-secretase inhibitory activity of this class of compounds.

Long- Term Morphine Exposure Alters Cocaine-Induced Behaviors Chinwe A. Nwaneshiudu *and Ellen M. Unterwald. Dept. of Pharmacology and Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA 19140

The purpose of this study was to examine the effects of chronic morphine exposure using different administration regimens on behavioral responses to cocaine in a rat model. Saline or morphine filled 2 ml Alzet osmotic mini pumps (20 mg/kg/day) were implanted subcutaneously in 60-day-old male Sprague Dawley rats under 3-5% isofluorane anesthesia. Fourteen days after pump implantation, rats received an ip injection of either saline or cocaine (20 mg/kg) and activity was monitored for 60 mins. In a separate study, rats received once daily subcutaneous injections of either saline or morphine (10 mg/kg) for 5 days. Ten days after the last morphine injection, rats received an ip injection of either saline or cocaine (15 mg/kg) and locomotor activity of rats was monitored for 60 mins. Data were analyzed for statistical significance using a repeated measures two way ANOVA. Rats exposed to a continuous infusion of morphine for 14 days showed higher levels of stereotypic activity when challenged with cocaine than control rats. Administration of morphine daily for 5 days also caused an increase in response to a cocaine challenge 10 days later, mostly due to increases in stereotypic activity. In conclusion, these data suggest that chronic morphine exposure enhances cocaine-induced activity.

References

DeMaria Jr et al. *Am J Addict*, 2000.
Glauser et al. *J Emerg Med*, 2007.

Kosten et al. *J Nerv Ment Dis*, 1988.

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CXCL12 Potentiates the Behavioral Effects of Cocaine in the Rat. J Trecki* and EM Unterwald. Dept. of Pharmacology, Center for Substance Abuse Research (CSAR), Temple University School of Medicine, Philadelphia, PA 19140

CXCL12 (stromal-cell derived factor 1 alpha, SDF-1α) is a chemokine that has been shown to play an important role in various biological processes including neuronal development, inflammation, and tumor pathogenesis. CXCL12 binds to a single receptor, CXCR4, which belongs to the family of seven trans-membrane G-protein coupled receptors. Both CXCL12 and CXCR4 have been identified via immunohistochemical analysis within the substantia nigra, the ventral tegmental area and the caudate putamen. Cocaine, a widely abused psychostimulant, binds to transport proteins and prevents the reuptake of dopamine, serotonin, and norepinepherine into presynaptic neurons. Exposure to cocaine in naïve animals results in increases in ambulatory and stereotypic behaviors. The following study was designed to investigate the effects of CXCL12 on cocaine-induced activity. Male Sprague-Dawley rats underwent surgery and were evaluated using locomotor chambers. Animals received an ICV injection of CXCL12 followed by cocaine IP across a range of doses. Upon concomitant administration of cocaine and CXCL12, ambulatory and stereotypic activity was potentiated at both 25 and 50 ng doses of CXCL12 as compared to those treated with cocaine or CXCL12 (Two-way ANOVA, $p<.01$). To evaluate the pharmacological properties of CXCL12, AMD 3100, a selective CXCR4 antagonist, was administered 60 minutes prior to CXCL12 and cocaine. AMD 3100 was able to block the potentiation of ambulatory and stereotypy activity as compared to CXCL12 and cocaine alone (Two-way ANOVA, $p<0.01$). Current studies include the evaluation of synaptic dopamine and glutamate levels via in vivo microdialysis and the possible co-localization of CXCR4 and dopamine receptors using immunohistochemistry and fluorescence. These results demonstrate a functional interaction between CXCL12 and cocaine and future experimentation will investigate the cellular mechanism underlying this interaction. P30 DA13429 (MW Adler), PA Dept. of Health/TU (EMU) and T32 DA07237 (EMU).

Mu Opioid Receptors in The Nucleus Accumbens and Ventral Tegmental Area are Necessary for Cocaine-Induced Conditioned Reward. A.Soderman* and EM Unterwald. Department of Pharmacology and Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA

The purpose of the present study was to determine the role of mu opioid receptors in the behavioral effects of cocaine, specifically cocaine-induced reward and hyperlocomotion. The focus was to determine whether mu opioid receptors within the ventral tegmental area (VTA) and the nucleus accumbens are important for the development of cocaine-induced conditioned place preference. In addition, the role of mu opioid receptors within the nucleus accumbens in the expression of cocaine place preference was assessed. Injection cannulas were implanted bilaterally into either the rostral or caudal VTA or the core or shell region of the nucleus accumbens of adult male Sprague Dawley rats. Cocaine-induced reward was assessed using an unbiased conditioned place preference procedure. Animals were conditioned once daily for four days for a total of two pairings with each saline and cocaine. Twenty minutes prior to conditioning, animals received either intra-VTA or intra-accumbens injections of the selective mu opioid receptor antagonist CTAP (0.5 µg in 0.5 µl/side) or vehicle. Place preference was determined on day 5 in a drug-free state. Locomotor activity was recorded during the conditioning sessions. Results demonstrate that animals receiving CTAP into the accumbens core or rostral VTA, but not the caudal VTA or accumbens shell, during conditioning showed an attenuation of cocaine-induced place preference. Intra-accumbens shell but not core CTAP attenuated the expression of cocaine place preference. Both intra-accumbens core and intra-caudal VTA CTAP significantly attenuated cocaine-induced hyperlocomotion. These results demonstrate the importance of mu opioid receptors in the nucleus accumbens and VTA in cocaine-induced hyperlocomotion and the development of conditioned reward, and suggest that some aspects of the behavioral effects of cocaine are mediated by endogenous activation of the mu opioid receptors in these brain regions. [This work was supported by NIH/NIDA DA09580 (EMU) and P30-DA13429 (MW Adler/EMU)]

Inhibition Of GSK3-Beta Attenuates Cocaine-Induced Behaviors In Mice. J.S. Miller* and E.M. Unterwald. Dept. of Pharmacology, Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA 19140

Glycogen synthase kinase (GSK3-beta) is a critical central mediator for a host of intracellular signaling systems. Originally isolated from skeletal muscle, this enzyme is widely expressed in all tissues with abundant levels in the brain. The activity of GSK3-beta is regulated by a number of kinases, with activation occurring via tyrosine phosphorylation and subsequent inactivation via serine phosphorylation. Aside from kinase inhibition, previous studies have used compounds such as sodium valproate (VPA) and/or the selective GSK3-beta inhibitor SB216763 to inactivate GSK3-beta. Here, we investigated whether inhibition of GSK3-beta by VPA and/or SB216763 would attenuate cocaine-induced behavioral activity in mice. Adult male CD-1 mice were pretreated with an i.p. injection either vehicle, VPA (50-300 mg/kg), or SB216763 (0.25-7.5 mg/kg). Following pretreatment, mice were administered a second i.p. injection of either vehicle or cocaine (20 mg/kg), and both ambulatory and stereotypic activity were recorded for 60 minutes post-injection. Pretreatment with VPA (300 mg/kg) or SB216763 (1.0-7.5 mg/kg) prior to cocaine yielded a statistically significant attenuation of both ambulatory and stereotypic activity as compared to pretreatment with vehicle prior to cocaine. These results indicate that pharmacological inhibition of GSK3-beta reduced the behavioral responses to cocaine in mice, therefore suggesting a role for GSK3-beta in the regulation of dopaminergic neurotransmission.
(Supported by NIH R01 DA09580)

Human Prostaglandin E_2 Receptors Show Different Localization Patterns in Polarized Epithelial Cells. J.N. Albano* and B. Ashby. Department of Pharmacology, School of Medicine, Temple University, Philadelphia, PA 19140

The underlying mechanisms of protein sorting in polarized epithelial cells are poorly understood. Several studies have determined membrane targeting of G protein-coupled receptors using epithelial cells such as Madin-Darby canine kidney cells. Polarized epithelial cells are composed of apical and basolateral plasma membrane domains with specific protein compositions separated by tight junctions. Purinergic, muscarinic, and adrenergic receptors are a few examples of G protein-coupled receptors (GPCRs) that have been shown to localize to specific membranes in MDCK cells. The current work seeks to determine the differences in subcellular localization of the human prostaglandin E_2 receptors. The EP receptors are all GPCRs, which differ in their second messenger pathways. The EP3 receptor is unique in that it has eight different isoforms that differ in the lengths of the carboxyl tail. Previous studies in our laboratory determined that the EP3 isoforms, as well as the EP2 and EP4 receptors, display different agonist-induced internalization patterns in HEK293 cells. We have also shown the EP3 isoforms have tissue-specific distribution patterns. These differences among the receptor subtypes and isoforms may correspond to the differences in function among them. To further study the differences among the PGE_2 receptors, we examined their subcellular localization patterns in Madin-Darby canine kidney (MDCK) and human bronchial epithelial (BEAS-2B) cells. We have determined the unique subcellular localization patterns for EP2, EP4, EP3.I, EP3.II, EP3.VI, and EP3.f, as well as three mutants in MDCK cells. Studies have also been done using the bronchial epithelial cell line BEAS-2B. We have shown the localization patterns for EP2, EP4, EP3.I, and the three receptor mutants and observed results similar to those obtained in MDCK cells, suggesting that receptor localization is not dependent on cell type. Current work is focused on constructing various receptor chimeras to locate structural motifs responsible for apical or basolateral localization. The aim of this work is to define the role of receptor localization in receptor function, as this may lead to a more complete understanding of the physiological role of the various human prostaglandin E_2 receptors.

Immunosuppressive Effect of Morphine on *Acinetobacter baumannii* Infection. Jessica M. Breslow*[1,2], Joseph J. Meissler, Jr. [1,2], Phillip B. Spence[1,2], John P. Gaughan[3], Martin W. Adler[1], M. Alexandra Monroy[4], and Toby K. Eisenstein[1,2] . Center for Substance Abuse Research[1], Departments of Microbiology and Immunology[2], Physiology[3], and Surgery[4] Temple University School of Medicine, Philadelphia PA 19140

Multiply drug-resistant *Acinetobacter baumannii* are usually nosocomial pathogens causing infection in immunosuppressed patients in intensive care units. Infections among healthy, but wounded, military personnel in Iraq have caused concern. We proposed that morphine, administered for analgesia on the battlefield, is immunosuppressive and predisposes to *A. baumannii* infection. To test this hypothesis, an intraperitoneal (i.p.) infection model was established in 2 strains of mice, examining male and female animals using a strain of *A. baumannii* obtained from Walter Reed Army Institute of Research. Morphine administered continuously for 48 hr by subcutaneous implantation of a slow-release morphine pellet resulted in 100% mortality of animals challenged with a 0.1 LD_{50} dose of *A. baumannii*, whereas all animals receiving placebo pellets survived. The lethal effect could be blocked by administering the opioid receptor antagonist, naltrexone. *Acinetobacter* burdens in the blood, spleens, livers, and lungs of morphine-treated mice, assayed 12h after i.p. challenge, were significantly higher than those in placebo-treated mice, confirming that mortality was due to potentiated growth of the bacteria. No effect of morphine on growth or viability of *A. baumannii* was observed over a 10^6-fold dose range when added to cultures in vitro. These results support the hypothesis that morphine potentiates *A. baumanii* infection in mice.

Interactions of Endogenous Vasoactive Peptides Examined In Vitro in Rat Aorta: Angiotensin II and Urotensin II. N Lamarre*, J Michener, and RJ Tallarida. Department of Pharmacology, Temple University School of Medicine, Philadelphia PA 19140

Urotensin II (U-II), a peptide found in the circulation of humans and animals, has been described as a potent vasoconstrictor. Human studies have revealed highest concentrations in the kidney and motor neurons, and its plasma levels are known to be elevated in hypertensive patients. Angiotensin II (Ang II) is a peptide whose vasoconstricting properties are well characterized and its importance in hypertension is well known. Because these are endogenous agents that may interact synergistically, we conducted a rigorous study in the isolated rat aorta. The aim was quantitation of the vasoconstrictor actions (measuring isometric tension) of the individual agents and their combined effect. Adult male Sprague-Dawley rats (300-400 g) were used following a minimum acclimation period of 3 days. Animals were euthanized via CO_2 asphyxiation, and the aorta excised in a manner aimed at preserving the integrity of both the endothelium and adventitia. The integrity of the endothelium was confirmed with carbachol-induced relaxation following precontraction with an 80 % dose of norepinephrine. Preliminary observations confirmed previously published reports demonstrating tachyphylaxis with the individual agents, therefore, each tissue specimen received only a single dose (or dose combination) in these studies. Contraction following dosing was prolonged (occasionally 35 min to maximum). The effects were normalized to a 120 mM KCl response. For U-II, the maximal effect was 71.3 % KCl and its half-maximal concentration was 5.81 ± 1.53 nM. The corresponding values for Ang II were 45.2 % KCl and 30.2 ± 4.04 nM. The combination analysis used several different fixed-ratio proportions of the constituents. In one such set, 5.9 % U-II and 94.1 % Ang II, this ratio of constituents yielded effects suggestive of synergism. This finding may have important implications in our understanding and treatment of hypertension.

NMDA-Like Receptor Activation and Nitric Oxide Synthesis Mediate the Development and Expression of Methamphetamine Physical Dependence in Planarians. Christopher Roth*, Robert Raffa, PhD, & Scott Rawls, PhD. Department of Pharmaceutical Sciences, Temple University School of Pharmacy, Philadelphia, PA

A role for glutamate and nitric oxide in methamphetamine physical dependence was investigated at the behavioral and neurochemical levels using a simple, established planarian model of drug withdrawal. A behavioral sign of methamphetamine withdrawal (planarian spontaneous locomotor velocity, *p*LMV) was determined in the presence of four drugs: a NMDA antagonist (LY 235959); an AMPA antagonist (DNQX); a glutamate release inhibitor (riluzole); and a nitric oxide synthase inhibitor (L-NAME). Glutamate levels in whole planarians were measured following spontaneous withdrawal from methamphetamine. Experiments demonstrated that methamphetamine (0.1-100 μM)-exposed planarians placed into drug-free water displayed a dose-related decrease in planarian spontaneous locomotor velocity (*p*LMV). No change in *p*LMV occurred when methamphetamine (10 μM)-exposed planarians were placed into water containing methamphetamine (10 μM). For combined administration, methamphetamine (10 μM)-exposed planarians placed into water containing LY 235959 (1, 10 μM), L-NAME (10 μM) or riluzole (10 μM) did not display withdrawal. Withdrawal was not observed in planarians that were co-exposed to solutions containing methamphetamine (10 μM) and LY 235959 (0.1-10 μM), L-NAME (10 μM) or riluzole. The AMPA receptor antagonist DNQX did not alter methamphetamine-evoked withdrawal. Glutamate levels increased in direct proportion to the magnitude of the dose-related abstinence-induced withdrawal. The present experiments demonstrate that methamphetamine physical dependence develops in planarians and that NMDA-like receptor activation and nitric oxide production is required for both the development and expression of the dependence.

Flumazenil-Sensitive Dose-Related Physical Dependence in Planarians Produced by Two Benzodiazepine and One Non-Benzodiazepine Benzodiazepine-Receptor Agonists. Federica Cavallo*, Anna Capasso, PhD, & Robert Raffa, PhD. Department of Pharmaceutical Sciences, University of Salerno (FC, AC) & Department of Pharmaceutical Sciences, Temple University School of Pharmacy, Philadelphia (RR)

Two benzodiazepine (midazolam and clorazepate) and one non-benzodiazepine (zolpidem) benzodiazepine-receptor agonists produced dose-related physical dependence, as evidenced by abstinence-induced decrease in planarian locomotor velocity (*p*LMV) when drug-exposed planarians were placed into drug-free water, but not when they were placed into drug-containing water (*i.e.*, abstinence-induced withdrawal, since the effect was only obtained in the removal of drug and not in the continued presence of the drug). We have previously shown that the decrease in *p*LMV is associated with specific and transient withdrawal signs. In the present study, the selective benzodiazepine receptor antagonist flumazenil significantly antagonized ($P < 0.05$), by co-application, the ability of each agonist to produce the withdrawal. These results: (1) suggest that two different structural categories of benzodiazepine receptor agonists produce a dose-related physical dependence in planarians that is manifested as abstinence-induced withdrawal in this simple and convenient model, and that (2) in the absence of published cloning or radioligand binding literature, suggest a possible specific interaction site (receptor?) for these compounds in planarians.

Voluntary Alcohol Consumption Differentially Alters Cortical $GABA_A$ Receptor Sites in Wistar-Kyoto and Wistar Rats. Irene Yaroslavsky* and Shanaz Tejani-Butt. Pharmaceutical Sciences, University of the Sciences in Philadelphia, 19104

The Wistar-Kyoto (WKY) rat strain has been previously described as an animal model of depressive behavior. Previously reported strain differences in dopamine (DA) transporter and DA-2 receptor sites in the ventral tegmental area and the nucleus accumbens suggested an inherent deficit of DA in the mesolimbic pathway. Since the mesolimbic DA system is thought to mediate alcohol abuse, DA deficits in this pathway may predispose these animals to drink more alcohol. Further investigations have noted that WKY rats consume 200% more alcohol under basal conditions. Given that deficits in GABAergic processes are implicated in alcohol abuse, we investigated $GABA_A$ receptor binding in WKY and WIS rats under control and alcohol conditions using quantitative autoradiography. In order to study the effects of 24 day alcohol consumption on $GABA_A$ receptor sites, the present study measured the specific binding of [^{3}H] SR95531 to $GABA_A$ receptors in the brains of WKY and WIS control and 24-day alcohol treated rats. The results showed a significant strain and treatment interaction. The specific binding of [^{3}H] SR95531 to $GABA_A$ receptors was significantly increased in the cingulate cortex (CC) of WKY rats following 24 day alcohol consumption; with no differences seen in the motor cortex, caudate putamen and the nucleus accumbens. Within the alcohol groups, the effect of alcohol consumption on $GABA_A$ receptor sites in the CC was significantly greater in WKY as compared to WIS rats. Increased $GABA_A$ receptor density may be indicative of low GABA levels in the CC of WKY rats following chronic alcohol consumption. Current literature has noted that deficits in GABA may be one contributing factor to both substance abuse and mood disorders. Deficits in mesolimbic DA and cortical GABA neurotransmission have been suggested to play an important role in alcohol and other substance abuse disorders. Furthermore, the CC is one of the principle structures involved in emotion and behavioral manifestations and plays a critical role in impulsive behaviors such as drug addiction and alcohol abuse. The results of the current study together with previous differences in DA receptor binding provide support for the involvement of corticolimbic mechanisms in the increased propensity of WKY rats to voluntarily consume more alcohol compared to WIS rats (Research funded by USPHS Grant AA 015921 to S.T-B).

Use of EA.Hy926 Cells and Putative NO-Specific Fluorescent Dyes to Explore Endothelial Cell Function *In Vitro*. L. D'Angelo* and D.W. Morel. Dept. Pharmaceutical Sciences, University of the Sciences in Philadelphia 19104

Endothelial dysfunction is thought to be one of the hallmarks of atherosclerosis and diabetes-induced cardiovascular disease. One commonly used measure of endothelial dysfunction *in vivo* is increased vasoconstriction, thought to be mediated by reduced nitric oxide (NO) production by endothelial nitric oxide synthase (eNOS, NOSIII) as a result of cellular oxidative stress. In these studies we explored the use of an endothelial cell line, EA.hy926, a hybridoma of human umbilical vein endothelial cells and a lung carcinoma, with endothelial characteristics as an *in vitro* model in which to monitor changes in endothelial cell function related to NO production. Since early experiments showed very low and variable levels of NO using the classic Griess reaction as an index of NO, in these studies we

employed the purportedly highly sensitive and NO-specific dye, 4-amino-5 methylamino-2',7'-difluorofluorescein (DAF-FM, Molecular Probes ®), to measure intracellular (using the diacetate form) and extracellular NO production. The dye reacts directly with NO to produce a fluorescent adduct with Ex_{max} at 488 nm, Em_{max} at 515 nm. Intracellular DAF-FM fluorescence increases in a time dependent manner, and is subject to modulation by changes in cellular oxidative stress as monitored separately by 2',7'-dichlorodihydrofluorescein diacetate (H_2DCF-DA) fluorescence. However, DAF-FM fluorescence was unaffected by L-NAME, a competitive inhibitor of eNOS. Extracellular DAF-FM fluorescence was also modulated by changes in intracellular oxidative stress but also unaffected by L-NAME. A cell-free NO-generating system (DETA-NoNoate) produced time and concentration-dependent increases in DAF-FM fluorescence. Thus, studies to date are equivocal in the use of DAF-FM dyes to measure endothelial cell function via NO production in EA.hy926 cells *in vitro*

Elucidation of the Mechanism for *E.col i* topoisomerase III –Mediated DNA Catalysis. Pejvak Soltany*, Russell J. DiGate, James C. Pierce, James R. Johnson. Pharmacology Program, Bioinformatics Department, Biology Department, University of the Sciences in Philadelphia, Philadelphia, PA, 19104

A variety of cellular processes, including DNA replication, transcription, and chromosomal condensation, require enzymes that can regulate the ensuing torsional stress introduced into DNA. DNA topoisomerases have the capacity to relieve this stress within the chromosome by altering DNA topology. DNA topoisomerases are classified into two categories: type I and type II. The two types can be further divided into four subfamilies: IA, IB, IIA and IIB. Members of the same subfamily are structurally and mechanistically similar, whereas those of different subfamilies are distinct. Escherichia coli consist of the two type IA (DNA topoisomerase I and III) and two type IIA (DNA gyrase and DNA topoisomerase IV) topoisomerases. Previous studies have demonstrated that a strain lacking type IA topoisomerase activity is inviable. Interestingly, cells lacking either topoisomerase I (Topo I) or topoisomerase III (Topo III) alone are viable. This suggests that type IA topoisomerase activity is absolutely required for cell survival under normal circumstances but that the Topo I and III have at least partially overlapping activities. Our laboratory has also showed that inactivation of both type IA topoisomerases leads to improper chromosomal segregation. In addition, we have shown that the inability to separate newly synthesized chromosomes is not due to improper chromosomal segregation but due to improper resolution of recombination intermediates. In order to further dissect the role of topoisomerase in DNA metabolism we will attempt to isolate suppressors mutations Δ*topA topB*-mediated lethality. These suppressor mutations may identify proteins and enzymes involved in the same metabolic pathway as the type IA topoisomerase. In addition we are also examining the effect type IA deactivation has upon gene expression using microarray technology. This may also give clue to the role of type IA topoisomerase in DNA metabolism. DNA topoisomerases (type II) are the known targets for the fluoroquinolone antibiotics; however, there are no known inhibitors of type IA enzymes. Elucidating the mechanism of this enzyme is important because it may allow the identification of inhibitors of topoI and topoIII.

Exogenous Activation of the Transient Receptor Potential V4 Channel Causes Endothelial Failure and Circulatory Collapse. Weike Bao*, Sandhya Nerurkar, Tian-li Yue, Chris P Doe, Gerald Stankus, Haisong Ju[2], Heath Thomas[2], Cynthia Fishman[2], Anthony Sulpizio, David Behm, Sandra Hoffman[1], Zuojun Lin, Irina Lozinskya, Linda N Casillas[1], Min Lin[1], Robert E. Lee Trout[1], Bartholomew J. Votta[1], Robert Marquis[1] Xiaoping Xu, Robert N. Willette. Cardiovascular-Urogenital and Oncology[1] Centers of Excellence in Drug Discovery, Safety Assessment[2], GlaxoSmithKline Pharmaceuticals, King of Prussia, PA

Transient receptor potential V4 (TRPV4) is an osmo/mechano-sensitive non-selective cation channel expressed in the endothelium that contributes to intracellular Ca^{2+} homeostasis and regulation of cell volume. The purpose of the present study was to evaluate the cardiovascular effects of GSK1016790, a novel potent small molecule TRPV4 activator, and to examine it's mechanism of action. In three species (mouse, rat and dog), the intravenous administration of GSK1016790 induced a dose-dependent reduction in blood pressure, followed by profound circulatory collapse. In contrast, GSK1016790 had no acute cardiovascular effects in the TRPV4-/- null mouse. Hemodynamic analysis in the dog suggested that the terminal event was related to a profound reduction in cardiac output. However, GSK1016790 had no effect on rate or contractility in the isolated, buffer-perfused rat heart. In contrast, GSK1016790 produced potent endothelial-dependent relaxation of rodent isolated vascular ring segments that was abolished by NOS inhibition (L-NAME), ruthenium red and eNOS gene deletion. Surprisingly, the in vivo circulatory collapse was not altered by NOS inhibition (L-NAME) or eNOS gene deletion but was associated with (concentration and time appropriate) profound microvascular leakage and tissue hemorrhage in the lung, intestine and kidney. GSK1016790 potently induced rapid electrophysiological and morphological changes (retraction/condensation) in cultured endothelial cells. These results demonstrate that inappropriate activation of TRPV4 produces acute circulatory collapse associated with endothelial activation/injury and failure of the pulmonary microvascular permeability barrier. It will be important to determine the role of TRPV4 in vascular disease and disorders associated with microvascular congestion.

Compensatory Role for Sgk2-Mediated Sodium Reabsorption During Salt Deprivation in Sgk1 Knockout Mice. C.G. Schnackenberg[1], M.H. Costell*[1], R.E. Bernard[1], K.K. Minuti1, E.T. Grygielko1, M.J. Parsons[2,3], N.J. Laping[1], G. Duddy[2]. [1]Center for Excellence in Cardiovascular and Urogenital Drug Discovery, [2]Transgenics and Gene Cloning, GlaxoSmithKline, [3]Department of Surgery, Johns Hopkins University School of Medicine

The purpose of this study was to investigate the role of Sgk2 in the regulation of salt and water homeostasis. Kidney function and expression of Sgk1, Sgk2, Sgk3, and alpha-ENaC were determined during normal and 0% salt intake in Sgk1-/-, Sgk2-/-, and Sgk1-/-,Sgk2-/- double KO mice (DKO). During normal salt intake, renal function of Sgk1-/-, Sgk2-/- and DKO mice were similar to wild type mice. The renal response to salt deprivation was impaired in Sgk1-/- but not in Sgk2-/- mice. DKO mice on 0% salt diet gained less body weight, had higher urine flow, sodium and chloride excretions, and similar glomerular filtration rate than Sgk1+/+,Sgk2+/+ mice.

Plasma concentrations of sodium, chloride and potassium were increased, renal cortical Sgk3 expression was increased, and there was no difference in renal alpha-ENaC expression in DKO compared to wild type mice. DKO mice had an impaired ability to reabsorb water, sodium, chloride, and potassium during salt deprivation compared to Sgk1-/- or Sgk2-/- mice. In conclusion, Sgk2 has a minimal role in the regulation of salt and water homeostasis during normal or reduced salt intake in vivo. However, Sgk2 significantly contributes to water and electrolyte homeostasis during salt deprivation in the absence of Sgk1, suggesting that Sgk2 can compensate for functional changes in Sgk1.

Chronic DOI Reduces 5-HT2A-Mediated PI Hydrolysis in Rabbit Frontal Cortex. Emmanuelle A Schindler*, Vincent J. Aloyo, Joel Horwitz and John A. Harvey. Drexel University College of Medicine, Department of Pharmacology & Physiology, 245 N.15th St, MS488, Philadelphia, PA 19102

Serotonin2A (5-HT2A) receptors are G-protein coupled receptors that signal through phosphatidylinositol (PI) hydrolysis. The 5-HT2A receptor is also implicated in psychotic disease and remains a point of interest in treatment. Our lab has previously established that rabbits serve as a better model than rodents for human 5-HT2A receptors; there are, however, no published reports of serotonergic PI hydrolysis in rabbit brain tissue. The purpose of this study was to establish the assay in rabbits and test the validity of performing chronic treatments followed by PI hydrolysis measurements. Frontocortical tissue from naïve rabbits was chopped into slices, incubated with [^{3}H]*myo*inositol, the radiolabeled precursor to PI, and then exposed to agonists. Both serotonin (5-HT) and 5-HT2A/2C agonist (±)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) increased signals over basal. Pretreatment of tissue with the 5-HT2A antagonist ketanserin reduced agonist signals back to basal levels, isolating the effects to 5-HT2A receptors. In another group, rabbits were given daily injections of DOI (3µmol/kg) or saline for eight days. One, two, or three days after the last injection, animals were sacrificed and frontocortical tissue assayed for signaling. In all groups, DOI treatment reduced the 5-HT and DOI-mediated responses by approximately half without affecting basal signals. We have previously shown that identical treatment with DOI reduces frontocortical 5-HT2A density by 60%. These findings are similar to rodent studies that show correlation between receptor density and PI hydrolysis. This study also validates the use of rabbits for investigating drug-mediated changes in 5-HT2A-mediated PI hydrolysis.

Chronic SR46349b Up-Regulates 5-HT$_{2A}$ and 5-HT$_{2C}$ Receptors in the Rabbit Brain. L.C. Scarlota*, J.A. Harvey, V.J. Aloyo. Pharmacology & Physiology, Drexel University College of Medicine, Philadelphia, PA, 19102

Current pharmacology indicates that chronic antagonist administration results in receptor up-regulation. However, in the serotonergic system, chronic antagonist administration results in a paradoxical down-regulation of 5-HT$_2$ receptors. Currently, only two antagonists are known to up-regulate the 5-HT$_{2A}$ receptor, and there are no published reports of 5-HT$_{2C}$ receptor up-regulation. In rabbits, chronic administration of the 5-HT$_{2A}$ antagonist, MDL11,939, up-regulates the 5-HT$_{2A}$ receptor with no change in 5-HT$_{2C}$ density. In rodents, the 5-HT$_{2A/2C}$ antagonist SR46349B also up-regulates the 5-HT$_{2A}$ receptor, but 5-HT$_{2C}$ density was not examined. The current study was designed to determine if chronic administration of SR46349B (a gift from Sanofi-Synthelabo Recherche) also modifies 5-HT$_2$ receptors in the rabbit brain. To investigate receptor modification, male New Zealand rabbits were injected once daily with SR46349B (10 mg/kg, sc) for 8 days. Twenty-four hours later, rabbits were sacrificed and frontal cortex and hippocampus were obtained. 5-HT$_{2A}$ and 5-HT$_{2C}$ receptor densities were measured by saturation binding using [^{3}H]ketanserin, and [^{3}H]mesulergine, respectively. As reported for rodents, repeated administration of SR46349B significantly increased cortical 5-HT$_{2A}$ receptor density. However, decreased affinity indicated the presence of residual drug. A novel finding is that the density of 5-HT$_{2C}$ receptors was also significantly increased in the frontal cortex. To determine the regional specificity, 5-HT$_{2C}$ receptors were also measured in the hippocampus. Again, 5-HT$_{2C}$ receptor density was increased. These findings suggest that SR46349B has affinity for 5-HT$_{2A}$ and 5-HT$_{2C}$ receptors, and at both may be acting as an inverse agonist rather than an antagonist. [Grant MH-16841-38; J.A.Harvey]

Morphine-Induced Antinociception in Mice After Either Pharmacological Blockade or Genetical Deletion of Opioid Receptors. S. Inan*, R.J. Tallarida and A. Cowan. Department of Pharmacology and Center on Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA 19140

Morphine binds to three main opioid receptors known as mu, kappa and delta. To establish the degree to which each morphine-occupied receptor contributes to the antinociceptive effect of morphine, we examined dose-effect relations with one, two or all three opioid receptors blocked with selective, pharmacologic antagonists using the mouse abdominal constriction test. Also, we ran mu receptor knockout (k/o) mice in this test after a fixed dose of morphine (1 mg/kg, s.c.). Male Swiss-Webster mice (n=8-10; 20-25 g) and the aforementioned male k/o mice (C57Bl/6 background; n=6-8; 20-25 g) were used. β-FNA (10 mg/kg, s.c. at -24 h), norBNI (20 mg/kg, i.p. at -20 h) and naltrindole (3 mg/kg, s.c. at -1 h) were administered to block mu, kappa and delta receptors, respectively. After morphine (0.1-10 mg/kg, s.c. at -30 min) and 0.6% acetic acid (i.p. at -5 min) injections, the number of writhes was counted for 15 min. Morphine (1 mg/kg) antagonized nociception similarly in mu receptor k/o mice and animals pretreated with ß-FNA (36.8 ± 12 % and 43 ± 11 % inhibition, respectively). When morphine occupied all three receptors, the A_{50} value was calculated as 0.74 (0.37-2.62) mg/kg. A_{50} values of 0.95 (0.35-2.63), 1.34 (0.46-5.58), and 1.03 (0.48-5.76) mg/kg were obtained during specific occupation by morphine of mu, kappa and delta opioid receptors, respectively. When two receptors are occupied by morphine, A_{50} values were: 0.69 (0.45-3.56) for kappa + delta occupation; 0.86 (0.37-2.55) for mu + kappa occupation; and 1.18 (1.11-4.24) mg/kg for mu + delta occupation. Blocking all three receptors displaced the morphine dose-response curve 6.32 times to the right. *Despite using standardized/literature doses of the pharmacological antagonists, morphine is still a potent and efficacious antinociceptive agent in the test.*

Validation of the Delayed Non-Match to Place Task as an Assay for Working Memory in Alzheimer's Drug Discovery Research. Jason Smucny*, Gene Kinney, and Lone Veng. Merck and Co., West Point, PA 19486

Alzheimer's disease is a devastating neurodegenerative disorder that is characterized by a progressive decline in cognitive abilities, including spatial and working memory. Discovery and characterization of drugs to treat Alzheimer's disease thus necessitates the use of a functional assay of working memory in laboratory animals. To that end, we have developed and validated the delayed non-match to place (DNMTP) task for use in mice. The DNMTP task requires mice to use an alternating search strategy to locate a nourishing reward in a Y maze, using a variety of time delays between acquisition and retrieval trials.

In this study, we first trained male C57/B6 mice (n = 8) to retrieve the reward with 85% accuracy using a minimal time delay (1 second or less). We then measured their performance after a 90s delay, and found that choice accuracy decreased to near chance level (50%), suggesting that memory for the rewards' location was labile within this interval, matching the definition of working memory. To validate our assay, we tested the performance of mice under the influence of compounds that have been previously shown to improve or impair working memory in rodents. As expected, the PDE4 inhibitor rolipram (s.c., 0.3 mpk) improved performance at the 90s interval relative to saline control, whereas the amnestic muscarinic antagonist scopolamine (i.p., 0.5 mpk and i.p., 0.75 mpk) impaired performance. These results suggest that our version of the DNMTP is a reliable measure of working memory and can be used to test the pro-cognitive effects of novel agents for Alzheimer's disease.

Syntheses and Physicochemical Property Studies of Noncompetitive NMDA Receptor Antagonists. Shengguo Sun* and Adeboye Adejare. Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA 19104

Neurodegenerative diseases, such as Parkinson's and Alzheimer disease, are a growing problem as the global senior population increases. N-methyl-D-aspartate (NMDA) receptor is believed to be a therapeutic target to treat these diseases. It is also believed to play a role in epilepsy and stroke. During states of ischemia, NMDA receptors are over-activated causing membrane potential collapse by allowing too much Ca^{2+} entry. Phencyclidine (PCP) binds inside of NMDA receptor in the neuron and blocks excessive ion flux. The designed compounds are derived from PCP and are expected to act as noncompetitive NMDA receptor antagonists, preventing excitotoxicity even in the presence of excitants. The purpose of this study was to synthesize and evaluate novel target compounds, and determine physicochemical properties of a model compound. All of the target compounds were synthesized in good yields via four steps and yields varied from 10 to 50%. Compounds were characterized by NMR, MS, and other spectra. Several of the target compounds were evaluated as anticonvulsants using the maximal electroshock (MES) test. One compound exhibited significant anticonvulsant properties at therapeutic doses and with minimal side effects. *In vitro* binding studies showed anticonvulsant activity was in part due to blocking the NMDA receptor.
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Anxiolytic Behavior Induced by Delta Opioid Receptor Activation in the Central Nucleus of the Amygdala in Rats Using the Elevated Plus-Maze Test. Jovita F. Randall-Thompson* and Ellen M. Unterwald. Pharmacology Dept. & CSAR, Temple University School of Medicine, Philadelphia, PA 19140

Recent research has shown that anxiety-like behavior can be altered by delta opioid receptor modulation. Specifically, decreases and increases in anxiogenic behavior following systemic administration of the selective delta opioid receptor agonist SNC80 and selective delta-opioid receptor antagonist naltrindole, respectively, have been reported (Perrine et al., 2006; Saitoh et al., 2005). The neural site of action underlying these effects however is not known. One brain region that may be involved is the amygdala, which has been reported to be directly involved in both the acquisition and expression of fear conditioning (Rosen, 2004), with the central nucleus of the amygdala (CeA), in particular, being implicated in the modulation of stress response and anxiety-like behaviors (Kang et al., 1999). In addition, delta opioid receptors are expressed in the CeA (Poulin et. al, 2006). The following study, therefore, examined delta opioid receptor activation in the CeA using an animal model test of anxiety-like behavior. Male Sprague Dawley rats were anesthetized and cannula guides were implanted bilaterally into the CeA. Following a six day recovery period, subjects were microinjected with the delta opioid receptor agonist [D-PEN ^{2,5}]-Enkephalin (DPDPE) at either 100 ng (50 ng bilaterally), 1 µg (0.5 µg bilaterally) or 3 µg (1.5 µg bilaterally) or were given saline. Twenty minutes after microinjections subjects were tested for 5 min on the elevated plus-maze. Analysis of the following conditions indicated that subjects microinjected with 100 ng, 1 µg and 3 µg of DPDPE within the CeA spent significantly more time in open arms and had greater number of open arm entries in comparison controls. These findings reveal that delta opioid receptor activation within the CeA can reduce anxiety-like behavior and therefore open the possibility to examine in more detail the effect of delta opioid receptor activation in the CeA on anxiety. *Supported by NIH/NIDA T32 07237 (EMU/JRT) & DA018326 (EMU).*

References: Kang et al., *Ann N Y Acad Sci.,* 1999; Perrine et al., *Br J Pharmacol.,* 2006; Poulin et al., *J Comp Neurol.,* 2006; Rosen, *Behav Cogn Neurosci Rev.,* 2004; Saitoh et al., *Psychopharmacology (Berl),* 2005

Corticotropin Releasing Factor Is Implicated in the Sensory and Affective Components of Pain Behavior in a Rodent Nerve Injury Model. M. Hummel*, T. Cummons, P. Lu, N. Sullivan, and G. Whiteside. Wyeth Research, Discovery Neuroscience-Pain Department, Princeton, New Jersey 08543

Corticotropin releasing factor (CRF), the principal neuropeptide of the hypothalamic-pituitary-adrenal axis (HPA), plays a major role in controlling the body's behavioral response to stressful stimuli. Because chronic pain states cause both physical and psychological stress, these pathological conditions may impart changes in CRF-HPA function. Additionally, chronic pain often leads to affective disorders, such as anxiety and depression, which are also accompanied by known disturbances in this stress-response system. This study investigated whether the sensory and affective components of neuropathic pain-related behavior are related to aberrations in CRF. To this end, male Sprague-Dawley rats, 21 days post-spinal nerve ligation (SNL) or sham surgery, were subjected to a place aversion conditioning paradigm (CPA) whereby both nociceptive and affect-related pain behavior were assessed. For the procedure, rats were pre-tested, then alternately conditioned with a painful stimulus paired with a novel object in one chamber for 20 min and 3 h later conditioned in the opposite chamber with a non-painful stimulus paired with the same novel object. The sequence of pairings was alternated over 5 days using different objects. Rats were tested for CPA on day 7, immediately after which blood, brain and spinal cord were removed for analyses. Results showed that neuropathic rats have a significant aversion to the pain-paired environment. Furthermore, neuropathic rats displayed an increased number of foot withdrawals as well as reduced novel object interactions compared to sham controls during conditioning sessions. Biochemical analyses revealed that neuropathic animals had reduced CRF levels. In addition, reduced intensity of immunohistochemical staining was observed in the hypothalamus and the ipsilateral dorsal horn of the spinal cord as compared to controls. Together, these findings suggest that CRF may modulate both the sensory and affective components of neuropathic pain behavior in rodents. Ultimately, these findings may underscore the importance of CRF as being a critical mediator in the complex pathobiology associated with chronic painful conditions.

Age-Dependent Effects of the Cannabinoid CB1 Antagonist SR141716 on Food Intake, Body Weight Change, and Head-Scratching Behavior in Rats. Sara Jane Ward*, Timothy W. Lefever, Ellen A. Walker. Department of Pharmaceutical Sciences, Temple University School of Pharmacy, Philadelphia PA 19140

The cannabinoid CB1 selective antagonist SR141716 (Rimonabant) has been shown to decrease appetite and body weight in laboratory animals and humans and is approved for the treatment of adult obesity. Recent evidence suggests that while SR141716 modulates appetite via blockade of central CB1 receptors, its weight decreasing effects may be partially modulated by blockade of peripheral CB1 receptors involved in energy metabolism. In addition, SR141716 can also elicit scratching behavior in laboratory animals by a less well understood mechanism. Although childhood obesity is a rising health issue, it is unknown whether SR141716 is equipotent at modulating food intake and weight loss in younger subjects, and whether age affects scratching behavior elicited by SR141716 as well. To determine whether CB1 receptor blockade is equipotent at modulating these behaviors at different ages, the effect of a range of SR141716 doses on food intake, body weight change, and head scratching behavior in food-deprived 18 day old weanling, 28 day old adolescent, and 60 day old adult male rats was investigated. SR141716 dose-dependently suppressed food intake and body-weight gain and elicited head-scratching at all ages tested. SR141716 was most potent at decreasing food intake in weanlings, followed by adolescents, with adults requiring the highest dose of SR141716 to decrease feeding. SR141716 was also most potent at eliciting head-scratching behavior in weanlings, and was equipotent at eliciting head-scratching behavior in adolescents and adults. In contrast, there was no significant effect of age on SR141716's ability to suppress body-weight gain. These results indicate that the modulation of food intake and scratching behaviors by SR141716 are age dependent, while its effects on body-weight gain are not, suggesting that some populations of CB1 receptors change in sensitivity throughout development while others do not. These data further suggest that CB1 receptor modulation of food intake and metabolism are mediated by separate receptor populations (central versus peripheral). Supported by grants F32-DA01931 (SJW) and R01-DA014673 (EAW)

Effects of Anandamide on Amphetamine-Induced Locomotor Responses. Rasmussen, BA* and Rawls SM. The Department of Pharmaceutical Sciences, Temple University, Philadelphia, PA, 19140

Evidence suggests that endogenous cannabinoids (e.g. anandamide) modulate the behavioral effects of psychostimulants. Cannabinoid agonists are known to inhibit the reinforcing, rewarding, and toxic properties of cocaine by activating cannabinoid CB_1 receptors. However, the specific role of endogenous cannabinoids in this regard is unclear as most pharmacological studies have used synthetic cannabinoid receptor ligands. The goal of the present study was to elucidate a role for anandamide, the prototypical endogenous cannabinoid, in the behavioral effects of amphetamine in the rat. Rats were pretreated with (R)-(+)-methandamide (5mg/kg i.p.) 20 minutes before amphetamine (2mg/kg i.p.) administration, in paradigms designed to assess the effects of anandamide on acute and sensitized amphetamine-induced locomotor responses. No significant acute effects of anandamide on stereotypy or ambulation were found. Similarly, anandamide did not block the expression of amphetamine-sensitized stereotypy or ambulation. These data suggest that anandamide does not play a significant role in the acute hyperactivity caused by amphetamine. Current experiments are examining the effect of anandamide on the development of amphetamine-sensitization of locomotor behavior.

PTX-Insensitive G_z Transduction Pathway Contributes to Buprenorphine-Induced Supraspinal, But Not Spinal, Antinociception. Zhe Ding* & Robert B. Raffa. Department of Pharmaceutical Sciences, Temple University School of Pharmacy 19140

Buprenorphine is known as an opioid analgesic. Although it shares some of the general characteristics of other opioids, it displays preclinical pharmacology and clinical attributes distinct from opioids such as morphine and fentanyl. As a way of elucidating some of the differences, we investigated the contribution of G proteins in buprenorphine-induced antinociception. Subcutaneous (s.c.) administration of buprenorphine, morphine or fentanyl induced antinociception in the warm-water (48°C) tail-dip/flick test in mice in a dose-related manner. The antinociception induced by all three agonists was attenuated by intrathecal (i.t.) administration of either pertussis toxin

(PTX) (1 μg, 48h) or the opioid receptor antagonist naloxone (20 μg). However, intracerebroventricular (i.c.v.) PTX or naloxone administered attenuated only morphine- and fentanyl-induced antinociception. Pretreatment with Gz antisense (14.6 μg, 24 h) i.t. had no effect on any agonist-induced antinociception. However, pretreatment with Gz antisense (but not control) i.c.v. inhibited buprenorphine-induced, but not morphine- or fentanyl-induced antinociception. These results reveal that a PTX-insensitive, Gz transduction pathway plays an important role in buprenorphine-induced supraspinal antinociception distinct from, or to a greater degree than, morphine or fentanyl. This difference might account for one or more of the unique clinical attributes of buprenorphine.

In Vitro Toxicity Study of Novel Neuro-Protective Agents. Natalia Coleman*, Katrina E. Meachem, Adeboye Adejare. Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA 19104

Our group is involved in the design and syntheses of gamma-secretase inhibitors and N-methyl-d-aspartic acid (NMDA) receptor antagonists as possible therapies for Alzheimer's disease (AD). In this study, we compared toxic effects of novel lead compounds resulting from both projects (TLR-I-04 and SS-IV-055) with Memantine, and FDA approved therapy for AD acting via NMDA receptors. Toxicities of the compounds on two cell lines, namely MDCK (to mimic blood brain barrier) and CCL-131 (a neuronal cell line) were evaluated at various concentrations. Individual wells of a 96 well plate were seeded with cell concentrations of 10,000 and 5,000 in 100 µL of DMEM/F12 media supplemented with 10% fetal bovine serum and Penicillin/Streptomycin, and incubated for 24 h at 37 ^{o}C/ 5% CO_2. Cells were dosed at final concentration of 0 – 700 µM of each agent in triplicates for 30 min and up to 3 h. Viability was determined by AlamarBlue assay. Results show that the compounds and Memantine have acceptable toxicity profiles on MDCK cells. Unlike Memantine, both TLR-I-04 and SS-IV-055 displayed concentration dependent viability for neuronal cells with significant toxicity at higher concentrations. Based on results from this and similar studies, both compounds show acceptable toxicity profiles and are thus good lead compounds. Examination of these compounds in other cell lines is on-going.

The Use of Embryonic/Fetal Cells Against Neurodegeneration. Godfrey Caesar*. 209 West 137th Street, New York, NY 10030

It is becoming increasingly acceptable that many diseases may be of genetic origin (mutation in, loss of, or defect in protective gene/s).

Embryonic/fetal cells have (1) the ability to grow and proliferate, (2) the ability to undergo cell and tissue differentiation (intrinsic plasticity (3) the ability to produce growth factors, and (4) reduced antigenicity compared with adult tissue.

Embryonic/fetal cells could be profoundly important to the understanding of human disease/s. They can help to understand the processes underlying cell differentiation and biological development to prevent and treat diseases.

Neurons could be transplanted into the brains of patients with neurodegenerative disorders such as Parkinson's Disease.

These specific embryonic/fetal cells can be considered as a form of gene therapy to compensate for the defective or missing protective gene/s.

They may also be a source of rejuvenation.

I would suggest embryonic/fetal cell injections or implants.

This concept is further explained in *Medical Hypotheses*, Vol.58, No.5, 371-3, May 2002

Pharmacological and Anatomical Evidence that Brainstem Endocannabinoids Selectively Increase Feeding of Palatable Foods Via CB1Rs. *Nicholas V. DiPatrizio and Kenny J. Simansky. Drexel University College of Medicine, Dept. of Pharmacology and Physiology, Philadelphia, PA 19102

Feeding and energy balance are regulated by a complex network of brain regions and their associated receptor pathways, including cannabinoid signaling systems. In this series of experiments, we examined properties of activating cannabinoid CB1 receptors (CB1Rs) in the pontine parabrachial nucleus (PBN--brainstem region associated with integrating neurotransmission from multiple sensory systems, including information regarding ingestion) on intake of a palatable high-fat (60%)/sucrose diet (HFS) and/or standard-chow (SC). Additionally, coupling of PBN CB1Rs to their G-proteins were evaluated by [^{35}S]GTPγS autoradiography following incubation of tissue sections with the endogenous CB1R agonist (endocannabinoid), 2-arachidonoylglycerol (2-AG; 50µM). Separate groups of 6-7 male Sprague Dawley rats were implanted with bilateral cannulae aimed at the lateral PBN (LPBN) and food intake was measured for 4hr. By 30min post-infusion, 2-AG (1nmol) increased ingestion of HFS (from 6.2±0.4 to 10.1±0.8g) above control (vehicle). In order to confirm that the actions of 2-AG were mediated via CB1Rs, we pretreated (20min prior to 2-AG) animals with the CB1R selective antagonist, AM251 (1nmol). Intake of HFS following 2-AG administration (separate group of animals=5.0±0.4 to 7.8±0.9g) was completely reversed by pretreatment with the CB1R antagonist, AM251 (both=4.5±0.8g). To verify anatomical specificity for hyperphagic effects of 2-AG in the LPBN, animals were challenged with infusions ~0.5mm caudal to anatomical loci where 2-AG successfully increased intake. In these off-target controls, 2-AG failed to alter intake of HFS at 30min (5.4±1.2 to 5.0±0.8g). In contrast to HFS, 2-AG failed to modify eating of SC (0.1±0.1 to 0.1±0.1g). Furthermore, in the assay assessing G-protein coupling in tissue sections, 2-AG dramatically increased coupling in the LPBN. Importantly, this effect was attenuated by co-incubation with AM251, again identifying 2-AG effects as mediated by CB1Rs. Our data suggest that hedonically-positive sensory properties of food enable endocannabinoids at CB1Rs in the LPBN to increase eating and that 2-AG induced G-protein coupling in the LPBN is CB1R mediated. USPHS DK067648 to KJS.

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