

# ASIP Pathways

Research

Scientific  
DiscoveryTranslational  
ResearchImproved  
Medical Care

AMERICAN SOCIETY FOR INVESTIGATIVE PATHOLOGY

**News for Scientists Taking First Steps to Biomedical Discovery & Disease Cures**

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## **ASIP Representatives Participate in Translational Research Forum at Howard Hughes Medical Institute**

In early 2010, FASEB's Clinical Research Committee formed a **Translational Research Steering Committee** to focus on creating a national forum of leaders to discuss the role of basic scientists in the translational research enterprise. An agenda was developed and speakers were selected and invited over the course of 2010 for the Forum that was held on March 24 and 25, 2011 at the Bethesda campus of HHMI. Participants in the Steering Committee could not have foreseen just how timely and relevant the Translational Research Forum would be, with the simultaneous development of the National Center for Advancing Translational Sciences at NIH.

The Steering Committee recognized there is widespread interest in accelerating the pace at which basic research discoveries are translated into improved medical care. Lack of effective, systematic collaboration among basic, clinical, and translational researchers is frequently cited as one of the obstacles to moving promising discoveries from the bench to the bedside. Although there have been numerous initiatives aimed at addressing this concern, few have specifically focused on the importance of engaging basic scientists. The Forum's specific goal was to address the critical role that basic researchers play in translation, to examine approaches to increasing the participation of basic scientists, particularly those at an early career stage, and to explore new ways to foster collaboration among researchers working at all points along the bench-to-bedside continuum.

The Steering Committee, with assistance from FASEB society leaders, invited a select group of ~150 participants, including guest speakers, association members and staff, who they believed would make valuable contributions and facilitate the discussions. ASIP had substantial and broad representation from members: **Stanley Cohen, MD** (Chair of the Department of Pathology at UMDNJ-New Jersey Medical School), **James M. Crawford, MD PhD** (Senior Vice President and Chair of the Department of Pathology and Laboratory Medicine at the North Shore-Long Island Jewish Health System Laboratories), **Mary JC. Hendrix, PhD** (President and Scientific Director of the Children's Memorial

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## Welcome New Members!



**Mark E. Sobel, MD, PhD**  
Executive Officer

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<b>Salomé Creighton</b>	Executive Assistant
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<b>John W. Nelson, PhD</b>	Scientific Editor

### Milestones in Investigative Pathology Editor

**William K. Funkhouser, MD, PhD**

### ASIP Pathways Editor

**Mark E. Sobel, MD, PhD**

### ASIP Pathways Contributing Writers

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ISBER News - **James Douglas**

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### Regular Members:

**Gianfranco Alpini PhD**, Texas A&M Health Science Center  
**Robert Belloch MD, PhD**, University of California - San Francisco  
**Connie Cepko PhD**, Harvard Medical School  
**Kris K. Chadee PhD**, University of Calgary  
**Domenico Coppola MD**, H. Lee Moffitt Cancer Center  
**Piyali Dasgupta PhD**, Marshall University  
**Ram Datar MPhil, PhD**, Biomedical Nanoscience Institute of University of  
Miami  
**Maria DeTolve Donoghue DO**, G&M Consulting Services  
**Michael Feldman MD PhD**, University of Pennsylvania  
**Benedicte Fournier PhD**, Emory University  
**Michael S. Goligorsky MD PhD**, New York Medical College  
**Metin Gurcan PhD**, Ohio State University Medical Center  
**Ali Hafezi-Moghadam MD, PhD**, Harvard Medical School  
**Daniel Hayes MD**, University of Michigan Comprehensive Cancer Center  
**Timothy Koh PhD**, University of Illinois at Chicago  
**William A. LaFramboise PhD**, University of Pittsburgh School of Medicine  
**Jochen Lennerz MD, PhD**, Massachusetts General Hospital/Harvard Medical  
School Pathology Services  
**Peter Lucas MD, PhD**, University of Michigan Medical School  
**Haresh Mani MD**, Penn State Milton S. Hershey Medical Center  
**Paul McMenamin DSc**, Monash University  
**Stanley B. Prusiner MD**, University of California, San Francisco School of  
Medicine  
**Nasir M. Rajpoot PhD**, University of Warwick  
**Jenny Sabin M.ARCH**, University of Pennsylvania  
**Jennifer Sanders PhD**, Rhode Island Hospital  
**Phillip Scherer PhD**, University of Texas Southwestern Medical Center  
**Stacey Schultz-Cherry PhD**, St. Jude Children's Research Hospital  
**Melissa Schutten DVM PhD**, Genentech  
**Patrick M. Sluss PhD, MA**, Harvard Medical School/Massachusetts General  
Hospital  
**Carolyn J. Smith PhD**, New York Medical College  
**Federica Sotgia PhD**, Thomas Jefferson University  
**Elizabeth Uhl PhD DVM**, University of Georgia  
**Jouni Uitto MD, PhD**, Thomas Jefferson Medical College  
**Alexander Von Ruecker**, University Hospital Bonn  
**Betsey Wagener PhD**, Independent Consultant  
**Wendy Woodward MD, PhD**, University of Texas MD Anderson Cancer  
Center  
**M. James You MD, PhD**, University of Texas MD Anderson Cancer Center  
**Youli Zu MD, PhD**, The Methodist Hospital

### Trainee Members:

**Alice May Chang MD**, University of Washington  
**Crystal J. DiCosmo-Ponticello**, UMDNJ - New Jersey Medical School  
**Kristen Funk**, The Ohio State University  
**Grant Kolar MD, PhD**, Washington University  
**Prashanthi Menon PhD**, Harvard Medical School/BIDMC  
**Nayden Gueorguiev Naydenov PhD**, University of Rochester  
**Emmanuel Okoro MD**, Meharry Medical College  
**Ronen Sumagin PhD**, Emory University  
**Geeta Upadhyay PhD**, Georgetown University  
**Xuying Xin PhD**, Pennsylvania State University College of Medicine  
**Lili Zhang MD**, Baylor College of Medicine

### Associate Member:

**Mahadevan Venkatachalam MS**, Primex Healthcare & Research Pvt Ltd

(Continued from Page 1 - Public Affairs)

Research Center), **James Mallory Musser, MD PhD** (Chair of the Department of Pathology and Laboratory Medicine at The Methodist Hospital System), **John A. Smith, MD PhD** (Director of the Division of Laboratory Medicine at the University of Alabama, Birmingham), and **Mark L. Tykocinski, MD** (Dean of the Jefferson Medical College). **Mark E. Sobel, MD PhD**, Executive Director, and staff member **Priscilla Markwood** also attended on behalf of ASIP.

Francis Collins, Director of the National Institutes of Health, gave the keynote talk, providing a comprehensive but concise overview of the phases of translating basic scientific discoveries into therapeutics and therapeutics into improved medical care. Other sessions focused on: 1) the role of basic researchers in translation, highlighting examples of good and poor cooperation among basic, clinical, and translational researchers, which led to or inhibited breakthroughs; 2) a review of current initiatives aimed at increasing basic scientists' engagement in translational research, including training and education, institutional incentives, and funding opportunities; and 3) new approaches to fostering collaboration between basic and applied scientists, with the goal of identifying specific, actionable policy recommendations aimed at increasing basic science engagement in translational research. These primary topics were addressed through expert panels, break-out sessions and table discussions. Questions from the audience were encouraged and well-addressed.

In the end, attention centered on several issues: 1) individually, how to 'spark' the interest of basic researchers into studying human disease pathobiology; 2) locally, how to incentivize inter-departmental cooperation and engagement in translational research; and 3) nationally, how to better characterize funding opportunities and evaluate grant applications to fit translational research paradigms. Understandably, the 2-day Forum only scratched the surface of inquiry into these challenging and complex issues. However, the Steering Committee is now in the process of reviewing the transcripts of the meeting and devising a white paper, which they hope will enable stakeholder communities to take this critical dialogue steps further. The white paper will be published in fall 2011.

In general, the reaction of ASIP member participants to the Forum was a realization that our members, having occupied the human disease research 'space' far longer, have to some degree addressed many of the obstacles still being evaluated by other basic sciences. In that sense, ASIP can play a key role in enabling more translational research, and educating and facilitating the careers of basic scientists interested in pursuing these options. **James Mallory Musser, MD PhD**, Vice President-Elect of ASIP and member of ASIP's Public Affairs Working Group, is currently drafting an editorial on pathology's role in translational research and ASIP's unique perspective on related issues. Look for the editorial in a fall issue of *The American Journal of Pathology*.

If you would like to contribute your thoughts on pathology's role in translational research to Dr. Musser's editorial, to the ASIP Public Affairs Working Group, or to the FASEB Translational Research Steering Committee, please contact Priscilla Markwood at [pmarkwood@asip.org](mailto:pmarkwood@asip.org) or 301-634-7408.

## Scientific Interest Group News

### Are you interested in Neuropathology?

Are you looking for a way to get more involved in the Society?

We are in need of members to assist with development of the **Neuropathology Scientific Interest Group (SIG)**. As you may or may not know, these groups provide a forum to interact with other trainees and experts in the field and allow members to initiate discussions, foster collaborations and network. Importantly, SIGs help determine scientific programming for the Annual Meeting as well as social/networking events. If you are interested in becoming an active participant of this SIG, please email Tara Snethen, ASIP Senior Director of Society Services at [tsnethen@asip.org](mailto:tsnethen@asip.org).

### Neuropathology Symposium: ASIP 2012 Annual Meeting at Experimental Biology April 25, 2012

#### Innate Immunity in the Brain

Chair: Clayton A. Wiley

- **Microglia in vivo**, Axel Nimmerjahn
- **Monocyte Trafficking to Brain**, Richard Ransohoff
- **Microglia in vitro**, Julia Kofler
- **MicroRNA Modulation of Microglia**, Howard Weiner

## Save the Date! Biobanking Meeting!

# ISBER 2012 Annual Meeting & Exhibits

*Keeping Step in an Evolving Global Research Environment: BioBanking for Now and for the Future*

May 15-18, 2012

Westin Bayshore Hotel

Vancouver, British Columbia, Canada

Save the date and plan to attend the International Society for Biological and Environmental Repositories (ISBER) 2012 Annual Meeting. This meeting will feature plenary sessions, educational workshops, corporate workshops, contributed papers, poster sessions, and working group discussions on **biobanking**. Vendors from around the world will demonstrate the latest products, services, and technology in the field of repository and specimen collection!



International Society for Biological and Environmental Repositories

A Division of ASIP

[www.isber.org](http://www.isber.org)

## Call for Nominations for the 2012 ASIP Cotran Early Career Investigator Award

Provided through an unrestricted grant from Elsevier

Deadline: July 15, 2011



The ASIP Cotran Early Career Investigator Award recognizes an *early career* investigator with demonstrated excellence as an investigator who has recently established independence and a research focus leading to an improved understanding of the conceptual basis of disease. The award is named in honor of Dr. Ramzi Cotran. Awardees will receive an honorarium and a plaque at the ASIP Annual Business Meeting and will present a lecture at the ASIP Annual Meeting that will form the basis of a publication in *The American Journal of Pathology*. Please note that the lecture is part of the CME content of the annual meeting. **IMPORTANT:** There is no age eligibility requirement for this award however awardees will be several years beyond the initial faculty appointment and have received extramural grant support as a principal investigator (or equivalent) beyond the level of a career development award. Nominations for the 2012 award require: 1) letters from two members of the Society describing the basis for recommendation; 2) the candidate's curriculum vitae including bibliography; and 3) ASIP membership in good standing for at least three years. Previous Awardees include: Monte Willis, MD, PhD (2011), Diane Bielenberg, PhD (2010), and Carlos Moreno, PhD (2009).

For more information visit:

<http://www.asip.org/awds/cotran.htm>

## Join the Visiting Mentoring Corps!

The Committee for Career Development, Women and Minorities is seeking volunteers for the new **Visiting Mentoring Corps!** Members of the Visiting Mentor Corps will mentor trainee travel awardees during the ASIP 2012 Annual Meeting at Experimental Biology in San Diego. Why is this important? Because each year, several trainees receive a trainee travel award to attend the annual ASIP meeting and present their research. For many of these trainees, this is their first scientific meeting and their mentor is not available to attend. Matching up a trainee award winner with a mentor at the meeting will be a great resource, contact person, and support system in a new environment. Please consider serving in this important role for our trainees at the upcoming meeting. A survey will be sent out later this year asking for volunteers. We hope you will be able to join us!

## President's Message



As my tenure as President of ASIP nears the end of its term on June 30 of this year, I reflect on major accomplishments and ongoing challenges facing our Society. Perhaps one of the biggest accomplishments in recent years for ASIP was the transition from self publishing its journals, *The American Journal of Pathology (AJP)* and *The Journal of Molecular Diagnostics (JMD)*, to that of post-production managed publishing through Elsevier. Given that the *AJP* represents the majority of the Society's net revenue stream, I am pleased to report that, while some details are still being worked out, the transition

has been successful, in large part through tireless and diligent efforts of the ASIP office staff in close collaboration with the Publications Committee under the leadership of **Dr. Bill Stetler-Stevenson**. Because of fruitful negotiations and collaboration between ASIP and Elsevier, I am confident that the flagship journals of our Society will continue to be among the top tier journals in the fields of experimental and molecular pathology and that new opportunities for enhanced global visibility will be possible. I would like to thank all of the members of the Council and leadership for continued strong efforts and involvement in societal activities. With major changes in the Journal management, there have necessarily been adjustments in the administration of ASIP. Our Executive Officer, **Dr. Mark Sobel**, has worked tirelessly on adapting to the many administrative challenges faced this past year regarding our transition to managed publishing.

During my tenure, ASIP has continued to explore its relationships with managed societies in our office (Association for Molecular Pathology, Association of Pathology Chairs, Intersociety Council for Pathology Information). There have been many ASIP Council meetings over the past few years that debated pros and cons of ASIP's role in managing societies. Despite recent decisions to end management of certain societies that have left our office, there remains significant support for bi-directional mutually beneficial arrangements in which cooperating societies can use ASIP to support their mission(s) and also help to grow interest in ASIP. The latter issue remains a significant challenge to ASIP as we explore new and innovative ways to increase membership and participation in our Society. I have had the privilege of working with many talented ASIP members and have been impressed by the deep commitment to the mission of ASIP and the discipline of experimental pathology. Through the commitment and hard work of the ASIP staff and committees, the annual meeting this April in Washington DC was a great success with outstanding scientific sessions and excellent attendance. Despite these successes, membership in our Society fails to grow. In an effort to increase involvement in ASIP, new efforts are underway to stimulate formation and/or support of Scientific Interest Groups (SIGs). I urge the membership to reach out to colleagues with shared scientific interests and to submit ideas for new SIGs to [asip@asip.org](mailto:asip@asip.org). I believe that these Science Interest Groups, such as Breast Cancer, Club Hepatomania (Liver Pathobiology), and Veterinary Pathology for example, can bring a critical mass of investigators together and stimulate increased participation in our Society. I also urge leadership within the ASIP membership to continue reaching out to trainees and junior faculty. ASIP is easy to get involved in and everyone can make a difference. This is a fantastic way to participate in a national service activity that can help advance one's academic career both in terms of promotion and increased visibility within the experimental pathology community. In closing, it has been an honor to serve ASIP in this leadership role and I look forward to continued active participation in my Society. I wish next year's president, **Martha Furie** the best of luck, and will be happy to help in any way I can.

Chuck Parkos

# American Society for Investigative Pathology 2012 Annual Meeting at Experimental Biology



## SAVE THE DATE!

### ASIP 2012 Annual Meeting at Experimental Biology

April 21-25, 2012  
San Diego, CA (USA)

Abstract Submission Deadline:  
November 8, 2011

Look for the *Call for Abstracts* in your mailbox in September 2011 for a complete list of topic categories!

#### GUEST SOCIETIES

- American College of Veterinary Pathologists (ACVP)
- American Society for Matrix Biology (ASMB)
- International Society for Analytical and Molecular Morphology (ISAMM)
- International Society for Biological and Environmental Repositories (ISBER)
- Società Italiana di Patologia/Italian Pathology Society (SIP)
- Society for Cardiovascular Pathology (SCVP)

For more information, contact:

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Email: [meetings@asip.org](mailto:meetings@asip.org)

Or visit:

[www.asip.org](http://www.asip.org)

**CME & SAM Available**

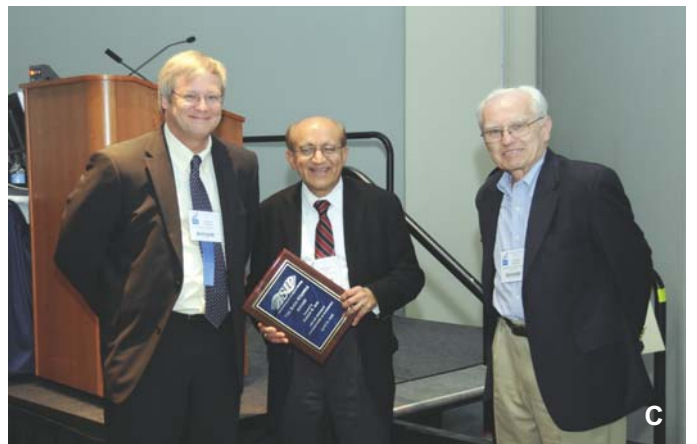


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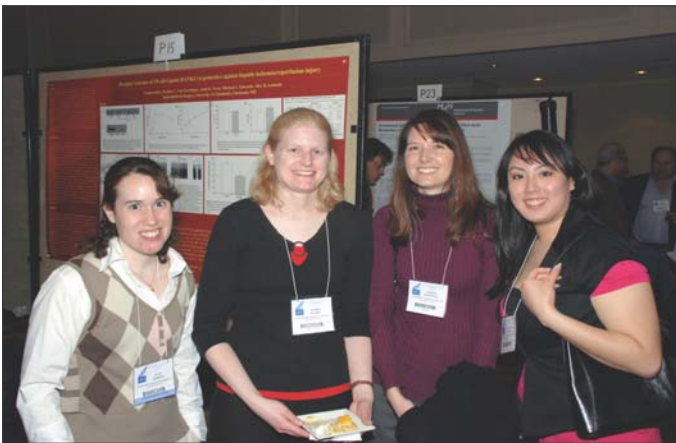
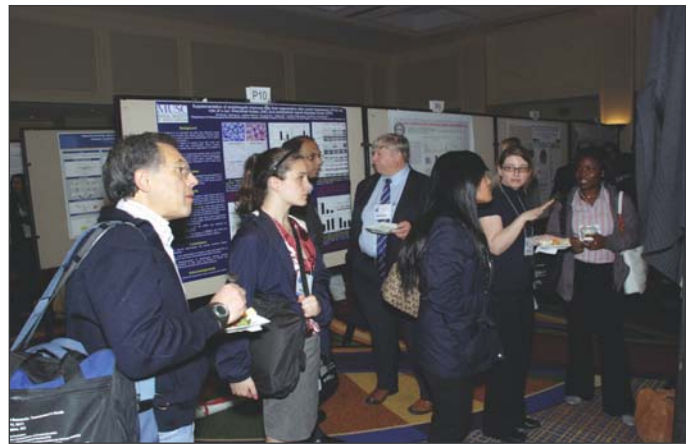
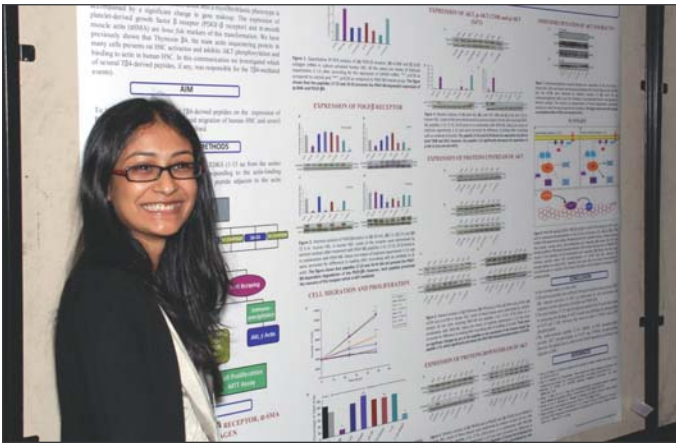
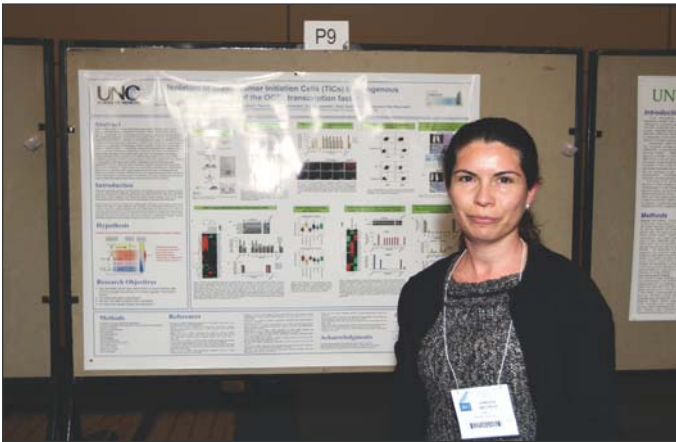
#### Preliminary Program

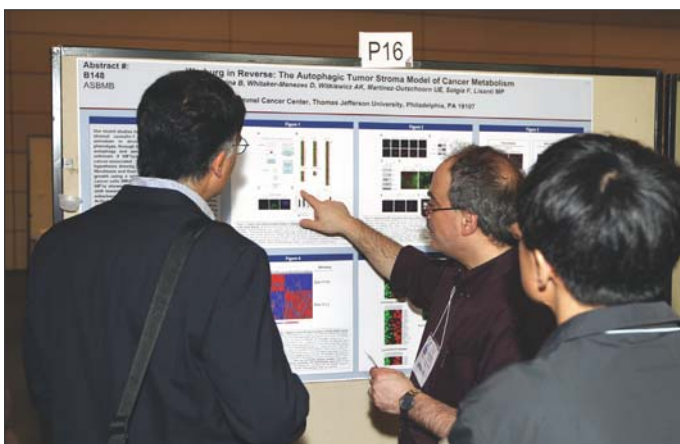
- **Breast Cancer Workshop: Personalized Medicine & Breast Cancer**  
Chairs: Ashley G. Rivenbark & William B. Coleman  
*Sponsored by the ASIP Breast Cancer Scientific Interest Group*
- **Mesenchymal Stem Cells and Lung Disease**  
Chairs: Michael A. Matthey & Dani Zander
- **Highlights: Graduate Student Research in Pathology**  
Chair: Diane Bielenberg  
*Sponsored by the ASIP Committee for Career Development, Women & Minorities*
- **iPS CELLS: Are We There Yet!**  
Chair: S. Paul Monga
- **The Myofibroblast: Biological Features and Therapeutic Perspectives**  
Chair: Cory M. Hogaboam
- **ASIP EXCELLENCE IN SCIENCE AWARD LECTURE: Mechanisms of TDP-43 Mediated Neurodegeneration in ALS and FTL D**  
Award Recipient: Edward B. Lee
- **Career Development Workshop & Breakfast: Getting Your Dream Job: Preparing Your CV and Managing Your Interview**  
Chairs: Tara Sander & Roberto Barrios  
*Supported by the ASIP Committee for Career Development, Women & Minorities and the FASEB Minority Access to Research Careers (MARC) Office*
- **Molecular and Cellular Basis of Disease: Liver Pathobiology**  
Chair: S. Paul Monga  
*Sponsored by the ASIP Liver Pathobiology Scientific Interest Group*
- **Computational Phenomics: The Potential of Whole Animal Image Analysis in Elucidating Gene Function and Chemical Toxicity**  
Chairs: Keith C. Cheng & Anant Madabhushi
- **Regulation of Epithelial Junctions in Development and Diseases**  
Chairs: Andrei Ivanov & Asma Nusrat
- **12th Annual Career Development Program and Lunch: Fundamental Basics for Success: How to Write Award-Winning Grants**  
Chairs: Titus A. Reaves & Jayne Reuben  
*Sponsored by the ASIP Committee for Career Development, Women & Minorities, the American Association of Anatomists & the FASEB MARC Office*
- **Blood Vessel Club: Vascular Development**  
Chair: David S. Milstone
- **Resolution of Inflammation**  
Chairs: Sean P. Colgan & Andrew S. Neish
- **ASIP ROUS WHIPPLE AWARD LECTURE: The Many Roles of VEGF in the Adult**  
Award Recipient: Patricia D'Amore
- **ACVP Symposium: Evolutionary Aspects of Animal Models**  
Chairs: Michael Oglesbee & Elizabeth Uhl  
*Sponsored by the ASIP Veterinary Pathology Scientific Interest Group & ACVP*
- **ISBER Symposium: Better Disease Biomarkers Through Biobanking**  
Chairs: Michael Hogan & Galen Hostetter  
*Sponsored by ASIP & ISBER*
- **Stowell Symposium: Trends in Experimental Pathology: Metabolism & Cancer**  
Chairs: Sebastiano Andò & Alberto Mantovani  
*Sponsored by ASIP & SIP*  
*Supported by an unrestricted educational grant from the Robert E. Stowell Endowment Fund*
- **ASIP OUTSTANDING INVESTIGATOR AWARD LECTURE: Lost in Ubiquitination, Found by Mass Spectrometry: Identification of E3 Ligase Substrates Controlling Critical Cellular Events & Cancer**  
Award Recipient: Kojo S. J. Elenitoba-Johnson
- **Presidential Symposium: Pathogen-Host Interactions: Provoking and Evading the Immune Response**  
Chair: Martha Furie
- **Molecular & Cellular Basis of Disease: Host-Microbe Interactions: New Concepts in Vascular Biology: Endothelial Bacterial Interactions**  
Chair: Francis W. Luscinskas
- **SCVP Symposium: The Pathogenesis and Molecular Diagnosis of Cardiomyopathies**  
Chairs: Jon Seidman & L. Maximilian Buja  
*Sponsored by ASIP and the SCVP*
- **Mechanisms and Biological Roles of Autophagy**  
Chairs: Andrei Ivanov & Monte S. Willis
- **Molecular & Cellular Basis of Disease: Host-Microbe Interactions: The Microbiota & Systemic Disease**  
Chair: Andrew S. Neish
- **Protein Misfolding Diseases & Chaperonopathies**  
Chairs: Monte S. Willis & Jonathan Lin
- **Innate Immunity in the Brain**  
Chair: Clayton A. Wiley
- **Recent Advances in the Pathobiology of Diabetic Complications**  
Chairs: Sridevi Devaraj & Ishwarlal Jialal

# ASIP 2011 Annual Meeting at Experimental Biology









## ASIP Congratulates the following Members who had papers accepted to *The American Journal of Pathology* between January 1st, 2011 and May 1st, 2011.

Ali Hafezi-Moghadam	Michelle Manni
Andrew Lackner	Joanne Murphy-Ullrich
Marcos Rojkind	Mehrnaz Gharaee-Kermani
Beatrice Knudsen	Nicholas Lukacs
Brooke Mossman	Per Westermark
Charles Alpers	Philipp Scherer
Samuel Chacko	Renza Spelat
Carlos Moreno	Richard Pestell
Dontscho Kerjaschki	Richard Phipps
Katerina Dorovini-Zis	Sebastiano Andò
Gary Striker	le-Ming Shih
Gerald Shadel	Sem Phan
Cory Hogaboam	Steven Kunkel
Isaiah Fidler	M.Sambasiva Rao
Jochen Lennerz	Takahiko Nakagawa
Leslie Obert	Themis Kyriakides
Mauro Perretti	Xiuhua Sun
Michael Lisanti	Y. James Kang
Michael Prystowsky	Zaher Radi
Michael Roehrl	Jing Zhang
Michael Cohen	

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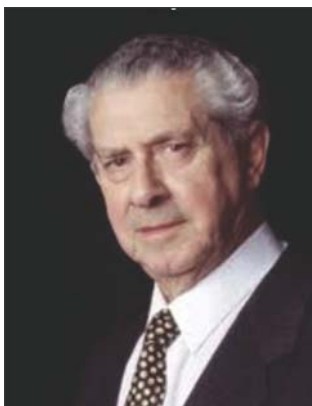
- A. ASIP Council and executive staff, 2010-2011
- B. 2011 Awards Presentation and Business Meeting (Dr. Jay McDonald in foreground)
- C. The 2011 Rous-Whipple Award is presented to Rakesh Jain, PhD by Drs. Harold Dvorak and Charles Parkos
- D. The 2011 Cotran Early Investigator Award (supported by Elsevier) is presented to Monte S. Willis, MD, PhD by Drs. S. Paul Monga and Charles Parkos
- E. Drs. George Perry and Xiongwei Zhu accept the 2011 Outstanding Investigator Award on behalf of Dr. Mark A. Smith, PhD
- F. The 2011 Excellence in Science Award is presented to Cecelia Yates, PhD by Drs. Mark Sobel and Charles Parkos
- G. The 2011 Robbins Distinguished Educator Award (supported by Elsevier) is presented to Avrum I. Gotlieb, MDCM, FRCPC by Drs. Bill Luscinskas and Charles Parkos
- H. The 2011 Gold-Headed Cane Award is presented to Jay McDonald, MD by Drs. Kevin Roth and Charles Parkos
- I. The 2011 Rous-Whipple Award is presented to Jordan S. Pober, MD, PhD by Drs. Mark Sobel and Charles Parkos
- J. 2011 Graduate Highlights in Student Research graduate student participants
- K. Breast Cancer Scientific Interest Group Leaders (Drs. Mark Sobel, Ashley Rivenbark and Bill Coleman)

# Milestones... in Investigative Pathology

by William K. Funkhouser, MD, PhD

## The Role of the Thymus in Lymphocyte Development

- (1) Miller JFAP. Immunological function of the thymus. *Lancet* 2: 748-749, 1961
- (2) Miller JFAP. Role of the Thymus in Transplantation Immunity. *Ann NY Acad Sci* 99: 340-354, 1962.
- (3) Miller JFAP and Mitchell GF. The thymus and the precursors of antigen-reactive cells. *Nature* 216: 659-663, 1967.



Jacques Francis Albert Pierre Miller

As you recover from your latest workplace cold virus infection, you should thank **Dr. Jacques FAP Miller** for discovering the role of the thymus in lymphocyte development<sup>1,2,3</sup>. Now you can understand how the viral infection was cleared, even if you can't speed the process. Before 1961, the thymus was thought to be irrelevant to the cellular immune response, likely because of the absence of secondary lymphoid follicles, the absence of measurable effects after adult thymectomy, and the general absence of immunologic reactivity of thymocytes<sup>4</sup>. Circulating small lymphocytes were thought to be

a homogeneous population able to generate both cellular and humoral immune responses. Dr. Miller's discoveries clarified the role of thymus-derived (T) lymphocytes in generation of an initial immune response to antigen, and the dependence on T lymphocyte function for antibody production. His work has led to our view of a unified role for T lymphocytes in the specific cellular immune response to non-self, whether virus or allograft.

Dr. Miller was an intentional scientist, but an unintentional immunologist, discovering thymus function while trying to study leukemogenic viruses in mice<sup>1</sup>. One arm of one experiment required thymectomy on neonatal mice, a novel surgical procedure that he was the first to perfect. His early observation was: "Between 50 and 120 days of age, about 70% of the mice in the neonatally thymectomized group developed a syndrome characterized by progressive wasting, lethargy, ruffled fur, hunched posture, diarrhea, and death within 1-3 weeks. This syndrome was rare in mice thymectomized between 1 and 3 weeks of age, and has never been seen in mice thymectomized after 3 weeks of age"<sup>2</sup>. The wasting was preceded by decreased lymphocyte concentration in peripheral blood, and absence of secondary follicle formation in secondary lymphoid organs<sup>2</sup>. He noted that this wasting syndrome was less common if the neonatally thymectomized mice were raised in cleaner conditions. He concluded that "mice without a thymus from birth were susceptible to infection." We could add that the importance of the thymus for generating xeno-reactive lymphocytes decreases over time after birth.

It was known by the mid-1940s that skin graft rejection had a predictable time course, was a function of Major Histocompatibility Complex (MHC) differences, and was lymphocyte-mediated<sup>5</sup>. However, it was not known in 1961 that the thymus had a role in allograft rejection. Dr. Miller did skin graft experiments from other strains of mice and rats onto mice that had been thymectomized at

different times. He found that neonatally thymectomized mice tolerated both allo- and xeno- skin grafts (most grafts survived >50 days), whereas thymectomy after 3 weeks of age showed normal allograft rejection (most grafts survived <25 days)<sup>2</sup>. Different colors of donor fur illustrated the tolerance of neonatally-thymectomized mice for allo- and xeno- skin grafts. As an example of following through on Koch's postulates, he injected splenocytes pre-sensitized to one of the skin grafts into a stable adult skin graft recipient, and saw rejection of the allograft within 12 days. He concluded that the neonatal thymus plays a critical role in transplantation rejection, noting that "thymectomy of the neonatal mouse is associated with marked depletion in the lymphocyte population and serious impairment of the maturation of the faculty for transplantation immunity"<sup>2</sup>.

Dr. Miller proceeded to show by 1967 that there are two major subsets of lymphocytes with different functions. His experiments dissected the role of thymocytes and bone marrow cells in the generation of antibody. Using a model of immune response to sheep red blood cells (RBC) in mice, he found that sensitization of thymocytes to sheep RBC was required, and that sensitized splenocytes from these sRBC-immune mice required bone marrow cells to generate hemolysin (antibody). Neither thymocytes nor bone marrow cells alone were pluripotent, and both together were required in this model to generate antibody<sup>3</sup>. He concluded that "sRBC-antigen-reactive cells are the progeny of antigen-independent precursor cells, the differentiation of which is dependent on the thymus. Our failure to detect precursors of antigen-reactive cells in populations of thymus lymphocytes would suggest that the precursors of the hemolysin-producing cells are derived from marrow"<sup>3</sup>. In this one set of elegant experiments, Dr. Miller dissected out the existence and roles of the two major types of lymphocytes, "T" for thymic and "B" for bursal or bone marrow. His work laid the groundwork for others to dissect the cellular interactions in the thymus that facilitate self-tolerance, the molecular events leading to Ig and TCR receptor rearrangements in the primary lymphoid organs, the protein- level process of mature T cell activation upon binding the 2-body ligand of self-MHC and processed antigen, the role of soluble lymphokine in mature T- and B- lymphocyte activation, and the longevity of memory T cells associated with thymic involution by adulthood.

So, take your pseudoephedrine for your cold, and head back to work. But instead of thanking your pharmacist, please thank Dr. Jacques Miller, who has helped you to understand the major lymphocyte subsets that drive your specific immune response to rhinoviruses, and your T cells, which allow you to control the infection itself.

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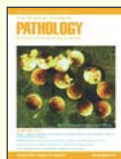
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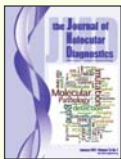
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