President's Welcome
Asma Nusrat, MD

It is truly an honor to serve as president of the American Society for Investigative Pathology (ASIP). I begin my term after a dynamic year at ASIP during which Dr. Mark Sobel retired as Executive Officer, and two senior executives were added: Dr. William Coleman, our new Executive Officer, and Dr. Martha Furie, Editor-in-Chief of our flagship journal, the American Journal of Pathology (AJP). The energy Dr. Coleman and Dr. Furie bring to the table is galvanizing our efforts, as exemplified by our Editor-in-Chief's newly-expanded article submission categories that has led to a rise in the AJP's impact factor. Cultivating an environment in which new ideas and fresh approaches to challenges are encouraged is a fundamental aspect of my tenure as president.

As we turn towards the future, I feel it is important to honor and build upon the work of our predecessors, who worked tirelessly to promote the advancement of experimental pathology: Mark Sobel. I am particularly indebted to Mark Sobel for his guidance and encouragement through my years at the ASIP. As president, my vision is to capitalize on the pathogenesis of disease as a common thread that can unify and build up our membership. In addition to promoting basic research, ASIP builds bridges that link scientific investigation, clinical practice, and public understanding of research. Like other societies, ASIP is faced with challenges, many caused by resource constraints, compounded with increases in the number of societal options available to researchers. However, I believe that together, we can overcome many challenges and raise ASIP to new heights of success. I ask all members, particularly our junior members and trainees to become engaged and actively participate in these efforts - to bring new ideas to the table and volunteer your services within ASIP. This is a fantastic way to network with other researchers and build your career.

I look forward to working with our Society members to explore new ways to grow our Society and foster awareness of experimental pathology as an interdisciplinary approach to understanding the fundamental mechanisms of disease. I am excited to mentor trainees and junior faculty, and engage with them as they bring their ideas to the table. Most of all, I look forward to serving together with you and welcome this opportunity to grow together.

To view entire Welcome, please go to http://www.asip.org/about/welcome.cfm

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Now Accepting Nominations for 2020 ASIP Meritorious Awards
Deadline: October 31, 2018

For details and instructions, go to: http://asip.org/awards/how-to-nominate-meritorious.cfm

Accepting nominations for:
- ASIP Gold-Headed Cane Award
- ASIP Robbins Distinguished Educator Award
- ASIP Rous-Whipple Award
- ASIP Outstanding Investigator Award
- ASIP Cotran Early Career Investigator Award
- ASIP Young Scientist Leadership Award

Awards to be presented at 2020 ASIP Annual Meeting at Experimental Biology in San Diego, CA (April 4-8, 2020)

If you have any news of note please submit to dpellerin@asip.org
### #PISA2018: Welcome from the Meeting Host

*Charles Parkos, MD, PhD*

A SIP is proud to host the fourth Pathobiology for Investigators, Students, and Academicians (PISA) conference at the University of Michigan in Ann Arbor, Michigan on October 20-22, 2018 ([http://pisa2018.org/](http://pisa2018.org/)). This focused, interactive, abstract-driven scientific conference is entitled "Molecular Mechanisms of Disease: Tissue Homeostasis, Immune Responses and Cancer" and aims to deliver to attendees the most exciting up-to-date concepts in pathogenesis and translational medicine. The dynamic scientific program features lectures by invited speakers, including world-acclaimed scientists, comingled with abstract-driven talks and short abstract-driven poster blitz sessions. Similar in format and feel to Gordon and FASEB Summer Research Conferences, PISA is well-suited to trainees and junior faculty. We invite you to attend and present your research at PISA in Ann Arbor, Michigan in 2018!


### #ASIP2019: Welcome from the Program Chair

*David C. Williams, Jr., MD, PhD*

On behalf of ASIP, I am very excited to invite you to the 2019 ASIP Annual Meeting to be held April 6-9, 2019 in Orlando, Florida ([https://asip19.asip.org/](https://asip19.asip.org/)). Held in conjunction with Experimental Biology 2019, the organizing principle for this year is "From Molecules to Pathobiology: Exploring Molecular and Cellular Etiologies for the Diagnosis and Treatment of Disease" and includes an exciting lineup of basic and translational research talks presented by both well-known senior and up-and-coming junior scientists. These sessions will not only illuminate the molecular origins to pathological processes but also highlight molecular and cellular targets for the prevention, detection, diagnosis, and treatment of human disease. Two key components of the four-day program are the multiple ASIP-sponsored abstract-driven minisymposia and poster sessions. The meeting will also include cutting-edge symposia and workshops, commingled with educational and professional development sessions that reflect ASIP’s strong commitment to supporting young investigators and trainee members. As members of the investigative pathology community, your participation in the ASIP Annual Meeting is absolutely vital to the Society’s success. We look forward to seeing you at EB 2019 in Orlando.

To view entire Welcome, please go to [https://asip19.asip.org/](https://asip19.asip.org/)
Sarah Hosking  
University Honors College, University at Buffalo, NY

This summer I gained invaluable experience working with Dr. Wendy Mars in her lab in the Department of Pathology at the University of Pittsburgh. Through lab meetings, seminars, and departmental lectures, I was exposed to myriad disciplines and inspiring and accomplished professionals. I had the privilege of working in a cutting-edge research lab, studying liver microstructure and pathology with a focus on the proteins involved in regulating lipid metabolism — in particular low density lipoprotein receptor-related protein 1 (LRP1) and hepatocyte nuclear factor 4 alpha (HNF4a). Specifically, my summer project focused on confirming that HNF4a is able to bind to LRP1 and analyzing the effect diet may have on the location and abundance of the complex. LRP1 is a multi-functional receptor that has a significant role in lipid homeostasis via its role as an apolipoprotein E and chylomycin remnant receptor. HNF4a is a nuclear receptor and transcription factor that regulates multiple genes connected with lipid metabolism. Previous data from the Mars Lab showed that these two proteins are able to form a complex, and we hypothesized that the complex may regulate HNF4a target genes related to dietary metabolism.

I initially ran western blots on cytoplasmic and nuclear-enriched extracts from livers of plasminogen activator inhibitor type 1 (PAI-1) wild type (WT) and knockout (KO) mice fed either a normal chow (NC) or high fat diet (HFD) in order to confirm the presence of the complex and its location. We used PAI-1 mice because LRP1 controls PAI-1 turnover and there is evidence that the absence of PAI-1 in obese mice protects animals from developing type 2 diabetes. I later ran an immunoprecipitation (IP) on total cell lysates in which I immunoprecipitated LRP1 and probed with HNF4a to verify that the two proteins were bound to each other. Immunohistochemistry (IHC) was performed to visualize and interpret the results. After I analyzed and quantified the western blots, it was apparent that in both the WT and KO mice, there was less HNF4a bound to LRP1 in the cytoplasmic-enriched HFD samples than the cytoplasmic-enriched NC samples. Furthermore, the IP confirmed that the complex was in fact real and that overall, complex formation was more prevalent in HFD-fed animals than their NC counterparts. Interestingly, IHC also showed differences in the localization of HNF4a, with loss of nuclear staining for HNF4a in areas of fat deposition in the HFD-fed KO animals. These findings confirm that LRP1 and HNF4a are forming a complex affected by diet and provide evidence that PAI-1 plays a regulatory role in the localization of HNF4a.

I am extremely grateful to have been a part of this program, which was made possible through the University of Pittsburgh and ASIP. This program allowed me to experience working in a lab, performing research that may potentially have clinical applications. As a result of this experience, I now know that I want to incorporate research in my future career as a veterinarian, possibly by pursuing a PhD after earning a DVM. I feel fortunate to have been paired with Dr. Mars, who continues to mentor me through my undergraduate experience. I also wish to acknowledge Dr. George Michalopoulos and the Department of Pathology, who were very helpful and accommodating. I am glad to have participated in a program that is dedicated to providing students with such enriching experiences and can confidently say that as a result, I am one step closer to becoming a veterinary scientist.

Dana Julian  
Research Assistant, Yates Research Lab, University of Pittsburgh, PA

This summer, I had the privilege of working with Dr. Cecilia C. Yates in her laboratory at the University of Pittsburgh through the ASIP Summer Research Opportunity Program in Pathology (SROPP). The Yates Lab focuses on the dynamics of macrophages and fibroblasts play in excessive scarring formation during tissue remodeling. This area of research was new to me and I was surprised to learn that most fibrosis-related diseases are treated with anti-inflammatory medications, which slow the progression. This knowledge kindled a keen interest in my part to investigate the specific interplay that exists between macrophages, fibroblasts (extracellular matrix modulators or ECMs) and fibroblasts (extracellular matrix modulators or ECMs) to better understand the cellular mechanisms that govern the inflammatory state of a tissue. I found it interesting that as the polarization of macrophages alters their cytokine and chemokine release patterns, this in turn shifts fibroblasts’ behavior through paracrine pathways, resulting in a distinct composition and micro-environment within the ECM. The Yates Lab reported that the mechanism by which macrophage phenotypes differentially alter fibroblasts’ pro- and anti-fibrotic matrix production is regulated, in part, by CXC-type chemokines in the absence of TGFβ. This finding inspired my summer project which sought to uncover the mechanisms by which macrophages-secreted chemokines drive or inhibit fibroblast to myofibroblast conversion and matrix production. This project allowed me to create a model system that mimics the interstitial cross-talk between macrophage-specific phenotype and fibroblast.

The data derived from this project points to macrophage-specific phenotype-fibroblast crosstalk dependency on proper tissue repair.

In addition to working in the lab, the research-focused atmosphere at the University of Pittsburgh contributed significantly to the multi-faceted training I received this summer. For example, I had the opportunity to attend workshops hosted by Pitt’s Health Science Library that introduced Bioinformatics software analyses to me such as CLC Genomics Workbench, Correlation Engine, and Ingenuity Pathways Analysis; I found astonishing the vast amount of research capabilities available to me. I also attended weekly collaborative lab meetings and data and journal clubs. In particular, I enjoyed discussions related to the mapping of fibroblast populations from normal patients and patients with scleroderma using single-cell RNA sequencing (scRNA-seq) methods and exposure to in-depth bioinformatics as these related to techniques directly applicable to the research I was conducting.

This SROPP experience served to broaden my scope of knowledge of different research approaches and techniques and solidified my desire to pursue biomedical research in pathology. I feel very fortunate to have had the opportunity to work with Dr. Yates and could not have accomplished what I did without her mentorship, enthusiasm for research, and encouragement. I look forward to continuing investigating possible treatments in wound healing and fibrosis as a senior Neuroscience major at the University of Pittsburgh this fall. I will continue to work with Dr. Yates and plan to expand the scope of my project using different knockout cell lines and signaling molecules to find more specific modes of interplay between macrophages and fibroblasts.

Orlane Destin  
Gordon College, Wenham, MA

Over the summer, I worked in the lab of Dr. Diane Bielenberg, a cancer biologist at Boston Children’s Hospital. We focused on pancreatic ductal adenocarcinoma (PDAC), specifically the role of neuregulin-2 (Nrp2) in metastasis. We hypothesized that PDAC tumors require vascular expression of Nrp2 in order to grow in vivo and tested this hypothesis by injecting syngeneic tumors into genetically altered mice and measuring tumor growth and angiogenic potential. Luciferase-labeled Panc021Y mouse PDAC cells were injected orthotopically into the pancreas of mice, and tumor growth/metastasis was monitored using luminescence. Vascular density, measured by immunohistochemistry for CD31, was analyzed in normal pancreas and PDAC tumors and compared between Nrp2+/+ wildtype (WT) and Nrp2−/− knockout (KO) mice.

Our results indicated that the static endothelium in the normal pancreas of adult mice lack Nrp2 and baseline vascular density was comparable between WT and KO mice. However, Nrp2 expression was upregulated in angiogenic PDAC tumor vessels in WT mice. PDAC tumors grew poorly in Nrp2−/− mice and showed reduced tumor microvascular density. We next analyzed tumor vascular density in PDAC tumors treated with SEMA3F in vivo and our results indicate that SEMA3F is anti-angiogenic. Lastly, the direct effect of SEMA3F on PDAC tumor cells was analyzed in vitro in a migration assay. SEMA3F inhibited the migration of PDAC in a dose-dependent fashion. Taken together, our data suggest that Nrp2 may be an important target in both tumor cells and endothelial cells in PDAC tumors. Targeting of Nrp2 with antibodies or its inhibitory ligand may prevent liver metastasis.

Over the course of the summer I learned many new techniques including sterile culture of tumor cells, immunohistochemistry to detect blood vessels in cryosections, quantifying blood vessel density using ImageJ, polymerase chain reaction (PCR), breeding and genotyping mice, orthotopic injection of cancer cells into the pancreas of mice, and xenogen imaging on live mice to detect luciferase-labelled tumor cells in vivo. Other weekly activities included seminars focused on cancer research and cancer treatment given by local experts, a journal club where we discussed cancer-related published articles from basic research to clinical trials, evening seminars that included a panel discussion on career opportunities in biomedical sciences, weekly laboratory meetings in which we took turns sharing our data, and a book club where we read and discussed The Immortal Life of Henrietta Lacks by Rebecca Skloot. At the end of the summer, I prepared an abstract and presented my research in the form of an E-poster to the Harvard Community. I plan to present my studies at the upcoming ABRCS morning meeting in 2018 and at Experimental Biology in 2019. My future goals are to continue a career in the health professions and to apply to medical school following my graduation from Gordon College in 2021.
Recent ASIP member publications

Group 2 Innate Lymphoid Cells (ILC2s) Are Key Mediators of the Inflammatory Response in Polymicrobial Sepsis; Alfred Ayala et al. September 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.05.009

Hyaluronan-Binding Protein Involved in Hyaluronan Depolymerization Is Up-Regulated and Involved in Hyaluronan Degradation in Human Osteosarctic Cartilage; Yasunori Okada et al. September 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.05.012

High MUC2 Mucin Biosynthesis in Goblet Cells Impedes Restitution and Wound Healing by Elevating Endoplasmic Reticulum Stress and Altered Production of Growth Factors; Kris Chadee et al. September 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.05.013


Lymphocyte-Specific Protein-1 Controls Sorafenib Sensitivity and Hepatocellular Proliferation through Extracellular Signal-Regulated Kinase 1/2 Activation; George K. Michalopoulos et al. September 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.06.005

Hepatocyte-Derived Lipocalin 2 Is a Potential Serum Biomarker Reflecting Tumor Burden in Hepatoblastoma; Satdarshan P. Monga et al. August 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.05.006

Hepatic Knockdown of Splicing Regulator Slu7 Ameliorates Inflammation and Attenuates Liver Injury in Ethanol-Fed Mice; Min You et al. August 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.05.004

Impaired Fastig-Induced Adaptive Lipid Droplet Biogenesis in Liver-Specific Atg5-Deficient Mouse Liver Is Mediated by Persistent Nuclear Factor-Like 2 Activation; Wen-Xing Ding et al. August 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.04.015

Increasing Cardiomyocyte Atrogin-1 Reduces Aging-Associated Fibrosis and Regulates Remodeling in Vivo; Monte S. Willis et al. July 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.04.007

High MUC2 Mucin Expression and Misfolding Induce Cellular Stress, Reactive Oxygen Production, and Apoptosis in Goblet Cells; Kris Chadee et al. June 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.02.007


Plasminogen Activator Inhibitor-1 Reduces Tissue-Type Plasminogen Activator–Dependent Fibrolysis and Intrahepatic Hemorrhage in Experimental Acetaminophen Overdose; James P. Luyendyk et al. May 2018, DOI: https://doi.org/10.1016/j.ajpath.2018.01.010

Microbiota-Derived Indole Metabolites Promote Human and Murine Intestinal Homeostasis through Regulation of Interleukin-10 Receptor; Sean P. Colgan et al. May 2018, DOI: https://ajp.amjpathol.org/article/S0002-9440(17)30875-1/fulltext

The ASIP Research & Science Policy Committee continues to focus on a variety of policy issues such as funding for: pathology research; human subjects research protections; and the physician scientist workforce including support for the next generation for researchers. ASIP’s recent science policy accomplishments include the following:

- Submitted comment letter on EPA Notice of Proposed Rulemaking (NPRM)
- Joined 69 other organizations opposing EPA NPRM
- Released blog postings by two RSPC members on EPA NPRM
- Requested and received clarification from NIH leadership on clinical trials case study, and continued participation in coalition concerned with expanded definition of clinical trials
- Joined coalition letter on fetal tissue

To inform our membership of recent science policy developments, four newsletters have been sent out so far this year. We would enjoy hearing your feedback on these newsletters; please email jdreyfus@asip.org.

For more on the ASIP Research and Science Policy Committee see http://www.asip.org/SciencePolicy/