

AMPSC 2017, Oaxaca

AMSPC 2017 Oaxaca Day 1:

Welcome & Introductions



Mary-Ann Bjornsti
President (2015-17)



In memoriam:

Jonathan Tigue
Dale Birkle
Nancy Zahniser
Carol Faingold



Improving Openness and Reproducibility Project in Cancer Biology

Tim Errington, PhD
Project Manager, Center for Open Science

Dr. Errington described the work of the Center for Open Science to “improve openness and reproducibility of scientific research”. He focused on the efforts of the group to *encourage, embrace, enact and enable* change. He discussed the role of Norms and Counter-norms in Science and Research and the fact that most scientists feel that they personally fall into the Norms group but believe that most other scientists have behaviors that place them in the counter-norm group. He described barriers to success in scientific research reproducibility and emphasized that the “**Incentives for success are focused on getting it published, not getting it right**”. Scientists pursue innovative ideas that accelerate knowledge, but the information must be transparent and reproducible at several levels: Computational; Empirical; and Replicable.

The Problems encountered in this effort include: Flexibility in analysis; Selective reporting; Ignoring nulls; Lack of Replication; Disorganization; Loss of Materials and Data; and Infrequent Sharing. He went on to describe some studies conducted by the group in the evaluation of clinical trials and other studies that were part of the Open Science Collaboration, and specifically in relationship to the Reproducibility Project in Cancer Biology.

As part of the incentives to *embrace* change, he suggested that OP Guidelines (Transparency and Openness Promotion) should become incentives: Making Behaviors Visible Promotes Adoption (suggested badges or rewards to individuals for “Open Data”, “Open Materials”). Links to these ideas and the many resources (e.g., free statistical tools) that are being made available to the public are available at <https://cos.io/>. Considerable discussion followed the presentation.

A link to his presentation can be found at: <https://osf.io/v38j5/>

Note: Most of the other presentations can be viewed at the AMSPC web site.



Know Thy Cells (and Antibodies): Improving Biomedical Research Reproducibility

Leonard Freedman, PhD
President, Global Biological Standards Institute

Dr. Freedman pointed out that causes of irreproducibility are complex but often revolve around reagent variability and lack of validation. He described the mission of GBSI and the emphasis placed on cell line authentication, research antibody validation guidelines, tissue procurement, standard operating procedures, and good research practices training and assessment tools.

He discussed the STR Cell Authentication Standard: ANSI/ATCC ASN-0002-2011 and the fact that currently only 1 journal requires cell authentication. He mentioned a study published in *Biotechniques* 59:189-192 (2015) that polled scientists about their research procedures, especially related to the use of cells and cell lines in culture and described the issues that were uncovered by this poll. A major concern was the fact that 74% of surveyed researchers NEVER use STR profiling.

Since antibodies pose an even greater problem, there were some recommendations regarding the need to standardize the quality of the antibodies that are used in research. In particular, he pointed out that there currently are NO universally-accepted guidelines or standardized methods for validation. He suggested a number of ways to remedy the lack of standardization of antibodies.

Leonard discussed another topic of concern with research reproducibility: methods for procuring clinical samples and the lack of details about how samples are procured. He suggested that Biospecimen Commons may be a useful mobile application for a repository that could provide SOPs for procuring specimens. Dr. Freedman described an NIH R25 award to create a “training” module on good cell authentication and practices. PREPaRED: Producing Reproducible Experiments by Promoting Reverse Experimental Design conducted a poll focused on 5 questions related to: Study Design; Preparation and Staging; Data Management and Analysis; Experiment Execution and Reporting Results. The survey was distributed to 8000 researchers and received > 1000 responses. The results identified areas of concern related to reproducibility and the need to train individuals in appropriate methodologies.



Institutional Policies and Responsibilities

Pam Bounelis, PhD
Asst. Vice President for Research
University of Alabama, Birmingham

Dr. Bounelis discussed her role as an institutional official responsible for oversight of Research Misconduct, which she defined as involving **Falsification**; **Fabrication**; and/or **Plagiarism**. She emphasized that it does not include honest errors or differences of opinion. Pam discussed issues of Research Misconduct and pointed out that our Canadian colleagues operate from a slightly different perspective, with levels of misconduct based on magnitude (i.e. Major/Minor Research Misconduct).

Pam described various practices that institutions employ to manage research misconduct evaluations that involve the Research Integrity Office. The levels of evaluation consist of **Inquiry** and **Investigation**. Both involve faculty, but should utilize different faculty members. She pointed out the frequency of Research Misconduct is currently about 35%, of which the majority (~53%) are dismissed for lack of sufficient evidence. She also described some of the administrative actions that can be imposed on individuals when sufficient evidence in support of a finding of research misconduct is found. She also described some examples of individuals who were sanctioned for research misconduct issues.

She admonished the group to be certain to maintain accurate records of research findings, including actual raw data, and to frequently review laboratory personnel notebooks.

AMSPC 2017 Oaxaca Day 2



Challenges of Drug Discovery in Academia: Virginia Drug Discovery Consortium

John Lazo, PhD
Associate Director for Basic Science
University of Virginia Cancer Center

Dr. Lazo discussed the development of the Virginia Drug Discovery Consortium. John has been interested in drug development and discovery for several years and began by emphasizing the fact that drug discovery is increasing in complexity and interdisciplinary activity. This is due in part to the increasing number of molecular targets, the increasing number of diseases for which we have defined molecular bases, and the development of personalized medicine. John distinguished between discovery and development and identified several issues that will always be present in an academic endeavor devoted to drug discovery. He used examples of drug development centers at a number of institutions including Vanderbilt (Vanderbilt Center for Neuroscience Drug Discovery), University of Pittsburgh (Pittsburgh Drug Development Center), University of Connecticut and the Virginia Drug Discovery Consortium. He described the process by which the VaDDC was developed and the steps that were involved in bringing together individuals from multiple institutions.



Patient Derived Xenografts in Drug Development: What is Their Value?

Peter Houghton, PhD
Director, Greehey Children's Cancer Research
Institute, Univ Texas Health Sciences Center

Dr. Houghton described the efforts to develop patient-derived xenografts as an attempt to overcome the extraordinarily high failure rate (90%) of therapeutics identified using cell line-derived xenografts to succeed in clinical trials as experienced by NCI drug discovery efforts. He described the PDX model system, i.e. transplantation of human-derived cancers into mice, and posed the question of whether PDX models truly are the best representation of the patient tumor.

Peter discussed the potential uses of PDX models as a means to identify new agents that have therapeutic activity, to assist with selection of analogs for clinical development, and as a possible mechanism to prioritize/focus clinical development. At the same time, he identified the limitations of PDX models that mainly focused on the fact that immune-deficient hosts were required and that the differences between the animal model (i.e. mice) and humans could pose a significant challenge to overcome, including unpredicted toxicities and whether tumor models recapitulate the human disease at the molecular level. Peter presented the concept of an N of 1 approach using PDX models (many different PDXs sampled in singlicate, rather than a single PDX model sampled in replicate), which may be a useful approach to consider and employ in the future.



**Chair Presentation:
*Paracrine Hormone Hypothesis of Colorectal Cancer***

Scott A. Waldman, MD, PhD
Thomas Jefferson University

Dr. Waldman presented an interesting story about the work ongoing in his laboratory investigating the role of GUCY2C (Guanylyl cyclase C) hormone in preventing colorectal cancer. He described the importance of managing colorectal cancer and the argument that guanylyl cyclase C (GCC or GUCY2C) was an ideal candidate and that the natural ligands guanylin and uroguanylin might be useful ligands in the battle against colorectal cancer.

Scott presented some compelling data suggesting that linaclotide (a GCC activator used for IBS and constipation that is derived from the enterotoxin) might be a useful therapeutic agent in the treatment of colorectal cancer. He demonstrated that the Guanylin-GCC axis was universally silenced early in tumorigenesis and that the disease appeared to be due to, at least in part, a hormone sufficiency disease that activation of GCC may address in a therapeutically-useful manner.



FASEB Update

Howard Garrison, PhD
FASEB, Director of Public Affairs

Dr. Garrison presented a measured reflection of the current state of affairs at FASEB and in Washington. He posed three questions: Where are we now? Where are we going? What is FASEB going to do? He indicated that there were several positive things that occurred in 2016 including increases in FY 2016 appropriations. Howard added that there is were bills reported out of committee with increases for NIH in FY 2017 and some new funding from the 21st Century Cures Act was added to the continuing resolution. NIH had been authorized for 3 more years with some modifications to budget and direction to review and address some of the regulatory burdens that researchers face. Howard also pointed out legislation that calls for review of existing policies related to sub-recipient grant monitoring and laboratory animal regulations that was overwhelmingly passed by Congress.

Predictions are difficult, but there is good news in the “new” Washington that suggests that NIH funding COULD increase, that animal rights legislation may face obstacles and that regulatory reform could be possible. No idea what will become of the ACA and stem cell research. FASEB plans to continue to bring the fight to Congress for continued funding increases that target investigator-initiated research.

Finally, Howard admonished us to keep our heads down, don't worry about "What ifs", and to avoid being perceived as the problem rather than the solution. The advocates that FASEB has in Congress are still there so we need to pick the battles to fight carefully. He left us with the following quote:

"There are, in every age, new errors to be rectified and new prejudices to be opposed." - Samuel Johnson

AMSPC 2017 – Oaxaca Day 3



T32 Training Programs: Where is Pharmacology?

Stella E. Tsirka, PhD
Director, Scholars in BioMedical Sciences
Former T32 Pharmacology Graduate Program Director
Stony Brook University

Dr. Tsirka presented information regarding the current state of T32 Training Programs, with special emphasis on the increasing decline in T32s that could be identified as associated with Pharmacology training programs. Stella provided an excellent overview of the T32 Programs and the application process. Training programs in the Pharmacological Sciences should incorporate a quantitative and systems approach to pharmacology, enable students to conduct research in the development of therapeutic agents and provide training in regulatory sciences that includes pharmacy ethics, principles of absorption, distribution, metabolism, excretion and toxicology (ADME-Tox). There are currently 30 Pharmacology T32 programs (Program Officer: Dick Okita). Stella also identified some of the areas that reviewers focus on to enable individuals to provide the appropriate allocation of effort toward. The increasing emphasis on Diversity Enhancement is one primary area of evaluation that is taken very seriously.

Stella ended her presentation with an invitation to send graduate program directors to the Director of Graduate Studies (NDoGS) meeting this summer at Stony Brook. Several individuals made a point to support this program and the value that it brings to Graduate Studies Directors in Departments of Pharmacology. AMSPC is financially supporting this meeting.



MSPC / ASPET Update on POPs

Robert Theobald, PhD
Kirksville College of Osteopathic Medicine

Dr. Theobald updated the group on the status of the POPs Project. He identified the members of the group that have taken on the task of updating the POPs. Bob also provided the historical context surrounding the development of this particular educational instrument. He also identified the bases for re-examining the POPs and making changes in them. The structure of the POPs is fairly rigid and unlike previous editions that were only available in paper format, are now able to be delivered

electronically. AMSPC currently own the copyright for these documents but is planning to investigate the possibility of shared ownership with ASPET.

Bob asked the group to think about constructive ways to improve the series and particularly think about new topics that could be development and included. He also encouraged us to think about the frequency with which the topics need to be updated. Finally, he pointed out that this may provide a method to reintroduce pharmacology into the newer curricula that seem to be developing with increasing less overt exposure to the discipline.



ASPET Strategic Planning: Future of Pharmacology and Pharmacology Departments

Mary-Ann Bjornsti and Scott Waldman

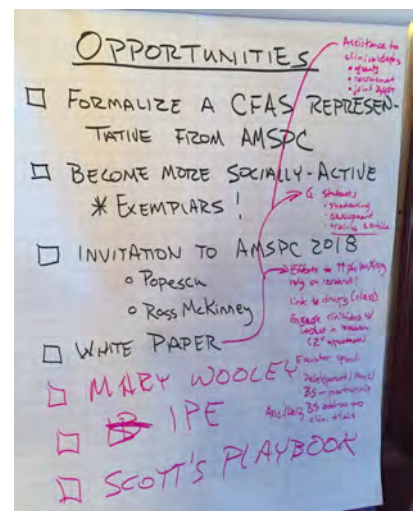
Mary-Ann Bjornsti and Scott Waldman provided an update on ASPET and the Strategic Planning that is currently being conducted by the society. There is a “draft” strategic plan developed on the basis of a survey of members that is currently being reviewed with the anticipated presentation in March. Both Mary-Ann and Scott urged us to broadly advocate for the discipline.



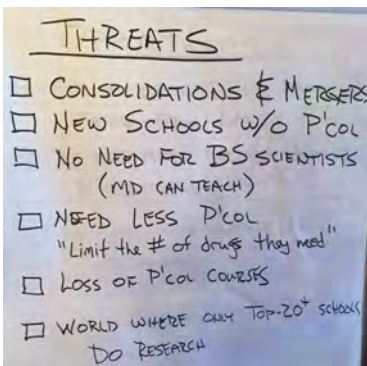
CFAS discussion – AAMC symposium “Brexit of PhDs from SOM”

Kent Vrana, PhD
Penn State University

Dr. Vrana led a lively discussion regarding the recent announcement of an AAMC Symposium or Discussion to be held at the spring Council of Faculty and Academic Societies meeting. The topic: “Brexit of PhDs from SOM” was placed on the agenda for the Council of Faculty and Academic Societies with the additional questions: What are the arguments for and against keeping basic science departments in medical schools?; What is the role of



the basic scientists in the medical school or in basic science or clinical departments?



Kent described the furor that apparently surrounded this issuance that has led to a Change in title: “**The Place for PhDs in the Medical Schools of Tomorrow**”. The Moderator: Gabriela Popescu hopes to lead discussion surrounding the following statement: “**The role of basic science research and education in the medical health center has been undergoing a transformation for years. What are the arguments for and against the role of the basic scientist in the medical school? In basic science departments? In clinical departments?**”

This debate and discussion will seek to both raise questions and develop answers to the critical questions about the essence of our medical schools. The objectives identified in this new discussion included:

1. Understand the history of basic science department in academic medicine, and how their impact is changing;
2. Recognize the interconnectedness of basic science and clinical care in the academic health center;
3. Investigate different paradigms for the basic sciences at your institution and in academic medicine generally

Kent's passionate presentation led to an even more passionate discussion of the threats and opportunities that departments are facing in the light of an apparent effort on the part of the AAMC to marginalize the basic sciences.

The threats discussed by the group included:

1. Consolidations and mergers
2. New schools developing without Pharmacology Departments
3. Lack of perceived need for basic scientists (MD or Pharm Ds can provide instruction)
4. Need less Pharmacology than is available (i.e. only discuss the drugs that they need to know).
5. Increasing decline in independent pharmacology courses due to integration of curricula.
6. Are we developing a world where the workload is distributed differently (i.e. to 20+ schools do research and the rest teach)?

Opportunities that were identified included:

1. Formalize a CFAS representative
2. Become more socially active
3. Invite a representative from CFAS (Gabriela Popescu or Ross McKinney) to next year's meeting
4. Invite someone from Research America (Mary Wooley)
5. Write a White Paper
6. Develop a playbook

There was some discussion surrounding the solution to the threats by implementing the opportunities to become better engaged with development offices to generate the financial resources to reduce dependency. Ideas discussed included:

1. Use collaboration with clinicians
2. Have graduate students engage potential donors
3. Develop better ability to tell the story in an understandable way to encourage donors to provided support



Treasurer's report

David Busija, PhD
Tulane University

David Busija closed the formal session with the Treasurer's Report which was more positive than in past years. Dues have been increased and the Treasurer's office is becoming more assertive in pursuing people to be active in the Association. The financial future of the organization is improving.

- Dues increased to \$200/year
- Increased balance by several thousands of dollars

Next meeting will be in Panama (GAMBOA resort for part and Hyatt on the ocean for the other). Those who have been to GAMBOA will remember it fondly.