AMSPC 2019 Meeting Minutes
Kauai, Hawaii

Sunday, January 13

Welcome and Introductions
President Dr. Michael Frohman welcomed everyone and asked all attendants to introduce themselves.

Two new chairs were present:

- Richard Wojcikiewicz, PhD, SUNY Upstate Medical University, Syracuse, NY
- Phillip Kopf, PhD, Midwestern University, Downers Grove, Illinois.

Dr. Frohman also described the venue change from St. Thomas to Kauai, Hawaii due to the hurricane that severely damaged St. Thomas.

New Approaches to Drug Development
Dr. Haian Fu, Moderator, Emory University introduced each speaker and topic beginning with Dr. Arkin.

"Drug Discovery Challenges, Large and Small"
Michelle Arkin, Ph.D., Co-Director Small Molecule Discovery Center (SMDC), UCSF

Dr. Arkin raised the issue of drug development failures (only 10% success at each step of the process), possibly due to:

- Selecting the wrong target (or an undruggable target)
- Selecting the wrong model system
- Focusing too much on target affinity or activity as opposed to therapeutic index


Michelle Arkin

She described the SMDC- A large collaborative effort to develop small molecules to treat various diseases.

Her approach is to change the paradigm using team science, best practices, and advanced technologies (e.g., High Throughput screening, Artificial Intelligence, High Content Imaging, Fragment-based discovery).

Arkin's lab focuses mainly on protein-protein interactions.

Dr. Arkin discussed the challenges associated with proteins as drug targets:

- Complex molecular recognition sites and epitopes
- Many proteins interact with multiple targets
- Overcoming biases in pharmaceutical knowledge

She discussed studies focused on p97, a master regulator of protein homeostasis.

- Adapter proteins
- Orthosteric targets
- Targeting ATP Hydrolysis
- Phenyl indoles-uncompetitive inhibitors of p97
- Searching for allosteric inhibitors
- Future studies-designing function specific inhibitors, conformational blocks

She also discussed studies focused on 14-3-3 proteins (adaptor proteins involved in multiple cellular processes).

- Development of small molecules to systematically stabilize the 14-3-3-ERα complex to treat cancers.

Dr. Arkin ended with her Vision for Academic Drug Discovery and Recommended Sources and meetings:

- Assay Guidance Manual
- SLAS 2019 (Feb 2-6, Washington DC), Specifically Short Courses Sponsored by Cisbio. https://www.slas2019.org
- Academic Drug Discovery Consortium: http://addconsortium.org
  "Better Leads, Better Drugs - Innovation in Screening Libraries" Meeting May 8-9, 2019, Harvard University.

"Hurdles and Opportunities of Academic/Biotech Drug Discovery"
Garth Powis, DPhil, Director, Sanford Burnham Cancer Center


Garth Powis

- In 2004, the innovation gap in Pharmaceutical R&D began to be recognized. Dr. Powis referred to the "Red Queen Effect" – It takes all the running you can do, to keep in the same place. Lewis Carroll, "Through the Looking Glass".
- Traditional (all-inclusive) Pharma no longer exists. Companies now hold specific portfolios. Example - Astra Zeneca now has only two divisions, Biopharmaceuticals & Cancer.
- Mergers and acquisitions are now the norm. Examples include Bristol Myers Squibb buying Celgene, Eli Lilly buying Loxo Oncology.
- The question of how this affects academia was raised.
- Typically, one lead compound takes 10-15 years to develop from 5,000-10,000 original compounds. Big Pharma now wants a clinic-(IND) ready drug.
- Academia is in the very early phase: Academia (10K projects) → Biotech (250 preclinical compounds) → Big Pharma (5 IND ready compounds).

Dr. Powis then moved on to addressing the question of "What happened to Cancer prevention? Prevention is better than a cure, but is it realistic for cancer? Currently there are very few prevention trials going on.

Cancer prevention strategies (Inhibit and delay)

- Vaccines (e.g., HBV, HPV)
- Diet-related approaches (vitamins, beta-carotene, folic acid, flavonoids, selenium)
- Preventative agents
- Target drugs

The sad story of dietary selenium as a prostate cancer prevention strategy was discussed.

- SELECT study-35K healthy men >55 YO took 200 ug selenium daily with vitamin E-Results-no effect, trial stopped early.
- Lesson-Faulty Science: Study out of date, based on secondary cancer endpoint, used pharmacologic doses of Se, combined Se with vitamin E.

Target drugs (e.g., aspirin, metformin, antiestrogens, antiandrogens)-mixed success and many side effects noted.

Summary:

- Vaccines-very effective but limited in scope so far
- Dietary approaches-spectacularly unsuccessful
- Target Drugs-mixed success

Take Home Message:

- Observational studies and epidemiology don't work.
- Target approach has to be based on a well-defined (rational) target

- It is not acceptable to use healthy subjects in cancer prevention studies.
- A high-risk group with a precancerous condition needs to be targeted.

Other subjects addressed:

- NCI PREVENT: helps with taking compounds through IND.
- Cancer drug resistance – can it be overcome or is it inevitable?
    - Cause: could be existing or new mutations, or amplification to increase activity to bypass signaling pathways.
    - Solutions:
        - Target conditions – hypoxia, ROS
        - Target ancestral mutations in cancer development
        - Target the tumor microenvironment
        - Identify subclones of cells that give rise to resistance
- Resistance to EGFR TKI–targeted therapy in advanced non-small cell lung cancer. Multiple drugs can buy patients 28 months or a bit longer; but maybe not enough for Big Pharma?
- Hypoxic: PX-487 Zhao et al., Oncotarget 2015: 64; 2250 – blocks HIF translation. Went through Phase I trials, but company taken over and new company uninterested in it.

"Drug Discovery in an Academic Setting"
Alan Frazier, Ph.D., Chair, University of Texas HSC at San Antonio


Alan Frazer

Dr. Frazier provided a general overview of the various drug discovery-related projects currently in progress, in the Department of Pharmacology at UTHSC at San Antonio.

He discussed the recent discovery that the anesthetic ketamine can be an effective medication for treatment-resistant depression, but that it has a number of side effects including psychedelic effects and that it is a drug of abuse. Selective negative allosteric modulators (NAMs) of α5-$GABA_A$ receptors, such as L-655,708 have antidepressant-like effects similar to ketamine, but not the adverse effect profile. Some of these NAMs can also exhibit cognitive enhancing effects.

Dr. Frazier provided a brief overview of the Cancer Drug Discovery work of Susan Mooberry and April Risinger. Their work is focused on the identification of new anticancer agents from natural products and from small molecule chemical libraries. With collaborators all over the world they evaluate extracts and compounds from soil samples, fungi and plants to identify new drug leads. Collaborations involve the Cichewicz laboratory at the University of Oklahoma and they engage lay people in this process through the website: https://whatsinyourbackyard.org

Dr. Frazier also discussed Dr. Jim Woods' work with methocinnamox, an irreversible mu opioid receptor antagonist for opioid overdoses and its comparison to naloxone.

Next, he discussed the work of Randy Strong and his involvement in NIA's Interventions Testing Program (ITP). Dr. Strong's work is focused on the metabolic and antiaging effects of rapamycin and its effects on longevity in mice as well as its ability to prevent AD and PD-like symptoms in animal models. Dr. Strong is also working on a microencapsulated formulation of rapamycin for the treatment of age-related diseases.

Dr. Frazier finished his presentation by presenting a summary of some of Dr. Yuguang (Roger) Shi's work on links between mitochondrial dysfunction in aging and the onset of various age-related diseases such as AD and PD. Notably, Dr. Shi created a company called Perenna Pharmaceuticals, Inc., and has thus far raised ~$5 million from Angel Investors.

Summary and Discussion - Dr. Haian Fu, Moderator
A significant amount of discussion after the morning sessions focused on how individual contributors to drug discovery projects in academia are evaluated at the time of P&T. Many of the critical contributors to DD projects are not the PI on the projects.

- Michelle Arkin - Ask candidate "What do you want to be known for and have you done it"?
- Mary Ann Bjornsti - Indicate your critical role in the findings of papers even if you are not the corresponding author. Side note - Mentors are often reluctant to put students on multi-PI projects.
- Andrew Thornburn - UC very old school and rigid. How is your salary being covered? There is no mechanism to keep key individuals who are not the grant PIs. For students, you cannot get a Ph.D. unless you are first author on one or more papers.
- Ray Dingledine - Evaluation not as black and white at Emory - Council of Chairs reviews the results of P&T committees for Assistant to Associate Professors.
- ENeuro asks that individual contributions be explicitly identified in the figures. This approach could be extended to other journals. Those on journal editorial boards should raise this issue.
- Haian Fu indicated that Patents are now considered scholarship contributions at Emory. He also mentioned that chairs have influence to change how their institutions operate.

Other comments and suggestions:

- Drug Companies are now mostly focused on Cancer (with some CV research) as opposed to aging and neuroscience.
- When approaching other sources of funding for DD work (e.g., VCs), you have to determine what they are most excited about. Since Cancer is saturated, there are openings for aging and neuroscience-related projects.
- In academic DD projects, chemists are needed both for target identification and development, but they do not always exist in Medical Schools. May need to partner with Pharmacy schools.
- Target discovery is not patentable and thus not (typically) of interest to drug companies.

AMPSC Business Meeting
Dr. Frohman - Nominations for Nominating Committee
Rick Neubig, Ken Tew, and Scott Waldman were nominated.

Monday, January 14

Kent Vrana - In Memorium

- Don Coffee
- John Maggio
- Elliott Vesell
- Deepak Bhalla
- Fusao Hirata
- Jim Butler
- Edson Albuquerque
- Lou Arrano
- Al Gilman

Kent asked for a moment of silence after the names were announced.

"Post-Tenure Review & Management: Experiences and Lessons"
Dr. Scott Waldman, Thomas Jefferson University Moderator

Introductory comments - At Jefferson, most faculty had not heard of post-tenure review until recently. Jefferson has ~ 1000 faculty, ~100 are tenured, 90 grandfathered in. Now there are new policies that are much less generous. Only well-funded faculty pass and all are reviewed every 5 years. All have passed so far, however.

"Economic Challenges of Non-productive Faculty"
Michael Frohman, MD, PhD, Chair, Department of Pharmacological Sciences, Stony Brook University

Dr. Frohman began his comments by indicating that Stony Brook faculty are unionized, a fact that clearly limits the ability of the Chair to make effective financial decisions. For the university, tenure is expected to occur within 6 years. The medical school is an exception and this is not set. The average is 7 years, but one Assistant Professor has been at Stony Brook for more than 12 years without achieving tenure.


Michael Frohman

Dr. Frohman then moved on to describing Stony Brook, its unique architecture and history, and its desirable location (midpoint of Long Island, close to the beach, 45 min to vineyards, 60 min to Manhattan, flights available to most anywhere). The Department of Pharmacological Sciences at Stony Brook is eclectic with faculty focused on neuropharmacology, metabolic disorders, cancer, etc. The department has very high caliber junior faculty. There is excellent infrastructure and

equipment for proteomics, imaging (high-resolution microscope, CryoEM), flow cytometry, etc. and a considerable amount of shared equipment is also available. The Department has a strong educational component, holds three T32 grants with 40 students currently enrolled in the Molecular and Cellular Pharmacology graduate program including MD/PhD students.

Dr. Frohman provided a brief history of the medical school administration and how their philosophy has changed over the last several years. Prior to ~ 10 years ago, the major focus of the president was on undergraduate education. Then Jim Simons, a billionaire and former Stony Brook faculty member donated $100's of millions to the university with the stipulation that physician scientists be hired into higher administration to lead the university. This led to the hiring of Samuel Stanley, MD, President, and Kenneth Kaushansky, MD, Senior Vice President, Health Sciences and Dean of the medical school. These individuals changed the landscape at Stony Brook. New Cancer Center and Children's Hospital buildings were erected as were many other buildings. An expansion fever ensued, but there were cost overruns, and only soft money was available to support people and eventually financial stress ensued. Dr. Frohman then cited a reference by Henry R Bourne: "*Opinion: Expansion fever and soft money plague the biomedical research enterprise*" PNAS 115: 8647-8651, 2018.

Historically, faculty salary at Stony Brook medical school was supported 100%, and grant effort and 9% of the IDCs were returned to the departments, but then the Dotcom bust and the recession of 2008 occurred. This led to many state cuts. Given the guaranteed faculty salaries, large department deficits ($100s of thousands per year) occurred and left the department heads waiting on retirements to become more financially sound. The pharmacology department size has now decreased.

The Dean has become more focused on this issue of full life-time salary guaranteed for unproductive faculty and now only guarantees 50% salary. He will personally send faculty members' letters notifying them of a salary cut when they have not been able to cover the other 50%. However, this approach also means that all of the faculty effort on grants is being used to support salary instead of becoming departmental revenue. The Dean proposed increasing the IDC return to 50% to offset the loss of salary effort funds, but the President refused and thus the Departments have now lost 80% of their historical revenue that was used for start-up packages, renovations, equipment, and bridging. Combined with the structural deficits, large challenges are faced in maintaining the research environment needed for success.

Final Comment from Dr. Frohman - Schools should contribute back to departments (structural deficits) when savings occur.

<u>Audience Discussion</u>
Different university models were discussed: salary formulas, incentives from grants, IDC return policies. In periods of largess, many Deans want the money back or to tap into savings, residual accounts.

Dr. Frohman - at Sony Brook, the 50% requirement does not apply to older tenured faculty and this cannot be changed unless the union is busted.

A Revamped Approach to Post-Tenure Review
David Hein, Ph.D., Chairman of the Department of Pharmacology & Toxicology, University of Louisville

Dr. Hein began by briefly describing the health sciences campus at the University of Louisville and indicated that they have recently revised the post-tenure review process. He then shared some of his experiences and lesions from his tenure at three universities over the last 35 years (Morehouse University, University of North Dakota, and University of Louisville).


David Hein

Morehouse University
- Never had a tenure system.
- 5 years contracts are provided with no peer review.

University of North Dakota
- A formal review is conducted every 3 years by a faculty committee.
- For the chairs, this is unsatisfying and there is not enough chair input.
- Every six years there is a full post-tenure review process by a faculty committee.
- Poor performance noted by the committee can result in appropriate action by the Dean.

University of Louisville
- There is a formal annual review by the chair.
- Peer review must be used in the process.
- Salary increases are based entirely on this review and must be non-uniform.
- The Dean only monitors this process.
- There is a formal review of faculty every 5 years and the evaluation is basically a faculty vote.
- The results of this vote are submitted to a PTR committee with the chair's recommendation.
- If the results are negative, the Dean has the discretion as to how to deal with it.

More recently, the university has revised the criteria.
- Faculty must now demonstrate excellence in their area of expertise and proficiency in all other area they are involved in.
- The same original standards are on the books for research excellence, but the process is now much more money driven.
- Currently there is no formal mechanism for recognizing team science, but the topic is being discussed. Outside reviewers can evaluate team science, multi-PI grants, etc. Letters from the chair are also important here.
- Patents can count in the process.

For Post-Tenure review;

- Full professors must demonstrate national and international reputation.
- Teaching proficiency is required.
- Service excellence must be demonstrated.
- Senior faculty members must also demonstrate leadership roles in the development of research programs.
- Many other (very granular) descriptions of responsibilities must be provided.

Audience Discussion

George Corcoran - Union contracts, at Wayne State there are 13 different unions. They are very powerful and can render the department chairs nearly powerless.
There is now a more rigorous performance evaluation of faculty and the university can (at least on paper) de-tenure an individual.

Mark Nelson - At the University of Vermont, faculty at the main campus are unionized, but they are not at the medical college. Working with tenured mid-career faculty who are struggling is the most challenging situation.

"Nil Sine Fundus - Nothing Without Funding Colorado State Motto"

Andrew Thornburn, DPhil, Chairman, Department of Pharmacology University of Colorado, Denver.

Dr. Thornburn began his presentation by indicating that things at UC are not too bad:

- The Dean is supportive of the basic sciences.
- From faculty surveys, the basic science faculty are happier than clinical faculty and faculty in the pharmacology department are the happiest.

Andrew Thornburn

One problem is that the post-tenure policies are reasonable, but the chairs have not been effective in adhering to the policies.

UC has 3400 University paid faculty, 278 have tenure, 650 have a PhD or MD/PhD. There are 5 basic science departments with ~125 tenure-track faculty, 85 have tenure and the rest expect to get tenure.

Promotion to Associate Professor is separate from tenure and there is no time or rank requirement for tenure. There is no tenure in the clinical departments except for department chairs and this is likely to change when current chairs retire.

What tenure means at UC:

- Base salary for Full Professor is $107K plus benefits
- Chair can only reduce salary for unproductive faculty by up to 15% per year, but can only go down to the base.

- You don't need many unproductive faculty to cause a departmental deficit that negatively affects the rest of the faculty.
- Tenure only benefits nonproductive faculty.

Departmental Policies:

- You are expected to pay 60% of your salary from non-departmental funds.
- Research track faculty are the responsibility of the PI.
- Assistant professors get 3 years of full salary, then are expected to pay 35% rising up to 60% by the time they are promoted to Associate Professor.
- If you cover more of your salary than the percentages highlighted above, you get the difference back as an incentive.

Other departmental features:

- The department has one master educator who does a majority of the medical teaching.
- There is one tenured faculty member who is moving toward being a full-time educator.
- Average extramural funding in the department is ~$540K in direct costs/year/ faculty member, which includes six assistant professors with no funding.
- For established faculty, your performance is considered below expectations if you do not have two RO1 equivalents.

Dr. Thornburn then showed a plot (Pearson correlation) clearly indicating that the more grant applications you submit the more grant $$ you get.

Other comments;

- The department is very productive in general, but has four faculty members who are chronic under-performers and there are no real options to increase their teaching loads.
- Graduate school teaching is not associated with any revenue streams and graduate school tuition is actually a tax on faculty mentors.
- Post-tenure review is conducted every five years by an ad hoc committee in each department.
    - If performance is unsatisfactory, a performance improvement agreement is developed and progress is periodically evaluated by the chair.
    - If this approach does not work, additional review is conducted by peers, a 2-year agreement is formulated, and progress is then evaluated by the Dean.
    - Poor performance at this stage can result in salary reduction, reduction in rank, or tenure revocation. Sanctions require approval of the president and chancellor, but to date none of this has happened. Essentially the system has not worked.
- The basic science chairs are now working on policies to make post-tenure review more rigorous and consistent.

- The chairs have agreed to carefully select PTR review committees and they must be composed of departmental faculty members + 1 (or preferably 2) members from outside of the department.
- They are lobbying for a policy that allows for the 15% salary reduction for unproductive faculty members to go below the base and to continue afterwards indefinitely.
- A caveat here is that any changes have to be approved by the faculty senate and the associate dean for faculty affairs so this endeavor may not work.

Final comments and take home messages:

- UC has some problems regarding faculty performance, but many of the issues could be alleviated if the chairs were more rigorous and consistent in their evaluations.
- Extensive changes to the system are needed, but the chairs and deans need to carefully pick the right people to serve on the relevant committees.

"Lessons About Cerebral Small Vessel Disease from Mouse Models"
Mark Nelson, Ph.D., Chairman, Department of Pharmacology, University of Vermont

Dr. Nelson began with a slide titled "The Shadow Nervous System: The Pharmacology of Turning Thoughts into Local Blood Flow in the Brain"


Mark Nelson

He then described his long-term interest in the capillary hyperemic response.

- In the brain, blood flow remains constant even when peripheral blood pressure changes.
- The brain possess intrinsic mechanisms by which vascular supply can be varied locally and there are many challenges to understanding this process.
- The human brain has approximately 1000 miles of blood vessels and 100 billion endothelial cells which is similar to the number of neurons in the brain.
- Endothelial cells account for BBB
- Capillary endothelial cells are sensors of neural activity to integrate sensory information and translate it into blood flow (i.e., functional hyperemia).

Next, Dr. Nelson discussed his funding and participation in "The Fondation Leducq Transatlantic Networks of Excellence Program" Pathogenesis of Small vessel Disease of the Brain. He discussed CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) as a leading cause of heritable cognitive decline and disability.

He also mentioned the recent increase in NIH funding for Vascular Cognitive Impairment.

In CADASIL, early deficits in the control of cerebral blood flow lead to dementia. Dr. Nelson described the CADASIL mouse model where during whisker stimulation-induced hyperemia there is a loss of the inward rectifier K+ component which cripples the communication between capillaries and arterioles in response to K+. He went on to describe the critical role of the phospholipid, PIP2, in altering endothelial potassium channel signaling and controlling cerebral blood flow and cited some of his recently published work (Harraz et al., 2018, PNAS).

Dr. Nelson concluded his presentation by describing some emerging concepts:
The Holy Grail: Will restoration of normal CBF control in small vessel disease (SVD) improve cognitive function?

The legacy of August Krogh:
In what way can the capillaries be excited, chemical, electrical, or mechanical?

"ASPET – Strategic Planning for Pharmacology and Discussion"
Judy Siuciak, Ph.D., Executive Officer, ASPET

Dr. Siuciak began her presentation by mentioning that ASPET elections are open through February 8th for president-elect, secretary/treasurer-elect, and councilor.

Strategic Planning Efforts are underway:

Key components and topics:

1. Promoting Pharmacology and ASPET
    a. Community engagement platform
    b. ASPET Fellows Program coming in 2019 with honorary distinction: FASPET
    c. Participation in Health Professions week
2. Attracting and developing the next generation of pharmacologists
    a. Precollege and undergraduate
    b. Graduate students and postdocs
    c. Early career and mid-level scientists
    d. Enhance gender and ethnic diversity within the profession and in ASPET leadership
3. Reimagining the annual meeting experience
    a. Joint opening lecture
    b. Joint opening reception
    c. Recruitment table
    d. Data blitz poster sessions
    e. No Wednesday program
    f. Dedicated poster presentation times
    g. Restructure session slots
    h. Career center improvements
    i. Program Committee review-score all abstracts submitted


Judith Siuciak

    j. New for 2019 - Top 5% of abstracts designated as “Top Picks” to be highlighted at the meeting.
4. Enhancing ASPET Journals
    a. Highlighting trainee authors for molecular pharmacology
    b. Utilize online services to expand the visibility of ASPET’s titles
    c. Special topics
5. Advocating for critical science policies
    a. Science policy committee
    b. Updated advocacy web pages
    c. Advocacy tool kit and targeting social media
    d. Increases collaboration with FASEB and other community partners
    e. Washington fellows program
6. Strengthening ASPET
    a. Financial analysis
    b. Global partnerships
    c. Governance review
    d. Philanthropy and related activities
    e. Dr. Siuciak described the laborious two-year process of relocating the ASPET office.
        i. New location is 1801 Rockville Pike, Rockville MD
        ii. New, very modern space.

Educational Topics
Dr. Brian Cox, Uniformed Services University, Moderator

Dr. Cox gave a brief introduction of the topic and then introduced Dr. Ray Dingledine. Dr. Dingledine was one of the first people that Dr. Cox met at Stanford University. Ray was a very unique and unusual student who convinced his mentor to pursue novel approaches to studying opiate pharmacology that had not previously been tried in the lab.

Why Is It So Hard To Do Good Science?
Ray Dingledine, Ph.D., Professor, Department of Pharmacology Emory University School of Medicine


Ray Dingledine

Dr. Dingledine began his presentation by stating that good science is about answering the important questions convincingly. However, it is increasingly being recognized that there is a systemic problem. In the realm of pharmacology, most investigational drugs fail. The reasons may be multifactorial (power failure, poorly designed clinical trials, fickle p values). The subject is reviewed in Nat Biotechnol: 32:40-51, 2014.

These failures are now in the popular press and they slow us down and decrease public confidence in the scientific process. There needs to be improvements in experimental design and improved statistical design. Dr. Dingledine

then defined “exploratory” versus “definitive” experiments. Exploratory experiments are often done in house, not blinded, and considered pilot projects or feasibility studies. Definitive experiments are much more rigorous, slower, and require blinded conditions replication, large Ns etc.

Dr. Dingledine then cited Begley and Ellis, Nature 483, 531–533, 2012. In oncology and hematology only 11-22% of landmark preclinical studies could be replicated by Amgen or Bayer. Six rules or red flags for Scientific Reproducibility were proposed:

1. Were the studies blinded?
2. Were all results shown?
3. Were experiments repeated?
4. Were positive and negative controls shown?
5. Were reagents validated?
6. Were the statistical tests appropriate?

Dr. Dingledine then summarized several topics that are reviewed in his recent publication: *Why Is It so Hard to Do Good Science*? eNeuro. 2018 Sep 6;5(5).

The results of informal discussions with staff include:

- The PI can become distant and his/her expectations and reality can diverge.
- Lab members can often have insufficient training for the particular studies.
- It may be difficult to replicate the methods from other labs and it may be difficult to get all parameters of an experiment under control. The experiments can become very laborious.

The Psychology of drawing conclusions:

- A question was asked about environmental factors that influence cancer rates in rural communities. The problem was that the number could go up and down every year and low Ns lead to high variance.
- Our tendency to build a narrative around new data however relevant is strong.
- The law of small numbers:
    - We have an inclination to expect the whole population to be mirrored by that of a small sample
    - Larger samples provide more precise data, while small samples can lead to extreme results
    - The London Bombing during WWII example was given. A very large-scale aerial view indicated that bombing affected almost every section of the city, but small-scale views could identify some neighborhoods with no damage. This led some to suspect that spies lived in these areas (an incorrect assumption).

Dr. Dingledine then discussed the psychological aspects of decision making where our preconceived ideas and preferences cloud our scientific judgment. He essentially reproduced the results of a study carried out on undergraduates by Kahneman and colleagues in 1973 with a group of 43 scientist (respondents) at Emory in 2018. The respondents were given a description of an individual named Chris: *Chris is of high*

intelligence, although lacking in true creativity. He has a need for order and clarity, and for neat and tidy systems in which every detail finds its appropriate place. He is dull, mechanical, corny with little sympathy for others…. Respondents were asked to rank order of nine fields by the likelihood that Chris works in that field (1=most likely, 9=least likely). 67% of the respondents felt that Chris was more likely to be in library science than in business administration, a field that has 64-fold higher employment.

Dr. Dingledine then briefly discussed the works of Nobel laureates Daniel Kahneman and Richard Thayer (a student of Kahneman) which generally concluded that preconceived notions and unconscious emotions often dominate decision-making when one is presented with new or unfamiliar data. He also introduced the two general approaches to decision-making, fast thinking - unconscious, intuitive and reflexive, and slow thinking - conscious, deliberate and reflective. Fast thinking is easily influenced by cognitive biases, whereas slow thinking is more resistant.

He ended his presentation by making the following recommendations when performing experiments:

- Use a slow thinking strategy.
- Clearly separate experiments into exploratory and definitive experiments.
- Employ good experimental practices.
- Before embarking on a new line of research, perform a premortem approach to identify what components can go wrong (as opposed to a postmortem analysis).
- Act more like Prometheus, and less like his brother, Epimetheus. Prometheus symbolizes “forethought” and effective planning, while Epimetheus represents “afterthought”. Prometheus helped advance mankind, whereas Epimetheus, in a rush, married Pandora and opened her box.

“The CTSA TRE$_x$ Drug Discovery Training Program at UTMB”
Kathryn Cunningham, Ph.D., Vice Chairman, Department of Pharmacology and Toxicology University of Texas Medical Branch, Galveston

Dr. Cunningham began her presentation with a brief description of UTMB. The university has 4 campuses with ~$22 billion in revenue. Faculty are well supported with financial resources.


Kathryn Cunningham

She next introduced the TRE$_x$ program (The Translational Research and Entrepreneurial Exploration Program). Its original name was “Innovation in Molecular Therapeutics and Devices”. The program was created by Dr. Massoud Motamedi who now co-directs the program with Dr. Cunningham. The purpose of the program is to create an integrated and focused paradigm for the accelerated conversion of basic science discoveries to clinical products. The program facilitates technology development and commercialization at UTMB by supporting investigators through technology management tools, intellectual property assistance, mentorship, and funding.

The TRE$_x$ Mission:

- Accelerate translation of our fundamental science toward the clinic
- Promote the cultural environment to value and foster translation of our discoveries
- Engender core competencies in entrepreneurship to incentivize the next generation of translational scientists
- Coordinate and leverage resources and expertise into an integrated, focused paradigm

The TRE$_x$ Vision:

- Offer Technology Commercialization Program (TCP) grants
- Provide mentoring and expertise for protecting intellectual property
- Promote collaborations with industry partners

UTMB Health - Technology Commercialization Program (TCP) - goal is to support and promote technology transfer and commercialization of research discoveries at UTMB. The funds are made available from the UTMB Health President's Royalty Fund. Through a partnership between the Chief Research Office and The Office of Technology Transfer, this program is usually offered twice a year in the fall and spring. The distribution of funds are handled by the Office of Sponsored Programs.

Other components of the program:

- TRE$_x$Talks is an engaging lecture series open to the entire UTMB community that promotes a cultural environment that values and fosters translation of our discoveries. Dr. Cunningham gave representative titles of some of the recent lectures.
- TRE$_x$Studio is an interactive consultation service and forum to assist and accelerate projects with down to earth discussions
- TRE$_x$Coach-for internal and external reviews and consultation
- TRE$_x$Quest is a forum led by junior faculty, postdoctoral, and predoctoral mentees.

Dr. Cunningham ended her presentation by summarizing the current opportunities for TRE$_x$:

- Finalize the TRE$_x$ website
- Establish targeted infrastructure to establish and operate startups
- Extend collaborations with industry for Phase 1 and Phase II clinical studies
- Engage community involvement in attracting talent and financial resources needed to support entrepreneurship and startups.

"Pharmacology Teaching and Training Programs for Graduate Students"
Lorraine Gudas, Ph.D., Chairman, Department of Pharmacology, Weill Cornell Medicine

Dr. Gudas began her presentation by describing the Pharmacology PhD program at Weill Cornell Medical College in NYC. There are several key aspects of the program:


Lorraine Gudas

- 40 faculty mentors from Weill Cornell and The Sloan Kettering Cancer Center.
- Currently there are 65 pharmacology PhD students enrolled.
- The average time to graduation is six years.
- The program has 3 pharmacology training grants (from NIGMS, NCI, and NIDA).
- Dr. Gudas showed the names of all of the faculty mentors.

Next Dr. Gudas showed a slide that provided all of the required courses in the curriculum and gave a brief overview of the courses. She then discussed two new courses that are now offered as electives:

- Accelerating BioVenture Innovation (Qtrs. I & II)
    - Teaches basic financial analysis and principles of entrepreneurship. Lectures cover the process of evaluating the market potential of a technology, building basic financial models, funding mechanisms, and writing and presenting a business plan to potential investors.
- Drug Development Course: From Molecule to Prescription
    - This course was designed in collaboration with drug development experts from Roche and provides an introduction to the multidisciplinary process of developing a new medication. It includes real world challenges encountered in the areas of discovery, development, manufacturing, global regulatory approval and commercialization of new medicines. In addition, the impact of emerging technologies to healthcare and the development process is discussed.

Next, Dr. Gudas next provided an overview of the Tri-Institutional Therapeutics Discovery Institute and its Mission. The Institute connects researchers from Memorial Sloan Kettering Cancer Center, The Rockefeller University and Weill Cornell Medicine with collaborators from across the globe and is a joint venture with Takeda Pharmaceuticals. The overall goal is to remove the barriers that impede drug discovery in academic settings and to advance academic discoveries along the path from bench to bedside. Takeda sends chemists to Weill Cornell Medical College to synthesize compounds and is a great resource for faculty as well as post docs and graduate students.

<u>Audience Discussion</u>

- The subject of PhD educational training versus the students serving as a work force for NIH grants was raised.
- We may have swung from treating students as indentured servants too far in the opposite direction.
- It was suggested that “apprentice” was a much better designation than “indentured servant”

- Additional discussion centered on graduate programs that require a "core curriculum" versus those that do not and how we fill the gaps when students are not trained well enough in their particular discipline.
- We really need to take more of an apprentice approach and also realize that the majority of Pharmacology PhD students do not go into academia. Accordingly, they need more diverse training experiences.
- Often times basic science faculty are skeptical of the educational mission, which may not include enough input from active basic scientists.
- At UAB, the new RCM model (Responsibility Center Management) does associate state dollars with graduate teaching. This has increased enthusiasm; however, IDC returns are decreased to compensate for the difference in funding streams.

"Knowledge Objectives and On-line Resources: To Infinity and Beyond!"
Kent Vrana, Ph.D, Chair of Pharmacology, Penn State University
Incoming AMSPC President


Kent Vrana

Dr. Vrana began his presentation by stating that "We need visible products to provide to the community". He also stated that we need to make pharmacology relevant to our bosses. He then mentioned the work of John L. Szarek, PhD at Geisinger Commonwealth School of Medicine (a speaker at last year's AMSPC meeting) where there is one department for all basic sciences. He followed by briefly describing the contributions of Dr. Szarek to the Pharmacology Education Project, a web resource of the International Union of Basic and Clinical Pharmacology. Web site: http://www.pharmacologyeducation.org

Dr. Vrana moved on to a discussion of the "Knowledge Objectives (KOs) in Medical Pharmacology". These KOs were created by AMSPC members and are endorsed by the association. He then discussed survey questions to pharmacology faculty and the KOs and related topics:

- Are you familiar with the AMSPC?
- AMSPC should continue the own KOs.
- Are the KOs applicable across health professions?
- Are the KOs applicable for graduate students?
- The highest cause of drug error is drug interactions. Knowledge is available at one's fingertips (e.g., cell phones), but will this lead to fewer errors?
- Do we need to revise the KO format? It's time to update (2012); is currently organized by drug class; could be organized by organ system instead.
- Can we get the knowledge streamlined, web based, and searchable?
- KOs are helpful in creating presentations for students, but, again, they need to be updated.
- Pharmacology faculty - Are you familiar with the KOs - most are not unless they are the course director.
- Drug names should be hyperlinked to content about the drug.

- Are there too many drugs?
- A student oriented set of objectives would be helpful.
- KOs could be written at a higher level and somehow make them more relevant and accepted by the medical school offices of medical education. Currently they are too granular. 180 pages of KOs is not reasonable. How do we stay relevant?
- Students are routinely questioned on clinical rounds on drug topics and often complain that they have not received the proper training. How can we address this more effectively?

Options and Suggestions:

- Provide a brand to generic pocket guide, which helps students on rotation (e.g., have pharmacology department distribute Kelly's pocket guide during intro week?).
- The students should know the top 10 drug classes for any rotation. We could prepare a "top-Ten Drug Classes" guide for students entering the clinics.
- AMSPC could prepare a document and put it on our website. Could integrate wwww.guidetopharmacology.org (IUPHAR/BPS) and pharmacologyeducation.org.
- Invite OME to pharmacology departments; bring inside the tent.
- Get pharmacology educator faculty into OME.

Discussion

- Pharmacology is losing its presence.
- Course directors should review all slides and tag them with a "pharmacology" label.
- The perception in many departments is that we are not training MDs to be prepared for the real world even though board scores have not changed and remain high.
- Decisions are being made by a small number of people.
- We need to get students to access a website that we create.
- We should provide two drug examples per drug class.
- We need to recognize the importance of "branding" in everything we do.
- 180 pages of KOs is daunting, very prescriptive, and Medical Education Administrators can't use them. This issue has to be addressed.
- What else can we do to get the proper credit from our medical schools for us as pharmacologists?
- One potential solution to improving our department's educational contributions is to hire PharmD-trained educators.

Treasurer's Report

David Busija, Ph.D., Chairman, Department of Pharmacology at Tulane University Medical Center

Provided by Alvin V. Terry, Jr., Ph.D., Chairman, Department of Pharmacology and Toxicology, Medical College of Georgia at Augusta University
Incoming Secretary AMSPC


Alvin Terry Jr.

Dr. Terry provided a Handout of the financial status of AMSPC. Finances are doing well and there is a substantial residual fund. Residual funds are managed by ASPET to allow for easy access.

We are down by 10 members (~$2K). Dave and Nancy Busija have been contacting new chairs and members who have not paid dues.
Expenses for the past year:

- AAMC annual dues
- 2018 AMSPC meeting
- 2018 EB Mixer
- Website maintenance
- Office costs (postage, paper, ink, misc. state MN and LA reg. fees)
- Tax and document preparation by CPA
- Donation to ASPET DPE for travel award to EB18

<u>Audience Discussion</u>
Ways to attract new members and get better attendance at the annual meeting:

- Provide membership and/or meeting discounts to new chairs.
- Each attendant at this year's meeting should contact and invite at least one chair who did not attend this year.
- Invite Chairs of Pharmaceutical Sciences Departments in Pharmacy Schools

Election of Nominating Committee
Michael Frohman, President

Ken Tew
Scott Waldman
Rick Neubig
Kathryn Cunningham

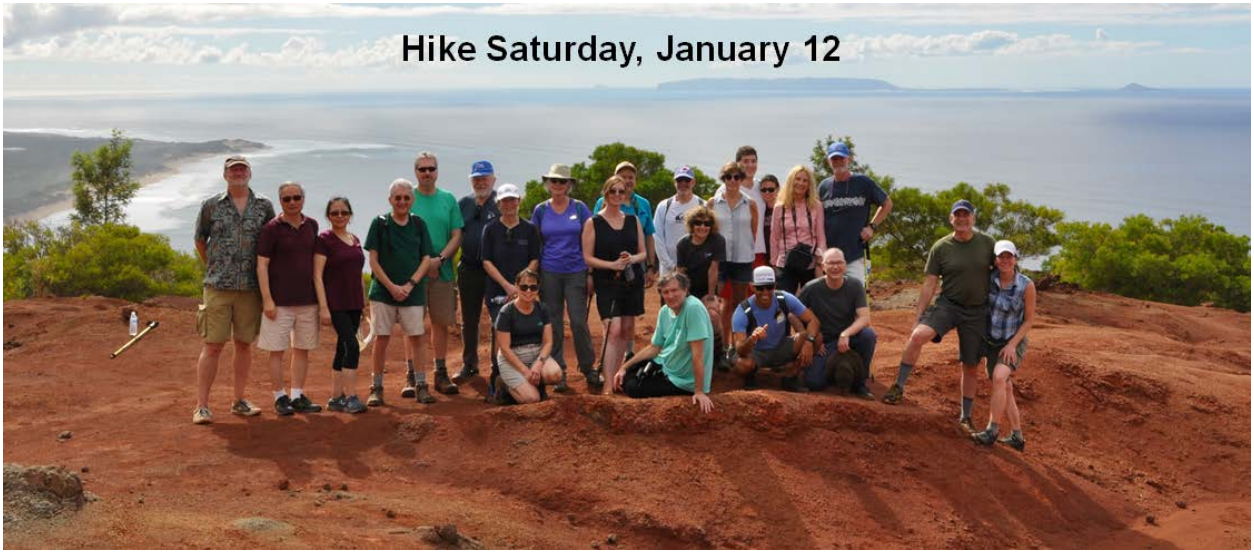
Preview of 2020 AMSPC Meeting
Kent Vrana, Incoming AMSPC President

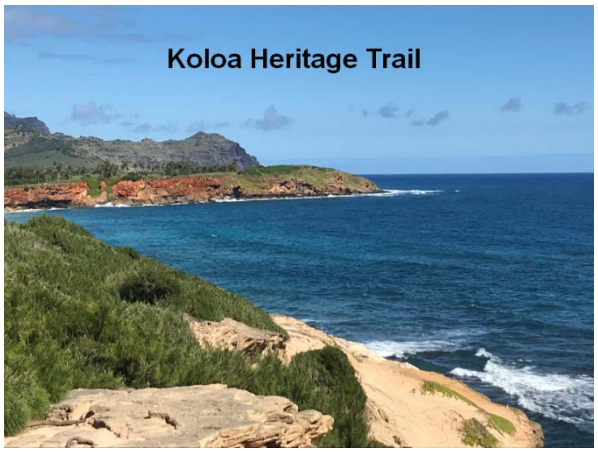
Nassau Paradise Island, Bahamas
Cost ~1/3 of the Kauai trip
Breakfast included, flights-~1/2 the cost and 3.5 hr travel time from east coast.
British Colonial Hilton Hotel ~$185/night

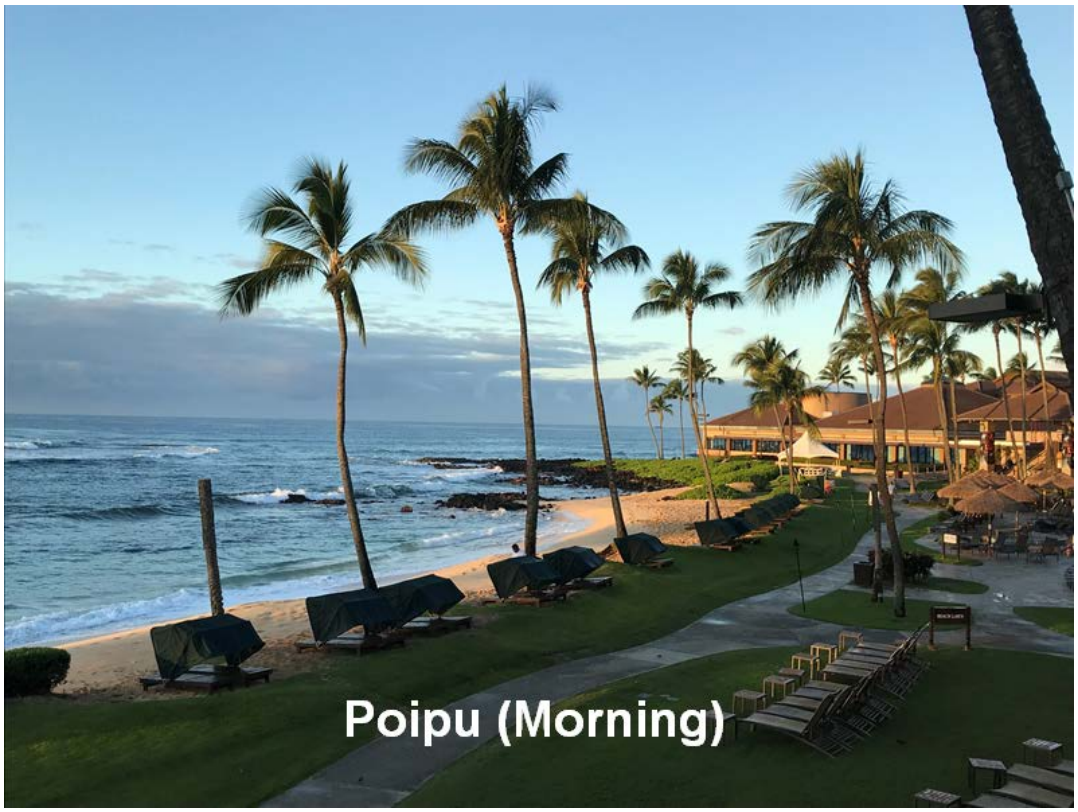
2021 meeting - potential destinations (most preferred the Quito, Ecuador choice)
Quito, Ecuador followed by cruise to Galapagos
Belize- Ramon's on Ambergris Cay and Anderson's Cave

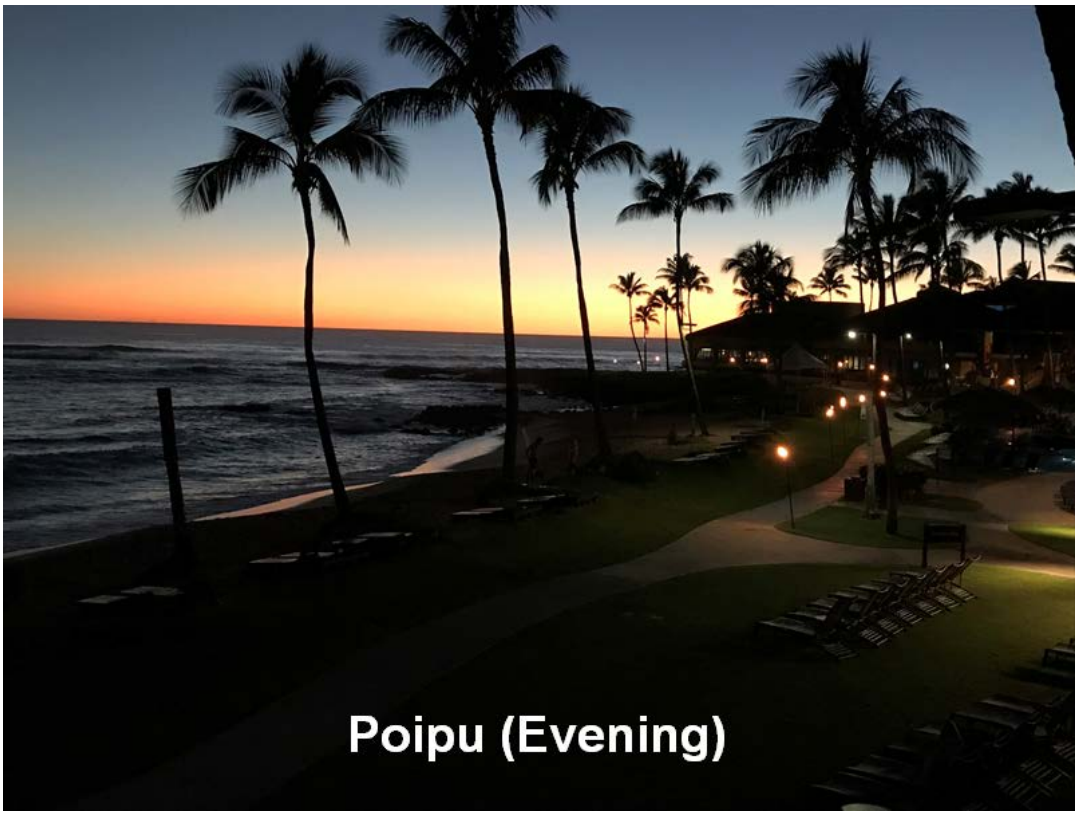
Some potential topics for next year:
Dealing with faculty who have International relationships
Regulatory Topics

Pictures, Special Events, and Excursions






Poipu (Morning)


Poipu (Evening)