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JeffPost

(Enhancing Scientific Communication and Career Transitions at Jefferson)

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Jefferson Postdoctoral Association (JPA) Executive Board 2020-2021

Top row, left to right:
President: Dr. Larissa Ishikawa; VP, Communications: Dr. Ankit Rochani; Secretary: Dr. Ahmad Sweid
Middle row, left to right:
VP, Social Affairs: Dr. Kristen Davis; Senior VP: Dr. Daniel Rubinstein; Faculty Advisor: Dr. Lisa Kozlowski
Bottom row, left to right:
Postdoc Advisor: Dr. Jenny Schneider; VP, Election and Nominations: Dr. Xi Chen; Treasurer: Dr. Daniela Muio (Not pictured: VP, Career Development: Dr. Arjun Singh)

The JPA has been actively executing virtual social hours and their Technical Skills Seminars Series (TSSS), with average viewership of nearly 20 participants from various departments of Jefferson. We will continue to conduct events remotely until at least the end of 2020. Drs. Ahmad Sweid, Kristen Davis, Daniela Muoio and Arjun Singh are the newly joined JPA executive board members for 2020. The following are a few messages from our new executive board members

"I intend to foster a sense of community among postdocs at Jefferson, enhancing it where I can. I also hope to further our sense of community with the rest of the city." *- Dr. Kristen C. Davis*

"[I plan to] build relationships between industry and academic personnel to interact with JPA and also organize events, seminars, and other activities to serve Jefferson postdocs in their career development. And to reach out to every postdoc and graduate student in Jefferson to improve their tech skills through our tech series events and networking with outside Jefferson people." *- Dr. Arjun Singh*

JPA Alumni Interview Series for Postdoctoral Insights

By Ankit Rochani Ph.D.

As JPA VP of Communications, I have interviewed two JPA Executive Board (EB) alumni to learn their transition stories and career paths. We have created an alumni page for previous JPA EB members from the last 15 years to develop cross talks and networking. A list of previous EB members can be found at:https://www.jefferson.edu/academics/colleges-schools-institutes/life-sciences/postdoctoral-affairs/postdoctoral-association/Jefferson-Postdoctoral-Association-Alumni.html. Here, I present two former Jefferson postdocs-turned-faculty to share their stories and views about their transitions. The basic idea behind this effort is to develop networking between faculty, postdocs, and senior PhD students to generate healthy collaborations.

Dr. Anastasios (Tassos) Lymperopoulos

Associate Professor of Pharmacology and Pharmaceutical Science at Nova Southeastern University

Before moving to the US, Dr. Lymperopoulos did his PhD in Pharmacology in his native country, Greece. As a postdoctoral researcher at Jefferson, he worked with Dr. Walter Koch (former Jefferson faculty). He is a Fellow of the American Heart Association and of the European Society of Cardiology, as well as a recipient of a 5-year Scientist Development Grant award from the American Heart Association. Before he was elected as a Fellow and recipient of these grants, he was a postdoc at Jefferson and an active JPA board member from 2008-2009. He trained in Dr. Koch`s laboratory in molecular cardiology, specifically on the roles of G protein-coupled receptors (GPCRs) in heart failure pathophysiology.

Please introduce your lab and the broad questions you are trying to solve:

I continued to work and focus my career on cardiovascular biology/pharmacology, in combination with cutting-edge, biomedical, translational research. My current work focuses on GPCR function and signal transduction in relation with cardiovascular function and heart failure. The main goal of my laboratory is discovery of new and innovative drugs for countering the cardio-toxic actions of catecholamines and angiotensin II (and other hormones) in heart failure. Special emphasis is given on the functions of GRKs and ß-arrestins, two protein families with important signaling implications in the adrenal gland. These proteins are druggable targets for developing new therapies for cardiovascular diseases. The lab is working on the now proprietary (patented) concept of ß-arrestin being responsible for increased production of aldosterone, which precipitates and confounds cardiac failure. Hence, my laboratory is currently working on identifying new inhibitors that could block ß-arrestin pro-aldosteronic function with the end-goal of curbing or preventing heart failure.

Could you share your experience as a JPA board member?

Being a member of JPA was a great experience. It was really pleasant working with other postdoctoral fellows, and of course Lisa was a great mentor. She was very keen in providing directions and showed us the enthusiasm to be active participants in JPA events. It has been 11 years; time flies! The most memorable event for me is the 2008 JPA's Postdoctoral Research Symposium (PRS). I used to participate in every PRS during my time at Jefferson; I earned best poster (2006) and oral presentation (2008) awards. It was interesting to organize such scientific events, where we learned about fellow researchers and had brainstorming discussions about exchanging technologies and research insights focused on stem cell, gene, and other state-of-the-art therapies and diagnostics.

The JPA events and seminars help postdocs to develop and widen their networks and to appreciate the scope of different job opportunities present in the market. JPA events are something different from every day work and every postdoc should participate in them, not only engage in regular lab work. It provides new perspectives to postdocs and also helps in building postdoctoral community at Jefferson. Even senior PhD graduate students should become a vital part of PRS seminar. Postdocs can give them insights into what's coming next for them and even exploring the different labs. It provides an interdisciplinary environment to develop new ideas and ventures.

When did you think you should transition?

I belonged to the era of 2004-2009, at the end of which there was a period of great recession and financial market meltdown. For me the transition to independence was quite abrupt as the job market during those days during recession was really tough; today is probably even tougher with the current COVID-19 situation. I was unable to go back to my home country due to financial crisis/instability. Thus, I decided to explore job opportunities in the United States. In 2009, I was able to get a faculty appointment at Nova Southeastern University. At the same time, I was fortunate enough to secure a Scientist Development Grant from the American Heart Association to continue my research in the field. Today, I have one issued patent and two provisional ones. My laboratory is pretty much a standard molecular biology/pharmacology laboratory pursuing the quest for identifying new treatment options for cardiovascular and other diseases.

Dr. Heather Montie

Associate Professor of Neuroscience, Physiology and Pharmacology, Philadelphia College of Osteopathic Medicine

Introduction

Dr. Heather Montie is currently an Associate professor in the Department of Bio-Medical Sciences at Philadelphia College of Osteopathic Medicine (PCOM). She received her PhD from Wayne State University in Physiology. She was a postdoctoral fellow at Thomas Jefferson University in Dr. Merry's lab from 2005 to 2013. Her research mainly focused on understanding how polyglutamine-expanded androgen receptor (AR) causes spinal and bulbar muscular atrophy (SBMA, Kennedy's Disease), in order to identify therapeutic targets. Later in her fellowship, she expanded her work to include investigating the AR in prostate cancer. She was JPA Vice President of Social Affairs from 2007-2008 and JPA President from 2008-2009. She also co-chaired the PRS in 2007 and wrote a JeffPost article about it. During her postdoc, she obtained two research grants, one from the Kennedy's Disease Association and one from the Prostate Cancer Foundation (John A Moran PCF Young Investigator Award) to study the role of AR acetylation in SBMA and prostate cancer, respectively.

Please introduce your lab and the broad questions you are trying to solve.

Currently Dr. Montie's lab continues to study the role of the AR in SMBA and prostate cancer. SBMA is an X-link neuromuscular disease caused by the expansion on a CAG tract in the AR gene, encoding a glutamine-tract in the protein. Thus, SBMA is a polyglutamine expansion disease. AR ligands are mainly androgens (men have higher levels than women), such as testosterone and dihydrotestosterone (DHT), and they are critical for disease. The mutant AR confers some loss of function, but the major effect on disease is that it gains a toxic function in lower motor neurons and skeletal muscle. This causes men to have adult-onset, slowly progressive loss of motor function. To date there is no disease-modifying treatment available for SBMA patients. The goal of the studies in Dr. Montie's lab is to identify cellular pathways that can be targeted to mitigate the toxicity of the mutant AR and slow disease progression. For these studies her group utilizes cell and mouse models to investigate disease processes, as well as the effects of interventions aimed at pathways that have been identified to be critical for disease. Her group has recently developed a transgenic zebrafish model of SBMA that are currently characterized and research is focused on utilizing it as a high-throughput system to screen potential therapeutic strategies. One of the major goals of all research programs at PCOM is to provide medical and graduate students research experiences, the zebrafish model was also created to enable small, yet impactful projects for students with limited time in the lab.

In prostate cancer, the majority of tumors rely upon the AR and androgens for growth and viability. Thus, her research also aims to identify mechanisms to block AR function and reduce tumor growth and viability. Her group has been specifically interested in the castrate-resistant form of disease, wherein the AR maintains function to support tumor growth in the absence of androgens. They are currently targeting post-translational modifications of the AR to impede its function in this setting.

Could you share your experience as a JPA board member?

Dr. Montie met some of her best colleagues and friends in life during her time as a postdoc at Jefferson. Such friends/colleagues included those from her research lab, and those garnered from her involvement with the JPA (other postdocs and graduate students). She was also able to work with many faculty and administrators (Dr. Merry, Dr. Karen Knudsen, Dr. Byrne, Dr. Gomella, and Dr. Grunwald, to name a few) that served as mentors/champions of her career endeavors. Through this time, she also gained a mentor and friend in Dr. Lisa Kozlowski.

The various research seminars and career seminars/panels/workshops provided by the institution and also specifically by the Office of Postdoctoral Affairs, separate or in collaboration with the JPA, gave her a perspective of various career paths, and solidified and supported her goal to continue research in academia. Due to her involvement with the JPA and the professional relationships she made within the institution, she was given an opportunity to be mentored in teaching, by participating in some JCLS Post-baccalaureate Pre-Professional Program lectures. This experience not only helped her identify her passion for teaching, but it also served as an experience that contributed to her ability to obtain her current faculty teaching and research position at PCOM. Her leadership roles in the JPA were also noted as a positive experience/skill-set in her interview for her current position.

When did you think you should transition?

According to Dr. Montie, deciding upon the right time to transition from a postdoc is generally dependent upon one's ultimate career goal. She says it is important to make a career development plan early and keep tabs on building one's portfolio of experiences, so that when the time is right, and positions pop up, one is prepared to be competitive for it.

Although Dr. Montie was originally interested in a research-centric faculty position, the teaching opportunity she had at Jefferson made her more open to consider faculty positions that focused more on teaching. Therefore, when she saw a posting for a teaching/research faculty position at PCOM, she was well positioned with her research, teaching, and leadership experiences to be competitive and was ready to make that transition.

Comments from the author

Dr. Lymperopoulos' and Dr. Montie's journey are inspirational for Jefferson postdocs and senior PhD students. They both are open for productive collaborations with Jefferson researchers and clinicians who are working in the field of finding treatment for a) cardiovascular diseases, b) spinal and bulbar atrophy (SMBA, Kennedy's disease), and c) prostate cancer through novel approaches.

Thomas Jefferson University fights COVID-19 with vaccine development and clinical trials

By Aurore Leburn Ph. D.

We are now in our seventh month facing the COVID-19 pandemic, and the development of an effective vaccine against SARS-CoV-2 is still far from a reality. The recent announcement of yet another vaccine trial delay by AstraZeneca, coined a wake-up call by the WHO, has dampened hopes of returning to normal even further. However, hope is on the horizon! The vaccine developer Bharat Biotech and Thomas Jefferson University have signed an exclusive deal to develop a new vaccine candidate for COVID-19. Invented at Jefferson, in Professor Matthias Schnell's laboratory, the vaccine candidate is based on a deactivated rabies vaccine (more information is available at fal.cn/3acsL). In addition to vaccine development, Thomas Jefferson University has joined the fight against the virus with six clinical trials. These trials target the disease through various angles, from plasma therapy to boosting the immune system while preventing the deleterious cytokine storm. Here is an overview of the current clinical trials underway in Jefferson Hospital facilities.

Convalescent plasma therapy trial underway

A trial for convalescent plasma therapy is underway at Thomas Jefferson University under the direction of Drs. Mike Baram and AnnaMarie Chang. This protocol provides access to convalescent plasma for patients in acute care facilities infected with SARS-CoV-2, who have severe or life-threatening COVID-19 or who are judged to be at risk of progression to severe or life-threatening disease. Passive immunization with convalescent plasma, as a treatment for human infectious diseases, can be traced back to the 20th century. This technique can achieve immediate, short-term vaccination against infectious agents by administering pathogen-specific antibodies. It had proven a lifesaving tool, in particular, when vaccines or other therapies were not available. Convalescent plasma has appeared to be of benefit for the treatment of infections from respiratory viruses, including COVID-19.

Remdesivir in combination with Tocilizumab in the Remdacta (Covacta 2.0) clinical trial

Another treatment that attracted a lot of attention in the press is a drug called Remdesivir. Remdesivir is a broad-spectrum nucleotide prodrug that inhibits RNA-dependent RNA polymerase activity among a diverse group of RNA viruses, including coronaviruses. Principal Investigator Dr. Katherine Belden is currently studying the use of Remdesivir in combination with Tocilizumab in the Remdacta (Covacta 2.0) clinical trial. Tocilizumab is a recombinant humanized, anti-human monoclonal antibody of the IgG1 subclass directed against soluble interleukin-6 receptor (sIL-6R) and membrane-bound IL-6R. Tocilizumab binds specifically to both sIL-6R and membrane-bound IL-6R and has been shown to inhibit both soluble and membrane-bound IL-6R-mediated signaling. This study will evaluate the efficacy and safety of combination therapy with Remdesivir plus Tocilizumab compared with Remdesivir plus placebo in hospitalized patients with COVID-19 pneumonia.

Pharmacologic administration of ascorbic acid (vitamin C) to promote immune function

Lymphocytes are a crucial component of the body's defense against viral disease progression and adaptive immunity. By utilizing physiologic intracellular hydrogen peroxide as a second messenger, lymphocyte activation occurs after viral antigen presentation by dendritic cells. Pharmacologic administration of ascorbic acid (vitamin C) can increase extracellular hydrogen peroxide generation, confer epigenetic changes that include DNA demethylation, and promote lymphocyte activation *in vivo*.

In his trial, Dr. Dagan Coppock is evaluating the safety and efficacy of ascorbic acid in the form of sequential intravenous infusions for patients with suspected COVID-19 who are unlikely to require mechanical ventilation within 24 hours of the study intervention.

The use of Ruxolitinib (Jakafi) to diminish the cytokine storm

Another hallmark of COVID-19 infection is the cytokine storm, a severe immune reaction in which the body secretes too many cytokines into the blood too quickly. Cytokines play an important role in normal immune responses, but having a large amount of them released all at once can be harmful and lead to multiple organ failure. Ruxolitinib is a well-established, potent, and selective inhibitor of JAK1 and JAK2. Ruxolitinib interferes with the signaling of several cytokines and growth factors that are important for hematopoiesis and immune function. Principal Investigator Michael Baram is currently testing the use of Ruxolitinib (Jakafi) to diminish the cytokine storm. Investigators hypothesize that JAK 1/2 inhibition with Ruxolitinib, an FDA-approved treatment for intermediate or high-risk myelofibrosis, could have a similar effect in patients with severe COVID-19, quelling the immune-hyperactivation, allowing for clearance of the virus, and reversing the disease manifestations.

Testing the virological efficacy of sirolimus as an add-on to standard therapies

The sirolimus trial, conducted by principal investigators Dr. Walter Kraft and Edwin Lam, along with co-investigators Drs. Ross Summer, Scott Waldman, Gagan Kaushal, Holly Ramage, and Ankit Rochani, is a clinical study designed to assess the virological efficacy of sirolimus as an add-on to standard therapies in patients diagnosed with COVID-19. Sirolimus is an immunosuppressant agent approved for organ transplant prophylaxis. It inhibits the mammalian target of rapamycin (mTOR), which effectively suppresses cytokine-driven T-lymphocyte proliferation. Sirolimus also inhibits progression from G1 to the S phase of the cell cycle. mTOR is a key factor in regulating viral replication, including for SARS-CoV-2.

Testing pamrevlumab for efficacy against symptoms associated with acute COVID-19

Finally, the treatment of symptoms of COVID-19, such as pulmonary edema, is being studied by Dr. Rafael Perez in the FGCL-3019-098 – FibroGen trial. Pamrevlumab is a recombinant fully human immunoglobulin G1 (IgG) kappa monoclonal antibody that binds to connective tissue growth factor (CTGF) and is being developed for the treatment of diseases in which tissue fibrosis has a pathogenic role. Observations suggest that the administration of Pamrevlumab may attenuate edema associated with virus-induced pneumonia and improve gas exchange. This randomized, double-blind, placebo-controlled, phase 2 study will evaluate the efficacy and safety of intravenous Pamrevlumab in hospitalized subjects with acute COVID-19 disease.

Call for Stories for Jeffpost

Postdocs, graduate students, and PIs interested in showcasing the following should contact the JPA:
-Technologies or services in labs at Jefferson for postdocs and the research community at Jefferson
-Research stories from Jefferson laboratories
-Articles related to Jefferson's actions associated with improving the life of postdocs and students

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Contact: Ankit Rochani, PhD, VP Communication, JPA jpa@jefferson.edu
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