University of Washington Postdoctoral Association
Annual Research Symposium 2016

November 18th, 2016
Orin Smith Auditorium
UW Medicine - South Lake Union Campus

Schedule

1:30 pm **Welcome and Session 1 Talks**

Session 1

Shannon Oda, Department of Immunology, UW & Fred Hutch
Immunomodulatory fusion proteins enhance adoptive immunotherapy of leukemia

James Laing, UW Atmospheric Sciences Department, UW-Bothell
How do wildfires affect air quality in the Pacific Northwest and global?

Alexander Zevin, Department of Pharmaceutics, Washington National Primate Research Center, UW
Antibiotic treatment affects gastrointestinal luminal and mucosal microbial communities in SIV-infected macaques

Julie Van De Weghe, Pediatric Genetics, UW
In search of the unifying mechanism of Joubert Syndrome

2:30 pm **Break**

2:45 pm **Session 2 Talks**

Ryan Niemeyer, Department of Civil and Environmental Engineering, UW
Do dams increase downstream river temperatures?

Rama Subba Rao Vidadala, Department of Chemistry, UW
Synthesis Of Bumped Kinase Inhibitors Against Taxoplasma Gondii Calcium-Dependent Protein KINASE 1 (TgCDPK1) To Treat Taxoplasmosis

Caitlin M. Hudac, Department of Psychiatry and Behavioral Sciences, UW
Infant brain correlates of fairness expectations

Chloé Lahondere, Department of Biology, UW
What makes mosquitoes attracted to Platanthera *orchids?*

3:45 pm **Break**

4:00 pm **Panel: Preparing to be a T-shaped Professional**

Chet Moritz, Associate Professor in Rehabilitation Medicine, UW

Melanie Roberts, Founding Director of Emerging Leaders in Science & Society

Ron Paulsen, Principal Program Manager, Medical Devices Group, Microsoft Research

4:45 pm **Prizes and Closing Remarks**

5:00 **Reception**

Thank you for attending our annual research symposium!

As the future leaders of research, we are proud to support the postdocs at UW and affiliated institutions. This annual event showcases a portion of the tremendous work conducted by postdocs.

The University of Washington Postdoctoral Association (UWPA) is a postdoc-lead organization that is dedicated to maximizing the experience of postdoctoral fellows at the University of Washington. We are dedicated to enhancing the welfare, and fostering the professional development and career advancement, of the postdoctoral community. The UWPA was formed in October 2004. Its formation was inspired by a Howard Hughes Medical Institute-sponsored workshop for postdocs on teaching and mentoring. Strikingly, this retreat offered the first opportunity for many postdocs working within the same department to meet each other.

We aim to establish an active professional and social network at UW and affiliated institutions to support the postdoc experience by providing information, resources, and services.

Join us for our regular monthly events, which include the UWPA Board meeting (open to all postdocs!), UWPA U-district social hour (second Thursday), and SLU happy hour (third Thursday). This year we have team up with the Office of Postdoctoral Affairs (OPA) to ensure that each month we have an informal conversation regarding issues relevant to all postdocs (e.g., funding, career development).

Thank you for your support! Enjoy the speakers and panelists.

2016 UWPA Research Symposium Chair
Robert Ono

UWPA Executive Committee
Caitlin Hudac, Outgoing Chair
Pedro Fonseca, Incoming Chair
Julie Van de Weghe, Incoming Chair

UWPA Board members:
Katharina Esser-Nobis, Toni Ferro, Tim Gallagher, Karla-Luise Herpoldt, Alison Kell, James Laing, Sandi Spencer, Manda Williams, Zhou Yu

UWPA Contact information:
Email: uwpa@uw.edu
Website: https://depts.washington.edu/uwpa/
Twitter: @UWPostDocs
Facebook: https://www.facebook.com/UWPostdocAssociation

UWPA
University of Washington Postdoctoral Association

ABSTRACTS

Shannon K. Oda

Department of Immunology, UW & Fred Hutch

soda@fredhutch.org

Immunomodulatory fusion proteins enhance adoptive immunotherapy of leukemia

Cancer is an increasing epidemic; 40% of people will develop cancer during their lifetimes. Acute myeloid leukemia (AML), the most common adult acute leukemia in the U.S., has the worst survival rate of all leukemias, with only 26% of AML patients surviving 5 years. T cell immunotherapy is an expanding field for cancer treatment that engineers a patients' own immune cells (T cells) to express a cancer-targeting receptor to kill their cancer cells. However, obstacles to achieving tumor clearance include diminished costimulation as well as increased inhibitory signals from the tumor, that can interfere with activation of T cells to recognize and kill leukemia cells. CD200 is an inhibitory protein expressed by leukemia and other cancers that inhibits antitumor T cell responses, and is associated with decreased patient survival. We hypothesized that we could overcome this inhibition and give T cells a costimulatory boost, by engineering T cells to express a CD200 receptor(R)-CD28 immunomodulatory fusion protein (IFP) that produces a costimulatory CD28 signal rather than an inhibitory signal. T cells engineered with the CD200R-CD28 IFP exhibited enhanced proliferation, accumulation and anti-tumor function in response to CD200+ target cells in vitro. Importantly, in an in vivo model of leukemia, these T cells protected mice from otherwise lethal disease and engineering human T cells with the IFP also improved antitumor activity, supporting clinical translation of this strategy. IFPs provide the opportunity to replace an immunological brake with an accelerator and are a novel platform that advances cancer immunotherapy to improve patient outcomes.

James Laing

UW Atmospheric Sciences Department, UW-Bothell

j.laing85@gmail.com

How do wildfires affect air quality in the Pacific Northwest and global?

Aerosols from wildfires have significant effects on air quality as well as global radiative forcing budgets. Radiative forcing pertains to how gases like CO_2 or aerosols influence the energy balance of the Earth's atmosphere by either absorbing or reflecting solar radiation. The direction and amplitude of the radiative forcing of aerosols depends on aerosol properties such as size, chemical composition, and shape. For wildfire aerosols, these properties can change significantly with atmospheric aging so it is important to determine the mechanisms that drive this change. Wildfires are a major contributor of aerosols globally and it has been predicted that these emissions are likely to increase due to climate change. This makes the proper characterization of these emissions an important area of research.

In my research we investigate the physical properties (mass and size distribution) and optical properties (how much light is scattered/absorbed) of wildfire particles at the Mt. Bachelor Observatory. The Mt. Bachelor Observatory is located at the top of Mt. Bachelor in central Oregon (2.8 km above sea level). Its location allows for the sampling of air masses transported over long distances with little influence from local anthropogenic pollution. In the summer of 2015 we observed wildfire plumes from regional fires in Northern California and Oregon in addition to fires in the Lake Baikal region of Siberia. The differences between the aerosols from these fire plumes will be discussed.

Alexander Zevin

Department of Pharmaceutics, Washington National Primate Research Center, UW

azevin@uw.edu

Antibiotic treatment affects gastrointestinal luminal and mucosal microbial communities in SIV-infected macaques

Mucosal barriers are critical for preventing acquisition and managing pathogenesis of HIV. Healthy gut-resident bacteria (i.e. the microbiome) promote proper function of mucosal barriers. However, during HIV infection, an altered microbiome is associated with disease progression. Antibiotics are widely used to treat bacterial infections, but can cause long-term changes to the stool-associated microbiome. However, little is known about their effects on the composition of mucosal microbiota. We treated six SIV-infected macaques with broad-spectrum antibiotics and then performed a fecal microbiome transplant (FMT), and collected stool, colon biopsies, and rectal swabs. We used 16S rRNA gene sequencing to profile the composition of the bacterial communities at each sampling site. We found that the mucosal bacteria were distinct from those associated with the stool. Further, antibiotics dramatically altered the composition of stool and mucosal microbiota, but stool-associated microbiota were more affected than mucosal microbiota. Following FMT, the communities at each site recovered, but the final microbiome differed between each animal. We concluded that antibiotic use has profound effects on the microbiome and that this can be partially restored by reintroduction of healthy communities through FMT. We also demonstrated that the sampling method can greatly influence the apparent microbiome composition, and that rectal swabs are more informative for evaluating mucosal microbiota than stool, which has important implications for study design regarding microbiome sampling.

Julie Van De Weghe

Pediatric Genetics, UW

julievdw@uw.edu

In search of the unifying mechanism of Joubert Syndrome

Joubert Syndrome (JS) is a genetic, multiple birth defect disorder defined by the appearance of “the molar tooth sign” on brain imaging. All people with JS have developmental delays, intellectual disabilities, abnormal eye movements, trouble breathing, and some have extra fingers/toes, and progressive problems with vision, kidney and liver function. To date, >35 genes have been identified to be associated with JS, all required for primary cilium function. The primary cilium protrudes from the surface of nearly every cell in the human body and functions like an antenna, allowing cells to sense and respond to their environment. Many different defects in cilia have been proposed to cause JS, but a unifying disease mechanism across all genetic causes has not been identified. The leading candidates are changes in the ciliary membrane and changes in the Hedgehog signaling pathway. Experiments with skin cell lines collected from a large number of people with JS will determine whether these changes are shared across all genetic causes of JS. Since this is an autosomal recessive condition, every cell harbors the causative mutations, one from mom and one from dad, which allows us to investigate the cellular dysfunction in skin cells. In contrast to animal models with completely absent function of JS genes, cells from people with JS more accurately reflect the abnormalities that cause the disorder. Using these cells is an efficient strategy to delineate the most important disease mechanisms for further study and to identify therapeutic targets for future treatments.

Ryan Niemeyer

Department of Civil and Environmental Engineering, UW

rniemeyr@uw.edu

Do dams increase downstream river temperatures?

Cool river temperatures are essential for salmon and other important fish in the Pacific Northwest. When rivers get too hot, fish die – as happened to 250,000 sockeye on the Columbia River during the record hot temperatures in 2015. Climate change threatens to further increase river temperatures. Recently, conservation groups sued the Environmental Protection Agency because they allege that dams on the Columbia River are the primary cause for these high river temperatures in 2015. But do dams always increase river temperatures? If not, when is this not the case? My presentation will describe two aspects of my current research related to dams and river temperature. First, I will briefly describe a new reservoir module I developed for a well-established river temperature model, and how it can improve our ability to predict how dams impact downstream river temperatures. Second, I will describe an analysis on measured river temperatures downstream of dams in the Pacific Northwest and California to determine where dams are currently impacting river temperature. This research helps us understand the complex influence dams have on downstream river temperatures, and better protect the iconic fish of the Pacific Northwest.

Rama Subba Rao Vidadala

Department of Chemistry, UW

ramsiict@gmail.com

Synthesis Of Bumped Kinase Inhibitors Against *Taxoplasma Gondii* Calcium-Dependent Protein KINASE 1 (TgCDPK1) To Treat Taxoplasmosis

New therapies are needed for the treatment of toxoplasmosis, which is a disease caused by the protozoan parasite *Toxoplasma gondii*. To this end, we previously developed a potent and selective inhibitor (compound **1**) of *Toxoplasma gondii* calcium-dependent protein kinase 1 (*Tg*CDPK1) that possesses antitoxoplasmosis activity in vitro and in vivo. Unfortunately, **1** has potent human ether-a-go-go-related gene (hERG) inhibitory activity, associated with long Q–T syndrome, and consequently presents a cardiotoxicity risk. Here, we describe the identification of an optimized *Tg*CDPK1 inhibitor **32**, which does not have a hERG liability and possesses a favorable pharmacokinetic profile in small and large animals. **32** is CNS-penetrant and highly effective in acute and latent mouse models of *T. gondii* infection, significantly reducing the amount of parasite in the brain, spleen, and peritoneal fluid and reducing brain cysts by >85%. These properties make **32** a promising lead for the development of a new antitoxoplasmosis therapy.

Caitlin M. Hudac

Department of Psychiatry, UW

chudac@uw.edu

Infant brain correlates of fairness expectations

Infants' sensitivity to fairness emerges over the first year of life. By 12 months, infants will look longer to unfair (unequal) distribution of a resource. We sought to evaluate the underlying biological response to fairness expectations to better specify the developmental processing for 12- and 6-month old infants. Infants watched video vignettes of an actress distributing crackers while high-density electroencephalography (EEG) was acquired. At 12 months, infants elicited larger brain responses (i.e., frontal P100 and late-slow wave, LSW, components) when observing unfair (unequal) compared to fair (equal) outcomes across frontal electrodes. In contrast, 6-month-old infants discriminated between fair and unfair distributions via a posterior P100 and LSW, specifically for outcomes in which the distribution was both unfair and exclusionary (i.e., 2:0 proportion). Our results suggest a topographic (i.e., posterior to frontal) shift, as well as a developmental shift between 6 to 12 months of age, such that younger infants discriminate fairness outcomes only when one recipient is excluded. These findings contribute to recent work on how concerns about fairness emerges within the first year of life by capturing underlying biological mechanisms involved in constructing fairness expectations.

Chloé Lahondère

Department of Biology, UW

lahonder@uw.edu

What makes mosquitoes attracted to *Platanthera* orchids?

Female mosquitoes not only feed on blood to produce eggs but they also use carbohydrates to sustain their metabolism. In nature, flowers provide a good source of carbohydrates and some plants such as *Platanthera* orchids take advantage of these visitors to get pollinated by the mosquitoes during their nectar intake. Although several observations have been made of mosquitoes pollinating these bog orchids, the signals used by the plant to attract both male and female mosquitoes remain unknown.

We first performed non-destructive head-space volatile collections in the field to study the scent of several *Platanthera* species, and analyzed these scent samples using Gas-Chromatography coupled with Mass-Spectrometry (GC-MS). Adult mosquitoes of different species and some of them carrying pollinia were also caught and identified in field sites where orchids were present. Then, using Electro-Antennograms coupled with Gas-Chromatography (GC-EAGs), we evaluated to which specific compounds from the orchid scents the mosquitoes are responding to. Delivering pulses of specific chemicals (EAGs) to the mosquitoes also provided a better understanding of the way orchids attract and use the mosquitoes to get pollinated. Inter-specific differences among orchid species and mosquito species will be discussed.

Panel

Preparing to be a T-Shaped Professional

All post-docs possess deep expertise in their area of study; however, in order to mature into a well-rounded professional, the development of a broad set of interpersonal skills must not be neglected. Increasingly, the "T-Shaped Professional" terminology is being used to describe professionals who possess the so-called 'soft skills' that allow him or her to collaborate across disciplines (the T-top) as well as unmatched knowledge of a highly demanded skill (the T-stem). As post-docs prepare for the next step in their careers, it is important to recognize and continue to build out both dimensions of their "T". In this panel discussion, we will hear from former PhDs and post-docs on their experiences and efforts toward becoming more T-shaped, as well as their perspectives on what current post-docs can and should be doing to develop their own "T".

Chet Moritz
Associate Professor
Rehabilitation Medicine
Physiology & Biophysics
University of Washington
ctmoritz@uw.edu
depts.washington.edu/moritlab/

Melanie Roberts
Founding Director
Emerging Leaders in Science & Society
roberts.m.r@gmail.com
elissfellows.org

Ron Paulsen
Principal Program Manager
Medical Devices Group
Microsoft Research
ropau@microsoft.com
http://research.microsoft.com/en-us/um/redmond/groups/medicaldevices/