

CSPS YSN NEWSLETTER

THIS MONTH'S NEWSLETTER COURTESY OF THE UNIVERSITY OF WATERLOO

CSPS YSN

JULY 2018

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ABOUT UW SCHOOL OF PHARMACY

'Bold Start. Bright Future.' The University of Waterloo School of Pharmacy celebrated its tenth anniversary in January 2018 under this slogan. Though the University of Waterloo (UW) officially opened its doors in 1957, it would be more than 50 years later before a School of Pharmacy could be established- a bold move as this would be the first new Canadian Pharmacy School to be founded in 20 years. Though the graduate program was established in 2010 with only 16 graduate students, that number has more than doubled today with a broad range of research disciplines including clinical pharmacy, pharmacokinetics, drug delivery, gene therapy, Alzheimer's and diabetes research- evidence of UW School of Pharmacy's bright future.

In addition to the most recent publications from the UW School of Pharmacy, this month's CSPS YSN issue features cutting-edge research highlights from our graduate students. This newsletter also features a one-on-one interview with Dr. Emmanuel Ho, former President of the Canadian Chapter of the Controlled Release Society (CC-CRS) and recipient of the 2014 CSPS/GlaxoSmithKline Early Career Award.

We hope that you enjoy this issue!

Be sure to follow us on Twitter @CSPS_YSN

2018 PUBLICATIONS FROM UW PHARMACY

Amyloid- β Inhibits PDGF β Receptor Activation and Prevents PDGF-BB-Induced Neuroprotection

Curr Alzheimer Res.

Liu H, Saffi GT, Vasefi MS, Choi Y, Kruk JS, Ahmed N, Gondora N, Mielke J, Leonenko Z, Beazely MA.

Cationic Gemini Surfactant-Plasmid Deoxyribonucleic Acid Condensates as a Single Amphiphilic Entity

J Phys Chem B

Shortall SM, Wettig SD.

Improving Pediatric Protein Binding Estimates: An Evaluation of α 1-Acid Glycoprotein Maturation in Healthy and Infected Subjects

Clin Pharmacokinet.

Maharaj AR, Gonzalez D, Cohen-Wolkowicz M, Hornik CP, Edginton AN.

Three-Dimensional Co-Culture Bioassay for Screening of Retinal Gene Delivery Systems

Methods Mol Biol.

Chen DW, Pauloff K, Foldvari M.

Implant delivering hydroxychloroquine attenuates vaginal T lymphocyte activation and inflammation

J Control Release.

Chen Y, Traore YL, Yang S, Lajoie J, Fowke KR, Rickey DW, Ho EA.

Vitamin D supplementation for bone health in adults with epilepsy: A systematic review.

Epilepsia

Fernandez H, Mohammed HT, Patel T.

Lambda phage nanoparticles displaying HER2-derived E75 peptide induce effective E75-CD8+ T response

Immunol Res.

Arab A, Nicastro J, Slavcev R, Razazan A, Barati N, Nikpoor AR, Brojeni AAM, Mosaffa F, Badiie A, Jaafari MR, Behravan J.

FEATURED YOUNG SCIENTISTS

PAUL MALIK

PHD CANDIDATE

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SUPERVISOR: DR. ANDREA EDGINTON



Few drugs are designed with children in mind. When drugs are used in children, doses are often extrapolated from adult doses by weight or body surface area. While these methods account for size differences between adults and children, they do not account for differences in physiologic maturity. Failing to account for these differences can lead to toxic doses for children.

For small molecule drugs, we know that protein binding in the blood, metabolism in the liver and excretion in the kidneys are lower in children than in adults. We can account for these differences using a physiologically-based pharmacokinetic (PBPK) model and adjust pediatric doses accordingly.

Extending further, my research is concerned with describing how children may absorb, distribute and eliminate large molecule drugs (e.g., monoclonal antibodies) differently than adults. My PBPK models can be used to guide pediatric clinical trial design, to reduce the number of children required for potentially dangerous trials and to individualize therapeutic doses.

AMNA EL SHATSHAT

MSC CANDIDATE

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SUPERVISOR: DR. PRAVEEN P. RAO NEKKAR



Over the course of the twentieth century, the life expectancy of populations has increased and correspondingly, a surge in senile dementia has been observed. Various disordered proteins are observed to play a part in the complex pathophysiology of Alzheimer's disease (AD), and while therapeutics currently exist to provide symptomatic relief, a preventative strategy does not. Unstructured proteins, including amyloid beta and tau, tend to aggregate into soluble dimers and insoluble fibrils. These aggregates accumulate in the brain and are the main constituents of the characteristic plaques and tangles found in AD patient brains. In the Nekkar medicinal chemistry group, our research involves the development of small novel drug molecules, using naturally occurring small molecules, with known anti-inflammatory and anti-aggregating properties, as

pharmacological tools and starting templates to synthesize novel small drug molecules. These small compounds are capable of directly interacting with the preliminary stages of protein aggregation, in an attempt to reduce the amount of plaques and tangles found in the brain. The anti-aggregating properties these compounds have on these disordered proteins are monitored, in order to characterize the important regions involved in the formation of these protein aggregates.

Due to the complexity of this disease, multiple intervention strategies must be put-forth. As a result, a shift is required from conventional one target, one drug targeting approaches, to the development of multi-targeting small molecules. Through the use of computational software to identify the forces involved in aggregation and disaggregation, various chemical synthesis techniques, *in vitro* biochemical techniques including aggregation kinetic assays, monitoring via fluorescence measurements, and transmission electron microscopy to monitor aggregation morphology, we are confidently able to characterize and understand the interactions between our synthesized small molecules and amyloid beta and tau proteins. While various hypotheses have been theorized to explain this perplexing disease, our collective understanding of AD's pathogenesis is still very limited. In characterizing these protein aggregates, we are one step closer to increasing our understanding of this prevalent disease.

GOKUL PULLAGURA

PHD CANDIDATE

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SUPERVISOR: DR. NANCY WAITE

Advancements in vaccinology have resulted in a sharp decline in the prevalence of vaccine preventable diseases, so much so, that they may have become victims of their own success. Influenza, a common infectious disease of the respiratory tract, affects millions of Canadians each year and is consistently among the leading causes of death. Influenza vaccine, the primary preventive measure against influenza, is available free-of-cost to all residents of Ontario through multiple providers, including pharmacists. Yet, uptake remains sub-optimal as individuals increasingly choose to delay or refuse vaccinations despite their availability, a phenomenon referred to as 'vaccine hesitancy'. My primary research interests lie in exploring and addressing the challenges related to poor vaccine uptake and vaccine hesitancy at the community pharmacy.



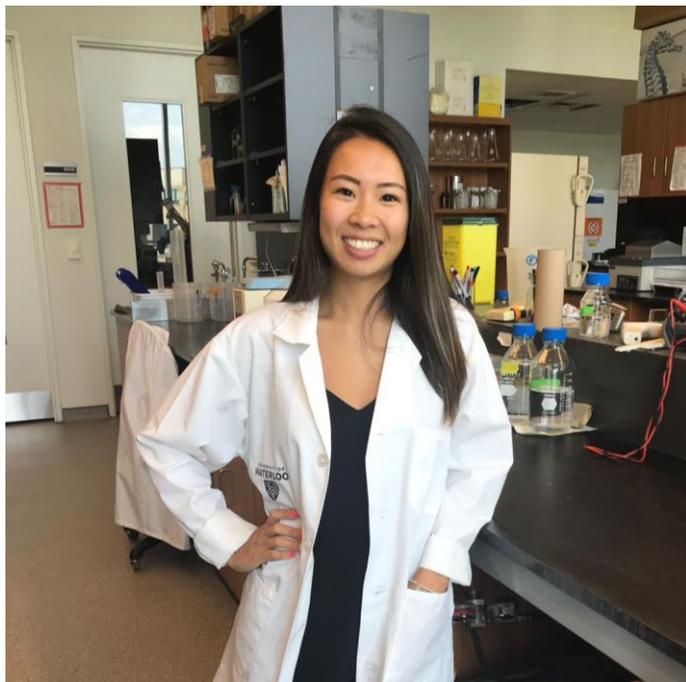
Pharmacists are an integral part of the immunizing work force; not only by providing convenient and accessible vaccination services, but also as trusted sources of high quality information on health and prevention to support their patients in making informed health care decisions. Our research aims to gain a nuanced understanding of Ontario community pharmacists' knowledge, attitudes and behavior towards influenza vaccine hesitancy through survey, interviews and decision analytic modeling research. This research will serve as a vital first step to understanding the challenges of vaccine hesitancy and poor vaccine uptake in the context of community pharmacy. Such insight is essential for the successful design and implementation of future interventions aimed at addressing vaccine hesitancy in the pharmacy setting.

MONICA HOANG

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SUPERVISOR: DR. JAMIE JOSEPH



Diabetes is a complex, multifactorial disease that affects many individuals and presents itself in many different forms. Unfortunately, diabetes is a global burden and has been identified by the International Diabetes Federation as ‘one of the largest global health emergencies of the 21st century’. Diabetes arises from abnormal glucose homeostasis due to impaired insulin secretion from β -cells or insulin resistance in target tissues. This is why it is so critical to develop a better understanding of the mechanism of β -cell insulin secretion, especially factors involved in the loss of insulin secretion. The goal of our research is to discover novel drug targets to stop or revert disease progression by enhancing β -cell function. One of our focuses is ARNT/HIF-1 β ; one of the most down regulated transcription factors in islets from type 2 diabetic

patients, which has been suggested to play a key role in maintaining β -cell function. Our research has shown a strong role for ARNT/HIF1 β in glucose sensing and insulin secretion *in vitro* as well as maintenance of β -cell mass.

As a CIHR-funded lab led by Dr. Jamie Joseph, we have access to some of the most innovative technologies for studying the biology and molecular metabolism of β -cells. Some of our most exciting methods include the use of a Seahorse XF Analyzer to measure oxygen consumption, glycolysis rates, ATP production and respiratory capacity in isolated islets and measurement of dynamic insulin release from pancreatic islets using a Biorep[®] Perfusion System. We also have access to both animal and human pancreatic islets, allowing us to test our theories across various models. With a global prevalence of almost 10%, a stronger understanding of the pathway of insulin secretion in β -cells is critical for the development of novel drug targets for treatment of type 2 diabetes.

PROFESSOR INTERVIEW

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Recently our group published on a new implant device capable of long-term release of hydroxychloroquine to locally induce T cell immune quiescence. A study conducted in Kenya on sex workers demonstrated that there are some women with natural immunity against HIV infection due to their low baseline in immune activation. Using hydroxychloroquine, which is an anti-inflammatory drug we want to mimic this quiescent state of HIV target cells. As we know, HIV infects preferably activated immune cells. If we are able to prevent immune activation by inflammation, we might be able to reduce HIV target cells, which in turn reduces the incidence of HIV infection. Our implant was successful in reducing T cell immune activation in a rabbit model. The next step for our research is using this implant to prevent HIV infection in a more appropriate animal model.

Please tell us about your research interests and the main focuses of your lab

Our research group is interested in developing drug delivery formulations, nanomedicines, medical devices and biomaterials for treating and preventing diseases. We also use drug delivery strategies as tools for delineating pathogenesis of disease as well as how diseases function and progress.

How did your earlier career choices lead you to where you are now?

I think it comes down to interests. The key was really finding an area I was interested in and also exploring contrasting career options. When I did my comparison, I appreciated certain aspects of academia- especially the freedom to choose my own research direction. In my group, we have an overall goal but our research can take different paths because of different interests that develop in time. I also enjoy the mentorship and being given the opportunity to guide young scientists as well as the teaching aspect. These are the main reasons why I chose academia over industry and other career options.

What career mistake has given you the biggest lesson?

One career mistake was having the preconception that initially industry was 'better' than academia or that getting into industry was easier than academia. So initially before choosing a career in academia, I was also set on industry because of what everyone tells you- that it is difficult to get into academia, super-competitive, grant-writing is difficult, obtaining tenure is scary. So my biggest mistake was giving up on academia before even trying. Surprisingly, finding a job in industry was not as easy as everyone made it out to be. Without any success in finding my "dream" pharma job, I decided to try applying for jobs in academia and I was more successful in landing interviews. So, while it was a mistake it was a lesson learnt: keep your options open. What others tell you may not be applicable to you because it really

comes down to what you are enthusiastic about and what your motivation and goals in life are. This mistake actually benefitted me because if I had gotten a job in industry, who knows where I would be today.

What is the best career advice you've ever received?

Don't give up until you try and remember to work hard, but also work smart. A lot of people say don't work hard, work smart but I think you need a combination of both to truly succeed.

What is one thing you wish someone would have told you about designing your own career path?

Go with what you are truly passionate about. Don't give up until you've given it a try. I mentioned this earlier but a lot of people don't even try to apply for academia jobs because they think it is difficult but if you are truly passionate about academia and want to be a professor, give it a shot. You just never know! That's what I wish someone would have told me in the beginning.

What impresses you the most when you are hiring a graduate student, post-doc or research assistant?

Well, a lot of students have very similar resumes and transcripts so I tend to consider each student as a clean slate. What I am truly looking for are enthusiastic students, students passionate about research and my research interests and really, a good fit in my group. I'm always looking for team players that are willing to work well with others to become successful. I have met a lot of students that I can tell from an interview, are not interested in research. They are pursuing graduate school only because they feel it is required to find a job. The trainees I do end up hiring are those that express enthusiasm and hope to use that research experience for something further down the line whether in academia, industry or even medicine. They have a plan. They know that doing graduate school is something that will benefit them rather than just obtaining a second degree.

What can graduate students do now to prepare themselves for a successful career?

My advice would be to just keep pushing. Work hard and don't be afraid to break some sweat. You will be enjoying the fruits of your labour later on. What you put in now, you will definitely see in your reward later on. I think a lot of students don't realize that you have to put in all this time and effort now to get what you want later. It is not an easy path but it will be worth it.

What do you enjoy most about your job?

I enjoy the research part definitely. Being able to discuss research, new research paths, research angles and the mentorship for sure. Guiding students and watching them succeed is a reflection of my own success. When they do well, I feel happy. I also feel that I am doing something correctly!

What skills have you found essential for success in this occupation?

Perseverance and thick skin (laughs). When you apply for grants you are going to get rejected which you have to accept is normal. Comments can be harsh but again, try to turn that into positive criticism and use it as motivation to work even harder.

What do you think the biggest revolution in the field of drug delivery or drug discovery will be in the next decade?

I think the biggest revolution in the next decade will hopefully be more products, more nanomedicines out there. Right now, the biggest struggle is that we have already gone through several decades of nanomedicine development and only a handful of nanomedicines have succeeded. I think what people need to realize is don't be discouraged. Sometimes it's not the 'fanciest' drug delivery systems that we should be focusing on but the understanding and mechanisms of actions of these drugs on the systems that will push this field forward.

Unfortunately, a lot of focus has been on the newer, fancier drug delivery systems- the ‘trends’, but I think to really get something to the clinic, we just need to focus on basic science.

Thinking back to when you were a graduate student conducting experiments in the lab, has the field changed at all? How so?

Compared to when I was a graduate student, the field has changed significantly. The research environment has also changed significantly. Back then, a lot of instruments were not available so that kind of required us to use a lot more creativity to find different alternatives but now, the breakthroughs in instrumentation and scientific techniques enable us to really answer the same question we had back then with a lot more ease. We can now be a bit quicker in answering some of the questions. Times have changed. The research field of drug delivery has evolved as well with all these different new techniques and these discoveries being made. This is what science is about, building on previous discoveries.

As a pioneer in your field, what does drug discovery and delivery look like to you in an ideal world?

In a perfect world, the development of drug delivery systems and even nanomedicine was intended to be a magic bullet. That is why people were working on nanomedicines- to develop a system that can target specific cell types while sparing other cell types in the body. So in an ideal world, I would hope that this magic bullet would actually be realized where we could design a system that could only target diseased cells such as HIV-infected cells and leave the normal, healthy cells alone for the patient.

Any final thoughts or advice for young scientists?

I would add that as a graduate student or young scientist, if you ever have questions or concerns either about career options or even research projects, don't be afraid to find mentors. Your supervisor does not have to be your only mentor. Feel free to talk to other professors either in the same department or even other departments to help gain an outside perspective. There are a lot of professors out there that are willing to mentor and guide students that are not even their own. Professors don't bite!