

CSPS-YSN

This month's newsletter from: *The University of Toronto*

Recent Publications from U of T

Journal of Controlled Release
July 2018

Hyperthermia-mediated drug delivery induces biological effects at the tumor and molecular levels that improve cisplatin efficacy in triple negative breast cancer

Dunne M, Dou YN, Drake DM, Spence T, Gontijo SML, Wells PG, Allen C.

#BRCA1 #BreastCancer
#Cisplatin #DrugDelivery
#Hyperthermia
#ThermosensitiveLiposome

Molecular Pharmaceutics
June 2018

Codelivery of Paclitaxel and Everolimus at the Optimal Synergistic Ratio: A Promising Solution for the Treatment of Breast Cancer

Houdaihed L, Evans JC, Allen C.

#DrugCombination #DrugDelivery
#Everolimus #Nanoparticles
#Paclitaxel



Welcome To YSN

Welcome to the Young Scientist Network! We are delighted to be presenting our first ever newsletter. Thank you to everyone who attended our talk at the CSPS conference in May and a special thanks to everyone who has volunteered to become a YSN Representative for their University. We hope that this network will bring together trainees pursuing pharmaceutical science across Canada and provide a platform where we can share success and learn from each other. Using this newsletter and our Twitter account (@CSPS_YSN) we want to share recent publications and exciting results as well as educate





Development

June 2018

Wnt signaling in development and tissue homeostasis

Steinhart Z, Angers S.

#Epigenetics #WntProtein

#WntSignalling

Molecular Pharmaceutics

June 2018

BRCA Status Does Not Predict Synergism of a Carboplatin and Olaparib Combination in High-Grade Serous Ovarian Cancer Cell Lines

Shen YT, Evans JC, Zafarana G, Allen C, Piquette-Miller M.

#BRCA #PARPinhibitor

#Carboplatin #DrugCombination

#Olaparib #OvarianCancer

#Synergy

Molecular Pharmaceutics

May 2018

Combined Effects of Supersaturation Rates and Doses on the Kinetic-Solubility Profiles of Amorphous Solid Dispersions Based on Water-Insoluble Poly(2-hydroxyethyl methacrylate) Hydrogels

Schver GCRM, Lee PI.

#AmorphousSolidDispersion

#DoseEffect #Indomethacin

#KineticStability #PHEMAhydrogels

#Posaconazole #SuperSaturationRate

people about the research and projects that are taking place in the different universities. Our newsletters will contain exciting interviews from professors who will share with us their secrets to success and their expert advice. While our inaugural newsletter showcases research at University of Toronto, each month will focus on a different Pharmacy school across Canada to get a taste of the research being conducted by trainees and professors across the country.

We would like to thank everyone who has sent in their ideas and suggestions. We hope to use them to build a network that will benefit everyone and so we encourage everyone to get involved and let us know what you want out of this community. Make sure to start following our Twitter account @CSPS_YSN and make sure to ask your representative to tweet about any new publications. Stay tuned for next month's newsletter which will be based on research happening at University of Waterloo.

Professor Interview

This month we had the pleasure of interviewing Dr. Keith Pardee from the University of Toronto. Dr. Pardee is an assistant professor at the Leslie Dan Faculty of Pharmacy as well as the Canada Research Chair in synthetic biology and human health. His research focuses is on the



potential of moving synthetic biology outside of the cell to create programmable materials that retain cellular transcription and translation properties. Dr. Pardee did his post-doctoral fellowship at the Wyss Institute (MIT/Harvard University) for Biologically Inspired Engineering. There, he developed the first safe and sterile method to deploy gene circuits out of the lab, creating a platform for programmable *in vitro* diagnostics. The Pardee Lab at the Leslie Dan Faculty of Pharmacy aims to build upon this work to bring low-cost, portable healthcare tools to under-served areas and patient populations

Recent Publications from UofT

Lab on a Chip
May 2018

A fully-integrated and automated testing device for PCR-free viral nucleic acid detection in whole blood

Liu W, Das J, Mephah AH, Nemi CR, Sargent EH, Kelley SO.

#HepatitisCvirus

#LabonaChip

#Electrochemicalassay

#Point-of-care diagnostics

Molecular Pharmaceutics
March 2018

Panitumumab Modified with Metal-Chelating Polymers (MCP) Complexed to ¹¹¹In and ¹⁷⁷Lu- An EGFR-Targeted Theranostic for Pancreatic Cancer

Aghevlian S, Lu Y, Winnik MA, Hedley DW, Reilly RM.

#Imaging #Indium-111

#Lutetium-177 #Metal-

ChelatingPolymer

#PancreaticCancer #Panitumumab

#Radioimmunotherapy

Angewandte Chemie International Edition
March 2018

Combinatorial Probes for High-Throughput Electrochemical Analysis of Circulating Nucleic Acids in Clinical Samples

Das J, Ivanov I, Safaei TS, Sargent EH, Kelley SO.

#EGFR

#CirculatingTumourNucleicAcids

#Electrochemistry #LiquidBiopsy

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

We do synthetic biology in a way that is cell-free. We're developing a branch of synthetic biology that is *in vitro*. We make gene circuits by imbedding freeze-dried, cell-free enzymes used in cellular transcription and translation either onto paper or into pellets. This way, they can be shipped to their end user in an easy, biosafe fashion. These systems can be used to make vaccines, conjugated antibodies, antimicrobial peptides, or even drugs. Just add water at the time of use and it's good to go. We can also use these systems to create diagnostic devices. We've recently made a gene circuit that is used as a sensor for nucleic acid sequences unique to different types of the Zika virus. These gene circuits are programmable, so you can make diagnostics for other infectious micro-organisms like Ebola.

2. How did your earlier career choice lead you to where you are now?

Hm. You mean the mistakes or...[laughs]. Well, my career path has been very diverse and I think that has allowed me to tackle things that maybe require breadth. It certainly made the progress slower but it has been good. I have two degrees in botany and my PhD is in molecular genetics. In my post-doc I did applied biology. I even have a diploma in carpentry! I've done a whole bunch of stuff. Maybe that's why a lot of the research I do involves hardware. That hardware then needs software, so we end up also making software. My career has been very winding in the long run but all my experiences have been very helpful.

3. What career mistake has given you the biggest lesson?

I think having fun is the most important thing. Of course, work hard! We all work hard. But if we don't have an underlying level of fun everything becomes harder. My PhD supervisor said that if you're not having fun then you're not doing it right! Especially during the days where nothing is working, having fun is important. Weeks and months can go by where you're working hard and pushing the boundaries towards one end when the answer could be right in front of you and you're just not seeing it because you're not having any fun.

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

Surround yourself with good people!

Recent Publications from Dr. Keith Pardee

Portable, On-Demand Biomolecular Manufacturing.

Pardee K, Slomovic S, Nguyen PQ, Lee JW, Donghia N, Burrill D, Ferrante T, McSorley FR, Furuta Y, Vernet A, Lewandowski M, Boddy CN, Joshi NS, Collins JJ. *Cell*. 2016 Sep 22;167(1):248-259.e12. doi: 10.1016/j.cell.2016.09.013.

Rapid, Low-Cost Detection of Zika Virus Using Programmable Biomolecular Components.

Pardee K, Green AA, Takahashi MK, Braff D, Lambert G, Lee JW, Ferrante T, Ma D, Donghia N, Fan M, Daringer NM, Bosch I, Dudley DM, O'Connor DH, Gehrke L, Collins JJ. *Cell*. 2016 May 19;165(5):1255-66. doi: 10.1016/j.cell.2016.04.059. Epub 2016 May 6.

Synthetic biology devices for in vitro and in vivo diagnostics.

Slomovic S, Pardee K, Collins JJ. *Proc Natl Acad Sci U S A*. 2015 Nov 24;112(47):14429-35. doi: 10.1073/pnas.1508521112. Review.

Paper-based synthetic gene networks.

Pardee K, Green AA, Ferrante T, Cameron DE, DaleyKeyser A, Yin P, Collins JJ. *Cell*. 2014 Nov 6;159(4):940-54. doi: 10.1016/j.cell.2014.10.004. Epub 2014 Oct 23.

5. What impresses you the most when you are considering hiring a grad student? A post-doc? A research associate?

I can say when I meet people it's mostly about positivity and fit. Basing that off a CV is hard. The easiest thing is to look at marks but it's not really the best way to do it. For a post-doc, papers are the obvious thing to look at. Looking for graduate students, I think it's just about finding out their broad interests and whether they are a nice person. I think that trumps straight As.

6. What is your biggest advice for achieving success?

I think it's all about hard work in combination with luck.

7. What do you enjoy most about your job?

All the new ideas! We build things and I love getting the new ideas. That process from conception of the idea to the execution and realization to the successful implementation; I love that.

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

Resilience? [Laughs] Endurance.

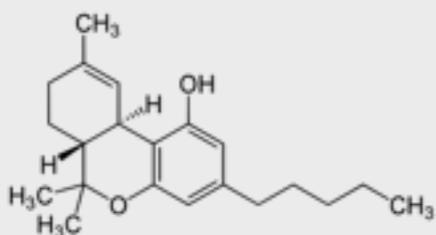
9. What does the future look like in your field? What trends do you see developing over the next few years?

I think the simple systems that we've developed so far will become more complex, more sophisticated, and be able to do even more things. Our technology is the way computers were in the 1950's. There's a lot of room for improvement. I guess seeing the things we are doing in the lab right now being used in people will be fantastic. We're currently leading a patient and field trial of our low-cost Zika virus diagnostics in Latin America so I'm excited about that. The whole theme of our lab is to take healthcare out of these big urban centers and make it more accessible.

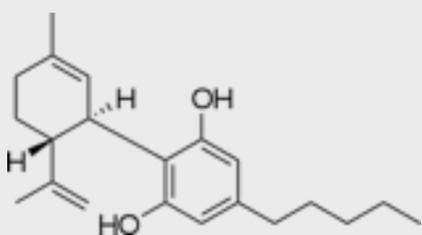
Link to website: <https://www.pardeelab.org/>



Figure 1: Chemical structures of the two major cannabinoids, THC (top) and CBD (bottom)



Tetrahydrocannabinol (THC)



Cannabidiol (CBD)

Exciting Projects at the University of Toronto

High Hopes: Canada poised to lead the way in Medical Cannabis Research

Jamie Evans, Leslie Dan Faculty of Pharmacy, University of Toronto

On June 18th 2018, Bill C-45 (also known as the Cannabis Act) was passed in a Senate vote, paving the way for the complete legalization of recreational cannabis in the coming months in Canada (with a date tentatively set for late August or early September). While there has been widespread speculation in media outlets about the possible ramifications to public health (in particular the risks to adolescents) that this may lead to, an area that is often overlooked is the area of medicinal cannabis. This is an area that many believe Canada can become a world leader in, with the medical cannabis market in the country valued at over \$1 billion.

Cannabis sativa is a herbaceous species originating in central Asia that, depending on the strain, can contain an array of over 100 different cannabinoid compounds [1]. Cannabinoids have been shown to have many medicinal applications including pain management, increasing appetite, controlling nausea and vomiting as well as lowering and controlling intraocular pressure in glaucoma patients [2-5]. In addition, many studies have highlighted the anti-tumour potential of cannabinoids (as monotherapies or in combination with existing chemotherapies) in a wide range of cancer models [6-8].

The two most studied cannabinoids are tetrahydrocannabinol (THC) (the psychoactive component of cannabis) and cannabidiol (CBD) (**Figure 1**) [9-11], with most cannabinoid formulations currently on the market containing one or both of these active compounds. Sativex® (Nabiximols; GW Pharmaceuticals) is an oromucosal spray composed of a 1:1 mixture of CBD:THC approved for use in multiple sclerosis spasticity and pain as well as chronic cancer pain [12,13]. Additionally, in June 2018, the FDA approved Epidiolex (also GW Pharmaceuticals), a CBD formulation used for the treatment of two drug-resistant forms of childhood epileps, Dravet Syndrome (DS) and Lennox-Gastaut Syndrome (LGS). This unprecedented approval by the US regulatory body marks a turning point for the medical cannabis field in North America (with obvious knock-on

effects worldwide), with the DEA expected to reclassify CBD from a Schedule I drug in the next 90 days.

Professor Christine Allen, Interim Dean at the University of Toronto has recently commenced a collaboration with Avicanna Inc. a medical cannabis biotechnology company based at JLABS (division of Johnson and Johnson (J&J)), Toronto. With over 20 years of formulation experience, Professor Allen's group is working with Avicanna Inc. to develop cannabinoid-based, advanced drug delivery systems with a range of therapeutic applications. It is hoped that this collaboration will advance the field of medical cannabis research and highlight Canada (and in particular, Toronto) as a major player in this budding industry.

[1] O. Aizpurua-Olaizola, U. Soydaner, E. Öztürk, D. Schibano, Y. Simsir, P. Navarro, N. Etxebarria, A. Usobiaga, Evolution of the cannabinoid and terpene content during the growth of *Cannabis sativa* plants from different chemotypes, *Journal of natural products*, 79 (2016) 324-331.

[2] M.A. Ware, C.R. Doyle, R. Woods, M.E. Lynch, A.J. Clark, Cannabis use for chronic non-cancer pain: results of a prospective survey, *Pain*, 102 (2003) 211-216.

[3] E.M. Berry, R. Mechoulam, Tetrahydrocannabinol and endocannabinoids in feeding and appetite, *Pharmacology & therapeutics*, 95 (2002) 185-190.

[4] L.A. Parker, E.M. Rock, C.L. Limebeer, Regulation of nausea and vomiting by cannabinoids, *British journal of pharmacology*, 163 (2011) 1411-1422.

[5] A. Porcella, C. Maxia, G.L. Gessa, L. Pani, The synthetic cannabinoid WIN55212-2 decreases the intraocular pressure in human glaucoma resistant to conventional therapies, *European Journal of Neuroscience*, 13 (2001) 409-412.

[6] G. Velasco, C. Sánchez, M. Guzmán, Anticancer mechanisms of cannabinoids, *Current Oncology*, 23 (2016) S23.

[7] K.A. Scott, A.G. Dalgleish, W.M. Liu, The combination of cannabidiol and Δ^9 -tetrahydrocannabinol enhances the anticancer effects of radiation in an orthotopic murine glioma model, *Molecular cancer therapeutics*, 13 (2014) 2955-2967. [8] S. Torres, M. Lorente, F. Rodríguez-Fornés, S. Hernández-Tiedra, M. Salazar, E. García-Taboada, J. Barcia, M. Guzmán, G. Velasco, A combined preclinical therapy of cannabinoids and temozolomide against glioma, *Molecular cancer therapeutics*, 10 (2011) 90-103.

[9] E. Eisenberg, M. Ogintz, S. Almog, The pharmacokinetics, efficacy, safety, and ease of use of a novel portable metered-dose cannabis inhaler in patients with chronic neuropathic pain: a phase 1a study, *Journal of pain & palliative care pharmacotherapy*, 28 (2014) 216-225.

[10] F. Grotenhermen, Pharmacokinetics and pharmacodynamics of cannabinoids, *Clinical pharmacokinetics*, 42 (2003) 327-360.

[11] A. Zgair, J.C. Wong, J.B. Lee, J. Mistry, O. Sivak, K.M. Wasan, I.M. Hennig, D.A. Barrett, C.S. Constantinescu, P.M. Fischer, Dietary fats and pharmaceutical lipid excipients increase systemic exposure to orally administered cannabis and cannabis-based medicines, *American journal of translational research*, 8 (2016) 3448.

[12] M.T. Fallon, E. Albert Lux, R. McQuade, S. Rossetti, R. Sanchez, W. Sun, S. Wright, A.H. Lichtman, E. Kornyeieva, Sativex oromucosal spray as adjunctive therapy in advanced cancer patients with chronic pain unalleviated by optimized opioid therapy: two double-blind, randomized, placebo-controlled phase 3 studies, *British journal of pain*, 11 (2017) 119-133.

[13] S. Giacoppo, P. Bramanti, E. Mazzon, Sativex in the management of multiple sclerosis-related spasticity: An overview of the last decade of clinical evaluation, *Multiple sclerosis and related disorders*, 17 (2017) 22-31