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## 2017 NanoOntario Conference Schedule:

Time	DAY 1 – November 9 <sup>th</sup> , 2017 Events
9:00AM-12:00PM	Pre-Clinical Imaging Workshop – STTARR (MaRS Discovery District, 101 College St.)
10:00AM-12:00PM	NCE Proposal NOI Discussion
12:00 - 1:00 PM	Registration
1:00 - 1:15 PM	Opening Remarks by Peter Mascher, McMaster U., Acting-Board Chair, NanoOntario
	<b>Session 1 – Drug Delivery, chaired by Frank Gu, U. Waterloo</b>
1:15 - 1:45 PM	Keynote: Christine Allen, U. Toronto – “Nanomedicines in Oncology: Successes and Challenges”
	Elizabeth Gilles, Western U. – “Amplifying Stimuli for Drug Release: Self-Immolative Delivery Systems”
1:45 - 2:50 PM	John Dutcher, U. Guelph. – “ PhytoSpherix Nanoparticles in Nanomedicine: Novel Drug Delivery, Anti-Infective and Immunomodulatory Agents”
	SPEAKER 3: TBA
2:50 - 3:05 PM	Health Break
	<b>Session 2 – Theranostics</b>
3:05 - 3:35 PM	Keynote: Shana Kelley, U. Toronto – “Profiling Cells Inside and Out Using Nanostructured Materials”
3:35 - 4:05 PM	Keynote: Gang Zheng, UHN – “ Porphysome Nanotechnology: Discovery, Clinical Translation and Beyond”
	Li-Lin Tay, NRC Ottawa – “Plasmonic Nanosensors for Biosensing and Imaging”
4:05 – 4:35 PM	Leyla Soleymani, McMaster U. – “Advanced Materials for Lowering the Limit-of-Detection of Handheld Biosensors”
4:35-5:05 PM	Poster Advertising Conga Line 1
5:05 – 7:00 PM	Poster Session and Industry-Academia Networking Reception
7:15 – 8:00 PM	Toronto NanoFabrication Centre (TNFC) Lab Tour

Time	DAY 2 – November 10 <sup>th</sup> , 2017 Events
8:00-8:30 PM	Registration
	<b>Session 3 – Nanoparticle Distribution, Toxicity and Analytical Methods, chaired by François Lagurné-Labarthe</b>
8:30 – 9:00 AM	Keynote: Warren Chan, U. Toronto – “Nanomedicine 2.0”
	Zoya Leonenko, U. Waterloo – “Nanotechnology approaches to study the molecular mechanism of Alzheimer’s disease”
9:00 – 9:40 AM	Shan Zou, NRC Ottawa – “Nanosafety and toxicity assessment using cellular model systems”

9:40 – 9:55 AM	Health Break
9:55 – 10:25 AM	Muhammad Rizwan and Evelyn Yim, U. Waterloo – “Micro and Nano-topography Patterned Substrates for Modulation of Cellular Response in Corneal Tissue Engineering Applications” Simone Pisana, York U. – “SPR and Magneto-optic-SPR-based Biosensors”
10:25 – 10:45 AM	Poster Advertising Conga Line 2
10:45 – 11:45 AM	Poster Session and Networking
11:45 AM-1:30PM	Lunch and Industry Panel – “Industry Needs: Moving to the Clinic and Enhancing Nanomedical Manufacturing in Ontario”
1:30 – 2:00 PM	<b>Session 3, continued</b>
	Kathryn Grandfield, McMaster U. – “Characterizing Nano-Biomaterials Interfaces: Correlative Microscopies for Bone Applications”
	Hendrick de Haan, U. Ontario Institute of Technology – “Self-Assembly of Gold Nanoparticles Driven by Iron and Iron-Containing Proteins”
2:00 – 3:30 PM	<b>Session 4 – Nanomedicine Researcher Awards, chaired by Hind Al-Abadleh, Wilfrid Laurier U.</b>
	Marianna Foldvari, U. Waterloo – “Needle-free nanomedicines – an overview of research, technologies and translation to the clinic”
	Jaclyn Brusso, U. Ottawa – “Exploring Tunable Nanoscale Metal Complexes Through Ligand Design”  Jin Zhang, Western U. – “Nanostructured Biosensor for Detecting Glucose in Tear by Applying Fluorescence Resonance Energy Transfer Quenching Mechanism”
3:30 – 3:45 PM	Closing Remarks
4:00 – 4:30 PM	Follow-up Discussion on NCE-NOI

## Workshops/Tours:

### Pre-Clinical Imaging Workshop at STTARR

Thursday, Nov. 9 at 9:00 AM at the Princess Margaret Research Tower at MaRS, 101 College St.

STTARR (Spatio-temporal Targeting and Amplification of Radiation Response) provides state-of-the-art imaging resources for translational drug discovery and radiation research. This workshop will include a lecture on animal models, imaging tools and contrast agents as well as a tour around the STTARR instrumentation areas. There will be chances to ask questions throughout the workshop. Learn more about this facility here: <http://www.sttarr.com>.

## Toronto NanoFabrication Centre (TNFC) Lab Tour

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Thursday, Nov. 9 at 7:15 pm in room B540 in the Sanford Fleming Building, 10 King's College Road

The Toronto NanoFabrication Centre is an interdisciplinary research and service centre at the University of Toronto providing access to state-of-the-art nanofabrication facilities, collaborative research networks and advanced education opportunities. Join us for a tour of their facilities, more information can be found at: <http://tnfc.utoronto.ca>.

## **2017 NanoOntario Achievement Awards:**

### Honorary Award for Outstanding Lifetime Achievements in Nanoscience and Nanotechnology in Ontario

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Recipient: Professor Marianna Foldvari

Dr. Marianna Foldvari is a Professor of Pharmaceutical Sciences at the University of Waterloo's School of Pharmacy in Canada. Dr. Foldvari received a BSc in Pharmacy and a Doctorate in Pharmaceutical Sciences, specializing in Pharmacognosy and Microbiology, both from Semmelweis Medical University in Budapest, Hungary and a PhD in Pharmaceutical Sciences from the College of Pharmacy at Dalhousie University in the area of targeted liposomal drug delivery systems in 1988. Between 1989-2006 she was a Faculty member at the College of Pharmacy and Nutrition, University of Saskatchewan. She held the Tier 1 Canada Research Chair in Bionanotechnology and Nanomedicine from 2007-2014.

Dr. Foldvari is an internationally recognized expert in nanomedicine. Her research program is focusing on pharmaceutical nanotechnology, non-invasive drug, protein and gene delivery system design (such as dermal, transdermal, transmucosal, ocular and intrapulmonary) for regenerative medicine in dermatology, ophthalmology and immunology.

Dr Foldvari's contributions to the drug delivery field in the past 28 years include both basic and applied research accomplishments with a total of 230 publications, 26 patents, 110 invited conference presentations, 90 abstracts, about \$23M in grant funding. She established the first pharmaceutical company, PharmaDerm Laboratories Ltd., in the province of Saskatchewan in 1991. Her pioneering work in topical protein delivery system development led to clinical trials and currently under commercial development.

Dr Foldvari's research is supported by grants from Canadian Institutes of Health Research (CIHR), Canada Foundation for Innovation (CFI), Natural Sciences and Engineering Research Council of Canada (NSERC), Ontario Centers of Excellence and industrial sources. Dr Foldvari is a member of the American Association for the Advancement of Science, American Association of Pharmaceutical Scientists, American Society for Gene and Cell Therapy and the Controlled Release Society.

She currently serves as Editorial Board Member of the Journal of Controlled Release (IF:8.4), Associate Editor for Frontiers in Neuroscience, OA Drug Design and Delivery and for the past ten years served as Associate Editor for Nanomedicine (2006-2016): NBM (IF: 6.9). Dr Foldvari serves as a grant reviewer on CIHR, NSERC, CFI and NIH panels and the Bill and Melinda Gates

Foundation Global Health Initiatives review board. Dr Foldvari is one of the Founding Directors of the American Society for Nanomedicine (ASNM) and the International Society of Nanomedicine (ISNM). She served as Board Member for Genome Prairie and was a Member of the Advisory Committee to the Prime Minister on Science and Technology and a Founder of the Canadian Society of Pharmaceutical Sciences (CSPS). She has received the YWCA Women of Distinction Award, the Saskatchewan Top 25 Science Achievement Award and the Sabex Award of Innovation.

## Honorary Award for Outstanding Mid-career Achievements in Nanoscience and Nanotechnology in Ontario

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Recipient: Professor Jin Zhang

Dr. Jin Zhang is an Associate Professor with the Department of Chemical and Biochemical Engineering, Western University, Canada. Dr. Zhang's research activities are related to the development of new biocompatible nanocomposites with enhanced magnetic, optical, electric, and mechanical properties. Her expertise lies in the interface between multifunctional nanostructures and biological systems. Currently, the Zhang group's research themes include (1) design and development of multifunctional nanocomposites through chemical and laser-assisted processes; (2) nanosystems for theranostics by combining therapeutics and diagnosis; and (3) nanostructured biosensors.

Dr. Zhang has published over 66 peer-reviewed papers, including *Biosensor & Bioelectronics*, *J. Eur. Cells & Mater.*, *J. Mat. Chem. B*, *Langmuir*, *RSC Advances*, *Appl. Phys. Lett.*, *J. Phys. Chem. B*, *J. Colloid interface Sci.*, etc.; her group has given over 90 presentations at national and international conferences. In 2014, Dr. Zhang was rewarded the Early Research Award of Ontario. She was recently recognized as the Grand Challenges Canada- Canadian Rising Stars in Global Health for her research work on "Non-invasive Diagnostic Tool for Diabetes". The device of non-invasive glucose sensor for diabetes invented by Jin Zhang has been successfully tested on animal model, and is moving forward for the clinical trial. Her research work was reported by the worldwide media, including the Discovery Channel, CTV, the Institute of Nanotechnology (IoN), and Nanotechnology Now, etc. In addition, Jin Zhang is an Associate Editor of the *International Journal of Nano and Biomaterials*. She has/had served as a guest editor for different journals, e.g. *Journal of Nanomaterials*.

## Honorary Award for Outstanding Early-career Achievements in Nanoscience and Nanotechnology in Ontario

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Recipient: Professor Jaclyn Brusso

Since joining the University of Ottawa in 2010, Dr. Jaclyn Brusso has successfully established a research program focused on addressing key challenges in the development of smaller, lighter, cheaper and more efficient optical, magnetic and electronic materials. Through design and development of finely tuned new organic systems she is achieving an exquisite understanding and control of the self-assembly process at the nanoscale. Her research extends to include tunable nanoscale metal complexes utilizing conjugated organic semiconductors and radical based materials as non-innocent ligands

capable of controlling their magnetic and conductive properties, essential for the nano- electronic devices of the future.

Jaclyn Brusso works to raise the profile of materials chemistry at the University of Ottawa through her success as an early researcher (such as Ontario Early Researcher Award, France Canada Research Fund and CNC-IUPAC Award) and as a founding member of uOttawa's Centre for Advanced Materials Research and part of the CFI teams that raised over \$25M. Jaclyn Brusso shows her leadership within the scientific community by dedicating time and effort to community and youth outreach activities (e.g., Women in STEM, Science Rendezvous, PopChem). Jaclyn is a rising star with an exceptional aptitude for innovation and academic leadership.

## **Keynote Talks:**

### Nanomedicines in Oncology: Successes and Challenges

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Christine Allen, University of Toronto

Thursday, November 9<sup>th</sup> at 1:15 pm in Session 1 – Drug Delivery

#### About Prof. Christine Allen:

Research in Professor Allen's laboratory is devoted to the development of nano and other delivery technologies for the detection, diagnosis and treatment of cancer. Current research projects include 1) the synthesis of new polymer materials for nanotechnologybased drug delivery; 2) pursuit of computational approaches to matching material-drug pairs and predicting solution behaviour of amphiphilic copolymer molecules; 3) development and evaluation of delivery systems for intraperitoneal administration of taxanes in the treatment of ovarian cancer; 4) image-based assessment of the in vivo pathway and fate of nanotechnologies at the whole body, tissue and cellular levels; 5) development of nanotechnologies for detection and diagnosis of lung and breast cancer; and 6) multifunctional nanotechnology for targeted auger electron radiotherapy of breast cancer.

Professor Allen has been a professor in the Leslie Dan Faculty of Pharmacy in the University of Toronto since 2007. She has been the GlaxoSmithKline Chair in Pharmaceutics and Drug Delivery since 2014, and has served as Associate Dean in the Leslie Dan Faculty of Pharmacy. Cross-appointed to the Department of Chemical Engineering and Applied Chemistry, University of Toronto, she is also appointed to the faculty of the STTARR Innovation Centre, University Health Network. She worked for 2 years at Celator Pharmaceuticals Corp. as an IRAP Project Leader, following her SERC Post-Doctoral Fellowship in the B.C. Cancer Agency. She earned her BSc and PhD at U Ottawa and McGill, respectively. She is an Associate Editor of Molecular Pharmaceutics. She has won a number of noteworthy awards, including the 2014 Gattefossé Canada/CSPS Award in Lipid-Based Drug Delivery, the 2011 CRS/Elsevier Journal of Controlled Release Jorge Heller Award for Outstanding Paper, an Innovation Award from the Ontario Research and Commercialization Program in 2008, a Career Award from the Canadian Institutes of Health Research, a new New Investigator Research Award from Association of Faculties of Pharmacy of Canada (AFPC)/AstraZeneca, and an Early Career Award from the Canadian Society for Pharmaceutics Sciences (CSPS)/GlaxoSmithKline.



## Profiling Cells Inside and Out Using Nanostructured Materials

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Shana Kelley, University of Toronto

Thursday, November 9<sup>th</sup> at 3:05 pm in Session 2 - Theranostics

To put disease-related biomarkers to work in the clinic, new high-performance technologies are needed to enable rapid and sensitive analysis of clinical specimens. Our group uses aspects of biophysical and materials chemistry to create new systems that permit biomolecular analytes and rare cells to be tracked and profiled. Nanomaterials play a central role in these efforts, as the unique properties of materials engineered at the nanoscale allow previously unreachable levels of sensitivity and specificity to be realized.

### About Prof. Shana Kelley:

The overarching theme of the Kelley group research program is the development of new molecules and devices that enable biological activities to be measured and manipulated. The projects underway involve aspects of diverse disciplines ranging from materials chemistry to chemical biology and nanotechnology.

Professor Kelley is appointed to multiple departments at the University of Toronto including: Pharmaceutical Sciences, Faculty of Pharmacy; the Institute of Biomaterials & Bioengineering, Faculty of Engineering; Chemistry, Faculty of Arts and Sciences; and Biochemistry, Faculty of Medicine. A few of her recent professional activities include Editorial Advisory Board, Journal of the American Chemical Society; Panel Member, NIH ISD; Associate Editor, ACS Sensors.

Professor Kelley has won many prestigious awards, including in the 2017 ACS Nanoscience Award, the 2017 Somorjai Visiting Miller Professorship (UC Berkeley), the 2016 SLAS Innovation Award, the 2016 NSERC Brockhouse Award, a 2013 University of Toronto Distinguished Professor Award, the 2011 Steacie Prize, the 2006 Pittsburgh Conference Achievement Award, the 2005 Camille Drefus Teacher-Scholar Award, a 2000 Dreyfus New Faculty Award, and a 2000 Research Innovation Award, and a 2004 NSF CAREER Award. In 2004 she was voted one of the top 100 innovators by Technology Review Magazine and won a 2004 Alfred P. Sloan Fellowship. She was named in 2016 as Fellow, American Institute for Medical and Biological Engineering, in 2016 as Fellow, Canadian Academy of Health Sciences, and in 2011 as University of Toronto Inventor of the Year, in 2010 as an NSERC E.W.R Steacie Fellow. In 2008 she was named one of "Canada's Top 40 under 40" by Globe & Mail/Caldwell.

## Porphysome Nanotechnology: Discovery, Clinical Translation and Beyond

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Gang Zheng, University Health Network/University of Toronto

Thursday, November 9<sup>th</sup> at 3:35 pm in Session 2 - Theranostics

Porphyrins are aromatic, organic, light-absorbing molecules that occur abundantly in nature, especially in the form of molecular self-assemblies. In 2011, we first discovered 'porphysomes', the self-

assembled porphyrin-lipid nanoparticles with intrinsic multimodal photonic properties. The high-density porphyrin packing in bilayers enables the absorption and conversion of light energy to heat with extremely high efficiency, making them ideal candidates for photothermal therapy and photoacoustic imaging. Upon nanostructure dissociation, fluorescence and photodynamic activity of porphyrin monomers are restored. In addition, metal ions can be directly incorporated into the porphyrin building blocks of the preformed porphyrinsomes thus unlocking their potential for PET and MRI. By changing the way porphyrin-lipid assembles, we developed HDL-like porphyrin nanoparticles (<20nm), porphyrin microbubbles (~2µm), giant porphyrin vesicle (~100µm), hybrid porphyrin-gold nanoparticles and metal chelating nanotexaphyrins. By mimicking light harvest systems in photosynthetic bacteria, we introduced high-ordered porphyrin aggregates into supramolecular assemblies, resulting unprecedented photonic properties (e.g., self-regulating photothermal effect). Such optical properties are also responsible for our discovery of the ultrasound-induced microbubbles-to-nanoparticle conversion phenomenon, which may open the door to bypass the enhanced permeability and retention effect when delivering drugs to tumors. We have now validated porphyrinsome's multimodal utilities in different cancer types, tumor models and animal species. The effort of moving porphyrinsomes towards first-in-human use is on the way. In summary, the simple yet intrinsic multimodal nature of porphyrinsomes represents a new nanomedicine paradigm and also confers its high clinical translation potential.

#### About Prof. Gang Zheng:

The Zheng lab develops nanoparticle and molecular platform technologies that could open up new possibilities in the fight against cancer. By conjugating a photoactive porphyrin molecule to a phospholipid, his lab has expanded the role of phospholipids in supramolecular architectures from simple structural components to intrinsic imaging and therapeutic agents. His lab is exploring lipoprotein-like nanocarriers, which are a novel class of biocompatible, biodegradable, and multifunctional nanoparticles based on chemically modified lipoproteins (LDL or HDL) or artificially engineered lipoproteinmimetic nanoscaffolds. They are specifically designed to address some common hurdles that limit many nanodevices from translating into the clinic. In addition, Zheng's group is well known for developing molecular beacons, which are target-activatable probes that use the fluorescent resonance energy transfer principle to control their fluorescence emission in response to specific biological stimuli.

Professor Zheng is a leading member of the University Health Network in Toronto. He has multiple appointments, including to the Department of Medical Biophysics, University of Toronto, the Institute of Biomaterials and Biomedical Engineering, and the Leslie Dan Faculty of Pharmacy. He is Senior Scientist and Tanenbaum Chair in Prostate Cancer Research at Princess Margaret Cancer Centre and Scientific Lead of Nanotechnology and Radiochemistry at Techna Institute, University Health Network. In addition, he is an adjunct Professor of Radiology at University of Pennsylvania.

Professor Zheng received his PhD in 1999 from SUNY Buffalo in Medicinal Chemistry. Following two years of postdoctoral training in photodynamic therapy at the Roswell Park Cancer Institute, he joined the University of Pennsylvania in 2001 as an Assistant Professor of Radiology, where he established the molecular imaging chemistry program and introduced photodynamic molecular beacons and lipoprotein-like nanoparticles. Since moving to Canada in 2006, his research has been focused on developing clinically translatable technology platforms to combat cancer. His lab discovered porphyrinsome nanotechnology (Nature Materials 2011), which was named one of the "top 10 cancer breakthroughs of 2011" by the Canadian Cancer Society. His lab also discovered that on exposure to low-frequency ultrasound, porphyrin microbubbles form nanoparticles that possess the same optical and therapeutic properties as the original microbubble, and can be used simultaneously for imaging and drug delivery (Nature Nano 2015). Dr. Zheng is an Associate Editor for Bioconjugate Chemistry and a Fellow of the American Institute for Medical and Biological Engineering.



## Nanomedicine 2.0

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Warren Chan, University of Toronto

Friday, November 10<sup>th</sup> at 8:30 am in Session 3 - Nanoparticle Biodistribution, Toxicity and Methods

Nanotechnology involves the engineering of structures, materials, and particle in the size range of 1 to 100 nm. These nanostructures have unique biological, optical, electrical and magnetic properties that are in direct relationship to their size, shape, and surface chemistry. As a result of these properties, nanotechnology is currently exploited in medicine for diagnosing and treating diseases. This seminar will discuss the current (1) current of nanomedicine research and development, and (2) challenges of clinical translation. This presentation will also discuss new and exciting opportunities in this area of research in the 21st century. Finally, I will describe the Canadian landscape and activities in this emerging field of research.

### About Prof. Warren Chan:

The Chan research group is currently interested in studying and understanding the proteomic and genomic changes associated with abnormal cells (e.g., cancer cells or virally-infected cells) and tissues. We aim to elucidate the cell's molecular dynamics by using recent developments in nanotechnology (e.g., inorganic nanostructures), microtechnology (e.g., micro-electromechanical systems and capillary flow systems), and molecular engineering (e.g., phage-display) as well as engineering new instrumentation and techniques to address biological questions. A fundamental understanding of molecular processes with technology developments should lead to the design of novel diagnostic schemes and therapeutic strategies.

Professor Chan is the Distinguished Professor of NanoBioEngineering at the University of Toronto. His primary appointment is to Institute of Biomaterials & Biomedical Engineering, and is additionally appointed to the departments of Chemical Engineering & Applied Chemistry, Chemistry, Materials Science & Engineering and to the Donnelly Centre for Cellular & Biomolecular Research (CCBR). He has won many awards, including the NSERC E. W. Memorial Steacie Fellowship (2012), the International Dennis Gabor Award (Hungary) (2009); Premier Research Excellence Award (2007), the Canadian Research Chair in Bionanotechnology (2006); Lord Rank Prize Fund, UK (2006), an NIH Training Grant, UCSD, (2001), the Winner of the BF Goodrich Collegiate Young Inventor's Competition (Graduate Level), (1999), and the Colgate-Palmolive Undergraduate Research Award (1996). He studied at the University of Illinois (1996) BSc, and earned his PhD from Indiana University. He is Associate Editor for ACS Nano.

## Speakers:

### Amplifying Stimuli for Drug Release: Self-Immolative Delivery Systems

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Elizabeth Gilles, Western University

Thursday, November 9<sup>th</sup> at 1:45 pm in Session 1 – Drug Delivery

Degradable polymers are of significant interest in nanomedicine, where they are frequently used to prepare nanoparticles that can encapsulate drugs and then release them as the polymers break down. Much progress has been made using polyesters such as polylactide and polycaprolactone. However, the ability to control drug release using these polymers is limited as they may degrade more rapidly or more slowly than desired. Many stimuli-responsive polymers have been developed over the past couple of decades, but these polymers typically require many stimuli-mediated events to achieve complete polymer degradation. To address these limitations, we have been developing self-immolative polymers (SIPs), which undergo complete end-to-end depolymerization following the cleavage of a single stimuli-responsive end-cap from the polymer terminus. This presentation will describe our group's development of polyglyoxylate SIPs and their applications in nanomedicine. We have prepared polyglyoxylates with end-caps responsive to a wide range of stimuli including light, heat, weak acids, hydrogen peroxide, and reducing agents, many of which are accessible *in vivo* and are associated with disease states such as cancer and inflammation. Their degradation was studied in solution, as assemblies of block copolymers, in the form of nanoparticles, and as coatings. In each case, the triggered polymers underwent rapid depolymerization whereas the untriggered controls remained quite stable. This provided triggered release of drug molecules. Overall, these studies have demonstrated that polyglyoxylates have great potential for drug delivery applications, and future work will focus on further *in vitro* and *in vivo* studies.

#### About Prof. Elizabeth Gilles:

The Gilles group is developing new polymeric platforms for applications in drug delivery and tissue engineering. They design and synthesize polymers with novel functions such as triggered degradation or the presentation of bioactive molecules and use these polymers to fabricate materials ranging from nanoparticles to coatings and 3-D scaffolds. They are working with collaborators across the faculties of Science, Engineering, and Medicine to apply these materials to challenges in the areas including musculoskeletal health, cancer, and immunology/microbiology.

Professor Gilles is appointed in the Department of Chemistry at Western University. She has won numerous awards, including most recently the NSERC E.W.R. Steacie Memorial Fellowship in 2017. In addition, she won the Fallona Interdisciplinary Science Award in 2016, the Faculty Scholar award, Western University in 2016, the Petro Canada Young Innovator Award in 2012, an Early Researcher Award from the Government of Ontario in 2008, a Tier 2 Canada Research Chair, Government of Canada in 2006, and the John Charles Polanyi Prize from the Government of Ontario in 2006.

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## PhytoSpherix Nanoparticles in Nanomedicine

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John Dutcher, University of Guelph

Thursday, November 9<sup>th</sup> at 1:45 pm in Session 1 – Drug Delivery

Phytoglycogen is a highly-branched polymer of glucose produced in the form of dense, monodisperse nanoparticles by some varieties of plants such as sweet corn. The particles are chemically simple, but have a special dendrimeric or tree-like structure that produces interesting and useful properties such as their unique interaction with water. Guelph-based Mirexus Biotechnologies is commercializing this safe, sustainable, natural nanotechnology as PhytoSpherix (Phx). Mirexus is currently selling Phx as ingredients for cosmetics formulations because of its unique moisturizing and anti-ageing properties, but there are even more promising applications of the Phx technology in nanomedicine. In addition to the particles being ideal drug delivery vehicles, we have found that certain chemical modifications of the particles result in promising candidates for novel anti-infectives, showing efficacy as broad spectrum antibiotics, and immunomodulatory agents, either enhancing or suppressing the innate immune response of organisms.

### About Prof. John Dutcher:

The Dutcher group studies soft matter and biological physics at surfaces. Soft and biological systems are very sensitive to their environment such that small changes in temperature and pH, as well as the application of external fields, can produce large changes in their properties. This sensitivity can be exploited to tune the properties of the systems and to achieve a deep understanding of the subtle interplay between different interactions. This research also leads naturally to the discovery of new and unique biomaterials, which can be exploited in new technological applications. The Dutcher group applies a broad range of surface-sensitive experimental techniques and fundamental, physics-based strategies to investigate the fundamental properties and practical applications of biophysical systems and novel biological molecules and materials.

Dutcher is Professor and Canada Research Chair in Soft Matter and Biological Physics in the Department of Physics at the University of Guelph. He is also Director of the Nanoscience Program at the University of Guelph. He serves on the Editorial Boards of Soft Matter, Journal of Polymer Science Part B: Polymer Physics, Colloids and Interfaces B: Biointerfaces and Scientific Reports. He is a Fellow of the American Physical Society. He is the founder of Mirexus Biotechnologies, a Guelph-based company that is commercializing natural nanoparticles discovered in his University of Guelph laboratory.

## Plasmonic Nanosensors for Biosensing and Imaging

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Li-Lin Tay, Jamshid Tanha, Jeff Fraser and John Hulse, National Research Council – Ottawa

Thursday, November 9<sup>th</sup> at 4:05 pm in Session 2 – Theranostics

Plasmon resonance of the noble metal nanoparticles (NP) manifests itself in a variety of extraordinary optical properties. Resonant excitation of the conduction electrons by incident radiation generates localized surface plasmon resonance (LSPR) which produces intense localized electromagnetic fields near the surface of NP and results in the well-known surface-enhanced Raman scattering (SERS) effect. In addition, the LSPR excitation results in the wavelength-selective absorption and scattering

in the visible region. In this paper, we will present a plasmonic biosensor which utilizes both SERS and light scattering properties of silver NP for the detection of pathogenic bacterium and imaging of cell surface receptors. In the pathogen detection study, silver NP was conjugated to a single domain antibody (Ag-SdAb) recognizing the pathogenic bacteria, staphylococcus aureus. Labeled cells can be detected with both light scattering and Raman imaging. Intense SERS signal were obtained from Ag-sdAb labeled cells. We will demonstrate the detection sensitivity of single cell can be achieved in the microfluidic device. We will also discuss the advantage of using such dual transduction detection platform and the instrumental development to enable this sensing and imaging scheme. In the cell surface receptor imaging study, NPs were co-functionalized with both antibody and Raman reporter to enable a labeled and targeted detection of specific cell surface receptor. In this report, we will show the correlation imaging from SERS, resonant Rayleigh images of the targeted cells.

#### About Dr. Tay:

Li-Lin Tay received her Ph.D. from the Department of Chemistry, University of Toronto in 2000. She joined NRC in 2002 as a research associate and studied III-V and group IV epitaxial thin films. She became a research officer in 2005 and focused her research on the development of integrated optical biosensor and fundamental properties of coupled plasmonic nanostructures. In 2015, she was the resource team lead for the photometry, radiometry, thermometry and Ionizing radiation disciplines in the measurement Science and Standards portfolio in NRC. She became the team leader of photometry and spectrophotometry in 2016. Her current research interest is in the study of optical properties in plasmonic-photonics coupled hybrid nanostructures.

## Advanced materials for lowering the limit-of-detection of handheld biosensors

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Leyla Soleymani, McMaster University

Thursday, November 9<sup>th</sup> at 4:05 pm in Session 2 – Theranostics

Since its commercialization in the 1980's, the handheld glucose biosensor has played a vital role in patient-centered management of diabetes. Motivated by this success, there is a major research effort towards developing a wide range of handheld biosensors for health monitoring and disease management. In this talk, I will discuss how advanced materials can be used to enhance the sensitivity of biosensors, and reduce their background signals associated with non-specific adsorption. More specifically, I will present new fabrication processes based on thin film wrinkling, self-assembly, electroless deposition, and pattern transfer for creating high surface area and self-cleaning electrodes on flexible substrate. I will then present the application of these materials in three classes of assays used for detecting nucleic acids, proteins, and small molecules. Finally I will demonstrate the use of these assays in clinical decision-making.

#### About Prof. Leyla Soleymani:

Leyla Soleymani obtained her PhD degree in Electrical and Computer Engineering from University of Toronto in 2010, and she has been a faculty member at the Department of Engineering Physics and the School of Biomedical Engineering at McMaster since 2011. She is currently the Canada Research Chair in Miniaturized Biomedical Devices and the recipient of the Ontario Early Researcher Award. She is working towards making new materials and methods for creating handheld and continuous monitoring biosensors.

# Nanotechnology approaches to study molecular mechanism of Alzheimer's disease

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Zoya Leonenko, University of Waterloo

Friday, November 10<sup>th</sup> at 9:00 am in Session 3 – Nanoparticle Distribution, Toxicity and Methods

Alzheimer's disease (AD) is a neurodegenerative disease characterized by dementia and memory loss for which no cure or prevention is available. Amyloid toxicity is a result of the non-specific interaction of toxic amyloid oligomers with the plasma membrane.

We studied amyloid aggregation and interaction of amyloid beta (1-42) peptide with lipid membrane using atomic force microscopy (AFM), Kelvin probe force microscopy, surface plasmon resonance (SPR) and black lipid membrane (BLM). We demonstrated that lipid membrane plays an active role in amyloid binding and toxicity. Effect of lipid composition, surface charge and presence of cholesterol or melatonin are discussed. We discovered that membrane cholesterol creates nanoscale electrostatic domains which induce preferential binding of amyloid peptide, while membrane melatonin reduces amyloid-membrane interactions. Using AFS we showed that amyloid inhibitors prevent amyloid-amyloid binding on a single molecule level, the first step which leads to the formation of toxic amyloid oligomers. These findings contribute to better understanding of the molecular mechanisms of Alzheimer's disease and aid to the developments of novel strategies for cure and prevention of AD.

**References:** Drolle et al, *PLOS ONE*, 2017, 12(8), e0182194; Robinson et al, *Biochim. Biophys. Acta*, 2017, 1865 (11), 1707-1718; Ollagnier, et al, 2016, *Conference proceedings: ALLSENSORS 2016*; Robinson et al, *AIMS Molecular Science*, 2015, 2(3): 332-358; Drolle et al, *J Drug Metabolism Rev.*, 2014, 46(2): 207-223; Hane et al, *J Biosensors & Bioelectronics*, 2014, 54, 492-498; Drolle et al, *Biophys. J.*, 2012, 103(4), L27-L29.

## About Prof. Zoya Leonenko:

The Leonenko group is interested in lipids, including the physics of lipids and lipidprotein interactions; the role of structural changes and physical properties of lipid monolayers and bilayers in controlling biological processes and diseases; and the application of lipid films in biomedical nanotechnology. Current Research Projects are focused on the role of lipid membrane in amyloid toxicity in relation to Alzheimer's Disease; testing amyloid inhibitor drugs using single molecule atomic force spectroscopy, interaction of antimicrobial peptides with lipid membrane and lung surfactant; lipid-based drug delivery systems, developing novel biosensing platforms using lipid membrane and surface enhanced spectroscopy.

Leonenko is a Professor in the Department of Physics and Astronomy holding a joint position with Department of Biology. Dr. Leonenko joined the University of Waterloo in 2007. Prior to this, she worked at the University of Maryland at Baltimore and the University of Calgary as an Assistant Professor. She was also a recipient of an Invited Professorship Award from the University of Burgundy, Dijon, France in 2006. Leonenko received her PhD in Chemical Physics from the Institute of Chemical Kinetics and Combustion, Novosibirsk State University, Russia and a Diploma (MS) in Physical Chemistry from Novosibirsk State University, Russia.

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# Nanosafety and toxicity assessment using cellular model systems

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Shan Zou, National Research Council – Ottawa

Friday, November 10<sup>th</sup> at 9:00 am in Session 3 – Nanoparticle Distribution, Toxicity and Methods

Nanoenabled smart and innovative products and processes have created a tremendous growth potential for a number of industry sectors. At the same time, many questions have been raised relating to the potential impact on human health and on the environment of these materials. The real concern is the lack of systematic characterization and standardization development of these nanomaterials. In vitro toxicity measurements are a popular and effective starting tool to understanding the cytotoxicity of nanomaterials. It is likely that monitoring toxic response of cellular model systems to nanoparticle exposure will provide the first step in monitoring the toxicity of these novel materials, as well as for further risk assessment. An AFM-based approach to investigate therapeutic compound induced ion channel effect in spontaneous beating cardiomyocytes is developed for prescreening drug development and serves as a cellular system for nanosafety studies. Complementary toxicity screening of a series of nanomaterials such as graphene oxide, boron nitride nanotubes and nanoparticles will be discussed using reference materials and cell assay based approaches.

## About Prof. Shan Zou:

The Zou group is focused on nanostructure design and nanophotonics for biosensing and cancer cell surface marker detection; self-assembly and supramolecular interactions; biophysics of membrane and membrane-protein interactions; and single molecule force spectroscopy and cancer cell mechanics by AFM. Dr. Zou's research interests include development of integrated multimodal techniques for characterization of nanomaterials and quantitative detection of cancer cells and cellular mechanical responses to drug treatments. Recently, she is working on the reference material development of boron nitride nanotubes and cytotoxicity of nanomaterials

Dr. Zou is Research Officer and Team Leader in the Measurement Science and Standards (MSS) portfolio at the National Research Council Canada in Ottawa. She is also an Adjunct Professor in the Department of Chemistry at the University of Carleton. She serves as Secretary of the Canadian National Committee for the International Union of Pure and Applied Chemistry and she is a Member-at-large of Committee E56 on Nanotechnology, at ASTM International: an international standards organization. She earned her Ph.D from the University of Twente, the Netherlands, and BSc and M.Sc. from Jilin University, P.R. China.

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# Micro and nano-topography patterned substrates for modulation of cellular response in corneal tissue engineering applications

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Muhammad Rizwan and Evelyn Yim, University of Waterloo

Friday, November 10<sup>th</sup> at 9:55 am in Session 3 – Nanoparticle Distribution, Toxicity and Methods

Fuchs corneal endothelial dystrophy (FED) is a degenerative disease of human corneal endothelial cells (HCECs) and is a major indication for corneal transplantations. Due to donor cornea shortage, alternative treatments are needed, which relies on the successful in-vitro culture of primary human corneal endothelial cells (HCECs). One of the challenge in corneal endothelial tissue engineering is the *in vitro* proliferation of primary HCECs. Primary HCECs are highly challenging to expand in-vitro. In the *in vivo* microenvironment, cells are surrounded by various biomechanical cues, including micro- and nano-topography that influence an array of cellular behaviours. Therefore, cell culture surface could be patterned with topographical cues to potentially control cell behaviour. We patterned regular polystyrene (PS) dishes with micro and nano-topography and demonstrated that the proliferation of HCECs increased close to 3-fold, and the expression and localization of Zona Occludens-1 (ZO-1) was significantly enhanced on PS pillars. 250 nm pillars induced an optimal hexagonal morphology of HCECs. Higher amount of ZO-1 expression was maintained even when the topographic cues were removed in the successive seeding, showing that the cells could “memorize” the topography-induced cell behavior, which is beneficial for corneal cell injection therapy. In subsequent work, we developed the nanoimprinted master molds for high resolution patterning of hydrogel films. The topography patterned gelatin methacrylate hydrogel films could be used for growth and transplantation of primary human corneal endothelial monolayer. Implantation of the hydrogel films in rabbit model demonstrated that the films were biocompatible and biodegradable. In summary, we demonstrated that nano-topographies play a vital role in dictating corneal endothelial cellular responses for tissue engineering and regenerative medicine application.

About Dr. Muhammed Rizwan and Prof. Evelyn Yim:

Dr Evelyn Lim joined the Department of Chemical Engineering at the University of Waterloo in 2016. Experienced with nanofabrication technologies and stem cell culture, Evelyn and her group are interested to apply the knowledge biomaterial-stem cell interaction to direct stem cell differentiation and tissue regeneration for neural, vascular and corneal tissue engineering. Her PhD is from the Johns Hopkins School of Medicine, USA.

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# SPR and Magneto-optic-SPR-based Biosensors

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Simone Pisana and Conrad Rizal, York University

Friday, November 10<sup>th</sup> at 9:55 am in Session 3 – Nanoparticle Distribution, Toxicity and Methods

Surface plasmon resonance (SPR) and Magneto optical SPR sensors created as heterostructure multilayer thin films have generated significant interest in recent years due to their ability to tune and enhance SPR. MO-SPR sensors show several advantages over conventional SPR sensors, including the possibility of probing highly dilute samples due to the large signal to noise ratio (SNR) and improved sensitivity.

In this work we aim to address three aspects of MO-SPR sensors. First, we focus on the theory of SPR and MO-SPR effects in multilayered materials. We discuss the conditions necessary to excite plasmon resonance and induce magneto-optic enhancement, compare these with conventional SPR sensors, and discuss the ways in which the sensitivity of the sensor can be enhanced.

Secondly, we focus on the optimization of the sensor using simulations based on the transfer matrix method. The configurations under consideration consist of plasmonic active, high refractory, soft-ferromagnetic, and diamagnetic materials. The multilayer structures serve as sensing layers due to their excellent magneto-optic and surface plasmon properties. The simulation results demonstrate that the inclusion of refractory, and ferromagnetic materials into a surface plasmon resonance sensor yields higher sensitivity and SNR.

Thirdly, this work explores the proof-of-concept device performance based on the optimization of the above configuration using a simple magneto-optical set-up. This MO-SPR sensor promises to be a compact device that can be used as a portable biosensor.

## About Prof. Simone Pisana:

Dr. Simone Pisana received his undergraduate education at the University of Toronto and received his PhD degree at the University of Cambridge in 2008. He then joined Hitachi Global Storage Technologies as Research Staff Member working on nanoscale magnetic field sensing devices and energy-assisted magnetic recording technologies. Dr. Pisana joined the Department of Electrical Engineering and Computer Science at York University in 2014 as Associate Professor. His research explores transport phenomena in nanoscale devices & materials for energy efficient nanoelectronic device engineering. He is Senior Member of the IEEE, and has authored 40 refereed journal articles, over 60 conference contributions and 8 patents.

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## Characterizing Nano-Biomaterials Interfaces: Correlative Microscopies for Bone Applications

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Kathryn Grandfield, McMaster University

Friday, November 10<sup>th</sup> at 1:30 pm in Session 3 – Nanoparticle Distribution, Toxicity and Methods

The lack of bonding at bone-implant interfaces causes the failure of up to 10% of orthopaedic and dental implants. This prompts us to question, what is happening at the bone-implant interface and how can we better design materials for this application? The influence of nanotechnology has prompted the development of nano-biomaterials surfaces for bone bonding applications. However, we still require a suitable method to investigate these interfaces to natural bone tissue with sufficient resolution. We are probing the interaction of titanium implants with human bone using a wide range of three-dimensional imaging techniques, ranging from X-ray tomography to on-axis scanning transmission electron tomography, to reveal bone structure at implant interfaces over multi-length scales. Mechanisms of biomineralization and bone ultrastructure are also explored. Elemental information as the “fourth-dimension” is added with the exploration of EELS-tomography and atom probe tomography of bone-implant interfaces. The advantages of using correlative microscopies to probe nano-biomaterials at multi-length scales will be highlighted.

### About Prof. Kathryn Grandfield:

Dr. Kathryn Grandfield is an Assistant Professor in the Department of Materials Science & Engineering and School of Biomedical Engineering at McMaster University. She is presently second Vice-President of the Microscopical Society of Canada, elected board member for the Canadian Biomaterials Society, and Director of User Operations at the Canadian Centre for Electron Microscopy. Dr. Grandfield is the 2017 recipient of the Petro Canada - McMaster University Young Innovator Award.

## Self-Assembly of Gold Nanoparticles Driven by Iron and Iron-Containing Proteins

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Hendrick W. de Haan, University of Ontario Institute of Technology

Friday, November 10<sup>th</sup> at 1:30 pm in Session 3 – Nanoparticle Distribution, Toxicity and Methods

The ability to form complex 3D architectures using nanoparticles (NPs) as building blocks remains a challenging objective within nanotechnology. In this talk I will present results a joint computational-experimental study that explores forming coordination-driven assemblies in a novel way by using iron ions to associate ligand-coated nanoparticles suspended in water. A multi-scale simulation approach to model the dynamics of the self-assembly will be introduced and described. Results from the

simulations will be shown to agree well with experiments in terms of cluster morphology. Details from the simulations give insight into the kinetics at short times and the mean growth rate at long times. As an extension of this mechanism of self-assembly, results from simulations and experiments that use iron-containing haemoglobin as the “glue” instead of iron ions will also be presented. These results suggest new methods for the generation of nanomaterials and also have applications to human-health related issues such as the detection and concentration determination of metals within drinking water and also determining haemoglobin levels within blood as related to conditions such as anemia.

#### About Prof. Hendrick W. de Haan:

Hendrick W. de Haan received his PhD from the University of Guelph in 2007. He then worked as Postdoctoral Fellow at the University of Ottawa before joining the University of Ontario Institute of Technology as an associate professor in 2013. His research employs many different computational methodologies and approaches to model and simulate biophysical systems – often with a focus on nanotechnology applications. Current projects center on devising nanopore-based nanofluidic devices to filter polymers such as DNA, studying the self-assembly of red blood cells into stacks via depletion forces, modeling the collective motion of “twitcher” bacterial cells on surfaces, and performing atomistic and coarse-grained simulations of PhytoSpherix particles which are biocompatible nanoparticles derived from sweet corn.

## Needle-free nanomedicines – an overview of research, technologies and translation to the clinic

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Marianna Foldvari, University of Waterloo

Friday, November 10th at 2:00 pm in Session 4 – Nanomedicine Researcher Awards

Nanomedicine is a recent term, used to define the medical applications of nanotechnology. One of the most important fields in nanomedicine is ‘drug delivery’. In particular, the development of safe and effective delivery systems for non-invasive administration is becoming increasingly important for both local and systemic treatments. The discussion will focus on some recent designs of needle-free technologies that provide specific advantages in drug delivery. An overview of nanoscale delivery technologies from our laboratory, such as liposomes, biphasic vesicles, gemini nanoparticles and carbon nanotubes as intelligent carriers for topically active compounds, including proteins and nucleic acids, and their applications, will be presented. The development of these technologies and their impact in dermatology, ophthalmology, regenerative medicine and infectious diseases will be discussed.

#### About Prof. Marianna Foldvari:

Dr. Marianna Foldvari is a Professor of Pharmaceutical Sciences at the University of Waterloo’s School of Pharmacy in Canada. Dr. Foldvari received a BSc in Pharmacy and a Doctorate in Pharmaceutical Sciences, specializing in Pharmacognosy and Microbiology, both from Semmelweis Medical University in Budapest, Hungary and a PhD in Pharmaceutical Sciences from the College of Pharmacy at Dalhousie University in the area of targeted liposomal drug delivery systems in 1988. Between 1989-2006 she was a Faculty member at the

College of Pharmacy and Nutrition, University of Saskatchewan. She held the Tier 1 Canada Research Chair in Bionanotechnology and Nanomedicine from 2007-2014.

Dr. Foldvari is an internationally recognized expert in nanomedicine. Her research program is focusing on pharmaceutical nanotechnology, non-invasive drug, protein and gene delivery system design (such as dermal, transdermal, transmucosal, ocular and intrapulmonary) for regenerative medicine in dermatology, ophthalmology and immunology.

She currently serves as Editorial Board Member of the Journal of Controlled Release (IF:8.4), Associate Editor for Frontiers in Neuroscience, OA Drug Design and Delivery and for the past ten years served as Associate Editor for Nanomedicine (2006-2016): NBM (IF: 6.9). Dr Foldvari serves as a grant reviewer on CIHR, NSERC, CFI and NIH panels and the Bill and Melinda Gates Foundation Global Health Initiatives review board. Dr Foldvari is one of the Founding Directors of the American Society for Nanomedicine (ASNM) and the International Society of Nanomedicine (ISNM). She served as Board Member for Genome Prairie and was a Member of the Advisory Committee to the Prime Minister on Science and Technology and a Founder of the Canadian Society of Pharmaceutical Sciences (CSPS). She has received the YWCA Women of Distinction Award, the Saskatchewan Top 25 Science Achievement Award and the Sabex Award of Innovation.

## Exploring Tunable Nanoscale Metal Complexes Through Ligand Design

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Jaclyn Brusso, University of Ottawa

Friday, November 10<sup>th</sup> at 3:00 pm in Session 4 – Nanomedicine Researcher Awards

Molecular nanomagnets, which embody a class of materials that exhibit magnet-like behaviour at the molecular level, represent ideal candidates for next generation high-density memory storage owing in large part to their nanoscale dimensions. In particular, each individual molecule within the molecular nanomagnet acts as a single-domain magnetic particle with bistability. As such, these systems enable a bottom-up approach to overcome the problems faced by Moore's law – the observation that the number of transistors in a dense integrated circuit doubles approximately every two years – and may provide a real solution to societies ever-growing demand for energy and data storage. Our approach to these highly sought-after systems focuses on the design of multidentate, non-innocent ligands and explores their use in the development of tunable nanoscale metal complexes in order to tap into their magnetic properties, and ultimately implement them into molecular and nano-electronic devices. This presentation will focus on heterocyclic  $\pi$ -conjugated materials currently being pursued in our lab as ligands in the development of multimetallic complexes, and the effect of their supramolecular self-assembly on their transport properties.

### About Prof. Jaclyn Brusso:

Since joining the University of Ottawa in 2010, Dr. Jaclyn Brusso has successfully established a research program focused on addressing key challenges in the development of smaller, lighter, cheaper and more efficient optical, magnetic and electronic materials. Through design and development of finely tuned new organic systems she is achieving an exquisite understanding and control of the self-assembly process at the nanoscale. Her research extends to include tunable nanoscale metal complexes utilizing conjugated organic semiconductors and radical based materials as non-innocent ligands capable of controlling their magnetic and conductive properties, essential for the nano- electronic devices of the future.

Jaclyn Brusso works to raise the profile of materials chemistry at the University of Ottawa through her success as an early researcher (such as Ontario Early Researcher Award, France Canada Research Fund and CNC-IUPAC Award) and as a founding member of uOttawa's Centre for Advanced Materials Research and part of the CFI teams that raised over \$25M. Jaclyn Brusso shows her leadership within the scientific community by dedicating time and effort to community and youth outreach activities (e.g., Women in STEM, Science Rendezvous, PopChem). Jaclyn is a rising star with an exceptional aptitude for innovation and academic leadership.

## Nanostructured Biosensor for Detecting Glucose in Tear by Applying Fluorescence Resonance Energy Transfer Quenching Mechanism

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Jin Zhang, Western University

Friday, November 10<sup>th</sup> at 3:00 pm in Session 4 – Nanomedicine Researcher Awards

Blood is often used in clinic to trace certain constituents to diagnose related diseases. To date, people with diabetes have to prick their fingers 4~8 times a day, over 2000 times a year, to check blood glucose level for management of this chronic disease. The test is uncomfortable and expensive. Furthermore, it is noted by an amount of infections reports caused by these blood glucose sensors. Consequently, development of non-invasive device for glucose monitoring is strongly requested. It has been spent several decades to verify that there is a correlation between tear and blood glucose levels. However, the challenges lie in quickly collecting tear samples and monitoring the low concentration of glucose in tear. This talk is focusing on the protein-incorporated hetero-nanostructures used as a biosensor to detect glucose in tear. Fluorescence resonance energy transfer (FRET) quenching mechanism is applied in developing the biosensor device. In the presence of glucose, the fluorescence intensity is restored. The photoluminescence intensity of the FRET sensor increases linearly with increasing concentration of glucose from 0.03 mmol/L to 3 mmol/L, which covers the range of tear glucose levels for both diabetics and healthy subjects. Meanwhile, the calibrated values of pixel intensities of the fluorescence images captured by a handheld fluorescence microscope increases with increasing glucose. Sprague-Dawley rats with different blood glucose concentrations were utilized to demonstrate the quick response of the FRET sensor to 2  $\mu$ L of tear samples.

### About Prof. Jin Zhang:

Dr. Jin Zhang is an Associate Professor with the Department of Chemical and Biochemical Engineering, Western University, Canada. Dr. Zhang's research activities are related to the development of new biocompatible nanocomposites with enhanced magnetic, optical, electric, and mechanical properties. Her expertise lies in the interface between multifunctional nanostructures and biological systems. Currently, the Zhang group's research themes include (1) design and development of multifunctional nanocomposites through chemical and laser-assisted processes; (2) nanosystems for theranostics by combining therapeutics and diagnosis; and (3) nanostructured biosensors.

In 2014, Dr. Zhang was rewarded the Early Research Award of Ontario. She was recently recognized as the Grand Challenges Canada- Canadian Rising Stars in Global Health for her research work on "Non-invasive

Diagnostic Tool for Diabetes". The device of non-invasive glucose sensor for diabetes invented by Jin Zhang has been successfully tested on animal model, and is moving forward for the clinical trial. Her research work was reported by the worldwide media, including the Discovery Channel, CTV, the Institute of Nanotechnology (IoN), and Nanotechnology Now, etc. In addition, Jin Zhang is an Associate Editor of the International Journal of Nano and Biomaterials. She has/had served as a guest editor for different journals, e.g. Journal of Nanomaterials.

## **Poster Abstracts:**

### Targeted Genetic Therapeutic Delivery to Glioblastoma Stem Cells

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Ellie Arnold<sup>1</sup>, Elise Malek-Adamian<sup>2</sup>, Phuong Le<sup>2</sup>, Masad J. Damha<sup>2</sup>, Kevin Petrecca<sup>2</sup>, and Molly Shoichet<sup>1</sup>

<sup>1</sup>University of Toronto

<sup>2</sup>McGill University

Glioblastoma stem cells are a major therapeutic challenge due to their invasion into surrounding brain tissue, resistance to chemotherapeutics, and capacity to re-initiate the glioblastoma following treatment<sup>1</sup>. The DRR gene has been identified as a driver of glioblastoma stem cells, and particularly involved in their invasive nature.<sup>2</sup> Antisense oligonucleotides (AONs) are potent genetic therapeutics that can be engineered to target proteins responsible for cancer cell characteristics. Damha and coworkers have synthesized AONs against DRR that include fluoro groups in the oligonucleotide chain. These modifications increase the intracellular half-life and therefore the duration of potency of the resulting AONs.<sup>3</sup> In this work, antibody-antisense oligonucleotide conjugates have been engineered to target glioblastoma stem cells through surface markers including CD44 and EphA2 and deliver an antisense oligonucleotide against DRR. We demonstrate successful internalization, accumulation, and DRR gene knockdown of antibody-antisense oligonucleotide conjugates in primary human glioblastoma stem cells. This represents the first example of antibody-antisense therapeutics against cancer stem cells. Future work will include in vivo studies in mice models of glioblastoma.

(1) Singh, S. K.; Hawkins, C.; Clarke, I. D.; Squire, J. A.; Bayani, J.; Hide, T.; Henkelman, R. M.; Cusimano, M. D.; Dirks, P. B. Identification of Human Brain Tumour Initiating Cells. *Nature* **2004**, *432*, 396–401.

(2) Dudley, A.; Sater, M.; Le, P. U.; Trinh, G.; Sadr, M. S.; Bergeron, J.; Deleavey, G. F.; Bedell, B.; Damha, M. J.; Petrecca, K. DRR Regulates AKT Activation to Drive Brain Cancer Invasion. *Oncogene* **2014**, *33*, 4952–4960.

(3) Deleavey, G. F.; Damha, M. J. Designing Chemically Modified Oligonucleotides for Targeted Gene Silencing. *Chem. Biol.* **2012**, *19*, 937–954.

Ellie is a PhD Student in the Shoichet lab at the University of Toronto, with a BSc in Chemistry from the University of Prince Edward Island. Her background is in synthetic chemistry, and she is currently developing a system to deliver antisense therapeutics to glioblastoma stem cells. She is passionate about finding ways to apply her chemistry background to biological problems and making a difference in the treatment of glioblastoma.

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# EGFR targeting Auger-electron emitting gold nanoparticles for treatment of small metastases from triple-negative breast cancer

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Zhongli Cai<sup>1</sup>, Priscilla Lai<sup>1</sup>, Simmyung Yook<sup>1,2</sup>, Yijie Lu<sup>3</sup>, Deborah A. Scollard<sup>4</sup>, Mitchell A. Winnik<sup>3</sup>, Jean-Philippe Pignol<sup>5</sup>, Raymond M. Reilly<sup>1,6,7</sup>

<sup>1</sup>Department of Pharmaceutical Sciences, University of Toronto, Toronto, Ontario, Canada

<sup>2</sup>College of Pharmacy, Keimyung University, Daegu, Republic of Korea

<sup>3</sup>Department of Chemistry, University of Toronto, Toronto, Ontario, Canada

<sup>4</sup>STTARR Innovation Centre, University Health Network, Toronto, Ontario, Canada

<sup>5</sup>Department of Radiation Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands

<sup>6</sup>Department of Medical Imaging, University of Toronto, Toronto, Ontario, Canada

<sup>7</sup>Toronto General Research Institute and Joint Department of Medical Imaging, University Health Network, Toronto, Ontario, Canada

Our objective was to develop a novel radiation nanomedicine for the treatment of small metastases of triple negative breast cancer (TNBC). AuNP were conjugated to lipoic acid (LA)-PEG-DOTA-<sup>111</sup>In or LA-PEG-panitumumab (PmAb). Stealth properties were assessed by changes in AuNP size measured by dynamic light scattering before and after incubation with mouse plasma. The effect of AuNP size, the amount of LA-PEG-DOTA and LA-PEG-PmAb reacted with AuNP on stealth properties were studied. The uptake of PmAb-AuNP-<sup>111</sup>In by BC cells with different EGFR density was measured by darkfield and fluorescence microscopy. The cytotoxicity of PmAb-AuNP-<sup>111</sup>In in vitro on MDA-MB-231/Luc BC cells was determined by clonogenic and  $\gamma$ -H2AX assays. Targeting of PmAb-AuNP-<sup>111</sup>In to MDA-MB-231/Luc lung metastases in nude mice was studied by microSPECT/CT, bioluminescence imaging and biodistribution studies. The smallest change in size (1 nm) after incubation with mouse plasma was demonstrated for 30 nm AuNP conjugating with 0.05  $\mu$ g LA-PEG-DOTA and 28.6  $\mu$ g LA-PEG-PmAb per cm<sup>2</sup> AuNP surface area, which was chosen for further evaluation. Binding and internalization of PmAb-AuNP-<sup>111</sup>In into EGFR-positive cells, but not EGFR-negative cells. PmAb-AuNP-<sup>111</sup>In caused 2-fold more DNA DSBs in MDA-MB-231/Luc cells and was significantly more effective in decreasing the survival than AuNP-<sup>111</sup>In or PmAb-AuNP. MicroSPECT/CT images showed more numerous foci of uptake in the lungs of mice at 3 hpi of *Auger-gold* than AuNP-<sup>111</sup>In. Biodistribution studies revealed 3-fold significantly greater lung uptake of *Auger-gold* than AuNP-<sup>111</sup>In at 24 hpi. PmAb-AuNP-<sup>111</sup>In is a promising radiation nanomedicine for treatment of small lung metastases from EGFR-positive TNBC.

Zhongli Cai is a radiobiologist and a radiation chemist. She received a B.Sc. degree in Applied Chemistry, a M.Sc. degree in Radiation Chemistry and a Ph.D. degree in Radiochemistry from Peking University, China and a PhD degree in Radiobiology from the Université de Sherbrooke, Quebec. She is studying <sup>111</sup>In-labeled and HER2 or EGFR-targeted gold nanoparticles for radiotherapy of breast cancer as well as the radiation dosimetry of targeted radiotherapeutics for cancer.



# Highly-Ordered Porphyrin J-Aggregate Assemblies in Lipid Membranes for Theranostic Nanomedicine

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Danielle M Charron<sup>1,2</sup>, Richard Liu<sup>1,3</sup>, Juan Chen<sup>1</sup>, Gang Zheng<sup>1,2,4,\*</sup>

<sup>1</sup> Princess Margaret Cancer Centre, University Health Network

<sup>2</sup> Institute of Biomaterials and Biomedical Engineering, University of Toronto

<sup>3</sup> Faculty of Science, McGill University

<sup>4</sup> Department of Medical Biophysics, University of Toronto

Corresponding author: gzheng@uhnresearch.ca, <http://zhenglab.utoronto.ca>

Porphyrins are a class of dyes that include the natural pigments heme and chlorophyll. Because of their endogenous origin and strong absorption within the visible and near-infrared region, porphyrins have been extensively studied as medical agents for phototherapy and optical imaging. We have expanded these applications by building highly-ordered porphyrin J-aggregate assemblies within the membrane of lipid nanomedicines. J-aggregation is a form of exciton coupling that relies on head-to-tail nanoscale organization of porphyrins, resulting in a strongly red-shifted and sharpened absorption band and similarly shifted emission. In this way, porphyrin J-aggregation encodes intact and disrupted nanomedicines with unique optical signals, which can be used to ratiometrically and responsively monitor their biological fate, or to deliver phototherapies in a structure-dependent and wavelength-selective manner. As a nanoscale phenomenon, J-aggregation is inherently sensitive to temperature and protein adsorption in biological environments. Therefore, simultaneously achieving stable porphyrin J-aggregation and responsive optical switching is a complex balancing act. Here, we investigate the influence of the host lipid environment on porphyrin J-aggregate formation and stability. We demonstrate that different porphyrin variants J-aggregate in structurally dissimilar ways, and are modulated by their environments to varying degrees. An in vivo optically-stable formulation was identified, which is now being applied for new applications in photoacoustic thermometry and combination phototherapy.

Danielle M Charron received a BAsC in Nanotechnology Engineering from the University of Waterloo in 2013. She is currently a PhD candidate in the Institute of Biomaterials and Biomedical Engineering at the University of Toronto under the supervision of Dr. Gang Zheng. Her research focuses on developing biologically-inspired photonic nanosystems for cancer theranostics. She serves as a Managing Editor for *Theranostics*.

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# Micelle Co-delivery of a Novel Endosomal Escape Peptide Modified Vitamin E Succinate and a pH sensitive prodrug of Doxorubicin Synergistically Kills Multi-Drug Resistant Breast Cancer Cells

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Petro P. Czupiel<sup>b,c,d</sup>, Vianney Delplace<sup>b,c,d</sup>, Molly Shoichet<sup>a,b,c,d</sup>,

<sup>a</sup>Department of Chemistry, University of Toronto, 80 St George Street, Toronto, ON, M5S 3H6, Canada

<sup>b</sup>Department of Chemical Engineering and Applied Chemistry, University of Toronto, 200 College Street, Toronto, ON, M5S 3E5, Canada

<sup>c</sup>Institute of Biomaterials and Biomedical Engineering, University of Toronto, 164 College Street, Toronto, ON, M5S 3G9, Canada

<sup>d</sup>Donnelly Centre, University of Toronto, 160 College Street, Toronto, ON, M5S 3E1, Canada

Severe toxicity of current chemotherapeutics and the common occurrence of multi-drug resistance (MDR) impede full cancer treatment. Doxorubicin is a broad-spectrum chemotherapeutic that frequently induces MDR in breast cancer. Vitamin E succinate is a potent cancer selective drug that inhibits MDR. Herein, we investigate the synergism of a micelle co-encapsulating a novel endosomal escape peptide-modified vitamin E succinate and a pH-sensitive prodrug of Doxorubicin in MDR breast cancer cells, EMT6/AR-1, in vitro. The endosomal escape peptide-modified vitamin E succinate exhibited cancer selective toxicity being 3.3-fold less potent in NIH/3T3, a murine fibroblast cell control, and 4-fold more potent relative to vitamin E succinate in EMT6/AR-1. The pH-sensitive prodrug of doxorubicin was synthesized through a pH-sensitive hydrazone bond with palmitic hydrazide, and when encapsulated in micelles, exhibited a pH-dependant release profile. Doubly-loaded micelles had a favourable diameter (58 nm), high total drug loadings ( $31.7 \pm 6.2$  wt%), and enhanced uptake of 1.6-fold in MDR breast cancer cells relative to singly loaded micelles. Moreover, doubly-loaded micelles synergistically lowered the total IC<sub>50</sub> against EMT6/AR-1 relative to singly-loaded micelles. Importantly, doubly-loaded micelles required 5.7-fold less of the pH-sensitive prodrug of doxorubicin and 3.2-fold less of the peptide-modified vitamin E succinate to achieve the IC<sub>50</sub>. The mechanism of synergy for doubly-loaded micelles included mitochondrial membrane depolarization, and induction of apoptosis. This work presents a micelle formulation co-encapsulating a pH-sensitive prodrug of doxorubicin and a peptide-modified vitamin E succinate that act synergistically against MDR breast cancer cells.

**Acknowledgments:** We thank Dr. Shirley Wu for generously donating the MDR EMT6/AR-1 cells. We are grateful to funding from NSERC (Discovery to MSS and CREATE in M3 scholarship to PC).

Petro P. Czupiel obtained an Honours Bachelor of Science in the biological chemistry specialist program from the University of Toronto. He continued his studies as a Ph.D. candidate at the University of Toronto studying nanoparticles and multi-drug resistant breast cancers under the supervision of Dr. Molly S. Shoichet.

# Multispectral Plasmonic Mode Localization in Width-Graded Gratings

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Moein Shayegannia<sup>1</sup>, Arthur Montazeri<sup>3</sup>, Nastaran Kazemi-Zanjani<sup>1</sup>, Katelyn Dixon<sup>1</sup>, Rajiv Prinja<sup>1</sup>, Nazir P. Kherani<sup>1,2</sup>

<sup>1</sup>Department of Electrical and Computer Engineering, University of Toronto, Toronto, Ontario, M5S 3G4, Canada

<sup>2</sup>Department of Material Science & Engineering, University of Toronto, Toronto, Ontario, M5S 3E4, Canada

<sup>3</sup>Lawrence Berkeley National Laboratory, 1 Cyclotron Rd., Berkeley, CA, 94720, USA

We describe plasmonic light localization phenomena in unique metal-insulator-metal gratings wherein the grating width is graded. Through computational modelling an understanding of the optical response of these nano-gratings is developed as a function of grating parameters including groove width, groove depth, and groove-to-groove separation. Surface plasmon polariton coupling and interaction mechanisms in these gratings conspire to produce plasmonic light trapping and waveguiding effects that result in multispectral mode-localization. Specifically, we show that plane wave illumination of the nano-gratings produces a maximally enhanced electromagnetic field at the narrowest groove situated at the center of the symmetrically graded grating. Using various fluorophores which luminesce at different wavelengths and confocal microscopy, we experimentally corroborate our theoretical findings. Fluorescence signal intensity enhancements of up to 2 orders of magnitude at various frequencies are observed at the surface of the width-graded gratings. The multispectral feature of width-graded nano-gratings enable enhanced fluorescence microscopy applications in the visible and near-infrared regions.

Katelyn Dixon is a first year M. A. Sc. student in the Department of Electrical and Computer Engineering at the University of Toronto. Her research is focused on the application of plasmonic nanogratings for SERS sensing, in particular biomarker sensing and disease detection. She recently completed her B. Sc. in physics at McMaster University and has conducted research in laser physics, flexible electronics, polymer physics, and solid-state physics.

## Stabilizing colloidal drug aggregates

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Eric Donders, Ahil N. Ganesh, Brian K. Shoichet and Molly S. Shoichet

Department of Chemical Engineering and Applied Chemistry, Institute for Biomaterials and Biomedical Engineering, Department of Chemistry, University of Toronto

Department of Pharmaceutical Chemistry, University of California – San Francisco

The authors are grateful for the funding for this project from the U.S. National Institute of General Medical Sciences (GM71896), the Natural Sciences and Engineering Research Council of Canada, and the Canadian Cancer Society.

The hydrophobicity of many small molecule drugs limits their water solubility. It has been recently discovered that ~25% of these drugs spontaneously aggregate into amorphous, nano-sized particles when their concentration exceeds the critical aggregation concentration. These colloidal drug aggregates produce false positives in drug screens by non-specifically adsorbing and sequestering enzymes. At the same time, the colloidal drug aggregates result in false negatives in cell-based assays due to reduced (if any) cell membrane penetration, leading to a lower intracellular drug concentration and subsequent loss of effectiveness.

While traditionally viewed as a nuisance, we hypothesized that colloidal drug aggregates could be useful as vehicles for drug delivery due to their drug-rich composition and small size. In particle-based formulations, the surface of the particle impacts how it behaves in a physiological environment and ultimately its biological fate. Therefore, we investigated the use of non-ionic surfactants to improve the stability of colloids under physiological conditions. Specifically, we found that surfactants prevent flocculation and growth of the colloids when exposed to salt solutions. The results of this work give further insight on how the physical properties of colloidal drug aggregates affect their behaviour in physiological conditions.

I am a second year MASc student in chemical and biomedical engineering, having previously completed my undergrad at Queen's in Engineering Chemistry. Previously, I have worked on nano-emulsions for automotive coating applications and drug nanocrystals for oral delivery; I have continued this theme by studying colloidal drug aggregates for cancer therapy. Coming from a mostly chemistry background, I am most excited to learn more about the complex behaviour of nanomedicines in the body, and the current and future role of nanomedicine in the clinic.

## Simulations of Self-Assembly of Gold Nanoparticles

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Christopher Drossis, Martin Magill, Michael Greenberg, Jacquelyn Egan, Dr. Olena Zenkina, Dr. Hendrick de Haan

Faculty of Science, University of Ontario Institute of Technology, Oshawa, Canada

Gold nanoparticles (NPs) are highly biocompatible, and depending on their proximity, they can change the colour of the solution they are suspended in. Because of these two properties, gold NPs can be highly useful in sensing applications. In the experiments that motivated this work, gold NPs were coated with citrate and heteroaromatic ligands, and put in a solution of either iron ions or hemoglobin, which bonds to the ligands and causes them to aggregate. Initially, simulations were coarse grained with interactions, ligands were rigidly bonded to the gold NPs and iron was modelled implicitly. These simulations were also run with hemoglobin instead of iron. Observations from those simulations allowed some simplifying assumptions to be made for simulations to run faster. Simulations could be divided into two scales, diffusion and collision. This would greatly speed up the simulations by simulating the diffusion with no interactions and only introduce interactions when collisions would occur. These simulations give an insight into the physical dynamics of the system that cannot be obtained in experiment.

Christopher Drossis obtained a Bachelor of Science in Physics with a specialization in Energy and the Environment. He is currently completing a Master's degree in Modelling and Computational Science at the University of Ontario Institute of Technology and is working in cNAB Lab under Dr. Hendrick de Haan.

## Poly(ethyl glyoxylate) nanoparticles for drug delivery

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Bo Fan<sup>1</sup> and Elizabeth Gillies<sup>1,2</sup>,

<sup>1</sup>Department of Chemical and Biochemical Engineering, <sup>2</sup>Department of Chemistry, The University of Western Ontario, London, Canada, N6G 1Z1

Stimuli-responsive polymers are one of the most pursued materials for biological and medicinal applications. However, the demand for high concentrations of stimuli and the generation of toxic

products from material degradation can create a bottleneck for many of the current stimuli-responsive polymers. To overcome these shortcomings, we have developed polyglyoxylates as a new class of stimuli-responsive materials, that can amplify stimuli by cascade polymer degradation, and the subsequent degradation products are expected to be benign species. This presentation will describe our recent development of stimuli-responsive linker end-caps that enable the conjugation of poly(ethyl glyoxylate) (PEtG) with poly(ethylene oxide) (PEO) to form amphiphilic block copolymers. These block copolymers were self-assembled to form nanoparticles in aqueous solution and these nanoparticles could be disassembled by low concentrations of stimuli. Specifically, by varying the linker end-caps it was found that PEtG-based nanoparticles could be prepared to respond to thiol reducing agents, heat, UV light, H<sub>2</sub>O<sub>2</sub>, and combinations of these stimuli. In addition, the fluorophore Nile red and the drug molecules doxorubicin and curcumin were encapsulated into these nanoparticles and could be selectively released once the stimulus was applied. We envisioned that this new system can further promote the application of stimuli-responsive polymers in the biological and medicinal fields.

Bo Fan is a Ph.D. candidate in the Gillies group at the University of Western Ontario. His research involves the synthesis of self-immolative (end-to-end depolymerizing) degradable polymers for a range of applications including intelligent degradable coatings, nanoparticles for drug delivery, and food quality sensors. Prior to beginning his PhD, he obtained a B. Eng. in Polymer Materials and Engineering at Sichuan University and an MSc in Chemistry at Western University.

## Exploiting Protein Adsorption to Stabilize Colloidal Drug Aggregates

Ahil N. Ganesh<sup>1</sup>, Christopher K. McLaughlin<sup>1</sup>, Da Duan<sup>2</sup>, Brian K. Shoichet<sup>2</sup> and Molly S. Shoichet<sup>1</sup>

<sup>1</sup>Department of Chemical Engineering and Applied Chemistry, Institute for Biomaterials and Biomedical Engineering, University of Toronto

<sup>2</sup>Department of Pharmaceutical Chemistry, University of California – San Francisco

The formation of colloidal aggregates by hydrophobic small molecule drugs is the major contributor of false hits during high-throughput drug screening<sup>1</sup>. Protein adsorption to the colloid surface leads to non-specific enzyme inhibition and false-positives in drug screening. While colloids are typically viewed as nuisance artefacts, their drug-rich composition makes them attractive as intentional formulations. However, the transient stability of colloidal aggregates limits their utility. In this study, we exploited the ability of colloidal aggregates to adsorb proteins to stabilize them for applications in drug delivery<sup>2</sup>. The formation of a protein corona reduced colloid size in a concentration-dependent manner. Protein coronas improved colloid stability over 48 h in both buffered saline and serum-containing media. Protein coronas composed of the targeting antibody, trastuzumab, could induce selective uptake by HER2-overexpressing cells but not by cells that have low expression of HER2. Colloids stabilized by a generic IgG were not internalized by either cell type. With these stabilized formulations, further investigation of how the properties of colloidal drug aggregates impact their biological fate is possible.

The authors are grateful for the funding provided by the U.S. National Institute of General Medical Sciences (GM71896), the Natural Sciences and Engineering Research Council of Canada and the Canadian Cancer Society.

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Ahil Ganesh is currently a PhD candidate in Chemical and Biomedical Engineering in the lab of Prof. Molly Shoichet at the University of Toronto. His research interests are in the areas of nanotechnology, drug delivery and tissue engineering. He completed his undergraduate degree at the University of Toronto in Engineering Science with a focus on biomedical engineering.

## Two-Pronged Biomimetic Approach to Create Porphyrin Aggregation-Induced Nanoassembly for Spectrally-Modulated Phototheranostics

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Kara M. Harmatys<sup>1</sup>, Juan Chen<sup>1</sup>, Danielle M. Charron<sup>1,2</sup>, Christina M. MacLaughlin<sup>1</sup>, Gang Zheng<sup>1-3</sup>

<sup>1</sup>Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario M5G 1L7, Canada; <sup>2</sup>Institute of Biomaterials and Biomedical Engineering, University of Toronto;

<sup>3</sup>Department of Medical Biophysics, University of Toronto, Toronto, Ontario M5G 1L7, Canada

Chlorosomes are ~100 nm sized supramolecular structures extracted from green sulfur bacteria, which contain >250 000 bacteriochlorophyll porphyrin dyes that can self-assemble absent protein via noncovalent interactions. They are efficient light-harvesting systems with photonic properties capable of spectral modulation depending on the dye-aggregation state; this phenomenon can be exploited for cancer imaging and phototherapy. Presently, this chlorosome biomimetic system has not yet been explored in the field of cancer nanomedicine, due to its hydrophobicity. To overcome this challenge, the Zheng lab has synthesized chemically-stable zinc chlorin porphyrin analogs intended for reconstitution in a lipoprotein scaffold. Lipoproteins contain a hydrophobic core used for lipid transport in the blood; we intend to use the core of this biomimetic nanoparticle as a stable center for dye self-assembly. When the lipoprotein is intact, dye fluorescence is quenched and the Qy band absorbance shifts from 653 nm to 715 nm, which is an ideal wavelength for photoacoustic imaging or photothermal therapy. The lipoprotein has inherent tumor-targeting capabilities, which results in structure and subsequent dye dissociation enabling restored fluorescence (660 nm). This is ideal for fluorescence monitoring and has the capability for photodynamic therapy using the monomeric porphyrin photosensitizer. Overall, depending on the state of dye-aggregation, these nanostructures can be useful for phototheranostics in cancer nanomedicine.

Kara M. Harmatys received her B.S. in Chemistry and Biochemistry from Lewis University in 2010. She completed her Ph.D. in 2015 under the supervision of Professor Bradley D. Smith from the University of Notre Dame. Her dissertation work focused on enhanced cell death fluorescence imaging using targeted small molecules. Currently, she is a postdoctoral research fellow in the Gang Zheng lab at the Princess Margaret Cancer Centre (PMCC). Her research interests include two major projects: (1) prostate-specific membrane antigen (PSMA)-targeted porphyrins for photodynamic therapy and (2) biomimetic self-assembled porphyrin nanoparticles for imaging and therapeutic applications.



# Functionalization of Polymer Vesicles with Glycopolymer Arms

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Josh J. Jadischke,<sup>1</sup> Brooke M. Raycraft,<sup>1</sup> John F. Trant,<sup>2</sup> Greg Whitton,<sup>1</sup> Elizabeth R. Gillies<sup>\*1,3</sup>.

<sup>1</sup>Department of Chemistry, <sup>3</sup>Department of Chemical and Biochemical Engineering, The University of Western Ontario, London, Canada, N6G 1Z1. <sup>2</sup>Department of Chemistry, The University of Windsor, Windsor, Canada, N9B 3P4.

Carbohydrates are involved in many important biological processes from cellular communication to viral and bacterial infection. As individual carbohydrate-based recognition events are weak, nature uses multiple simultaneous interactions to initiate biological events. These multivalent recognition events can potentially be mimicked or intercepted by nanomaterials presenting multiple carbohydrates. We have previously achieved this with dendrimer-functionalized nanomaterials such as micelles and vesicles. However, these may not provide optimal binding due to their limited flexibility. To improve the binding, we have explored the functionalization of vesicles with linear polysaccharide arms. Azide-functionalized polybutadiene-*b*-poly(ethylene oxide) (PBD-PEO) vesicles were prepared and conjugated with a linear polymer of  $\beta$ -galactose. Both the length and surface density of the pendant glycopolymer chains were varied to explore their effects on binding to a complementary carbohydrate-binding protein (lectin).

Josh is currently a candidate for an MSc in Organic Chemistry with the Gillies group at Western University. He received his BSc from Western University in Chemistry. Previously he held an undergraduate research position jointly supervised by Dr. Beth Gillies and Dr. Paul Ragogna at Western University. His chemistry experience is in nanocarriers, dendrimer synthesis, and polymers.

## DNA translocation through a nanopore under nanoscale pre-confinement

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Konstantinos Kastritis<sup>1</sup>, Martin Magill<sup>1</sup>, Kyle Briggs<sup>2</sup>, Vincent Tabard-Cossa<sup>2</sup>, Hendrick W. de Haan<sup>1</sup>

<sup>1</sup>Faculty of Science, University of Ontario Institute of Technology, Oshawa, ON, Canada

<sup>2</sup>Department of Physics, University of Ottawa, Ottawa, ON, Canada

Nanopores are nanoscale structures with a wide variety of native biological uses and promising scientific and technological applications. Solid-state nanopores allow for exploring the manipulation of single molecules and polymers. These pores are nanometric holes in thin membranes. An electric potential difference across the system then drives polymers through the membrane. However, the passage of molecules through the pore introduces a significant amount of variation in translocation times due to the conformational entropy of the molecule.

To reduce this variation we use a thin nanoporous silicon nitride membrane placed within molecular reach of a nanopore. Simulations were used to study the system and provide insight on the dynamics. The simulations were conducted using coarse-grained Langevin dynamics.

The experimental results demonstrate that the presence of the nanofilter minimizes variability during the translocation process. This effect is demonstrated as a global minimum in the coefficient of variation of translocation times. The simulations were able to recover the global minimum in the coefficient of variation and provide insight into the dynamics. We confirmed through simulations that the mechanism behind the reduction in variability was the elongation of the polymer. The nanofilter provides a way of reducing the conformational entropy of the molecule at the onset of translocation.



In addition the nanofilter increases the stability of the process as it eliminates the dependence of translocation on pore size (which help increase the variability due to fluctuations). This gives us cheaper access to reliable solid state nanopores.

Konstantinos Kastritis completed his B.Sc. in Physics at the University of Ontario Institute of Technology (UOIT). Since May 2016 he has been an M.Sc. candidate at UOIT in the Computational Nano-Biophysics Lab studying polymer physics and working on nanopore translocation under the supervision of Hendrick W. de Haan.

## Probing Prostate Cancer-Derived Extracellular Vesicles using Surface-Enhanced Raman Spectroscopy

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Kaufman, L. H.<sup>1</sup>; Lagugné-Labarthet, F.<sup>1\*</sup>; Dayarathna, T.<sup>2</sup>; Leong, H. S.<sup>2</sup>.

<sup>1</sup>Department of Chemistry, The University of Western Ontario, London, ON.

<sup>2</sup>Lawson Health Research Institute, St. Joseph's Health Care, London, ON

Extracellular vesicles (EVs), released by nearly all cell types within the human and animal body have been found to play diverse roles throughout the body. EVs may be classified into groups based on size. The size distribution ranging between 40 – 100 nm may be classified into a group known as 'exosomes'. Lacking all cellular machinery, these nano-sized biological exosomes carry functional proteins, DNA and RNA from their parent cells, providing direct insight into the biomarkers of healthy and cancerous cells. These small vesicles have attracted considerable attention over the past few decades, and have been found to play diverse roles in the human body including cell-to-cell communication, apoptosis and tissue repair. Since exosomes may be found *in vivo* in blood and urine samples, characterization of the chemical and physical compositions of exosomes holds extreme potential in developing less invasive cancer detection and treatment methods, in movement towards needle-core liquid biopsies.

We propose use of lithographic techniques to generate platforms capable of generating surface-enhanced Raman spectra (SERS). Probing exosomes onto these surfaces will allow for the generation of SERS spectra of individual exosomes, providing insight into individual spectroscopic signatures for classification, comparison and differentiation of biomolecular diversity. This research holds potential applications in cancer detection, diagnosis and point-of-care technologies.

Lauren Kaufman comes from Mississauga, Ontario where she attended The University of Toronto Mississauga. She graduated with an H.B.Sc in Biology and Chemistry in 2015. Lauren took on an exciting role during a gap-year in 2015-2016 within the Ontario Institute for Cancer Research, Drug Discovery Program. This position further nourished her interests in analytical chemistry. Lauren joined the FLL lab at the University of Western Ontario in September 2016 as a Masters student. Her research focuses on the development of plasmonic nanostructures for studies of biological extracellular vesicles.

# Molecular Dynamics Simulations of Glucose-based Carbohydrate Nanoparticles

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Mohammad Hassan Khatami, Hendrick W. de Haan

Faculty of Science, University of Ontario Institute of Technology, Oshawa, ON, Canada

PhytoSpherix™ is a dendritic, biodegradable carbohydrate-based nanoparticle, produced by Mirexus Biotechnologies from sweet corn. This particle consists of roughly 22,000 glucose units, with an overall experimental radius of ~17 to 35 nm (depending on the technique), which acts as an energy storage unit in plants. They are highly mono-dispersed particles and great water absorbents, which make them candidate as an additive to skin creams. Despite the extensive experimental studies, the detailed structure of this particle is unknown yet.

In this work, we employ large-scale molecular dynamics simulations to construct energetically feasible structures of Phytospherix-like particles in atomistic details. Here, we start with a simple glucose-chain structure as the initial base of our particle. Then, we solvate the system with explicit water molecules and conduct MD simulations using the GROMACS package. After the production run, we feed the simulated carbohydrate structure as an input to our home-made C++ code to grow the particle. In this step, the code adds glucose units to the ends of each branch and/or start new branches, based on our algorithm. Then, we solvate the new particle and simulate the system. We have implemented the first few cycles and built up to ~ 1000 glucose unit particle, where the simulation box contains more than 2 million atoms. Besides investigating the structure of PhytoSpherix-like particles, the goal of our project is to investigate growth mechanisms by which our particles could encapsulate, protect and deliver molecules of interest, e.g., release therapeutic drugs only at the location of the tumor.

Dr. Mohammad Hassan Khatami got his PhD in Physics from Memorial University of Newfoundland, where he conducted MD simulations of membrane-active proteins in lipid bilayers. He is now a Post-doctoral researcher under SOSCIP-TalentEdge Post-doctoral Fellowship Program at University of Ontario Institute of Technology. He is working under supervision of Dr. Hendrick W. de Haan on “Large Scale Atomistic Molecular Dynamics Simulations of Phytospherix™ Nanoparticles”.

## In vivo evaluation of treatment efficacy and toxicity from <sup>177</sup>Lu labeled gold nanoparticle incorporated into a nanoparticle depot

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\*Priscilla Lai <sup>1</sup>, Zhongli Cai <sup>2</sup>, Jean-Philippe Pignol <sup>3</sup>, David A. Jaffray <sup>1</sup>, Raymond M. Reilly <sup>2</sup>

<sup>1</sup> Department of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

<sup>2</sup> Department of Pharmaceutical Sciences, University of Toronto, Toronto, Ontario, Canada

<sup>3</sup> Department of Radiation Oncology, Erasmus MC, Rotterdam, The Netherlands

We previously reported the design of a nanoparticle depot (NPD) into which radiolabeled AuNP can be incorporated and released locally following implantation using permanent brachytherapy techniques. The current work evaluates the efficacy and toxicity of the NPD based treatment using <sup>177</sup>Lu-AuNP NPD implanted into two different breast cancer xenograft models. MDA-MB-468 and MDA-MB-231 tumors xenografts were established in female NOD/SCID mice. Three treatment groups were used (n=21); (1) PEGylated AuNP NPD, (2) <sup>177</sup>Lu-AuNP NPD, and (3) untreated

control. Tumor growth inhibition, body weight index, blood toxicity, serum Cr and ALT were measured, and organs were collected for biodistribution. Treatment with  $^{177}\text{Lu}$ -AuNP NPD resulted in tumor growth delay as compared to the tumors treated with PEGylated AuNP NPD and untreated controls. For MDA-MB-231 tumors, the delay in growth was approximately 3 days at 14 days post implantation (p.i.). MDA-MB-468 tumors had minimal regrowth of the tumor up to 78 days. There were no differences in body weight between treated and control groups for both xenograft models. The absence of toxicity was confirmed in hematology, kidney and liver function results, for mice bearing MDA-MB-231 xenografts. The biodistribution studies revealed that the majority of the radioactivity remained in the tumor up to 15 days p.i. of the NPD, with only minimal redistribution to other organs 1 day p.i.. The study demonstrates that radiation doses delivered are enough to result in a tumoricidal effect with no toxicities to other normal tissues, although the extent of response to treatment is dependent on breast cancer type.

Priscilla Lai completed her B.Sc. at McMaster University in Medical and Health Physics, and began her Ph.D. studies in 2012 in Medical Biophysics at University of Toronto. Prior to commencing her graduate studies, Priscilla conducted research in the area of microbubble mediated radiosensitization for breast cancer treatment. Currently, she is developing a novel unsealed source that incorporates radiolabeled gold nanoparticles for radiotherapy of breast cancer which can be implanted using existing permanent brachytherapy techniques. She is a recipient of the Ontario Graduate Scholarship, the Natural Sciences and Engineering Research Council award, and Geoff Lockwood and Kevin Graham Medical Biophysics Graduate Award.

## Specific and Direct Amplified Detection of MicroRNA with MicroRNA:Argonaute-2 Cleavage (miRACle) Beacons.

Luby, Benjamin M<sup>1,2</sup> and Zheng, Gang<sup>1,2,3</sup>

1 Princess Margaret Cancer Centre and Techna Institute, University Health Network, 101 College St., Toronto, ON, Canada.

2 Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada.

3 Department of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada.

Molecular beacons are elegant nanoscale sensors that can transform intracellular microRNA concentration into a fluorescence intensity. While target binding enhances beacon fluorescence, the degree of enhancement is insufficient for demanding applications. The addition of specialty nucleases can enable target recycling and signal amplification, but this process complicates the assay, and renders the assay inapplicable in cells. We have developed and characterized a class of beacons that are susceptible to the endogenous nuclease Argonaute-2 (Ago2). After purification of the complex by co-immunoprecipitation, microRNA:Ago2 cleavage (miRACle) beacons undergo site- and sequence-specific cleavage, and show a 13-fold fluorescence enhancement over traditional beacons. The system can be adapted to any microRNA sequence, and can cleave nuclease-resistant, non-RNA bases, potentially allowing miRACle beacons to be designed for intracellular use as a sensor, or integrated into a nanoscale system where a RNA-dependant cleavage event is required.

Benjamin M Luby received his Honours B.Sc. in Biochemistry at McGill University in 2012. He then relocated to University of Toronto in the Institute of Biomaterials and Biomedical Engineering, under the supervision of Dr. Gang Zheng for his Ph.D. work. Ben's work focuses on RNA biology, RNA interference, fluorescence, and oligonucleotide synthesis.

# Separation of Polymer Mixtures by Length Using a Series of Nanopores Connected by Nanochannels

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Martin Magill<sup>1</sup>, Ed Waller<sup>2</sup>, and Hendrick W. de Haan<sup>1</sup>

<sup>1</sup> Faculty of Science, University of Ontario Institute of Technology, Oshawa, Canada

<sup>2</sup> Faculty of Energy Systems and Nuclear Science, University of Ontario Institute of Technology, Oshawa, Canada

The separation of polymer mixtures by chain length is an important technology for modern biological analysis, and is likely to remain an essential step in nanomedical procedures of the future. Currently, gel-based separation techniques are the gold standard for this purpose. However, these generally entail manual labour, and cannot be easily miniaturized and automated. This has motivated interest in alternative separation technologies, especially those that might be more compatible with lab-on-a-chip designs.

Synthetic nanopores are promising candidates for such a technology. These devices consist of nanoscopic holes in thin membranes, through which polymers are driven by an electric field. The mean translocation time for polymers to cross the membrane increases monotonically with chain length. This length-dependent passage time might be exploited for separation purposes.

This study uses multiscale coarse-grained simulations techniques to demonstrate the sorting of polymers by length using a series of nanopores connected by nanochannels. Furthermore, we show that this sorting can be in increasing, decreasing, or non-monotonic order of length, depending on the parameters of the system. The different possible orders of sorting arise from interplay between polymer dynamics in the nanochannels and those in the nanopores. Since shorter chains diffuse more readily than longer chains, they explore more of the nanochannel volume as they cross the system. In other words, short chains cross the nanochannels more slowly than long chains, whereas long chains cross the nanopores more slowly than short chains. This suggests a variety of potential applications.

I completed a bachelor's degree in applied mathematics at the University of Waterloo before doing a master's degree in modelling and computational science at the University of Ontario Institute of Technology (UOIT) under the joint supervision of Hendrick de Haan and Ed Waller. In my master's thesis, I studied a solid state nanofluidic device for polymer manipulation consisting of a nanocavity in a thin membrane bounded by two nanopores. I am now pursuing a PhD at UOIT. My doctoral work consists of studying a variety of nanofluidic devices using both simulations and mathematical analysis.

## Lipid-Encapsulated Gold Nanoparticles for Cell Surface Protein Detection

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Samantha McWhirter and Gilbert C. Walker

Department of Chemistry, University of Toronto

B-cell chronic lymphocytic leukemia (B-CLL) is the most prevalent hematologic malignancy in western countries. The identification of the overexpression and spatial organization of B-lymphocyte specific membrane proteins, such as cluster of differentiation 20 (CD20), can be used in the diagnosis of B-CLL. Here we present lipid-encapsulated gold nanoparticles (AuNPs) with Raman dyes that have been conjugated to anti-CD20 antibodies through polyethylene glycol (PEG) linkers. The lipid/PEG coating provides stability and prevents non-specific adsorption of the AuNPs and the narrow emission

bands of the Raman dyes provide potential for multiplexing. The gold nanoparticle core enhances the Raman signal (surface enhanced Raman scattering) and allows for visualization of the spatial organization of surface proteins with dark field microscopy. The methods used to facilitate the encapsulation of the AuNPs with lipids and bioconjugation to antibodies will be discussed. We will also demonstrate the use of the AuNPs in surface protein detection with B-lymphocytes with dark field microscopy.

Samantha is a PhD student in the Walker lab in the Chemistry department at U of T, working on lipid-encapsulated gold nanoparticles to study cell surface proteins. She received her BSc from Mount Allison University, where she studied physical properties of gold nanoparticle films with Dr. Vicki Meli.

## An SPR Lipid Biosensor to Study Binding of Amyloid- $\beta$ to Lipid Membrane

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Stephen Turnbull<sup>1</sup>, Nanqin Mei<sup>1</sup>, Brenda Yasia Lee<sup>2</sup>, Liz Drolle<sup>2</sup>, Morgan Robinson<sup>2</sup>, Zoya Leonenko<sup>1,2,3</sup>

<sup>1</sup>Department of Physics and Astronomy, <sup>2</sup>Department of Biology, <sup>3</sup>Waterloo Institute of Nanotechnology, University of Waterloo, Canada

Alzheimer's Disease (AD) is a neurodegenerative disease that primarily develops in those above 65 years of age. These AD-inflicted individuals suffer from memory loss, cognitive decay and eventually, dementia and death. Worst of all, there is no cure yet. The amyloid hypothesis (first published in Science in 1992) has provided some insight into understanding AD, suggesting that the amyloid-beta ( $A\beta$ ) peptide contributes to neural cell loss upon aggregating in the brain. However, efforts to inhibit such aggregation have proven to be futile. Recently, melatonin has been shown to play a protective role in preventing the degeneration of neural cell membranes by  $A\beta$ . Melatonin is a hormone produced by the pineal gland, which regulates the sleep cycles of the brain. It has been documented that melatonin secretion decreases in AD patients and that melatonin supplementation has neuroprotective effects against  $A\beta$ . The molecular mechanisms behind melatonin's effect on neural cell membranes and  $A\beta$  interaction are unclear, and the research aims to expand on this knowledge using a nanotechnology tool, Surface Plasma Resonance. To accomplish the research, three mimicked neuronal membrane models: healthy model, early diseased model and advanced diseased model, are used as representatives of human neuro cell membranes under different stages of AD. The results so far have shown the reduced interaction strength in terms of binding signal between  $A\beta$  and mimicked neuronal membranes in the presence of melatonin.

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My name is Nanqin Mei, and I am currently a first-year physics (nanotechnology) graduate student at the University of Waterloo (UW). In the last year, I worked in Dr. Zoya Leonenko's nanoscale biophysics lab as an undergrad research student. During this time, I attended the 3<sup>rd</sup> Annual Meeting of Biophysics Society of Canada and Women in Physics in Canada 2017 conference, where I did poster presentations.

# Nanopores with an internal cavity can be used as length based filtering device for polymers

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Timothée Menais, Martin Magill, and Hendrick W. de Haan

Faculty of Science, University of Ontario Institute of Technology, Oshawa, Canada

Sorting polymers by chain length is important for conducting analysis for modern biology and is very likely to remain so in the near future as DNA sequencing becomes more widespread. Although it is currently commonly done by gel electrophoresis, this technique suffers from many drawbacks. Particularly, it cannot easily be miniaturized nor automated.

Nanopore-based devices are promising candidates to address those issues. The classic setup consists in a nanometric hole punched in a thin membrane, through which polymers can be driven by an electric field. This process is called translocation. The longer the chain length, the longer the mean translocation time.

We work on a device coupling two nanopores linked by a nano-cavity. Previous work using a generic polymer model has shown that the mean translocation time through such a device is not a monotonic function of the chain length. Hence the device is a good candidate as a selective polymer filter. Here we show results using improved polymer and electric field models that confirms the potential of the set up as an efficient polymer filtering device.

Timothée Menais graduated with a bachelor's and a master's degree in physics from ENS de Lyon (France). He then did a PhD in theoretical physics at Université Grenoble Alpes (France) during which he numerically studied the translocation of polymers through thin membranes. He is now a Post doctoral fellow at UOIT in Hendrick W. de Haan's cNAB LAB.

## Simulations of Various Models of Bacterial Twitchers

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Andrew Nagel, Michael Greenberg, and Hendrick W. de Haan

Twitching motility is a flagella-independent form of bacterial movement on a surface. Twitching bacteria undergo movement through the use of hair-like structures called Type IV Pili. These pili are used like grappling hooks to propel the bacteria across a surface. Twitching motility is a social behaviour and when used in large groups, allows bacteria to move collectively in order to explore their environment and form a biofilm.

This study uses coarse-grained simulation techniques to model the collective behaviour of twitching bacteria. Various models were created to explore and understand the effects of different types of pili attachment (on surface, on other twitchers, breaking criteria). Trajectory data and simulation movies are used to quantify the effect that density and reversal probability have on the emergence of collective motion.

Andrew Nagel completed a bachelor's degree in mathematics at the University of Guelph and is currently pursuing a master's degree in modelling and computational science at the University of Ontario Institute of Technology (UOIT). Under the supervision of Hendrick W. de Haan, his masters work consists of using computer simulations to study the motility of bacterial twitchers.



# Depletant Induced Stacking Of Red Blood Cells Into Rouleaux

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Austin Nehring, Hendrick W. de Haan

University of Ontario Institute of Technology, Oshawa Ontario L1H 7K4 [Austin.Nehring@uoit.net](mailto:Austin.Nehring@uoit.net)

Rouleaux is the organized structure of aggregated red blood cells observed in the human body. In pathological cases, such as malaria and sickle cell disease, aggregations of these rouleaux can block blood vessels. Currently there are two theories of how red blood cells can aggregate together in clusters. The first proposes plasma macromolecules (proteins) which bind the blood cells together. The second theory looks at how the depletant induced potential can cause aggregation. Depletant induced potentials are entropic interactions arising from the size difference between red blood cells and smaller particles in the fluid. The size of the potential is directly related to the density of the small particles in the fluid, the depletants.

Coarse-grained simulations of red blood cells subject to the depletant potential are explored over three different models. When the strength depletant interaction is less than the thermal fluctuations in the system, the red blood cells are free floating and do not aggregate. When the depletant interaction is larger than the thermal fluctuations the cells aggregate together into collapsed structures, this is a first order phase transition. After the collapse there exists a region where the cells can align and stack on top of each other creating stable, long lived rouleaux. Increasing the depletant interaction further reduces the rouleaux into amorphous aggregate structures. The red blood cells are modeled as disks made from spheres bound together. The motion cells is governed by Langevin dynamics within a system of periodic boundary conditions. In this work we present the depletant induced potential can cause rouleaux formation of red blood cells.

Austin Nehring received his BSc. in physics from UOIT. Since May 2015 he has been a graduate student in the material science program at UOIT working in the Computational NanoBiophysics laboratory (cNab.Lab).

# Gold Nanoparticle Probes for Dual-Mode Dark Field and Surface Enhanced Raman Scattering (SERS) Detection of Cell Surface Proteins

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Caroline Pao and Gilbert C. Walker

Department of Chemistry, University of Toronto

Due to the prevalence and diversity of hematologic cancers, such as chronic lymphocytic leukemia (CLL), there is a demand to develop multimodal detection techniques that limit the number of tests required for diagnosis. In this study, SERS-active reporter molecules have been incorporated into gold nanoparticle probes to impart dual-mode imaging functionality for both dark field and SERS microscopy. The capabilities of both techniques were exploited to provide complementary information to improve cell detection and disease diagnosis while limiting the number of discrete tests required. Briefly, various dyes were physisorbed onto the gold nanoparticles to create probes with fingerprint SERS-spectra of narrow bandwidths that allow for improved multiplexing capabilities compared to traditional fluorescent biomarkers. Polyethyleneglycol was used to protect the SERS-active nanoparticles to prevent aggregation and achieve improved stability and biocompatibility. The probes were then conjugated to monoclonal antibodies that selectively target diagnostic markers of B-



CLL cells, such as CD20. Dark field imaging was employed to investigate the spatial distribution of CLL surface proteins while SERS microscopy allowed for their identification through the distinct SERS spectra of the various probes. The success of these probes in the selective targeting of CLL cells and future applications in Raman mapping and flow cytometry will be discussed.

Caroline is a PhD student in the Department of Chemistry at the University of Toronto under the supervision of Professor Gilbert Walker. She received her BSc from the University of British Columbia where she gained experience in electrochemistry with Prof. Daniel Bizzotto and computation nanomaterials with Prof. Yan Alexander Wang.

## Beyond vascular confinement: ultrasound-triggered conversion of porphyrin microbubbles to nanobubbles

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Carly Pellow<sup>1,2,3</sup>, David Goertz<sup>1,2</sup> and Gang Zheng<sup>1,3</sup>

<sup>1</sup>Department of Medical Biophysics, University of Toronto;

<sup>2</sup>Sunnybrook Research Institute, Toronto, Canada;

<sup>3</sup>Princess Margaret Cancer Research Tower, Toronto, Canada

Photodynamic therapy is a minimally invasive strategy with potential to target infiltrative tumours while sparing surrounding normal tissue. However, reliance of nanoscale photosensitizers on passive targeting has resulted in insufficient delivery, prompting an exploration of ultrasound-stimulated microbubbles (MBs) to actively enhance blood-tissue drug permeability. Recently, novel porphyrin photosensitizer-shelled MBs demonstrated an ultrasound-triggered conversion to porphyrin nanostructures, found to contain gas. In addition to photoactive porphyrin, the presence of gas in the daughter nanobubbles (NBs) opens the possibility of stimulating further bubble-mediated ultrasound imaging and therapy beyond the confines of the vasculature.

Here I investigate the effects of size and a confining tissue environment on bubble behaviour through vessel and tissue phantom studies, providing a foundation for a physical understanding of NB behaviour and laying the groundwork for assessing their imaging and therapeutic potential beyond the vasculature. I also demonstrate preliminary insights into the microscale spatiotemporal extravasation induced by the conversion with ultrasound transducers integrated into a multiphoton window-chamber microscopy setting, acoustically inducing MB conversion and tracking subsequent fluorescent porphyrin-shelled NB extravasation. This setup will further leave us uniquely poised to investigate the imaging and therapeutic utility of these porphyrin NBs directly in the intra-tumoural space, working to extend phototherapeutic and bubble-mediated theranostic approaches to deep-seated solid tumours.

I completed my undergraduate studies in Engineering Physics at Queen's University in 2015, and am currently a PhD student in Medical Biophysics at the University of Toronto under the supervision of Dr. David Goertz and Dr. Gang Zheng, studying the behaviour of multimodal microbubbles and nanobubbles for drug delivery and cancer theranostics.

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# Use of Porphysomes for accurate intra-operative detection of lymph node metastases in an endometrial cancer model

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L. Philp<sup>1</sup>, H. Chan<sup>2</sup>, M. Rouzbahman<sup>3</sup>, J. Chen<sup>2</sup>, G. Zheng<sup>2</sup> and M.Q. Bernardini<sup>4</sup>.

<sup>1</sup>Institute of Medical Science, Department of Obstetrics and Gynecology, University of Toronto, Toronto, ON, Canada

<sup>2</sup>Princess Margaret Hospital, University of Toronto, Toronto, ON, Canada

<sup>3</sup>Department of Pathology, University Health Network, Princess Margaret Hospital, Toronto ON, Canada

<sup>4</sup>Division of Gynecologic Oncology, University Health Network, Princess Margaret Hospital, Toronto, ON, Canada

**Objective:** Establish the accuracy of intra-operative Porphysome fluorescence image-guided resection (PYRO-FGR) for the detection of uterine tumour, metastatic lymph nodes and abdominal metastases in a model of endometrial cancer.

**Methods:** Rabbits were inoculated with VX2 cells via intra-myometrial injection. At 30 days, Porphysomes were administered IV. At 24hrs the abdomen was imaged with a 675nm fluorescence endoscope. Fluorescent tissue was resected (PYRO-FGR). Complete pelvic and para-aortic lymphadenectomies were performed after confirming lymph node tissue was fluorescence negative. All resected tissue was examined for tumour by a gynecologic pathologist and histopathology including ultrastaging was used to detect VX2 cells in fluorescent tissue. Fluorescence signal to background intensity ratio (SBR) was calculated and VX2 (+) tissue compared to VX2 (-) tissue. Biodistribution was calculated and fluorescent VX2 (+) tissue compared to fluorescent VX2 (-) and non-fluorescent VX2 (-) tissue.

**Results:** 8 VX2 rabbits and 2 controls were used. 8 tumours, 19 lymph nodes (LN) and 27 abdominal metastases (AM) were fluorescence positive on PYRO-FGR and resected (Fig 1). Of these, 8 tumours, 15 LN and 22 AM were VX2 (+) and 2 LN and 1 AM were VX2 (-). 6 specimens were unable to be assessed and removed from analysis. 11 negative lymph nodes were identified in lymphadenectomy specimens, all fluorescence negative. No tumour was identified on histopathology that was not fluorescent intra-operatively. Control rabbits had negative fluorescence in all lymph node basins and low uterine fluorescence. Sensitivity and specificity of PYRO-FGR for VX2 (+) tissue based on current limited samples were 100% / 79% for all tissue, 100% / 100% for uterine tumour, 100% / 85% for LN and 100% / 92% for AM respectively. Increased SBR was seen in all VX2 (+) tissue ( $p=0.003$ ), LN ( $p=0.006$ ) and AM ( $p=0.007$ ). Increased Porphysome uptake was seen in all fluorescent VX2 (+) tissue including tumour ( $p<0.001$ ), LN ( $p=n/a$ , 1 (-) LN) and AM ( $p=0.018$ ).

**Conclusions:** Porphysomes are an IV agent that allows for accurate intra-operative detection of uterine tumour, metastatic lymph nodes and abdominal metastases using fluorescence in a model of endometrial cancer.

Dr. Lauren Philp is a fourth year resident in the department of Obstetrics and Gynaecology at the University of Toronto. She received her undergraduate degree from McGill University and her medical degree from Queen's University. During her residency she developed a strong interest in the care of women with gynaecologic malignancies and has been involved in clinical research regarding management of ovarian and cervical cancer. Her master's degree is investigating the ability of the Porphysome to diagnose lymph node metastases in a model of endometrial cancer. Lauren plans to pursue a fellowship in Gynaecologic Oncology following the completion of her training, and she hopes to dedicate her career to improving the lives of women with gynaecologic cancer.

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# SG pseudo-peptide amyloid- $\beta$ inhibitors: single-molecule force spectroscopy and cell viability study.

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M. Robinson<sup>1,2</sup>, J. Lou<sup>3</sup>, Arvi Rauk<sup>5</sup>, Michael Beazely<sup>1</sup>, Zoya Leonenko<sup>2,3,4</sup>.

<sup>1</sup>School of Pharmacy, <sup>2</sup>Department of Biology, <sup>3</sup>Department of Physics and Astronomy, <sup>4</sup>Waterloo Institute of Nanotechnology, University of Waterloo, Canada; <sup>5</sup>Department of Chemistry, University of Calgary, Alberta, Canada

E-mail: [zleonenk@uwaterloo.ca](mailto:zleonenk@uwaterloo.ca).

Alzheimer's disease (AD) is a neurodegenerative disorder that is a leading cause of death with no cures and limited treatment options. Amyloid- $\beta$  (A $\beta$ ) accumulation is the definitive neuropathological hallmark of AD which aggregates to form neurotoxic oligomers that bind to nanoscale electrostatic and topographical features of the neuronal membrane, disrupting membrane potential and neuronal function<sup>1,2</sup>. One potential strategy to prevent neurotoxicity associated with A $\beta$  is to stabilize the non-toxic monomer, inhibiting the formation of toxic oligomers. To that end, SG pseudo-peptide inhibitors have been rationally designed and optimized for affinity to A $\beta$  using molecular dynamics simulations by collaborators at the University of Calgary. The lead candidates from these simulations were then experimentally tested in our lab using nanoscale biophysics technique on an AFM platform. We have shown on a single-molecule level that the SG inhibitors prevent dimerization of A $\beta$  and shift the distribution of A $\beta$  binding forces<sup>3</sup>. We also have demonstrated that SG inhibitors ameliorate A $\beta$  toxicity in cell viability studies, indicating SG inhibitors as a potential preventative treatment for AD.

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Morgan (BSc Physics/Biophysics, MSc Biology) is a PhD student at the University of Waterloo in Pharmaceutical Sciences exploring the molecular and cellular mechanisms of Alzheimer's disease, under the tutelage of Dr. Zoya Leonenko and Dr. Michael Beazely. The focus of his research is to explore the interactions between the neuronal lipid membrane, A $\beta$  and neuronal signaling pathways, as it pertains to Alzheimer's disease, using functional neurophysiological assays in conjunction with biochemical analysis and nanoscale biophysical characterization of neuronal membranes.

## Multispectral SERS Using Symmetrically Width-Graded Nano-Gratings

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Nastaran Kazemi-Zanjani<sup>1</sup>, Moein Shayegannia<sup>1</sup>, Rajiv Prinja<sup>1</sup>, Arthur O. Montazeri<sup>3</sup>, Aliakbar Mohammadzadeh<sup>6</sup>, Katelyn Dixon<sup>1</sup>, J. Zhu<sup>4</sup>, Ponnambalam R. Selvaganapathy<sup>6</sup>, Anna Zavodni<sup>4</sup>, Naomi Matsuura<sup>2,4,5</sup>, Nazir P. Kherani<sup>1,2</sup>

<sup>1</sup>Department of Electrical and Computer Engineering, University of Toronto, Toronto, Ontario, M5S 3G4, Canada

<sup>2</sup>Department of Material Science and Engineering, University of Toronto, Toronto, Ontario, M5S 3E4, Canada

<sup>3</sup>Lawrence Berkeley National Laboratory, 1 Cyclotron Rd., Berkeley, CA, 94720, USA

<sup>4</sup>Department of Medical Imaging, University of Toronto, Toronto, Ontario, M5T 1W7, Canada

<sup>5</sup>Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario, M5S 3G9, Canada

<sup>6</sup>Department of Mechanical Engineering, McMaster University, Hamilton, Ontario, L8S 4L7, Canada

We report on the potential of a new class of nanoplasmonic width-graded gratings as sample substrates for multispectral surface enhanced Raman spectroscopy (SERS) in order to achieve unprecedented detection sensitivity, specificity and rapidity in sensing. Width-graded gratings of symmetric geometry are fabricated with nano-groove widths less than 200nm and narrowest groove width of 40nm. Electron beam lithography, reactive ion etching and sputter-deposition techniques are used to fabricate these metal-insulator-metal nanoplasmonic graded gratings.

Systematic SERS experiments are carried out on these gratings using phospholipids in dried and aqueous solution phases. Raman signal intensity enhancement of over four orders of magnitude are observed with laser illumination in the visible and infrared regions. These preliminary results indicate the viability of width-graded nano-grating based multispectral SERS for accurate and rapid compositional analysis of a diversity of molecular species.

Moein Shayegannia received his Bachelor of Science degree (Cum LAUDE) in Electrical Engineering from the American University of Sharjah in UAE in 2008, and his Master of Science degree in Engineering Science from the Simon Fraser University in Vancouver, Canada in 2012. After working as a research assistant for 1.5 years at SFU, Moein embarked on his PhD degree in the department of Electrical and Computer Engineering at the University of Toronto in 2014. His doctoral research pertains to the analysis, fabrication and characterization of novel plasmonic nanograting structures for SERS based bio-molecular sensing applications.

## Determining the size-dependence of the surface tension of iron nanoparticles using time-resolved laser-induced incandescence

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T. A. Sipkens, K. J. Daun

Mechanical and Mechatronics Engineering, University of Waterloo, 200 University Ave W, Waterloo, ON N2L 3G1

The surface tension of nanoparticles is known to deviate from the bulk value due to curvature in the nanoparticle surface. To date, there is no consensus on which model best describes this size-dependent property. The current work uses time-resolved laser-induced incandescence (TiRe-LII), customarily used as a soot diagnostic, to probe iron nanoparticles to determine this property. This technique uses a short laser pulse to heat nanoparticles to incandescent temperatures. The decay in the incandescence and temperature following the laser pulse is measured and related to nanoparticle characteristics using heat transfer and spectroscopic models. For many materials, the laser pulse superheats the nanoparticles so that cooling is initially dominated by free molecular evaporation, which is enhanced by the nanoparticle curvature. We use Bayesian model selection, an advanced statistical technique for choosing between competing models, to cross-examine available models describing the size-dependence of the surface tension, particularly examining the Kelvin equation, Tolman equation, and value for the Tolman length. The results will give researchers insight into this thermophysical property for iron nanoparticles and will illustrate how TiRe-LII can be used as a technique to determine fundamental nanoparticle properties.

Timothy Sipkens is a Ph.D. candidate in Mechanical Engineering at the University of Waterloo. His work on time-resolved laser-induced incandescence has earned him several Waterloo Nanofellowships and the Governor General's Gold Medal. His work focuses on advancements in TiRe-LII models, ranging from uncertainty quantification on model outputs to improvements in the basic heat transfer models. He has disseminated this work in 12 articles to prominent journal in his field, including several international collaborative projects.

# Polyglyoxalamides: Amide Analogues of Polyglyoxylates

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Quinton E. A. Sirianni,<sup>1</sup> Amir Rabiee Kenaree,<sup>1</sup> and Elizabeth R. Gillies,<sup>1,2</sup>

<sup>1</sup>Department of Chemistry, <sup>2</sup>Department of Chemical and Biochemical Engineering, The University of Western Ontario, London, Canada, N6G 1Z1

Stimuli-responsive polymers undergo changes in their physical or chemical properties when exposed to specific stimuli. Due to this capability, these polymers show promise in applications such as drug delivery and functional coatings.<sup>1,2</sup> Recently, our group reported a new class of stimuli-responsive polymers known as polyglyoxylates.<sup>3</sup> These polymers can be synthesized from commercially available precursors such as ethyl glyoxylate. Furthermore, polyglyoxylates can degrade upon exposure to specific stimuli such as light or changes in redox conditions or pH.<sup>3,4</sup> While polyglyoxylates possess the potential for use outside of academia, their long-term stability may be compromised by their reactive ester side chains. In addition, polyglyoxylates have mechanical and thermal properties that make them less than ideal for certain applications. To address these issues, we have worked to create analogues of polyglyoxylates that replace the ester side chains with amides, a more stable functional group. We have been able to synthesize these amide analogues (known as polyglyoxalamides) via a post-polymerization modification of poly(ethyl glyoxylate). This poster presents an overview of the synthesis of polyglyoxalamides as well as the investigation of these polymers.

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Quinton Sirianni attended Thompson Rivers University in Kamloops, BC, obtaining his BSc in Chemistry in 2014. Since 2016, he has been enrolled in the Chemistry doctoral program at The University of Western Ontario under the supervision of Dr. Elizabeth Gillies. His research focuses on the synthesis and applications of polyglyoxalamides, which are polymers that can be degraded in response to stimuli.

## High-intensity laser-induced incandescence of aerosolized nanoparticles: Interference of plasma thermal radiation with incandescence signal

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S. Talebi Moghaddam, T. A. Sipkens, K. J. Daun

Mechanical and Mechatronics Engineering, University of Waterloo, 200 University Ave W, Waterloo, ON N2L 3G1

Time-resolved laser-induced incandescence (TiRe-LII) is a technique for characterizing aerosolized nanoparticles that uses a laser pulse to energize aerosolized nanoparticles to incandescent temperatures and then measures the spectral incandescence from the nanoparticles they return to the ambient gas temperature. The nanoparticle volume fraction and size distribution are inferred from the incandescence decay using spectroscopic and heat transfer submodels. Obtaining robust estimates of nanoparticle characteristics from TiRe-LII data relies on the accuracy of the LII model used to link the observed incandescence with the nanoparticle temperature. In many instances, LII models fail to reproduce experimental trends, such as in the case of anomalous cooling and excessive absorption of the incident radiation by the nanoparticle compared to that predicted by Mie/Drude theory. Recent experiments suggest that these discrepancies may be a consequence of a laser-induced microplasma around the nanoparticles.

The current work investigates how thermal radiation from the microplasma surrounding the nanoparticle may corrupt pyrometrically-inferred temperatures. We consider two components for the LII model: (i) the microplasma, describing the global environment throughout the laser-induced microplasma based on its temperature and density; (ii) the nanoparticle, using traditional TiRe-LII heat transfer and spectroscopic submodels [1]. These two components of the LII model interact through heat and mass transfer. The detected radiation is given as the sum of the incandescence and bremsstrahlung radiation, and temperatures are inferred from pyrometry to determine how much bremsstrahlung radiation corrupts the inference of nanoparticle characteristics. The results show that pyrometry overestimates the nanoparticle's temperature due to bremsstrahlung radiation.

Sina Talebi Moghaddam is a Ph.D. candidate in Mechanical Engineering at the University of Waterloo. His work focuses on optical modeling of laser-nanoparticle interactions used for laser-based nanoparticle diagnostics. He has published four articles in recognized journals in this field since 2015. His work on the optical behavior of plasmonic nanoparticles adjacent to an atomic force microscope (AFM) probe helped understand previously baffling experimental results on using a probe to melt/evaporate nanoparticles. His work in developing multi-angle elastic light scattering (MAELS) optical modeling has received recognition by the community and opened future collaboration with Erlangen Graduate School in Advanced Technologies.

## Self-assembled bio-degradable polymeric nano-radiopharmaceutical for liver imaging; A potential probe for targeted radiotheragnostics

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Nashmia Zia<sup>1</sup>, Aadarash Zia<sup>2</sup>, Zafar Iqbal<sup>1</sup>, Abida Raza<sup>3</sup>

<sup>1</sup>Department of Pharmacy, University of Peshawar

<sup>2</sup>ARC Centre of Excellence in Convergent Bio-Nano Science and Technology, Monash Institute of Pharmaceutical Sciences, Monash University

<sup>3</sup>NNRL (NILOP Nanotheranostic Research Lab), NILOP (National Institute of Laser and Optronic

Noninvasive imaging is highly useful in diagnosis and monitoring of treatment progression, when tagged with efficient drug delivery systems. Paper aims at preparation and use of biodegradable polymer based nano- radionuclide as a potential radiotracer for liver imaging. Quaternary ammonium palmitoyl glycol chitosan (GCPQ) based nano-radionuclide formulation, 65 nm in size, was prepared at a concentration of 5mg/ml of GCPQ in sterile normal saline containing 500 MBq of sodium pertechnetate. Labeling efficiency and purity was checked by ITLC-SG. Rabbits were injected with labeled GCPQ NP at a dose of 80 MBq/5mg/ml/kg through marginal ear vein. Dynamic anterior and posterior images of whole body were acquired for 25 minutes using 165 frames followed by 1500 k-count spot views of the whole body at 0.5, 1, 2, 3, 4 and 24 hours. Biodistribution of <sup>99m</sup>Tc GCPQ NP vs. <sup>99m</sup>Tc showed intense uptake by liver. The time for the liver time-activity curve to reach 90% of its peak activity was approximately 13 minutes. Data suggested specific uptake of <sup>99m</sup>Tc GCPQ NP in hepatocytes giving a very good spatial resolution. The radionuclide can be used as a competitive liver imaging agent. Its optimum size, biocompatibility and specific retention in hepatocytes makes it a unique drug delivery system in liver disease.

I have done Doctor of Pharmacy from Department of Pharmacy, University of Peshawar in Feb 2013. Since March 2013 I am enrolled as a full-time PhD student at the said department. As facilities required for research are dispersed in different institutions in Pakistan, I had a chance to work in major institutions specialized in



their respective fields. I have worked as a researcher at my home department, **NORI** (Nuclear medicine and radiotherapy institute) Islamabad, **NILOP** (National Institute of Laser and Optronics), Islamabad and **IRNUM** (Institute of radiotherapy and nuclear medicine), Peshawar.

I am well trained in different techniques of Nano-formulations synthesis alone and in combination with fluorescent, technetium and iodine radiolabelling. I have worked on **HPLC, UV-Vis, PROBE SONICATOR, ZETA SIZER, PCR, ELISA Reader, GAMMA CAMERA, I-Box explorer (UV), ITLC, FTIR** cell culturing and geno-toxicity studies etc.

My main area of interest is development and characterization of polymeric and metal based Nano-theranostics formulation for cancer treatment and its genetic toxicity assessment employing In-vitro and In-vivo Micro-nucleus assays.