The Terry Fox Research Institute
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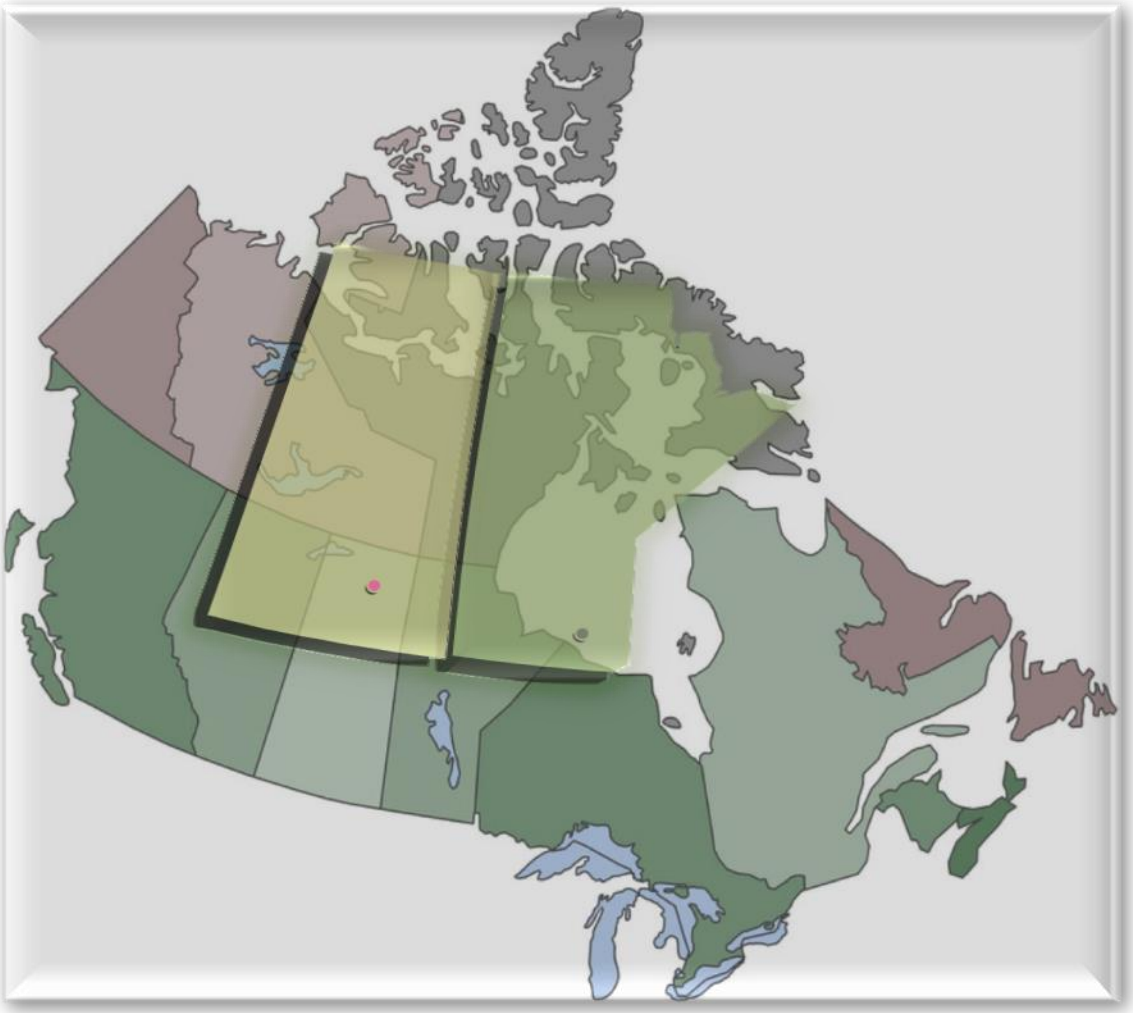
Cancer Researchers within the Terry Fox Research Institute Prairie Node



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Principal Investigators within the Manitoba Prairie Node

Clinical Trials Department of the Saskatchewan Cancer Agency
Dedicated to providing promising new cancer therapies

Lynn Dwernychuk, RN, BSN, MN, CON(C)

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Lynn Dwernychuk is the Director of Clinical Research at the Saskatchewan Cancer Agency. She is also an Adjunct Professor with the College of Graduate Studies and Research with the University of Saskatchewan. Lynn received her Bachelors of Science in Nursing in 1998 and completed her Masters in Nursing in April 2012 both at the University of Saskatchewan.

Lynn has been with the Saskatchewan Cancer Agency since 2002 in varying nursing and management roles and in 2012 became the Director of Clinical Research. She is the current the Chair of the NCIC Clinical Trials Group, Clinical Research Associates (CRA) Executive Committee. Lynn is a member of the Canadian Cancer Clinical Trials Network (3CTN) as a member of the Scientific Network Portfolio Committee. Lynn currently sits on the Alliance Oncology Nursing Board, the only Canadian Centre to hold a membership. She also is an integral part of the Clinical Trials Support Unit (CTSU); a joint research initiative between the Saskatoon Health Region, University of Saskatchewan and the Saskatchewan Cancer Agency. This unit provides onsite, in-house clinical research by having dedicated beds for inpatient treatment and monitoring. Lynn is the clinical advisor for this joint initiative.

The Clinical Research Department of the Saskatchewan Cancer Agency is an integral part of providing safe, quality care for patients. Through clinical trial, patients have access to cutting edge technologies and therapies. The Cancer Agency also supports physicians, researchers and staff in their in-house research and externally with the University of Saskatchewan.

The Clinical Research Department has participated in numerous national and international led clinical trials which has contributed to improved health outcomes for oncology patients. Clinical research conducted at the Cancer Agency incorporates studies offered through pharmaceutical sponsors and cooperative groups such as the NCIC Clinical Trials Group, Radiation Therapy Oncology Group (RTOG), the Children's Oncology Group (COG) and the Alliance. The Saskatchewan cancer Agency is the only Canadian Centre to hold a membership with the Alliance, a merged board consisting of the following groups: American College of Surgeons Oncology Group (ACOSOG), Cancer and Leukemia Group B (CALGB), and the North Central Cancer Treatment Group (NCCTG).

The Cancer Agency is an integral partner with the Clinical Trials Support Unit (CTSU). The CTSU is a joint research initiative between the Saskatoon Health Region, University of Saskatchewan and the Saskatchewan Cancer Agency. This unit provides onsite, in-house clinical research by having dedicated beds for inpatient treatment and monitoring.

The Saskatchewan Cancer Agency has the interdisciplinary expertise needed to conduct sponsor and in-house clinical research efficiently and effectively. Site management includes activities such as:

- Identifying potential sponsors for investigator-initiated basic-science or clinical studies
- Protocol development
- Review and revision of the consent forms
- Submission of all documents requiring ethical review/approval
- Completion of regulatory documents
- Contract and budget negotiation
- Patient recruitment and retention
- Consent and enrollment of patients
- Patient care and management
- Data capture tools
- Data management
- Training and quality assurance

Clinical Research at the Saskatchewan Cancer Agency: Dedication of a multidisciplinary team whose focus is providing excellence in patient care.

The Clinical Research Department website can be viewed at the following link:
http://www.saskcancer.ca/Default.aspx?DN=4874aa7d-fede-461a-bac1-69dc02174101

Epidemiology and Performance Measurement Department of the Saskatchewan Cancer Agency

Riaz Alvi

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The Saskatchewan Cancer Agency's Department of Epidemiology and Performance Measurement is led by the Director, Riaz Alvi, and comprised of a team of epidemiologists, a health economist and research associates.

The Epidemiology and Performance Measurement Department provides expertise in treatment outcomes, epidemiological research, risk factor surveillance, evaluation, spatial analysis and cancer surveillance for the Cancer Agency to determine effectiveness of programs, assist with planning and reduce the burden of cancer for the population of Saskatchewan. We work closely with the Saskatchewan Cancer Registry, Prevention, KPO, QSR, Research and Early Detection Departments which, with Epidemiology and Performance Measurement, comprises the Population Health, Quality and Research Division of the Agency.

The department produces the Saskatchewan Cancer Control Report, which is a status report on cancer surveillance for the province. Each report highlights a special topic with detailed information about cancer for the population of Saskatchewan. Past reports have highlighted cancer prevalence and cancer stage distribution.

Performance Measurement is a new function of the department. We have been tasked with monitoring and verifying high level performance of the cancer control program at the SCA. This also includes health economic analysis.

The epidemiologists carry out day to day analytical work, data cleaning, and analysis and report writing/presentation.

The research associates carry out detailed chart reviews, data cleaning and data entry.

The Department's information products are used within the Agency and externally (nationally and internationally) for surveillance, planning, research and evaluation.

The Epidemiology and Performance Measurement website can be viewed at the following URL:
http://www.saskcancer.ca/Default.aspx?DN=12e55492-0853-4e8d-9cd9-3fd74edb36b8

Dr. Deborah Anderson, BSc, PhD

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Dr. Deborah Anderson is the Director of Research and a Senior Research Scientist at the Saskatchewan Cancer Agency, Professor, Division of Oncology University of Saskatchewan and Adjunct Member, Department of Biochemistry, University of Saskatchewan.

Dr. Anderson received her B.Sc. (Hons) in 1984 and her Ph.D. in 1988, both at the University of Manitoba.

Receptor tyrosine kinase (RTK) overexpression is frequently observed in many human cancers and drives cell division and cell survival. One major pathway activated by these receptors is the phosphatidylinositol 3-kinase (PI3K)/Akt pathway. PI3K activity consists of a p110 catalytic protein that phosphorylates lipids that in turn activate Akt signaling. The p110 protein is stabilized and regulated by another protein, p85.

1. Regulation of PTEN

PTEN is a tumor suppressor protein that counteracts the PI3K pathway, since it is the lipid phosphatase that dephosphorylates PI3K lipid products. We have recently shown that the p85 protein that regulates p110-PI3K activity, also directly binds and positively regulates PTEN lipid phosphatase activity. Thus, p85 is a dual regulator of both the kinase and the phosphatase controlling lipid levels and the resulting Akt signaling. Our results have been developed into a model that explains the paradoxical phenotypes observed in transgenic mice containing reduced p110, PTEN and p85 levels. We are also pursuing experiments to further characterize the regulatory effects of p85 towards PTEN.

2. Regulation of Receptor Endocytosis and Down-regulation

We are studying mechanisms cells use to decrease receptor tyrosine kinase levels via uptake of cell surface receptors into cells (endocytosis) and degradation in lysosomal compartments. The p85 protein also binds to many activated RTKs and remains bound while receptors are taken up inside cells. We have found that p85 has GAP activity that regulates Rab5 and Rab4 GTPases. Rabs are important for the trafficking of RTK-containing vesicles during endocytosis, receptor deactivation and recycling back to the cell surface, and for receptor sorting for degradation. Defects in the Rab regulatory function of p85 are oncogenic. We are studying this new role for p85 and the effect of mutations within the GAP domain of p85 that have recently been discovered in human cancer samples. We are also studying receptor trafficking and using complementary strategies in an effort to enhance EGFR &/or ErbB2 degradation in breast cancer cells.

3. Metastasis Suppressor CREB3L1

We are characterizing the metastasis suppressor protein, CREB3L1, activated during the stressful conditions (low nutrients and low oxygen) present in tumors. This transcription factor represses the expression of genes involved in cell growth, cell survival, migration and invasion, and is lost in highly metastatic breast cancer cells.

Selected Publications:

1. Allonby, Odette, Amr M. El Zawily, Tanya Freywald, Darrell D. Mousseau, Jennifer Chlan, **Deborah Anderson**, Alexandre Benmerah, Vishaldeep Sidhu, Mohan Babu, John DeCoteau and Andrew Freywald (2014) Kinase-dead EphB6 receptor loses Hsp90 aid and is efficiently downregulated following stimulation. Cellular Signalling, Aug 23; 26(12):2645-2657.
2. Ross, Rebecca L., Julie E Burns, Claire F Taylor, Paul Mellor, **Deborah H Anderson** and Margaret A Knowles (2013) Identification of mutations in distinct regions of p85 alpha in urothelial cancer. PLoS One, 8, e84411.
3. Mellor, Paul, Leah Deibert, Brian Calvert, Keith Bonham, Svein A. Carlsen and **Deborah H. Anderson** (2013) CREB3L1 is a metastasis suppressor that represses expression of genes regulating metastasis, invasion and angiogenesis. Mol Cell Biol, 33, 4985-4995.
4. Mellor, Paul, Levi A. Furber, Jennifer N. K. Nyarko, and **Deborah H. Anderson** (2012) Multiple Roles for the p85 Isoform in the Regulation and Function of PI3K Signalling and Receptor Trafficking. Biochem J, 441, 23-37.
5. Chamberlain, M. Dean, Jennifer C. Oberg, Levi A. Furber, Sharon F. Poland, Andrea D. Hawrysh, Stacey M. Knafelc, Heidi M. McBride and **Deborah H. Anderson** (2010) Deregulation of Rab5 and Rab4 proteins in p85R274A-expressing cells alters PDGFR trafficking. Cell Signalling 22, 1562-1575.
6. **Anderson, Deborah H.** (2010) p85 plays a critical role in controlling flux through the PI3K/PTEN signaling axis through dual regulation of both p110 (PI3K) and PTEN. Cell Cycle, 9, 2055-2056.
7. Chagpar, Ryaz B., Philip H. Links, M. Chris Pastor, Levi A. Furber, Andrea D. Hawrysh, M. Dean Chamberlain and **Deborah H. Anderson** (2010) Direct positive regulation of PTEN by the p85 subunit of phosphatidylinositol 3-kinase. Proc Natl Acad Sci USA, 107, 5471-5476.

Search PubMed for a complete list of publications by Anderson DH

Dr. Terra Arnason, MD, PhD, FRCPC Adult Endocrinology

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Dr. Terra Arnason received her B.Sc. in Biochemistry from the University of Victoria and her Ph.D. (Biochemistry) degrees from the University of Alberta. Her post-doctoral training was in the area of yeast molecular biology, first in protein translocation into mitochondria (University of München, Germany) followed by discovery of chromatin assembly mechanisms in the lab of Dr. Schultz at the University of Alberta. She continued part –time postdoctoral work during the first 3 years of MD training in Edmonton. She completed specialization training in Internal Medicine followed by a subspecialty fellowship in Adult Endocrinology. She is currently a clinician scientist at the University of Saskatchewan and has an active Endocrine clinical practice and an active research lab, and conducts both clinical and molecular/basic research. She is part of several research teams including the Drug Discovery and Development Group, and is a team lead on collaborative research projects looking at multiple drug resistance in spontaneous cancer. The first team uses companion canine models of lymphoma under a project entitled *"Metformin and microarrays: an innovative approach to treating and monitoring drug resistant canine lymphoma"*. The second team, in conjunction with the surgical oncology team is using human breast cancer tissue to identify clinically relevant predictive biomarkers of multiple drug resistance; *"In vivo and in vitro evaluation of patient-derived breast cancer cells for early detection and treatment of drug resistant tumors"*. Her research interests include the metabolic and environmental adaptation to cell survival, whether under stress or starvation (yeast studies) or through acquired drug resistant to chemotherapeutic agents.

Despite the advances in early detection and effective cancer therapy, drug resistance to chemotherapy is frequently observed and is an unwelcome complication with a poor prognosis. Acquired drug resistance is notorious in the most common malignancies of breast, colon, and blood. There is an urgent need to identify, monitor, and reverse multiple drug resistance (MDR). Protein markers that correlate with MDR exist in multiple cancers, yet drugs targeting them are disappointing in clinical trials. Tolerable, nontoxic treatment options to reverse MDR are urgently required. We are using bioinformatics to identify novel markers that correlate with the emergence of MDR *in vitro* and find that the insulin-sensitizer Metformin (MET) can *resensitize MDR cells to therapy, reverse the expression of MDR protein markers, and prevent the development of MDR* in vitro. In collaboration with oncologists at the Western College of Veterinary Medicine and bioinformatics experts, a canine lymphoma model has been established to test whether MET translates to clinically relevant *in vivo* outcomes, and to correlate molecular changes with treatment responses. In collaboration with the surgical Oncologists at the Womens' Breast Health centre, we are receiving tumor samples linked to patient clinical response to therapy to advance our prediction of MDR behaviour and introducing this tissue into severe combined immunodeficiency (SCID) mouse models and grown as primary cell lines. These tumors and cell lines will be exposed to MET adjunct therapy. Our results using the PDX and cell culture models will be compared to patient outcomes after 1 year. It is our hope that the expected reversal of the MDR behavior will coincide with reduction in tumor size in PDX models, which will ultimately improve patient care.

Selected Publications:

1. Jiao, R., Postnikoff, S., Harkness, T. A., and **Arnason, T. G.,** The SNF1 Kinase Ubiquitin-associated Domain Restrains Its Activation, Activity, and the Yeast Life Span. *The Journal of biological chemistry, 2015,* 290, 15393-15404.
2. **Arnason, T.**, Harkness, T., Development, maintenance and reversal of multiple drug resistance: At the crossroads of anticoagulation and hypoxia *Cancers Basel* 2015, 7, 2063-2082.
3. Davies, G.F.; Berg, A.; Postnikoff, S.D.; Wilson, H.L.; **Arnason, T.G.**; Kusalik, A.; Harkness, T.A. Tfpi1 mediates resistance to doxorubicin in breast cancer cells by inducing a hypoxic-like response. *PLoS One* 2014, *9*, e84611.
4. Menzel, J., Malo, M. E., Chan, C., Prusinkiewicz, M., **Arnason, T. G.**, and Harkness, T. A. The anaphase promoting complex regulates yeast lifespan and rDNA stability by targeting Fob1 for degradation. *Genetics,* 2014, 196, 693-709.
5. Slabu, H., and **Arnason, T.,** Pituitary granulomatosis with polyangiitis. *BMJ case reports* 2013.
6. Gorka, J., Taylor-Gjevre, R. M., and **Arnason, T.,** Metabolic and clinical consequences of hyperthyroidism on bone density. *International journal of endocrinology* 2013.
7. Sehmer, B., and **Arnason, T.,** Pop-provoked paralysis: silent Graves' disease presenting as thyrotoxic periodic paralysis. *BMJ case reports* 2012.
8. Davies, G.F.; Ross, A.R.; **Arnason, T.G.**; Juurlink, B.H.; Harkness, T.A. Troglitazone inhibits histone deacetylase activity in breast cancer cells. *Cancer Lett* 2010, *288*, 236-250.
9. Davies, G.F.; Juurlink, B.H.; Harkness, T.A. Troglitazone reverses the multiple drug resistance phenotype in cancer cells. *Drug Des Devel Ther* 2009, *3*, 79-88.
10. **Arnason, T.G.**; Pisclevich, M.G.; Dash, M.D.; Davies, G.F.; Harkness, T.A. Novel interaction between apc5p and rsp5p in an intracellular signaling pathway in saccharomyces cerevisiae. *Eukaryotic Cell* 2005, *4*, 134-146.

Dr. Mohan Babu, PhD

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Dr. Mohan Babu is an Assistant Professor in the Department of Biochemistry at the University of Regina. After graduating in Microbiology from the TNAU in India, Dr. Babu received his post-doctoral training in functional genomics and systems biology at the Ohio State University, University of California Davis, and at the University of Toronto. As a molecular biologist, biochemist, and emerging leader in integrative and network biology, Dr. Babu has developed and applied advanced proteomic, functional genomic, and bioinformatic methods to address how: **(1)** microbial genes and proteins associate within physical (protein-protein) or functional (gene-gene, or genetic) interaction networks to affect cellular behavior; **(2)** soluble and membrane protein complexes and pathways in model organisms are organized and conserved across species, including humans; and **(3)** perturbations in protein-protein interactions or protein complexes lead to diseases such as cancers and neurodegenerative disorders. He is the editor of the book "Prokaryotic Systems Biology" (Springer), secretary treasurer for Canadian Society of Microbiologists, and an advisory board member of the international Mitochondrial Human Proteome Initiative. He has served on grant review committee panels (NSERC, SHRF, CIHR, and MRC (UK)). Dr. Babu currently holds a CIHR New Investigator award and is a Maud-Menten Finalist of the CIHR Institute of Genetics. His research interests include receptors in cancer metastasis, genome instability, mitochondrial function in neurodegenerative disorders, biomarker discovery in cancer detection, interaction maps to understand disease pathway relationships to human health and disease, and identifying new targets for therapeutic intervention.

Specially, the prevalence of chronic diseases, including cancer, and the tremendous burden they place on our health care system emphasizes the urgent need for effective means of disease prevention and treatment. To address this, the Public Health Agency of Canada has launched the Canadian Chronic Disease Surveillance System to monitor and ultimately prevent chronic diseases like cancer. Defects in mitochondrial protein function have emerged as causative factors in a growing number of malignancies. Since almost all drugs used to treat cancer target mitochondrial proteins, and because mitochondrial proteins rarely act in isolation, every mitochondrial protein that functions in a given biochemical pathway is a potential target for drug discovery. While decades of detailed reductionist investigations have elucidated important details for isolated membrane systems, the role of mitochondrial protein dysfunction in cancer is often difficult to pinpoint due to incomplete information about its interactions with other membrane components. One of the research program of Dr. Babu is to address the sparsity of physical interactions among cancer-causing mitochondrial proteins by generating a comprehensive mitochondrial protein interactome map to characterize the protein-protein interactions underlying the disease.

Selected Publications: (48 publications; 2246 citations, h-index = 20 (Google Scholar); #corresponding author)

1. Li, J., Ma, Z., Shi, M., Malty, R.H., Aoki, H., Minic, Z., Phanse, S., Jin, K., Wall, D.P., Zhang, Z., Urban, A.E., Hallmayer, J., **Babu, M** and Synder, M (2015) Integrative analysis of human protein complexes reveals biochemical activities and convergent mechanisms of action in autism spectrum disorders. ***Cell Systems*** - In press.
2. Wan, C., Borgeson, B., Phanse, S., Tu, F., Drew, K., Clark, G., Xiong, X., Kagan, O., Kwan, J., Berzginov, A., Chessman, K., Pal, A., Cromar, G., Papoulas, O., Ni, Z., Boutz, D.R., Stoilova, S., Havugimana, P.C., Guo, X., Malty, R.H., Sarov, M., Greenblatt, J., **Babu, M**., Derry, W. B., Tillier, E., Wallingford, J.B., Parkinson, J., Marcotte, E.M. and Emili, A. (2015) Panorama of ancient metazoan macromolecular complexes. ***Nature*** 525, 339-344.
3. Rajagopala, S.V#., Sikorski. P., Kumar. A., Mosca. R., Franca-Koh. J., Pakala. S., Vlasblom. J., Arnold. R., Phanse. S., Ceol. A., Hauser. R., Siszler. G., Wuchty. S., Emili. A., **Babu. M**., Aloy. P., Pieper. R and Uetz. P (2014) Binary Protein-protein Interaction Landscape of Escherichia coli. ***Nature Biotechnology*** 32, 285-290.
4. Snider, J., Hanif, A., Lee, M.E., Jin K., Yu, A.R., Graham C., Chuk, M., Damjanovic, D., Wierzbicka, M., Tang, P., Balderes, D., Wong, V., Jessulat, M., Darowski, K.D., San Luis, B-J., Shevelev, I., Sturley, S.L., Boone, C., Greenblatt, J.F., Zhang, Z., Paumi, C.M., **Babu, M**., Park, H-O., Michaelis, S and Stagljar, I (2013) Mapping the functional yeast ABC transporter interactome. ***Nature Chemical Biology*** 9, 565-572.
5. **Babu, M**., Vlasblom, J., Pu, S., Guo, X., Graham, C., Bean, B.D.M., Burston, H.E., Vizeacoumar, F.J., Snider, J., Phanse, S., Fong, V., Tam, Y.Y.C., Davey, M., Hnatshak, O., Bajaj, N., Chandran, S., Punna, T., Christopolous, C., Wong, V., Zhong, G., Li, J., Stagljar, I., Conibear, E., Wodak, S.J.W., Emili, A and Greenblatt, J.F (2012) Interaction landscape of membrane protein complexes in *Saccharomyces Cerevisiae*. ***Nature*** 489, 585-589.
6. Havugimana , P.C., Hart , G.T., Nepusz., T., Yang , H., Turinsky, A.L., Li, Z., Wang , P.I., Boutz , D.R., Fong , V., Phanse , S., **Babu , M**., Craig , S., Hu , P., Wan , C., Vlasblom, J., Dar , V.N., Bezginov , A., Clark, G.W., Wu, G.C., Wodak, S.J., Tillier , E.R.M., Paccanaro , A., Marcotte, E.M and Emili, A. (2012). A census of human soluble protein complexes. ***Cell*** 150, 1068-1081.

See Mohan Babu's other publications

Dr. Ildiko Badea, PhD

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Dr. Ildiko Badea received a bachelor in pharmacy degree from the University of Medicine and Pharmacy Targu Mures in Romania and a PhD from the College of Pharmacy and Nutrition at the University of Saskatchewan. She was a postdoctoral fellow at the Vaccine and Infectious Disease Organization in Saskatoon. Currently she is an associate professor in the College of Pharmacy and Nutrition and a member of the Drug design and Discovery research Group. Dr. Badea is the Chair of the Biomedical Research Ethics Board of the University of Saskatchewan. She has served as a panel member on the Saskatchewan Health Research Foundation Postdoctoral Peer Review Committee. Her research interests are revolving around the design of non-invasive dermal and mucosal delivery systems for macromolecules and small anticancer agents.

The application of biotechnology in medicine resulted in an explosion of new therapeutic agents, such as proteins, DNA, and RNA. The major advantage of these drugs over chemical agents is their specificity and selectivity. Dr. Badea's research focuses on the use of DNA as a biotechnology drug. Lipid-based soft nanoparticles and nanodiamond-based gene delivery systems, which have the ability to encapsulate or complex DNA and shuttle it into the cells are developed in her laboratory, Using synchrotron-based technologies and biological assessments the gene transfer efficiency of these novel nanoparticle is evaluated. A continuous improvement of the DNA delivery systems will lead to the development of in vivo gene delivery systems for topical non-invasive administration.

The development of novel delivery systems has also given new hope for synthetic therapeutic agents that are effective but cannot reach their full potential in clinical evaluations due to the lack of selectivity and poor bioavailability. Incorporation of novel, poorly soluble anticancer drugs and radiopharmaceuticals in delivery systems improves their pharmacokinetic profile and reduces their toxicity. In Dr. Badea's laboratory, the ability of the encapsulated drug to stop cell proliferation, and programmed cell death is evaluated. The successful targeted delivery of the cytotoxic agents and radiopharmaceuticals into cancer cells without affecting healthy cells will lead to applied research for cancers with poor outcomes, such as skin cancers.

Selected Publications:

1. Poorghorban M, Karoyo AH, Grochulski P, Verrall RE, Wilson LD, **Badea I**. A 1H NMR Study of Host/Guest Supramolecular Complexes of a Curcumin Analogue with β‑Cyclodextrin and a β‑Cyclodextrin- Conjugated Gemini Surfactant *Mol. Pharmaceutics* 2015, 12, 2993−3006
2. Singh J, Michel D, Getson H, Chitanda JM, Verrall RE, **Badea I**. Development of amino acid-substituted gemini surfactant-based mucoadhesive gene delivery systems for potential use as non-invasive vaginal genetic vaccination *Nanomedicine* 2015, 10(3):405-417
3. Mohammed-Saeid W, Michel D, El-Aneed A, Verrall RE, Low N, **Badea I.** Development of lyophilized gemini surfactant-based gene delivery systems: influence of lyophilization on the structure, activity and stability of the lipoplexes *J Pharm Pharm Sci* 2012, 15: 548-567
4. Kaur R, Chitandra JM, Michel D, Maley J, Borondics F, Verrall RE, **Badea I.** Functionalized nanodiamonds as facile delivery agents for nucleic acids. *Int J Nanomed* 2012, 7:3851–3866
5. Michel D, Chitanda J, Balogh R, Singh J, Das U, El-Aneed A, Dimmock J, Verrall R, **Badea I.** Design and evaluation of cyclodextrin-based delivery systems for incorporation of curcumin analogs for topical treatment of melanoma. *Eur J Pharm Biopharm* 2012, 81: 548-56
6. Singh J, Michel D, Chitanda JM, VerrallRE, **Badea I**.Evaluation of cellular uptake and intracellular trafficking as determining factors of gene expression for amino acid-substituted gemini surfactant-based DNA nanoparticles. *J Nanobiotech* 2012, 10:7

Search PubMed for a complete list of publications by Ildiko Badea

Dr. Keith Bonham, BSc, PhD

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Dr. Keith Bonham is a Senior Research Scientist at the Saskatchewan Cancer Agency, Professor, Division of Oncology University of Saskatchewan and Associate Member, Department of Biochemistry, University of Saskatchewan.

Dr. Bonham received his B.Sc. (Hons.) at the University of Salford (UK) in 1980 and his Ph.D. at the University of Calgary in 1986.

My major research focus has been in the general area of gene expression and how that becomes deregulated in cancer cells. Most recently we have been particularly interested in the mechanism of action of a relatively new class of anti-cancer drug call Histone Deacetylase (HDAC) Inhibitors. These drugs appear to act through a reprogramming of gene expression; turning on some genes and turning off others. This epigenetic regulation results in cell cycle arrest, differentiating and apoptosis. Work on our lab has focused on the mechanism of gene silencing by these drugs, since one such affected gene in the SRC tyrosine kinase, a gene studied for many years in my lab. In a related project Dr. Franco Vizeacoumar and members of my lab we are using a state of the art approach to identify potential "druggable" targets in cancer cells that might synergize with HDAC inhibitors. This would predict a rational approach to combination therapies in the clinic. In collaboration with Dr. Erique Lukong we are also studying the epigenetic regulation of FRK, a Src like kinase, which appears to play a role in breast cancer.

Selected Publications:

1. Miah S., Goel R., Dai C., Kalra N., Beaton-Brown E., **Bonham K.**, and Lukong K. (2014) BRK targets Dok1 for ubiquitin-mediated proteasomal degradation to promote cell proliferation and migration. PLOS ONE. Published Feb 11th 2014 DOI: 10.1371/journal.pone.0087684
2. Mellor P., Deibert L., Calvert B., **Bonham K**, Carlsen SA. and Anderson DH. (2013). CREB3L1 is a metastasis suppressor that represses expression of genes regulating metastasis, invasion and angiogenesis. Mol. Cell. Biol. 33 (24) 4985-95.
3. Hirsch CL., Ellis DJP, and **Bonham K.** (2010) Histone Deacetylase Inhibitors Mediate Post-transcriptional Regulation of p21WAF1 through Novel cis-Acting Elements in the 3' Untranslated Region. Biochem. Biophys. Res. Commun. 402(4) 687-92.
4. Dehm SM., Hilton TL., Wang EH. and **Bonham K**. (2004) SRC Proximal and Core Promoter Elements Dictate TAF1 Dependence and Transcriptional Repression by Histone Deacetylase Inhibitors. Mol. Cell. Biol. 24 (6) 2296-2307.

Dr. John DeCoteau, MD, FRCP(C)

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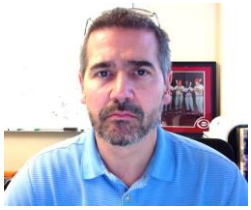

Dr. John DeCoteau, MD, FRCP(C) is a Professor of Pathology and Laboratory Medicine at the University of Saskatchewan and holds an associate membership at the Saskatchewan Cancer Agency. He received his MD at the University of Saskatchewan and specialty certification in Hematopathology at the University of Toronto. Following that, he pursued post-doctoral research studies at Harvard, MIT, and the University of Toronto. Dr. DeCoteau's expertise includes the molecular biology of leukemia, cancer diagnosis, classification and monitoring by Next Generation Sequencing, and minimal residual leukemia detection using high resolution flow cytometry. Dr. DeCoteau is the Medical Director of the Advanced Diagnostic Research Laboratory (ADRL) and is a co-leader of the Translational Cancer Research (TCR) Cluster at the University of Saskatchewan.

The field of oncology has been at the forefront of translating research discovery into improved diagnostics and targeted therapies. Consequently, the use of leading edge technologies, to support the diagnosis and monitoring of cancer patients, is now an essential element of clinical care. The Advanced Diagnostics Research Laboratory (ADRL) serves to develop and validate state-of-the-art diagnostic and monitoring tests for Saskatchewan cancer patients using new technology platforms such as 10-color flow cytometry and next generation sequencing (NGS). The information emerging from these tests can now be used to improve the diagnosis and classification of cancers, and to identify those cancer patients most likely to benefit from targeted therapies. New monitoring tests, having vastly increased sensitivity compared to standard approaches, are revolutionizing cancer care by allowing clinicians to safely reduce, or cease, potentially toxic therapies in those patients achieving 'deep' remissions, and by detecting early recurrence of cancer so that treatment approaches can be modified before unsalvageable disease progression occurs. ADRL holds a medical laboratory licence and performs validated assays to meet the oncology testing needs of clinical trial groups and the pharmaceutical industry. ADRL is also integrated with the Saskatchewan Therapeutic Antibody Resource (STAR) and the Centre for Biological Imaging Research and Development (C-BIRD) in the creation of a synthetic antibody discovery and validation pipeline. These entities use protein engineering and synthetic antibody technology to develop proprietary reagents and assays to improve the diagnosis and monitoring of cancer patients.

Current work undertaken by the ADRL includes assessing synthetic Fabs and antibodies generated against leukemia-associated surface proteins recently discovered by mass spectrometry based profiling of B-ALL cases. This work focuses on determining the diagnostic and therapeutic potential of these agents for improving the management of pediatric B-ALL. Another recently initiated project focuses on improving the monitoring of Non-Hodgkin Lymphoma (NHL) patients. Recent advances in NGS technology now permit tumor specific immunoglobulin gene clonotypes, and the mutational status of key genes implicated in lymphoma pathogenesis, to be efficiently determined in diagnostic biopsy material from individual NHL patients. This genetic information can be used to create predictive biomarkers, and to develop highly sensitive monitoring tools. Custom NGS based assays will be created to efficiently detect lymphoma clones in cell free DNA (cfDNA) present in plasma samples. This approach will be applied to serial plasma samples collected from NHL patients to test if noninvasive monitoring can identify evidence of molecular disease prior to clinical relapse and predict disease outcome after chemotherapy, transplantation or treatment with novel agents.

Selected Publications:

1. Yang Y, Sebra R, Pullman BS, Qiao W, Peter I, Desnick RJ, Geyer CR, DeCoteau JF, Scott SA. Quantitative and multiplexed DNA methylation analysis using long-read single-molecule real-time bisulfite sequencing (SMRT-BS). BMC Genomics. 2015 May 6;16:350.
2. Truitt L, Hutchinson C, DeCoteau JF, Geyer CR. Chaetocin antileukemia activity against chronic myelogenous leukemia cells is potentiated by bone marrow stromal factors and overcomes innate imatinib resistance. Oncogenesis. 2014 Oct 20;3:e122. doi: 10.1038/oncsis.2014.37.
3. Lakshmikuttyamma A, Scott SA, DeCoteau JF, Geyer CR. Reexpression of epigenetically silenced AML tumor suppressor genes by SUV39H1 inhibition. Oncogene. 2010 Jan 28;29(4):576-88.
4. Scott SA, Lakshimikuttysamma A, Sheridan DP, Sanche SE, Geyer CR, DeCoteau JF. Zebularine inhibits human acute myeloid leukemia cell growth in vitro in association with p15INK4B demethylation and reexpression. Exp Hematol. 2007 Feb;35(2):263-73.

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Dr. Oleg Dmitriev, PhD

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Oleg Dmitriev received his M.Sc. and Ph.D. degrees from Moscow State University in Russia. His post-doctoral training in biochemistry of ion transport across cell membranes, and in protein NMR spectroscopy was done at the University of Osnabrück in Germany in the laboratory of Karlheinz Altendorf, and at the University of Wisconsin in the laboratory of Bob Fillingame. Dr. Dmitriev was a recipient of the Alexander von Humboldt research fellowship in Germany. Oleg Dmitriev is currently a professor in the Department of Biochemistry at the University of Saskatchewan. He serves as an Academic Editor at PLOS One, and has been a member of the grant review panel for Prostate Cancer Canada. Research in Dmitriev lab is focused on the molecular mechanisms of membrane transport proteins including Wilson Disease Protein (ATP7B), ATP synthase, and bacterial multidrug resistance proteins. NMR spectroscopy remains one of the main techniques used in the lab to investigate dynamic behavior of these proteins, solve protein structures, and analyze protein interactions with small molecules.

The cancer connection in Dr. Dmitriev research developed from his interest in the mechanism of copper transport in human cells. Copper has remarkable chemical properties that make it indispensable in such diverse biological processes as respiration, hormone biosynthesis, connective tissue development, and neuronal function. At the same time, free copper is toxic, and the human tissues have sophisticated transport systems that deliver copper to its intended destinations within the cell, and at the same time prevent it from going astray and damaging the cell components. One of the most common anticancer drugs cisplatin, a chemical derivative of platinum, can bind to copper transport proteins, travel along the copper transfer pathways in the cell, and end up at the intracellular heavy metal detoxification facilities instead of its intended pharmacological target, DNA in the cell nucleus. This can make cancer cells resistant to cisplatin and other chemically similar platinum-based drugs. Dmitriev lab is studying the relationship between the transport of copper and platinum in the cell to improve pharmacological effectiveness of platinum-based anticancer drugs and reduce their toxicity during chemotherapy.

Selected Publications:

1. Huang, Y., Nokhrin, S., Hassanzadeh-Ghassabeh, G., Yu, C., Yang,H., Barry, A.N., Tonelli, M.. Markley, J.L., Muyldermans, S., **Dmitriev, O.Y.**, Lutsenko, S. (2014) Interactions Between Metal-Binding Domains Modulate Intracellular Targeting of Cu(I)-ATPase ATP7B, as Revealed by Nanobody Binding, *J. Biol. Chem.,* 289:32682-93
2. Dolgova, N.V., Nokhrin, S., Yu, C., George, G.N., and **Dmitriev, O.Y.** (2013) Copper chaperone Atox1 interacts with the metal-binding domain of Wilson disease protein in cisplatin detoxification. *Biochem. J.* 454:147-56.
3. **Dmitriev, O.Y.,** Bhattacharjee, A., Nokhrin, S., Uhlemann, E.E., and Lutsenko, S. (2011) Difference in Stability of the N-Domain Underlies Distinct Intracellular Properties of the E1064A and H1069Q Mutants of Cu-transporting ATPase ATP7B. *J. Biol.Chem.* 286, 16355-16362.
4. **Dmitriev, O.Y.** (2011) Mechanism Of Tumor Resistance To Cisplatin Mediated by the Copper Transporter ATP7B. *Biochem. Cell Biol.* 89, 138-147
5. Dolgova, N.V., Olson, D., Lutsenko, S., and **Dmitriev, O. Y.** (2009) The soluble metal-binding domain of copper transporter ATP7B binds and detoxifies cisplatin. *Biochem. J*, 419, 51-56
6. **Dmitriev, O.,** Tsivkovskii, R., Abildgaard, F., Morgan, C.T., Markley, J.L. and Lutsenko, S. Solution Structure of the N-domain of Wilson Disease Protein: Unique Nucleotide-Binding Environment and Effects of Disease Mutations (2006) *Proc. Natl. Acad. Sci. USA* **103:** 5302-5307

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Dr. Humphrey Fonge, PhD

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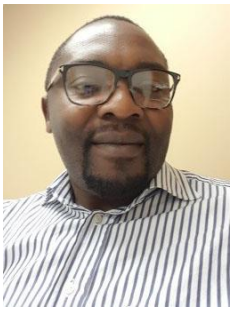

Dr. Fonge received an M.Sc and Phd in Pharmaceutical Sciences from Katholieke Universiteit Leuven (KU Leuven), Belgium. He then received post-doctoral training in molecular imaging and drug delivery at the University of Toronto under the supervision of Drs. R.M. Reilly and C. Allen. Dr. Fonge currently holds and adjunct and clinical assistant professor positions in the college of medicine of the University of Saskatchewan. He is also the radiopharmacist of the Royal University Hospital (RUH) Saskatoon. Dr Fonge has a number of awards and recognition in molecular imaging and radiotherapy and is funded by many provincial and national granting agencies/Foundations. His interests include the development of molecular imaging agents against cancer biomarkers using antibodies and antibody fragments, and the development of targeted alpha particle therapeutics using antibodies and multifunctional bionanomaterials.

Molecular imaging involves the non-invasive visualization of cellular and molecular events in living organisms in real time. ^{18}F-labelled Fluoro-deoxylglucose ([^{18}F]FDG) has been the workhorse of clinical positron emission tomography (PET/CT) and is used in over 90% of PET/CT procedures. [^{18}F]FDG measures glucose metabolism which is a common feature of most actively dividing cells but suffers of poor specificity in monitoring numerous cellular events and alterations involved in many diseases. To over this non-specificity issue we are developing engineered antibodies and antibody fragments against numerous biomarkers present in diseases and using these to develop molecular imaging agents. These agents can be used to 1) diagnose cancers; 2) select patients that will benefit from a particular anti-cancer therapy; 3) monitor response to cancer treatment 4) guide cancer surgery by aiding tumor visualization and improving the margin of resection. A second research focus of his group involves the development of targeted alpha particle therapeutics against resistant cancers. He group is working on innovative strategies to deliver multiple payloads of cytotoxic compounds to tumor cells using bionanomaterials and antibodies. This strategy can be used to overcome the issue of drug resistance encountered in clinical practice.

Selected publications:

1. Panosa C, **Fonge H**, Ferrer-Batallé M, Menéndez JA, Massaguer A, De Llorens R, Reilly RM. A comparison of non-biologically active truncated EGF (EGFt) and full-length hEGF for delivery of Auger electron-emitting 111In to EGFR-positive breast cancer cells and tumor xenografts in athymic mice. Nucl Med Biol. 2015 Aug 19. doi: 10.1016/j.nucmedbio.2015.08.003.
2. Panosa C1, Tebar F, Ferrer-Batallé M, **Fonge H**, Seno M, Reilly RM, Massaguer A, De Llorens R. Development of an epidermal growth factor derivative with EGFR blocking activity. PLoS One. 2013 Jul 30;8(7)
3. Banerjee N, **Fonge H**, Mikhail A, Reilly RM, Bendayan R, Allen C. Estrone-3-sulphate, a potential novel ligand for targeting breast cancers. PLoS One. 2013 May 22;8(5)
4. **Fonge H**, Leyton JV. Positron emission tomographic imaging of iodine 124 anti-prostate stem cell antigen-engineered antibody fragments in LAPC-9 tumor-bearing severe combined immunodeficiency mice. Mol Imaging. 2013 May;12(3):191-202.
5. **Fonge H**, Fasih A, Cai Z, Leyton JV, Tikhomirov I, Done SJ, Reilly RM.^{111}In-Bn-DTPA-nimotuzumab with/without modification with nuclear translocation sequence (NLS) peptides: an Auger electron-emitting radioimmunotherapeutic agent for EGFR-positive and trastuzumab (Herceptin)-resistant breast cancer. Breast Cancer Res Treat. 2012 Aug;135(1):189-200.
6. Chattopadhyay N, **Fonge H**, Cai Z, Scollard D, Lechtman E, Done SJ, Pignol JP, Reilly RM. Role of antibody-mediated tumor targeting and route of administration in nanoparticle tumor accumulation in vivo. Mol Pharm. 2012 Aug 6;9(8):2168-79.
7. **Fonge H**, Huang H, Scollard D, Reilly RM, Allen C. Influence of formulation variables on the biodistribution of multifunctional block copolymer micelles. J Control Release. 2012 Feb 10;157(3):366-74

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Dr. Fourney completed his medical school and residency training in Neurosurgery at the University of Saskatchewan in 2001. He did a fellowship in neurosurgical oncology at the University of Texas M.D. Anderson Cancer Center in Houston, Texas 2001-2002. He has a special interest in brain tumors as well as complex spinal disorders including tumors of the spine. He has authored more than 80 published peer-reviewed articles and book chapters. He directed the residency training program in Neurosurgery at the University of Saskatchewan form 2003-2013. He was President of the Canadian Spine Society from 2007 to 2009. He was Annual Meeting Chair for the American Association of Neurological Surgeons and Congress of Neurological Surgeons Joint Section on Disorders of the Spine and Peripheral Nerves in 2012.

Selected Publications:

1. Tymchak ZA, Epp A, **Fourney DR**. Lumbosacral discitis-osteomyelitis after mesh abdominosacrocolpopexy. Spine J. 2015 Jan 1;15(1):194-5. doi: 10.1016/j.spinee.2014.08.004. Epub 2014 Aug 10. PubMed PMID: 25117721.
2. Wilgenbusch CS, Wu AS, **Fourney DR**. Triage of spine surgery referrals through a multidisciplinary care pathway: a value-based comparison with conventional referral processes. Spine (Phila Pa 1976). 2014 Oct 15;39(22 Suppl 1):S129-35. doi: 10.1097/BRS.0000000000000574. PubMed PMID: 25299256.
3. Ivanishvili Z, **Fourney DR**. Incorporating the Spine Instability Neoplastic Score into a Treatment Strategy for Spinal Metastasis: LMNOP. Global Spine J. 2014 Jun;4(2):129-36. doi: 10.1055/s-0034-1375560. Epub 2014 Apr 28. Review. PubMed PMID: 25054100; PubMed Central PMCID: PMC4078113.
4. Paton GR, Hagel L, **Fourney DR**. Hospitalized head and spine injuries on Saskatchewan farms. Can J Neurol Sci. 2014 Jul;41(4):436-41. PubMed PMID: 24878466.
5. Kindrachuk DR, **Fourney DR**. Spine surgery referrals redirected through a multidisciplinary care pathway: effects of nonsurgeon triage including MRI utilization. J Neurosurg Spine. 2013 Nov 15. [Epub ahead of print] PubMed PMID: 24236668.
6. Choi D, Shaw A, Mendel E, **Fourney DR**. Comments. Neurosurgery. 2012Jul;71(1):66-7. PubMed PMID: 22893906.
7. **Fourney DR**, Skelly AC, DeVine JG. Treatment of cervical adjacent segmentpathology: a systematic review. Spine (Phila Pa 1976). 2012 Oct 15;37(22Suppl):S113-22. doi: 10.1097/BRS.0b013e31826d6284. PubMed PMID: 22885831.
8. **Fourney DR.** Expert's Comment concerning Grand Rounds case entitled "Aggressive vertebral hemangioma of the thoracic spine without typical radiological appearance" (Lei Dang, Chen Liu, Shao Min Yang, Liang Jiang, Zhong Jun Liu, Xiao Guang Liu, Hui Shu Yuan, Feng Wei, Miao Yu). Eur Spine J. 2012 Oct;21(10):2000-2. doi: 10.1007/s00586-012-2384-y. Epub 2012 Jun 26. PubMed PMID: 22732827; PubMed Central PMCID: PMC3463693.
9. Hnenny L, **Fourney DR.** Minimal access to the posterolateral lumbar spine. J Neurosurg Sci. 2012 Jun;56(2):97-103. Review. PubMed PMID: 22617172.
10. Wilkinson JS, **Fourney DR**. Failure of percutaneous remodeling of the ligamentum flavum and lamina for neurogenic claudication. Neurosurgery. 2012 Jul;71(1):86-92. doi: 10.1227/NEU.0b013e31825356f5. PubMed PMID: 22407072.

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Dr. Andrew Freywald, PhD

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Dr. Andrew Freywald received his Ph.D. degree in Molecular and Cell Biology at the Weizmann Institute of Science, Rehovot, Israel. His post-doctoral training in the area of signal transduction in normal and malignant T lymphocytes was done in the lab of Dr. Chaim Roifman at the Hospital for Sick Children, Toronto. Dr. Freywald is a Professor at the Department of Pathology, University of Saskatchewan. He has served as a panel member on CIHR, CRS and CBCF Peer Review Committees. He serves as a member of a Scientific Advisory Board at the Biomirex Inc. (MA, USA), a biotechnological company that specialises on the development of novel therapeutic antibodies. His research interests include investigation of molecular mechanisms that determine cancer aggressiveness, including invasiveness, metastasis, stemness and drug resistance. The ultimate goal of these investigations is to identify and characterize new targets for cancer therapies, and to support the development of new treatment approaches based on modulating activities of these targets in tumour cells.

Dr. Freywald's research program is currently focused on three main objectives, all related to the action of Eph receptor tyrosine kinases in various malignancies: **i)** Characterization of the functions of the EphB6 receptor in suppressing drug resistance in breast cancer tumours and breast cancer stem cells. **ii)** Generation and characterization of synthetic therapeutic antibodies targeting EphA2 and EphB6 receptors in various tumours. **iii)** Investigation of the role of EphB receptors in suppressing immunoelimination of leukaemic cells. These research projects are supported by CIHR, CBCF, CCSRI and SHRF granting agencies.

Selected Publications (within the last five years):

Reviews in refereed journals:

1. Paul J., Templeton S., Baharani A., **Freywald A.**, Vizeacoumar F. (2014) Building high-resolution synthetic lethal networks: a 'Google map' of the cancer cell., Trends Mol Med *20, 704-715*.
2. Truitt L, **Freywald A.** (2011) Dancing with the dead: Eph receptors and their kinase-null partners. Biochem Cell Biol 89(2):115-29. Funded by CIHR, Fund #: 73726.

Articles in refereed journals:

1. Jessulat M., Malty R., Nguyen-Tran D., Deineko V., Aoki H., Vlasblom J., Omidi K., Jin K., Minic Z., Hooshyar M., Burnside D., Samanfar B., Phanse S., Freywald T., Prasad B., Zhang Z., Vizeacoumar F., Krogan N., **Freywald A.**, Golshani A., Babu M. (2015) Spindle Checkpoint Factors Bub1 and Bub2 Promote DNA Double-Strand Break Repair by Nonhomologous End Joining., Mol Cell Biol *35, 2448-63*.
2. Kamstra R., **Freywald A.**, Floriano W. (2015), N-(2,4)-dinitrophenyl-L-arginine interacts with EphB4 and functions as an EphB4 kinase modulator., Chemical Biology & Drug Design [Epub ahead of print].
3. Allonby O., El Zawily A., Freywald T., Mousseau D., Chlan J., Anderson D., Benmerah A., Sidhu V., Babu M., DeCoteau J., **Freywald A.** (2014), Ligand stimulation induces clathrin- and Rab5- dependent downregulation of the kinase-dead EphB6 receptor preceded by the disruption of EphB6-Hsp90 interaction., Cell Signal *26, 2645-57*. Funded by CIHR and SHRF Funds #: COP-107969, RSN-132192 and 2891.
4. Umeshappa C., Nanjundappa R., Xie Y., **Freywald A.**, Xu Q., Xiang J. (2013) Differential requirements of CD4(+) T-cell signals for effector cytotoxic T-lymphocyte (CTL) priming and functional memory CTL development at higher CD8(+) T-cell precursor frequency., Immunology *138, 298-306.*
5. Munegowda M., Xu S., **Freywald A.**, Xiang J. (2012) CD4(+) Th2 cells function alike effector Tr1 and Th1 cells through the deletion of a single cytokine IL-6 and IL-10 gene. Mol Immunol *51, 143-9.*
6. Maddigan, A., Truitt, L., Arsenault, R., Freywald T., Allonby O., Dean J., Narendran A., Xiang J., Weng A., Napper S. and **Freywald A.** (2011) EphB receptors trigger Akt activation and suppress Fas receptor-induced apoptosis in malignant T lymphocytes, J Immunol *187, 5983-94*. Funded by CIHR, Funds #: 73726 and COP-107969.
7. Truitt, L., Freywald, T., DeCoteau, J., Sharfe, N. and **Freywald A.** (2010) The EphB6 receptor co-operates with c-Cbl to regulate the behaviour of breast cancer cells, Cancer Res *70, 1141-53*. Funded by CIHR, Fund #: 73726.

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Dr. C. Ronald Geyer, PhD

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Dr. Ron Geyer received his B.Sc. and Ph.D. degrees from the Simon Fraser University. His post-doctoral training involved using combinatorial biology to study signal transduction with Dr. Roger Brent at the Molecular Sciences Institute in Berkeley, CA and creating novel genetic systems with Dr. Steven Benner at the University of Florida.

Dr. Geyer is presently a Professor in the Department of Pathology and Laboratory Medicine at the University of Saskatchewan. He currently directs STAR and C-BIRD at the University of Saskatchewan and is the Director of Research and Development for ADRL. Through these centres, Dr. Geyer pursues his research interests in engineering synthetic antibodies for applications in antibody-based therapy, molecular targeted imaging, immune cell therapy, and diagnostics.

Significant progress has been achieved in developing personalized therapies and diagnostics for a variety of diseases using targeted antibodies against genetic abnormalities or cell surface antigens. To build on these successes, STAR was established in 2011 by Dr. Geyer at the University of Saskatchewan to meet the scale and scope of antibodies that are needed for validating diagnostic and therapeutic targets identified from genomic data. STAR houses a state of the art facility for rapidly generating antibody reagents. STAR combines novel synthetic human antibody libraries, automated screening, next generation sequencing, high throughput antibody characterization, and rapid antibody expression and purification procedures to develop and validate antibodies for personalized therapies and diagnostics. STAR's synthetic antibody technology platform includes all the necessary infrastructure for high speed antibody reagent production and characterization including: magnetic and fluorescent based cell sorting, next generation sequencing, high throughput ELISA and protein interaction technologies, robotics, large scale bacterial and phage culture facilities, tissue culture facilities, antibody bioreactors and purification systems, fluorescent microscopes, and animal facilities and imaging.

To meet the needs of using antibodies for molecular-targeted imaging, C-BIRD was established in 2014 to apply the principles of antibody engineering to the development of next generation molecular imaging agents for early and definitive diagnosis, improved disease characterization, and guided therapeutic intervention. C-BIRD is operates and has access to infrastructure for **(i)** generating and engineering antibody fragments for imaging probes with desired affinity, tissue penetration, body clearance, and pharmo-kinetics; **(ii)** producing PET/SPECT radionuclides with desired half-lives that can be matched with the biologic probe to optimize signal to noise and minimize side effects; and **(iii)** PET, SPECT, CT, and optical imaging infrastructure for analyzing small and medium size animals. Combined this expertise and infrastructure enables C-BIRD to develop and translate biologic molecular imaging agents from mice to human in one centre.

To meet the current deficiencies, and anticipated future testing needs for Saskatchewan cancer patients and to support clinical trials and translational cancer research projects, ADRL was established to develop and validate assays, and move these assays into the clinical arena through existing linkages with Saskatoon Health Region (SHR) Diagnostic Molecular Pathology (DMP) and Clinical Flow Cytometry Laboratories. ADRL develops and provides validated diagnostic assays using DNA sequencing (NGS and Capillary), RT-PCR, Flow Cytometry, and Cell Sorting infrastructure. ADRL holds a medical laboratory licence and performs validated assays to meet the oncology testing needs of clinical trial groups and the pharmaceutical industry. ADRL is integrated with STAR and C-BIRD and uses protein engineering and synthetic antibody technology to develop proprietary reagents and assays to improve the diagnosis and monitoring of cancer patients.

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Dr. Gary Groot, MD, Dip TM&H, PhD, FRCS(C), FACS

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Dr. Gary Groot began his medical career in Zaire after completing his medical school training at the University of Saskatchewan and a diploma of Tropical Medicine and Hygiene at the Institute of Tropical Medicine in Antwerp, Belgium. Upon returning to Canada he completed his General Surgery Residency Training at the University of Saskatchewan before going to Winnipeg where he completed a fellowship in General Surgical Oncology. Returning to Saskatoon in 1992, Dr. Groot established himself as a general surgical oncologist with a special interest in head and neck oncology. For 6 years, beginning January 1999, he was the Head of Surgery for the Saskatoon Health Region. He has since completed a PhD in Community Health and Epidemiology, and become actively involved health research.

Gary is a currently clinical co-lead with the Ministry of Health's appropriateness program, Director of Surgical Oncology at the University of Saskatchewan, and member of the national quality committee of both the Canadian Partnership against Cancer and the American Head and Neck Association. In these roles he bridges the evolving needs of the health care system with his research interests.

Dr. Groot's research program has three interrelated research concentrations designed to enhance appropriateness of care and facilitate clinical quality improvement: **i)** an exploration of **Shared Decision Making** models/frameworks, especially in areas known to have variation or potentially inappropriate care in Saskatchewan (breast cancer, prostate cancer, melanoma, thyroid cancer, depression, lower back pain); **ii)** a host of **Clinical Quality Improvement** projects that seek to apply scientific knowledge and interdisciplinary efforts to improve health outcomes; and **iii) Clinical Pathways** research, that seeks to understand the effects of provincial clinical pathways on professional practice, patient outcomes, economics and patient decision making.

Selected Publications:

1. Wanis KN, Hunter AM, Harington MB, **Groot G**, Impact of an acute care surgery service on timeliness of care and surgeon satisfaction at a Canadian academic hospital: a retrospective study, World J Emerg Surg. 2014 Jan 10;9(1):4. doi: 10.1186/1749-7922-9-4.
2. Wanis K, Oucharek J, **Groot G**, Quality of thyroid referrals in Saskatchewan, Quality in primary care, 2013 21(4): 247-52.
3. **Groot G,** Rees H, Pahwa P, Kanagartnam S, Kinloch M, Predicting Local Recurrence Following Breast-Conserving Therapy for Early Stage Breast Cancer: The Significance of a Narrow (=2mm) Surgical Resection Margin. J Surg Oncol. 2011 Mar 1;103(3):212-6. doi: 10.1002/jso.21826. Epub 2011 Jan 15.

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Dr. Azita Haddadi received his Pharm.D. From Tehran University of Medical Sciences. As a PhD student at the Tehran Shahid Beheshti University of Medical Sciences, she was awarded a scholarship and continued her studies at the Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta under Dr. John Samuel's supervision in 2003. Subsequent to her PhD defence she started her postdoctoral fellowship in Dr. Samuel's laboratory in the area of cancer immunology. Dr. Haddadi then joined Quest PharmaTech Inc. as a Senior Scientist while working as a Research Associate at the University of Alberta. Dr. Haddadi is an Assistant Professor of Pharmacy at the College of Pharmacy and Nutrition, University of Saskatchewan.

Dr. Haddadi's research program focuses on overcoming the ongoing challenges in cancer therapy. The main emphasis of her research group is to develop new biomedical and pharmaceutical nanotechnology strategies to achieve the critical issues in cancer chemo-immunotherapy.

Her research activities are in the following areas:

- Formulation and characterization of polymeric (PLGA) nanomaterials and protein therapeutics
- siRNA/Oligonucletide delivery in cancer treatment
- Targeted delivery systems for pharmaceutical applications (topical, iv. or sc. administration)
- Receptor-mediated nanoparticles as cancer vaccines
- Receptor-based tumor targeting for chemotherapy

Human epidermal growth factor receptor-2 (HER2) overexpresses in around 30% of breast cancers that creates an opportunity to design HER2 targeted therapeutic drug delivery system. Ongoing research is critical in the development of novel molecular targeted approaches that will have a clinical benefit in HER2- positive breast cancer and minimize unwanted drug-related toxicities and ultimately enhance patient outcomes. In a recent collaboration with Genentech, Dr. Haddadi's group have developed a targeted PLGA nanoparticle modified with Trastuzumab that carries the docetaxel to the HER2 positive breast cancer. This novel formulation has shown selective targeting to the site and significant inhibition of HER2 expression compared to the conventional formulations of docetaxel and trastuzumab (Herceptin) in the market.

In collaboration with Quest PharmaTech Inc, Dr. Haddadi has formulated a novel nanoformulation for cancer photodynamic therapy of squamous cell carcinomas (SCCVII). The formulation has been tested at BC Cancer Agency in comparison with two other nanoformulations, Quest's standard liposomal formulation and a polyvinylpyrollidone nanocluster developed at National Institute for Nanotechnology (NINT), Alberta. The Nanoparticle developed by Dr. Haddadi showed a more pronounced outcome over 85% survival rate, compared to the other two formulations showing 25-35% survival rate. This PLGA formulation has been patented by Patent Cooperation Treaty (PCT); and the results of study were published in Photochemistry and Photobiology.

Selected Publications:

1. Jahan ST and **Haddadi A*;** "Investigation and optimization of formulation parameters on preparation of targeted anti-CD205 tailored PLGA nanoparticles", Int. J. Nanomedicine, 2015, *in press*
2. Izadifar, M; Kelly, M E.; **Haddadi, A**; Chen, D; "Optimization of Nanoparticles for Cardiovascular Tissue Engineering", Nanotechnology, 2015, Jun;26(23):235301
3. Sadat SMA, Saeidnia S, Nazarali A and **Haddadi A**; "Nano-pharmaceutical Formulations for Targeted Drug Delivery against HER2 in Breast Cancer", Current Cancer Drug Target, 2015;15(1):71-86.
4. Rafiei P, Mitchel D and **Haddadi A**; "Application of a Rapid ESI-MS/MS method for quantitative analysis of docetaxel in polymeric matrices of PLGA and PLGA-PEG nanoparticles through direct injection to mass spectrometer"; American Journal of Analytical Chemistry 2015; 6(2):164-175.
5. Izadifar M, **Haddadi A**, Kelly ME and Chen XB; "Rate-programming of nano-particulate delivery systems for smart bioactive scaffolds in tissue engineering", Nanotechnology 2015; 26(1):012001.
6. **Haddadi A*,** Hamdy S, Ghotbi Z, Samuel J and Lavasanifar A; "Immunoadjuvant Activity of Nanoparticles Surface Modified with Mannan", Nanotechnology 2014, Sep 5;25(35):355101.
7. Korbelik M, Madyalakan R, Woo T and **Haddadi A***, "Antitumor Efficacy of Photodynamic Therapy Using Novel Nanoformulations of Hypocrellin Photosensitizer SL052", *Photochemistry and photobiology, 2012, 88 (1): 188-93.*

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Dr. Troy Harkness earned his PhD from the Department of Genetics at the University of Alberta in 1994, and then did postdoctoral training at the Universities of Munich (1995-96) and Alberta (1996-2001). Dr. Harkness is a full professor in the Department of Anatomy and Cell Biology (joined in 2001) and a member of the Drug Discovery and Development Research Group. He also served on the Biological and Clinical aspects of Aging peer review committee for CIHR.

Dr. Harkness' research interests are twofold: **i)** understanding the molecular genetics of aging and chromatin dynamics using yeast as a model organism; and **ii)** elucidating molecular mechanisms delineating the development of drug resistant cancers using *in vitro* and *in vivo* models. His research has been supported by grants from CIHR, NSERC, CBCF, CCS, SHRF and CFI.

Selected Publications: (total citations 774; H-index 15)

1. Ghavidel, A., Baxi, K., Ignatchenko, V., Prusinkiewicz, M., Arnason, T.G., Kislinger, T., Carvalho, C.E., and **Harkness, T.A.A.** (2015) A Genome Scale Screen for Mutants with Delayed Exit from Mitosis: Ire1-independent Induction of Autophagy Integrates ER Homeostasis into Mitotic Lifespan. PLoS Genetics 11:e1005429.
2. Jiao, R., Postnikoff, S., **Harkness, T.A.A.**, and Arnason, T.G. (2015) The SNF1 Kinase UBA Domain Restrains its Activation, Activity, and the Yeast Lifespan. J Biol Chem. 290:15393-404. ***Highlight article of the month*.**
3. Harkness, T.A. and Arnason, T.G. (2014) A Simplified Method for Measuring Secreted Invertase Activity in Saccharomyces cerevisiae. *Biochem Pharmacol* 3: 151
4. Davies, G.F., Berg, A., Postnikoff, S.D., Wilson, H.L., Arnason, T.G., Kusalik, A., and **Harkness, T.A.** (2014) TFPI1 Mediates Resistance to Doxorubicin in Breast Cancer Cells by Inducing a Hypoxic-Like Response. *PLoS One* 9: e84611. Impact factor: 3.73.
5. Menzel, J., Malo, M.E., Chan, C., Prusinkiewicz, M., Arnason, T.G., and **Harkness, T.A.** (2014) The Anaphase Promoting Complex Regulates Yeast Lifespan and rDNA Stability by Targeting Fob1 for Degradation. *Genetics* 196: 693-709. ***Highlight article of the month for March***. Impact factor: 4.39.
6. Postnikoff, S.D.L. and **Harkness, T.A.A.** (2012) Mechanistic insights into aging, cell-cycle progression, and stress response. *Frontiers in Physiology* 3: 183.
7. Postnikoff, S.D., Malo, M.E., Wong, B., and **Harkness, T.A.A.** (2012) The yeast forkhead transcription factors fkh1 and fkh2 regulate lifespan and stress response together with the anaphase-promoting complex. *PLoS Genetics* 8:e1002583. Impact factor: 8.52.
8. Goldberg, A.A., Beach, A., Davies, G.F., **Harkness, T.A.A.**, Leblanc, A., and Titorenko VI. (2011) Lithocholic bile acid selectively kills neuroblastoma cells, while sparing normal neuronal cells. *Oncotarget* 2:761-82. Impact factor: 9.14.
9. Islam, A., Turner, E.L., Menzel, J., Malo, M.E., and **Harkness, T.A.A.** (2011) Antagonistic Gcn5-Hda1 interactions revealed by mutations to the Anaphase Promoting Complex in yeast. *Cell Division* 6:13. Impact factor: 4.09.
10. Feser, J., Truong, D., Das, C., Carson, J.J., Kieft, J., **Harkness, T.**, and Tyler, J.K. (2010) Elevated histone expression promotes life span extension. *Mol. Cell* **39:** 724-35. ***Featured article***. Impact factor: 15.28.
11. Turner, E.L., Malo, M.E., Pisclevich, M.G., Dash, M.D., Davies, G.F., Arnason, T.G., and **Harkness, T.A.A.** (2010) The *Saccharomyces cerevisiae* Anaphase-Promoting Complex interacts with multiple histone-modifying enzymes to regulate cell cycle progression. *Eukaryot. Cell* **9:** 1418-1431. Impact factor: 3.59.
12. Davies, G.F., Ross, A.R., Arnason, T.G., Juurlink, B.H.J., and **Harkness, T.A.A.** (2010) Troglitazone inhibits histone deacetylase activity in breast cancer cells. *Cancer Lett*. 288: 236-50.

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Dr. Lorraine Holtslander, RN, PhD, CHPCN(c)

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Dr. Lorraine Holtslander, RN, PhD, CHPCN(c) is an Associate Professor in the College of Nursing in Saskatoon, Canada with the University of Saskatchewan. Her BScN, MN and PhD were granted by the University of Saskatchewan. The focus of her research with cancer patients is with family caregivers, specifically their experiences after caregiving ends and into bereavement. Family caregivers become cancer survivors and the experience of an often challenging and difficult caregiving experience can have profound impact on their experience of grief and bereavement. Lorraine has developed a Finding Balance Intervention, a self-administered writing tool to help caregivers identify their emotions, build a support network and find meaning in their caregiving story. She is in the process of completing a CIHR funded Knowledge Synthesis of the qualitative research with bereaved caregivers. Lorraine also teaches family nursing and qualitative methods. Her clinical expertise is in Palliative Home Care while the focus of her research is palliative care, grief and loss, and supporting family caregivers during bereavement.

Selected Publications:

1. Burles, M., Peternelj-Taylor, C., & **Holtslander, L.** A 'Good Death' for All? Examining Issues for Palliative Care in Correctional Settings (CMRT-2015-0016) *Mortality*, acceptance July 2015
2. **Holtslander, L.**, Baxter, S., Cooper, D., Dadgostari, T., Duggleby, W., Duncan, V., Hudson, P., Peacock, S. (2015). A metasynthesis of qualitative research with bereaved family caregivers of cancer patients, *Cancer Nursing*, 38, (4S), p. S18-19. Paper presented at the International Conference on Cancer Nursing (ICCN) 2015, July, 2015 in Vancouver, Canada
3. Ogunkorode, A. O. & **Holtslander, L.** (2015). Integrative review of literature on the determinants of health outcomes of women living with breast or cervical cancer in Canada and Nigeria from 1990-2014: A comparative study, *Cancer Nursing*, 38 (4S), p. S6. Paper presented at International Conference on Cancer Nursing, July 2015, Vancouver Canada
4. Duggleby, W., Kuchera, S., MacLeod, R., Holyoke, P., Scott, T., **Holtslander, L.**, Letendre, A., Moeke-Maxwell, T., Burhansstipanov, L., & Chambers, T (2015). "Indigenous people's experiences at the end of life." *Palliative and Supportive Care:* 1-13.
5. **Holtslander, L.**, & Bally, J. (2014) The concept of finding balance in bereavement: Applying theory and research to practice *Grief Matters: The Australian Journal of Grief and Bereavement* Volume 17 Issue 1 (Autumn 2014)
6. Bally, J. M., Duggleby, W., **Holtslander, L.**, Mpofu, C., Spurr, S., Thomas, R., & Wright, K. (2014). Keeping hope possible: A grounded theory study of the hope experience of parental caregivers who have children in treatment for cancer. *Cancer Nursing*, 37(5), 363-372.
7. **Holtslander, L.** F., Bally, J. M., & Steeves, M. L. (2011). Walking a fine line: An exploration of the experience of finding balance for older persons bereaved after caregiving for a spouse with advanced cancer. *European Journal Of Oncology Nursing,* 15(3), 254-259.
8. Duggleby, W., **Holtslander, L.**, Kylma, J., Duncan, V., Hammond, C., & Williams, A. (2010). Metasynthesis of the hope experience of family caregivers of persons with chronic illness. *Qualitative Health Research*, 20(2), 148-158.

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Dr. Anthony Kusalik, PhD

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Dr. Anthony (Tony) Kusalik received his B.Sc. in mathematics from the University of Lethbridge in 1978. He then completed M.Sc. and Ph.D. degrees from the University of British Columbia in computer science in 1982 and 1988, respectively. He has been a faculty member at the University of Saskatchewan since December of 1985. As well as being a professor in the Department of Computer Science and Director of the Bioinformatics Program at the U. of Saskatchewan, Dr. Kusalik is also a member of the university's Division of Biomedical Engineering and an Associate Member of the School of Public Health. He has served on the program committees of many leading bioinformatics conferences, has been a reviewer for grant competitions for NSERC, CIHR and Agriculture and Agri-Food Canada (AAFC), and served as a grant selection panel member for the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH. His research interests span a broad range of topics in bioinformatics and computation biology, especially as applied to health-related research. He has conducted successful research in proteomics, immuno-informatics, functional genomics, epi-genetics, and meta-genomics.

Selected Publications:

1. "A Framework of De Novo Peptide Sequencing for Multiple Tandem Mass Spectra", by Y. Yan, **A. Kusalik**, F-X. Wu, in *IEEE Transactions on NanoBioScience*, Vol 14, No. 4 (April 2015), pp. 478-484. doi: 10.1109/TNB.2015.2419194.
2. "Characterization of the Host Response to Pichinde Virus Infection in the Syrian Golden Hamster by Species-Specific Kinome Analysis" by S. Falcinelli, B. Gowen, B. Trost, S. Napper, **A. Kusalik**, R. Johnson, D. Safronetz, J. Prescott, V. Wahl-Jensen, P. Jahrling, and J. Kindrachuk, in *Molecular and Cellular Proteomics*, Vol 14, No. 3 (March 2015), pp. 646-657. doi: 10.1074/mcp.M114.045443.
3. "Using Crude Whole-Genome Assemblies of *Neisseria gonorrhoeae* as a Platform for Strain Analysis: Clonal Spread of Gonorrhoea Infection in Saskatchewan, Canada" by S. Vidovic, C. Caron, A. Taheri, S. D. Thakur, T. D. Read, **A. Kusalik** and J. R. Dillon, in *J. of Clinical Microbiology*, Vol. 52, No. 10 (October 2014): 3772-3776. doi: 10.1128/JCM.01502-14.
4. "Ebola Virus Modulates Transforming Growth Factor-β Signaling and Cellular Markers of Mesenchymal-Like Transition in Hepatocytes" by J. Kindrachuk, V. Wahl-Jensen, D. Safronetz, B. Trost, T. Hoenen, R. Arsenault, F. Feldmann, D. Traynor, E. Postnikova, **A. Kusalik**, S. Napper, J. Blaney, H. Feldmann, and P. Jahrling, in *Journal of Virology*, Vol. 88, No. 17 (September 2014), pp. 9877–9892. doi: 10.1128/JVI.01410-14.
5. "A better sequence-read simulator program for metagenomics" by S. Johnson, B. Trost, J. Long, V. Pittet, **A. Kusalik**, in *BMC Bioinformatics*, Vol. 15, No. S9, (September 2014), pg. S14. 10 pages. doi: 10.1186/1471-2105-15-S9-S14.
6. "Equivalent input produces different output in the UniFrac significance test" by J. R. Long, V. Pittet, B. Trost, Q. Yan, D. Vickers, M. Haakensen and **A. Kusalik** in *BMC Bioinformatics*, Vol. 15 (13 Aug 2014):278. 6 pages. doi:10.1186/1471-2105-15-278. "Highly Accessed" designation.
7. "NovoHCD: De novo Peptide Sequencing from HCD Spectra", by Y. Yan, **A. Kusalik**, F-X. Wu, in *IEEE Trans. Nanobioscience*, Vol. 13, No. 2 (June 2014), pp. 65-72.
8. "TFPI1 Mediates Resistance to Doxorubicin in Breast Cancer Cells by Inducing a Hypoxic-Like Response" by G. Davies, A. Berg, S. Postnikoff, H. Wilson, T. Arnason, **A. Kusalik**, T. Harkness, in *PLoS ONE*, Vol. 9 No. 1 (2014), pg. e84611. 16 pages. doi: 10.1371/journal.pone.0084611.
9. "PIIKA 2: An Expanded, Web-Based Platform for Analysis of Kinome Microarray Data" by B. Trost, J. Kindrachuk, P. Määttänen, S. Napper, and **A. Kusalik**, in *PLoS ONE*, Vol. 8 No. 11 (2013), pg. e80837. 12 pages doi: 10.1371/journal.pone.0080837.
10. "Kinotypes: stable species- and individual-specific profiles of cellular kinase activity" by B. Trost, J. Kindrachuk, E. Scruten, P. Griebel, **A. Kusalik**, and S. Napper, in *BMC Genomics*, Vol. 14 (2013), pg. 854. 12 pages. doi: 10.1186/1471-2164-14-854.
11. "Divergent Immune Responses to Mycobacterium avium subsp. paratuberculosis Infection Correlate with Kinome Responses at the Site of Intestinal Infection", by P. Määttänen, B. Trost, E. Scruten, A. Potter, **A. Kusalik**, P. Griebel, and S. Napper, in Infection and Immunity, Vol. 81, No. 8 (Aug. 2013), pp 2861-72. doi: 10.1128/IAI.00339-13.
12. "DAPPLE: a pipeline for the homology-based prediction of phosphorylation sites", by B. Trost, R. Arsenault, P. Griebel, S. Napper, and **A. Kusalik**, in Bioinformatics, Vol. 29, No. 13 (2013), pp. 1693-5. doi: 10.1093/bioinformatics/btt265.
13. "Computational phosphorylation site prediction in plants using random forests and organismspecific instance weights" by B. Trost and **A. Kusalik**, in Bioinformatics, Vol. 29, No. 6 (Mar. 2013), pp. 686-94. doi: 10.1093/bioinformatics/btt031.
14. "Pentamers Not Found in the Universal Proteome Can Enhance Antigen Specific Immune Responses and Adjuvant Vaccines" by A. Patel, J. C. Dong, B. Trost, J. S. Richardson, S. Tohme, S. Babiuk, **A. Kusalik**, S. K. P. Kung, and G. P. Kobinger, in PLoS ONE, Vol. 7, No. 8 (Aug 2012), pg. e43802. 13 pages. doi: 10.1371/journal.pone.0043802.

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Dr. Kiven Erique Lukong received his B.Sc. degree in biochemistry from Keele University, U.K. He obtained his M.Sc. and Ph.D. degrees in biochemistry from the University of Montreal under the supervision of Michel Potier and Alexey Pshezhetsky. He started his post-doctoral training in 2002, first at Harvard Medical School (Jae Jung lab), U.S.A. and second at McGill University (Stéphane Richard lab). He was hired as a tenure-tracked professor in the Department of Biochemistry at the University of Saskatchewan (U of S, Canada) in 2009. He is currently an Associate Professor and a member of the Cancer Research Cluster at the U of S. Since beginning his career as an independent researcher at the U of S, Dr. Lukong has obtained career awards from the Saskatchewan Health Research Foundation (SHRF, Top New investigator 2010) and from the Canadian Institutes of Health Research (CIHR, New investigator salary award). Dr. Lukong's research broadly involves elucidating the signalling mechanisms that control the growth of normal and cancer cells. His lab is investigating the cellular and physiological roles, the mechanisms of action and modes of regulation of the breast tumor kinase (BRK) family of non-receptor tyrosine kinases in breast cancer. The Lukong lab is also interested in defining the diagnostic, prognostic and therapeutic potential of the BRK family proteins in breast cancer. Research in the Lukong lab is funded by SHRF, CIHR and the Canadian Breast Cancer Foundation (CBCF).

Breast cancer is a serious public health issue globally and accounts for over 500,000 deaths annually with more than 1.6M new cases every year. The heterogeneity of the disease both histologically and at the molecular level has hampered therapeutic progress and drug resistance is also a major roadblock in the cure for breast cancer **(1, 2**). The BRK family kinases comprise 3 proteins, namely, BRK, FRK (Fyn-related kinase) and SRMS (Src-related kinase lacking C-terminal regulatory tyrosine and N-terminal myristoylation Sites) **(3)**. BRK, also known as protein tyrosine kinase 6 (PTK6) is overexpressed in over 80% of breast cancers. While BRK has oncogenic functions in breast cancers, FRK displays tumor suppressor activity. The cellular roles of SRMS are unknown. The Lukong lab is investigating the cellular and physiological roles, and the mechanisms of action and modes of regulation of all three kinases in breast cancer. Three recent publications from the Lukong lab have demonstrated that: 1) The enzymatic activation of BRK is important for BRK-promoted tumorigenesis **(4)**; 2) BRK potentially promotes tumorigenesis by inducing the degradation of the tumor suppressor protein Dok1 **(5)**; and 3) the enzymatic activity of SRMS is regulated by its N-terminal region **(6)**. The Lukong lab has also diversified into proteomic-related research to identify the interacting partners and substrates of the BFKs, crystalize the functional domains of these enzymes and to characterize their roles in signal transduction.

Selected Publications:

1. Goel RK, **Lukong KE**. 2015. Tracing the footprints of the breast cancer oncogene BRK - Past till present. Biochim Biophys Acta 1856: 39-54. PMID: 25999240
2. Nwabo Kamdje AH, Muller JM, **Lukong KE.** 2014. Signaling pathways in breast cancer: Therapeutic targeting of the microenvironment. Cellular signalling. PMID: 25093804
3. Nwabo Kamdje AH, Seke Etet PF, Vecchio L, Tagne RS, Amvene JM, Muller JM, Krampera M, **Lukong KE.** 2014. New targeted therapies for breast cancer: A focus on tumor microenvironmental signals and chemoresistant breast cancers. World J Clin Cases 2: 769-86. PMID: 25516852
4. Miah S, Goel RK, Dai C, Kalra N, Beaton-Brown E, Bagu ET, Bonham K, **Lukong KE.** 2014. BRK Targets Dok1 for Ubiquitin-Mediated Proteasomal Degradation to Promote Cell Proliferation and Migration. PLoS One 9: e87684. PMID: 24523872
5. Goel RK, Miah S, Black K, Kalra N, Dai C, **Lukong KE.** 2013. The unique N-terminal region of SRMS regulates enzymatic activity and phosphorylation of its novel substrate docking protein 1. The FEBS journal 280: 4539-59. PMID: 23822091
6. Miah S, Martin A, **Lukong KE**. 2012. Constitutive activation of breast tumor kinase accelerates cell migration and tumor growth in vivo. Oncogenesis 1: e11. PMID: 23552639

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Dr. David R. J. Palmer, PhD

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Dave Palmer completed a B.Sc. (Honours) and a Ph.D. in Chemistry Queen's University at Kingston, Ontario, where he studied carbohydrate synthesis and reaction mechanisms. He then studied enzymology as a postdoctoral research associate in the Department of Biochemistry at the University of Illinois, Urbana-Champaign. He became a member of the Department of Chemistry at the University of Saskatchewan in 1999, and he has served as Head of that department since 2010. Dr. Palmer was the head of the Molecular Design Research Group from 2009-2014, and was elected to the Executive of the University of Saskatchewan's PRISM Centre, which promotes science and training in proteins and proteomics. He has served on the Biomedical Establishment Grant Review Committee for the Saskatchewan Health Research Foundation (SHRF). Dr. Palmer has held continuous research funding support since 2000 from external agencies including NSERC, SHRF, CFI, the Canadian Breast Cancer Foundation, and the Sylvia Fedoruk Canadian Centre for Nuclear innovation. He has trained fourteen graduate students, six postdoctoral fellows, and over 35 undergraduates.

Dr. Palmer studies enzymes, which are proteins that catalyze chemical reactions. Practically every living process is controlled by enzymatic activity. Understanding the functions and mechanisms of enzymes will allow us and others to predict the function of other enzymes, modify enzymes to generate new catalysts, and design inhibitors that can serve as medicinal agents. We also are engaged in the design and synthesis of compounds modified with ^{18}F for use in medical imaging. The work in our laboratory is therefore not only geared toward a fundamental understanding of biological processes, but has many applications, particularly in the treatment of infectious diseases and in the detection and treatment of cancer. Our breadth of techniques, including organic synthesis, protein purification, reaction kinetics, and biophysical chemistry allows us to attack challenges comprehensively at the molecular level.

Selected Publications:

1. M. M. Galka, N. Rajagopalan, L. M. Buhrow, K. M. Nelson, J. Switala, A. J. Cutler, **D. R. J. Palmer**, P. C. Loewen, S. R. Abrams, and M. C. Loewen* (**2015**) Identification of Interactions between Abscisic Acid and Ribulose-1,5-bisphosphate Carboxylase/Oxygenase. *PLOS One*, 10(7): e0133033.
2. S. M. Forget, A. Jee, D. A. Smithen, R. Jagdhane, S. Anjum, S. A. Beaton, **D. R. J. Palmer**, R. T. Syvitski, and D. L. Jakeman* (**2015**) Kinetic evaluation of glucose 1-phosphate analogues with a thymidylyltransferase using a continuous coupled enzyme assay. *Organic and Biomolecular Chemistry*, 13, 866-875.
3. C. J. T. Conly, Y. V. Skovpen, S. Li, **D. R. J. Palmer*** and D. A. R. Sanders* (**2014**) Tyrosine 110 Plays a Critical Role in Regulating the Allosteric Inhibition of *Campylobacter jejuni* Dihydrodipicolinate Synthase by Lysine. *Biochemistry*, 53, 7067-7075.
4. K. E. van Straaten, J. B. Ko, R. Jagdhane, S. Anjum, **D. R. J. Palmer**, and D. A. R. Sanders* (**2013**) The structure of NtdA, a sugar aminotransferase involved in the kanosamine biosynthetic pathway in *Bacillus subtilis*, reveals a new sub-class of aminotransferases. *Journal of Biological Chemistry*, 288, 34121-34130.
5. H. Zheng, D. Bertwistle, D. A. R. Sanders and **D. R. J. Palmer*** (**2013**) Converting NAD-specific inositol dehydrogenase to an efficient NADP-selective catalyst, with a surprising twist. *Biochemistry*, 52, 5876-5883.
6. Y. V. Skovpen and **D. R. J. Palmer*** (**2013**) Dihydrodipicolinate synthase from *Campylobacter jejuni*: kinetic mechanism of cooperative allosteric inhibition and inhibitor-induced substrate cooperativity. *Biochemistry*, 52, 5454-5462.
7. N. D. Vetter, D. M. Langill, S. Anjum, J. Boisvert-Martel, R. C. Jagdhane, E. Omene, H. Zheng, K. E. van Straaten, I. Asiamah, E. S. Krol, D. A. R. Sanders, and **D. R. J. Palmer*** (**2013**) A previously-unrecognized kanosamine biosynthesis pathway in *Bacillus subtilis*. *Journal of the American Chemical Society*, 135, 5970-5973.
8. I. Gabriel*, N. D. Vetter, **D. R. J. Palmer**, M. Milewska, M. Wojciechowski, S. Milewski (**2013**) Homoisocitrate dehydrogenase from Candida albicans: properties, inhibition and targeting by an antifungal pro-drug. *FEMS Yeast Research*, 13, 143-155.
9. S. Anjum, N. D. Vetter, J. E. Rubin, and **D. R. J. Palmer*** (**2013**) Synthesis of 3,3'-Neotrehalosadiamine and related 1,1'-Aminodisaccharides Using Disarmed, Armed, and Super Armed Building Blocks. ***Tetrahedron***, **69**, 816-825.

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Dr. Meena Sakharkar obtained her PhD from the National University of Singapore, followed by postdoctoral training at Stanford University on discordant introns and intronless genes in eukaryotic genomes. She was assistant professor with concurrent appointments as head, Pharmacogenomics and deputy director for the Advanced Design and Modeling Lab at Nanyang Technological University, Singapore. Before joining the University of Saskatchewan Dr. Sakharkar was a professor at the Graduate School of Life and Environmental Science at the University of Tsukuba, Japan. Dr. Sakharkar is currently an Associate Professor at the University of Saskatchewan. She serves on several Editorial Boards of journals publishing in BioInformatics, Cell Biology and Molecular Biology. Dr. Sakharkar's research interests are in drug target identification and validation using multiple cross-disciplinary approaches. Currently, she is developing a framework for finding novel therapeutics for metastatic breast cancer. She has published more than 70 peer-reviewed articles and has recently co-edited two books in genomics and drug discovery.

Two research streams are pursued in her research program: **1.** Understanding the molecular mechanism of action of PPAR gamma which focuses on the link between the PPAR gamma activation and its regulated pathways. **2.** Identification and validation of novel ligands (small molecules) that have significant role in breast cancer therapeutics and have greater benefit: risk ratio.

Peroxisome proliferators activated Receptor (PPARs) belong to the nuclear receptor superfamily and are ligand activated transcription factors, regulating the expression of a wide variety of genes. PPAR gamma is most intensively studied and it is primarily involved in the regulation of lipid metabolism and insulin sensitivity reactions and hence plays important role in cell physiology. It has been suggested that PPAR gamma activation is involved in transcriptional regulation of genes involved in proliferation, angiogenesis, apoptosis, organogenesis, and energy metabolism and hence implicated in cell growth and viability. Even though the pathophysiological importance of PPAR gamma is clear in normal cellular functions and energy balance, the molecular mechanisms and pathways including the precise set of genes modulated by PPAR gamma to bring about these effects are not known. Her research interest is to decipher the biological pathways regulated by PPAR gamma.

Thiazolidinediones (TZDs), the insulin sensitizing drugs are known ligands of PPAR gamma. TZDs have been reported to be effective in several types of cancers. Due to lack of understanding of the precise molecular modulations caused by these drugs unwanted side-effects have been observed. Hence, there is a need to understand the intricacies of this nuclear hormone receptor's function and pharmacology, find novel ligands of PPAR gamma and targeted delivery of these ligands. Correlating the functions of this family of transcription factors with available clinical data including the data on adverse drug reactions will open new avenues to using PPAR gamma as a target in cancer therapeutics and related disorders.

Selected Publications:

1. Thangavel S, Yoshitomi T, **Sakharkar MK**, Nagasaki Y. Redox nanoparticles inhibit curcumin oxidative degradation and enhance its therapeutic effect on prostate cancer. J Control Release. 2015;209:110-9. PMID:25912409.
2. Shashni B, Sharma K, Singh R, Sakharkar KR, Dhillon SK, Nagasaki Y, **Sakharkar MK**. Coffee component hydroxyl hydroquinone (HHQ) as a putative ligand for PPAR gamma and implications in breast cancer. BMC Genomics. 2013;14 Suppl 5:S6. PMID: 24564733.
3. **Sakharkar MK**, Shashni B, Sharma K, Dhillon SK, Ranjekar PR, Sakharkar KR. Therapeutic implications of targeting energy metabolism in breast cancer. PPAR Res. 2013:109285. PMID: 23431283.
4. Shashni B, Sakharkar KR, Nagasaki Y, **Sakharkar MK**. Glycolytic enzymes PGK1 and PKM2 as novel transcriptional targets of PPARγ in breast cancer pathophysiology. J Drug Target. 2013 Feb;21(2):161-74. PMID: 23130662.
5. Venkatachalam G, Kumar AP, Sakharkar KR, Thangavel S, Clement MV, **Sakharkar MK**. PPARγ disease gene network and identification of therapeutic targets for prostate cancer. J Drug Target. 2011;19(9):781-96. PMID: 21780947.
6. Venkatachalam G, Kumar AP, Yue LS, Pervaiz S, Clement MV, **Sakharkar MK**. Computational identification and experimental validation of PPRE motifs in NHE1 and MnSOD genes of human. BMC Genomics. 2009; 10 Suppl 3:S5. PMID:19958503.

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Dr. Rajendra K. Sharma is a Distinguished Professor in the Department of Pathology and Laboratory Medicine at the University of Saskatchewan and a Research Scientist at the Saskatoon Cancer Centre. Dr. Sharma received his Ph.D. degree from the All India Institute of Medical Sciences (AIIMS), New Delhi, India and D.Sc from the University of Saskatchewan, Saskatoon, SK, Canada.

I have had a long standing interest in the biochemical mechanisms of signal transduction processes, with special emphasis on Ca^{2+}-calmodulin (CaM)-regulated enzymes. One of the central questions concerning signal transduction processes is how cells use the limited number of signaling cascades to achieve diverse responses to each of the multitude of cell stimuli. The existence of multiple regulatory activities at each step of the signaling cascades provides the potential mechanisms for achieving such diverse and specific cell responses. Multiple signaling cascades undergo complex and rigorously - regulated interactions to achieve a unique and integrated cell response. Biochemical studies have revealed numerous interactions in the signal transduction pathways and the number continues to increase. However, the contributions made by these regulatory reactions under any specific physiological condition are not yet fully understood.

Calmodulin Regulated Systems: I have focused my effort mainly on the regulation of CaM-dependent cyclic nucleotide phosphodiesterase isozymes, CaM-dependent protein kinases, CaM-stimulated protein phosphatase (calcineurin) and a high molecular weight CaM-binding protein (HMWCaMBP) which was discovered in my laboratory. Subsequently it was established that HMWCaMBP is homologous to calpastatin, an inhibitor of the Ca^{2+}-activated cysteine proteases, calpains. Our laboratory is currently working towards elucidating the role and expression of CaM-regulated proteins in cardiac ischemia and reperfusion. Besides this endeavour, the significance of the non-cardiomyocyte population in heart muscle is being investigated.

Protein Myristoylation: In addition, my interest in the role of spatial separation of regulatory activities during the process of signal transduction has led me to initiate a study of the lipid modification by myristic acid (a 14 carbon fatty acid). Protein myristoylation is catalyzed by the ubiquitously distributed eukaryotic enzyme N-myristoyltransferase (NMT). This lipid modification is important for the proper functions of several proteins including many of those involved in cancer progression. Originally we have established that NMT is more active in human colonic epithelial neoplasms than in normal colonic tissue. Since NMT activity is highest in colon cancer tissue, a limitation of assessing the activity and protein expression of NMT for prognostic / diagnostic purposes is difficult because endoscopic biopsy must be performed to obtain tumor tissue. Towards this direction, we demonstrated that altered expression and localization of NMT is found in the peripheral blood and bone marrow of colon cancer patients. Furthermore, immunohistochemical analysis revealed weak to negative staining for NMT in peripheral blood mononuclear cells (PBMC) chosen as controls, whereas strong positivity was observed in the PBMC of colon cancer patients. The different NMT expression offers the basis of a potential adjunct investigative tool for screening or diagnosis of patients at risk for, or suspected of, having colon cancer (**US Patent: Number; 7, 892,758B2, Date of Patent – February 22, 2011).**

We are working on understanding the regulation of this protein in vivo to develop therapies directed to NMT to inhibit the development and progression of cancer. We have identified that HSC70, a protein generally involved in cellular protection from stress, inhibits NMT function. We aim to understand the mechanisms of NMT inhibition by HSC70. Further we are also exploiting the roles of phosphorylation on the regulation of NMT function.

Selected Publications:

1. Kumar S, **Sharma RK** (2015) N-Terminal region of the catalytic domain of human N- myristoyltransferase 1 acts as an inhibitory module. PLoS One DOI: 10.1371/journal. pone. 0127661
2. Parameswaran S, **Sharma RK** (2014) Ischemia and reperfusion induce differential expression of calpastatin and its homologue high molecular weight calmodulin-binding protein in murine cardiomyocytes. PLoS One 9:e114653.Doi:10.1371/journal. pone. 0114653
3. Shrivastav A, Varma S, Senger A, Khandelwal R, Carlsen S, **Sharma RK** (2009) Overexpression of Akt/PKB Modulates N-myristoyltransferase Activity in Cancer Cells. J Pathol 218, 391-398.
4. Shrivastav A, Varma S, Lawman Z, Yang SH, Ritchie SA, Bonham K, Singh SM,Saxena A, and **Sharma RK** (2008)Requirement of N-myristoyltransferase 1 in the development of monocytic lineage. J Immunol 180, 1019-1028.
5. Shrivastav A, Varma S, Saxena A, Decoteau J, **Sharma RK** (2007) N-myristoyltransferase: A potential novel diagnostic marker for colon cancer. J Transl Med 5, 58.
6. Magnuson BA, Raju RV, Moyana TN, **Sharma RK** (1995) Increased N-myristoyltransferase activity observed in rat and human colonic tumors. J Natl Cancer Inst 87, 1630-1635.

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Dr. Uppalapati has a multidisciplinary educational background in materials science and bioengineering. He obtained his M.Sc. and Ph.D. degrees from The Pennsylvania State University. His postdoctoral training was in the area of combinatorial protein and antibody engineering under the guidance of Dr. Sachdev Sidhu at University of Toronto. He is affiliated with the Translational Cancer Research Cluster in the College of Medicine and is currently an Assistant Professor in the Department of Pathology and Laboratory Medicine at University of Saskatchewan.

Research Interests:

Protein-protein interactions (PPIs) play an important role in cell signaling and homeostasis. Aberrant signaling, due to overexpression or knockdown of certain proteins, is the hallmark of diseases such as cancer. The ability to identify and monitor these molecular signatures/biomarkers of cancer is essential for prognosis, diagnosis and monitoring disease progression.

Dr. Uppalapati is developing biologic affinity reagents that bind specifically to cancer biomarkers. His laboratory uses combinatorial protein engineering techniques (such as phage display) to generate new protein-based reagents (synthetic antibodies and proteins) that bind the target molecule with high affinity and specificity. These reagents when injected in patients will accumulate specifically at the tumor site and can be used as carriers for targeted delivery of drugs and imaging probes to cancer site, for applications in therapy and non-invasive imaging.

In addition to translational applications, protein-based affinity reagents are extremely useful tools in cancer proteomics. Genomic data from cancer patients enables the discovery of several new potential targets for personalized medicine. However, small molecule inhibitors are unavailable for many of these proteins to validate these targets for cancer therapy. Development of small molecule inhibitors is a resource intensive process and is not scalable for high-throughput target validation. Combinatorial protein engineering techniques, such as phage display, now allow rapid identification and development of protein-based inhibitors in a scalable manner.

Selected Publications:

1. **Uppalapati, M.,** D.J.Lee, K. Mandal, H.Li, L.P Miranda, J. Lowitz , J. Kenney, J. J. Adams, D. Ault-Riché, S. B. H. Kent, S. S. Sidhu**,** A Potent D-protein Antagonist of VEGF-A is Non-immunogenic, Metabolically Stable and Longer-Circulating In Vivo. (Submitted to ACS Chemical Biology)
2. Mandal, K., **M. Uppalapati**, D. Ault-Riché, J. Kenney, J. Lowitz, S.S. Sidhu, S.B.H. Kent. 2012. "Chemical synthesis and X-ray structure of a heterochiral {D-protein antagonist plus vascular endothelial growth factor} protein complex by racemic crystallography", Proc Natl Acad Sci USA, 109:14779-14784
3. Ahmed, S. M., B.L. Theriault, **M. Uppalapati,** C.W. Chiu, B.L. Gallie, S.S. Sidhu, S. Angers. 2012. "KIF14 negatively regulates Rap1a-Radil signaling during breast cancer progression", J Cell Biol, 199: 951-67.

Patents:

1. U.S. Patent Application 61/784,077 "Scaffolded peptidic libraries and methods of making and screening the same", **Maruti Uppalapati**, Sachdev S. Sidhu, Aaron Kerman. Filed March 13, 2013
2. U.S. Patent Application 13/294,072 "GB1 peptidic libraries and methods of screening the same", Sachdev S. Sidhu, **Maruti Uppalapati**. Publication date May 24, 2012
3. U.S. Patent Application 13/294,078 "Methods and compositions for identifying d-peptidic compounds that specifically bind target proteins", Dana Ault-Riche, Stephen B.H. Kent, Sachdev S. Sidhu, **Maruti Uppalapati**. Publication date July 12, 2012
4. U.S. Patent Application 61/548,817 "Antibodies and antibody fragments targeting SIRP alpha and their use in treating hematologic cancers", Jean C. Y. Wang, Jayne S. Danska, John E. Dick, Sachdev S. Sidhu, **Maruti Uppalapati**. Filed October 9, 2011

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Dr. Franco Vizeacoumar, PhD

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Dr. Franco Vizeacoumar received his Ph.D. degree from the University of Alberta under the mentorship of Dr. Richard Rachubinski. His post-doctoral training in the area of Cancer Genomics and Systems Biology was from the laboratories of Drs. Jason Moffat, Charlie Boone and Brenda Andrews at the University of Toronto.

Research Interest: My lab focuses on identifying targetable vulnerabilities of cancer cells by exploiting tumor genetics. Indeed, many developing drugs are repeatedly directed towards a narrow scope of molecules and identifying druggable cancer targets has been one of the major roadblocks for cancer research. Hence a broader method of assessment of the molecular machinery of cancer cells is urgently needed to increase the current range of targets and eventually improve treatment efficiency. In an effort to facilitate development of anti-cancer drugs directed at specific molecules, we have turned to exploiting the interactions between gene pairs that can cause lethality. Particularly, we take advantage of an approach called Synthetic Dosage Lethality (SDL), where an overexpression of a gene is lethal only when another, normally non-lethal, mutation or deletion is present. Since cancer cells often overexpress genes due to the effect of gene amplification, or other epigenetic modifications, discovering SDL interactions could reveal new therapeutic targets for cancer treatment. Importantly, normal cells would be unaffected as the gene whose expression is lost, is not essential for its survival. We use the genome-wide pooled *sh*RNA gene knockdown technology as well as genome-wide, pooled CRISPR system to systematically probe ~18,000 genes in the human genome to identify SDL interactions. Using this information, we aim to build a "Google Map" of the cancer cell to design novel cancer therapeutics.

Selected Publications:

1. Hornsby M, Paduch M, Miersch S, Sääf A, Matsuguchi T, Lee B, Wypisniak K, Doak A, King D, Usatyuk S, Perry K, Lu V, Thomas W, Luke J, Goodman J, Hoey RJ, Lai D, Griffin C, Li Z, **Franco J. Vizeacoumar**, Dong D, Campbell E, Anderson S, Zhong N, Gräslund S, Koide S, Moffat J, Sidhu S, Kossiakoff S, and Wells J. A High Through-put Platform for Recombinant Antibodies to Folded Proteins. **Mol Cell Proteomics. 2015 Aug 19. pii: mcp.O115.052209. [Epub ahead of print]** (Impact Factor 7.251)
2. Paul. JM, Templeton SD, Baharani A, Freywald A, **Franco J. Vizeacoumar***. Building high resolution synthetic lethal networks: a "Google map" of the cancer cell. Review in ***Trends in Molecular Medicine*** **2014 Oct 22; 20(12):704-715.** (Impact Factor 9.5) ***Corresponding Author**
3. **Franco J. Vizeacoumar,** R. Arnold, F. Vizeacoumar, M. Chandrashekhar, A.Buzina, J. T.F. Young, J. H.M. Kwan, A. Sayad, P. Mero, S. Lawo, H. Tanaka, K. R. Brown, A. Baryshnikova, A. B. Mak, Y. Fedyshyn, Y. Wang, G. C. Brito, D. Kasimer, T. Makhnevych, T. Ketela, A. Datti, M. Babu, A. Emili, L. Pelletier, J. Wrana, Z. Wainberg, P. M. Kim, R. Rottapel, C. A.O'Brien, B. Andrews, C. Boone and J. Moffat. A Negative Genetic Interaction Map in Isogenic Cancer Cell Lines Reveals Cancer Cell Vulnerabilities. ***Molecular Systems Biology 2013 Oct 8; 9:696).*** (Impact Factor 11.3)
4. Marcotte R, Brown KR, Suarez F, Ketela T, Sayad A, Koh JL, Krzyzanowski PM, Sircoulomb F, Medrano M, Fedyshyn Y, Karamboulas D, Van Dyk D, Fedyshyn B, Luhova M, Brito G. **Franco J. Vizeacoumar,** Vizeacoumar FS, Datti A, Kasimer D, Misquitta C, Normand J, Haider M, Wrana J, Rottapel R, Neel BG, and Moffat J. The topography of essential genes in breast, pancreas and ovarian cancer. ***Cancer Discov. 2012 Feb; 2(2): 172-89.*** (Impact Factor 13.1)
5. Li Z*, **Franco J. Vizeacoumar***, Bahr S, Li J, Warringer J, Vizeacoumar FS, VanderSluis B, Bellay J, DeVit M, Fleming JA, Stephens A, Haase J, Lin Z, Baryshnikova A, Min R, Lu H, Yan Z, Jin K, Datti A, Nislow C, Costanzo M, Bulawa C, Myers CL, Gingras AC, Zhang Z, Blomberg A, Bloom K, Andrews BJ, Boone C. Systematic Exploration of Essential Yeast Gene Function with Temperature-Sensitive Mutants. ***Nat. Biotechnol. 2011 Apr; 29(4): 361-7.*** (Impact Factor 32.4) ***Co-First Author**
   Highlights of this article: News in Brief: *Nature Methods, Vol. 8, No 5, 2011*
6. **Franco J. Vizeacoumar**, van Dyk N, S Vizeacoumar F, Cheung V, Li J, Sydorskyy Y, Case N, Li Z, Datti A, Nislow C, Raught B, Zhang Z, Frey B, Bloom K, Boone C, Andrews BJ. Integrating High-throughput Genetic Interaction Mapping and High-content Screening to Explore Yeast Spindle Morphogenesis. ***J Cell Biol. 2010 Jan 11; 188(1): 69-81.*** (Impact Factor 10.8)
   Highlights of this article:
   Review Commentary: Systems cell biology of the mitotic spindle. Saleem RA & Aitchison JD. *J Cell Biol. 2010 Jan 11; 188(1): 7-9.*
   Video Podcast: *http://jcb.rupress.org/biosights/biosights_jan_25_2010.dtl J Cell Biol. 2010 Jan 25 - Biosights.*
7. **Franco J. Vizeacoumar**, Chong Y, Boone C, Andrews BJ. A picture is worth a thousand words: genomics to phenomics in the yeast *Saccharomyces cerevisiae.* Review in Febs Lett. 2009 Jun 5; 583(11): 1656-61. (Impact Factor 3.6)

Dr. Kishor Wasan, RPh, PhD, FAAPS, FCSPS, FCAHS

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Dr. Wasan completed his undergraduate degree in Pharmacy at the University of Texas at Austin and his Ph.D. at the University of Texas Medical Center in Houston Texas at MD Anderson Cancer Center in Cellular and Molecular Pharmacology. After completing a postdoctoral fellowship in Cell Biology at the Cleveland Clinic, Dr. Wasan joined the Faculty of Pharmaceutical Sciences at UBC until 2014. In 2009, Dr. Wasan was named CIHR/iCo Therapeutics Research Chair in Drug Delivery for Neglected Global Diseases and in 2010, Dr. Wasan was named a Fellow of the Canadian Academy of Health Sciences. In 2011, Dr. Wasan was award the Canadian Society of Pharmaceutical Sciences Leadership award for outstanding contributions to Pharmaceutical Sciences in Canada. Dr. Wasan has received support from the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada (NSERC), and from several charitable foundations and pharmaceutical companies.

The plasma lipoprotein distribution of potential drug candidates is not commonly studied. For some hydrophobic drug candidates, attainment of similar plasma free drug levels has not been associated with uniform production of pharmacological activity in different animal species. It is well known that plasma lipoprotein lipid profiles vary considerably between different animal species. In addition, human disease states can significantly influence plasma lipoprotein profiles resulting in altered drug therapeutic outcomes. A plausible explanation for these findings may be a result of lipoprotein drug transport within the systemic circulation. Elucidation of the mechanisms that dictate the lipoprotein binding of drugs may yield valuable insight into the factors governing the pharmacological activity and potential toxicity of these compounds. Furthermore, utilizing these factors to target compounds specifically to one lipoprotein subclass over another could, potentially, improve the drug's efficacy and safety.

Over the past 14 years, Dr. Wasan and his research team have published a number of studies and established the experimental methodologies necessary to justify the importance of investigating the role of lipids and lipoproteins in modifying the biological activity of waterinsoluble drugs. With these research tools in place, Dr. Wasan and his team have demonstrated and provided the potential mechanisms by which water-insoluble drugs interact with lipids and lipoproteins and how these interactions impact on the absorption, distribution, efficacy, toxicity and metabolism of such compounds.

In the larger perspective, these studies have increased the understanding of the mechanisms involved in serum distribution of hydrophobic drugs. In contrast to albumin protein binding, lipoprotein binding of drugs is often overlooked and so the role of lipoproteins as possible intravascular carriers for hydrophobic compounds and their involvement in modifying the biological effects of drugs is a novel and pharmaceutically important discovery. In 2002, the FDA suggested that lipoprotein-drug distribution studies should be considered as part of any new IND application that contains a hydrophobic compound. In addition many pharmaceutical companies now screen hydrophobic compounds for plasma lipoprotein distribution.

Selected Publications:

1. Gershkovich P, **Wasan KM**, Ribeyre C, Ibrahim F, McNeill JH. Effect of variations in treatment regimen and liver cirrhosis on exposure to benzodiazepines during treatment of alcohol withdrawal syndrome. Drugs Context. 2015 Aug 7;4:212287. doi: 10.7573/dic.212287. eCollection 2015. PubMed PMID: 26322116; PubMed Central PMCID: PMC4544271.
2. Gordon JA, Midha A, Szeitz A, Ghaffari M, Adomat HH, Guo Y, Klassen TL, Guns ES, **Wasan KM**, Cox ME. Oral simvastatin administration delays castration-resistant progression and reduces intratumoral steroidogenesis of LNCaP prostate cancer xenografts. Prostate Cancer Prostatic Dis. 2015 Aug 4. doi: 10.1038/pcan.2015.37. [Epub ahead of print] PubMed PMID: 26238234.
3. **Wasan KM**, Sivak O, Bartlett K, Wasan EK, Gershkovich P. Novel oralamphotericin B formulation (iCo-010) remains highly effective against murinesystemic candidiasis following exposure to tropical temperature. Drug Dev IndPharm. 2015 Sep;41(9):1425-30. doi: 10.3109/03639045.2014.954587. Epub 2015 Jul21. PubMed PMID: 25170660.
4. Sachs-Barrable K, Darlington JW, **Wasan KM**. The effect of two novelcholesterol-lowering agents, disodium ascorbyl phytostanol phosphate (DAPP) andnanostructured aluminosilicate (NSAS) on the expression and activity ofP-glycoprotein within Caco-2 cells. Lipids Health Dis. 2014 Oct 1;13:153. doi:10.1186/1476-511X-13-153. PubMed PMID: 25273894; PubMed Central PMCID: PMC4195884.
5. Osei-Twum JA, **Wasan KM**. Does P-glycoprotein contribute to amphotericin B epithelial transport in Caco-2 cells? Drug Dev Ind Pharm. 2015;41(7):1130-6. doi:10.3109/03639045.2014.931970. Epub 2014 Jun 25. PubMed PMID: 24963546.

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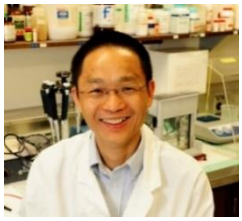

Dr. Yuliang Wu obtained his BSc and MSc from Zhejiang University, China in 1995 and 1998 respectively, and Ph.D. from International Centre of Genetic Engineering and Biotechnology (ICGEB), Delhi, India in 2002. In the following eight years, Dr. Wu did his postdoc training at the University of Alberta, Canada and the National Institute on Aging-NIH, where he studied the molecular and cellular basis of human genetic diseases characterized by genomic instability. Dr. Wu joined the Department of Biochemistry at the University of Saskatchewan, Canada in April 2011.

The integrity of our genomes is threatened continuously by DNA damage caused by replication, reactive oxygen species, radiation, and exogenous agents. All cells have developed a diverse range of repair pathways, which involve a large number of DNA repair proteins. When the DNA repair processes do not function correctly, a likely result will be instability of the genome that leads to human diseases, cancers, and aging. Our research focuses on DNA repair proteins, including helicase, recombinase and single strand DNA binding protein.

Helicases are molecular motors that couple the energy of nucleoside triphosphate hydrolysis to the unwinding and remodeling of structured DNA or RNA. They are involved in virtually all aspects of nucleic acid metabolism, including replication, repair, recombination, transcription, chromosome segregation, and telomere maintenance. Currently we are focusing on three helicases: **1)** FANCJ, also known as BRIP1 or BACH1, which mutations are linked to breast cancer, ovarian cancer and Fanconi anemia, **2)** ChlR1, also known as DDX11, is associated with a unique genetic disorder known as Warsaw Breakage Syndrome that is characterized by sister chromatid cohesion defects, and **3)** RTEL1, regulator of telomere elongation helicase 1 that participates in telomeric metabolism, mutations of which give rise to glioma, dyskeratosis congenital and Hoyeraal-Hreidarsson syndrome.

In addition, we are also interested in recombinase RAD51 and its paralogs, and single nucleic acid binding proteins (NABP1 and NABP2). Collectively, through structural and functional studies of these DNA repair proteins, we try to understand the molecular mechanisms underlying genomic instability. Ultimately the molecular information derived from these projects may be exploited to advance diagnosis, prognosis, and treatment of human diseases and cancers.

Selected Publications:

1. Guo, M., Hundseth, K., Ding, H., Vidhyasagar, V., Inoue, A., Nguyen, C. H., Zain, R., Lee, J. S. and **Wu, Y**. (2015) A Distinct Triplex DNA Unwinding Activity of ChlR1 Helicase. *J Biol Chem*. 290(8):5174-89.
2. Guo, M., Vidhyasagar, V., Ding, H., **Wu, Y**. (2014). Insight into the Roles of Helicase Motif Ia by Characterizing Fanconi Anemia Group J Protein (FANCJ) Patient Mutations. *J Biol Chem*. 289(15):10551-65.
3. Bharti, S.K., Khan, I., Banerjee, T., Sommers, J. A., **Wu, Y.**, Brosh, R. M. Jr. (2014). Molecular Functions and Cellular Roles of the ChlR1 (DDX11) Helicase Defective in the Rare Cohesinopathy Warsaw Breakage Syndrome, *Cell Mol Life Sci.* 71(14):2625-39.
4. Henderson, A., **Wu, Y**., Huang, Y., Chavez, L., Platt, J., Johnson, F.B., Brosh, R., Sen, D., and Lansdorp, P.M. (2014). Detection of G-quadruplex DNA in mammalian cells. *Nucleic Acids Res*. 42(2):860-8609.
5. **Wu, Y.**, Sommers, J. A., Loiland, J., Kitao, H., Kuper, J., Kisker, C., and Brosh, R. M. Jr. (2012). The Q Motif of FANCJ DNA Helicase Regulates its Dimerization, DNA Binding, and DNA Repair Function. *J Biol Chem*. 287(26):21699-21716.
6. **Wu, Y**., and Brosh, R. M. Jr. (2012). DNA Helicase and Helicase-Nuclease Enzymes with a Conserved Iron-Sulfur Cluster. *Nucleic Acids Res*. 40(10):4247-4260.
7. **Wu, Y**., Sommers, J., Khan, I., de Winter, J., and Brosh, R. (2012). Biochemical characterization of Warsaw Breakage Syndrome helicase. *J Biol Chem*. 287(2):1007-1021.
8. **Wu, Y**., Sommers, J. A., Suhasini, A. N., Leonard, T., Deakyne, J. S., Mazin, A. V., Shin-ya, K., Kitao, H., and Brosh, R.M. Jr. (2010). Fanconi anemia group J mutation abolishes its DNA repair function by uncoupling DNA translocation from helicase activity or disruption of protein-DNA complexes. *Blood* 116(19):3780-3791.

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Dr. Jim Xiang is a Senior Research Scientist at the Saskatchewan Cancer Agency, Professor, Division of Oncology, University of Saskatchewan and Associate Member, School of Public Health and Department of Pathology and Laboratory Medicine at the University of Saskatchewan. Dr. Xiang received his M.D. at the Shanghai University of Medial Sciences (Shanghai, China) in 1970 and his M.S. in 1983 and his Ph.D. in 1986 at the University Florida (USA).

Research Activities:

We are interested in **(i)** studying cellular and molecular mechanisms of cytokine's and mannose-6-phosphate receptor (M6PR)'s regulation and CD4+ T cell help in CD8+ cytotoxic T lymphocyte (CTL) contraction and memory, and **(ii)** in developing novel T cell-based immunotherapeutic vaccines for HER2-positive breast cancer and HIV-1 patients.

1. M6PR regulates CD8+ CTL contraction and memory. Molecular signaling for 90-95% cytotoxic T lymphocytes (CTLs) rapidly dying after proliferation subsequent to infection, leaving 5-10% as long-lived memory CTLs (mCTLs) is elusive. We demonstrate that a small fraction of KLRG-1^{low}CD62L^{high}IL-$7R^{+}$ mCTL precursors with down-regulated mannose-6-phosphate receptor (M6PR), the receptor for uptake of cytolytic granzyme-B (GB), survive the contraction following *Listeria monocytogenes*, and become functional KLRG-1^{low}CD62L^{high}IL-$7R^{+}$ mCTLs. Our study provides a novel insight into the role of M6PR in regulation of CTL contraction and memory, and is also critical for vaccine development. We are currently elucidating cellular and molecular mechanisms for regulatory role of M6PR in CTL contraction and memory.

2. A new concept "Sequential two cell interactions by CD4+ Th-APC in stimulation of CD8+ CTL responses": A long-standing paradox in cellular immunology concerns the conditional requirement for CD4+ T cells in priming of CD8+ CTL resp onses. We have proposed a new concept of T-APC. We found that CD4+ helper T (Th) cells can acquire antigen-presenting cell (APC) membrane pMHC I and II complexes and costimulatory molecules (CSM) when activated by APCs, and become Th-APC capable of stimulating central memory CD8+ CTL responses. We are currently studying the cellular and molecular mechanisms of CD4+ T cell help in three phases of CD8+ CTL immune responses. This new conceptual advance may also have great impact in developing novel vaccines.

3. Novel exosome-targeted T cell-based vaccines: Based upon this new T-APC concept, we developed novel T cell-based vaccines using active T cells with uptake of HER2 or HIV-1 Gag-specific dendritic cell (DC)-released exosomes (EXO). The novel vaccine HER2-Texo stimulated CTL responses leading to therapy against HER2-positive breast cancer in double transgenic HLA-A2/HER2 mice and eradication of trastuzumab-resistant BT474 breast cancer in athymic nude mice. The HIV-1 Gag-specific Gag-Texo vaccine stimulated Gag-specific CTL responses and therapeutic immunity in transgenic HLA-A2 mice, as well as counteracted T cell anergy and converted CTL exhaustion in chronic infection via its CD40L signaling the mTORC1 pathway.

Selected Publications in Recent 3 Years:

1. Ahmed K, Wang L, Griebel P, Mousseau D and **Xiang J**. Differential expression of mannose-6-phosphate receptor regulates T cell contraction. J Leuk Biol, 98: 313-318, 2015.
2. Wang R, Freywald A, Chen Y, Xu J and **Xiang J**. Transgene 41BBL-engineered vaccine stimulates potent Gag-specific therapeutic and long-term immunity via priming CD44+CD62LhighIL-7R+ CTLs with up- and down-regulation of anti- and pro-apoptosis genes. Cell Mol Immunol, 12: 456-465, 2015.
3. Wang L, Xie Y, Ahmed K, Ahmed S, Sami A, Chibbar R, Xu Q, Kane S, Hao S, Mulligan S and **Xiang J**. Exosomal pMHC-I complexes target T cell-based vaccine to directly stimulate CTL responses leading to antitumor immunity in transgenic FVBneuN and HLA-A2/HER2 mice and eradicating trastuzumab-resistant tumor in athymic nude mice. Breast Cancer Res Treat, 140: 273-284, 2013.
4. Umeshappa C S, Xu S, Nanjundappa R, Freywald A, Yulin Deng, Ma H and **Xiang J.** Th cells promote CTL survival and memory via acquired pMHC I and endogenous IL-2 and CD40L signaling and by modulating apoptosis-controlling pathways. PLos ONE 8: e64787, 2013.
5. Umeshappa C S, Nanjundappa R, Freywald A and **Xiang J**. Differential requirements of CD4+ T cell signals for effector cytotoxic T lymphocyte (CTL) priming and functional memory CTL development at higher CD8+ T cell precursor frequency. Immunol 138: 298-306, 2013.

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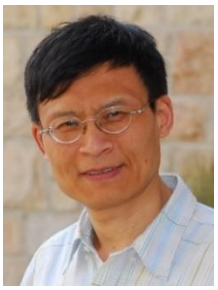

Dr. Xiao received his BSc degree in China, a MSc degree from University of Toronto and a PhD degree from University of Saskatchewan. Following two years of postdoctoral training at Harvard University, he became an Assistant Professor in the Department of Microbiology and Immunology, University of Saskatchewan, where he was promoted and remains as a Full Professor.

Ubiquitin (Ub) is an abundant, ubiquitous and highly-conserved small protein (76 amino acids) found in all eukaryotic cells, from unicellular yeasts to human. Through a series of enzymatic reactions, Ub is attached to the target protein with the help of a Ub-conjugating enzyme (E2 or Ubc) and a Ub ligase (E3), followed by the formation of a multimeric Ub chain known as the poly-Ub chain. Target proteins attached to poly-Ub are sent for degradation by the 26S proteosome, and this process serves as an important means of regulation involved in numerous cellular activities. Its importance is acknowledged by the 2004 Nobel Prize award to the discovery of ubiquitination and its involvement in target protein degradation. Careful investigation reveals that the above Ub chain is formed via a surface Lys48 residue of an incoming Ub attached to the C-terminal Gly residue. It was subsequently found that the Ub chain can also be formed via a surface Lys63 residue. Among over a dozen Ubcs found in any organism, only one, Ubc13, is capable of linking Ub through Lys63.

The unique feature of Ubc13 is due to its binding to another protein known as Uev (Ubc enzyme variant), which is also absolutely required for the process. More importantly, proteins attached to Lys63-linked Ub are not targeted for degradation, but for altering activities. Furthermore, among other types of ubiquitination, mono-ubiquitination is also believed to be a novel regulatory mechanism of the target protein activity, which expands the horizon of ubiquitination functions. Dr. Xiao is primarily interested in the discovery of the above unconventional ubiquitinaiton processes and in defining the molecular mechanisms of the related pathways. Since a few well-characterized unconventional ubiquitination target proteins are involved in cellular metabolisms such as DNA damage tolerance, cell cycle checkpoint, innate immunity and stress response, and these processes play critical roles in human diseases like cancer, this study will have direct impact on the diagnosis and treatment of cancers.

Selected Publications:

1. Zhang, C., Li, Z., Zhang, X., Yuan, L., Dai, H. and **Xiao, W**. (2015) Transcriptomic profiling of chemical exposure reveals roles of Yap1 in protecting yeast cells from oxidative and other types of stresses. *Yeast* (In press)
2. Wang, J., Zhang, Y., Hou, J., Qian, X., Zhang, H., Zhang, Z., Li, M., Wang, R., Liao, K., Wang, Y., Li, Z., Zhong, D., Wan, P., Dong, L., Liu, F., Wang, X., Wan, Y., **Xiao, W**. and Zhang, W. (2015) Ube2s regulates Sox2 stability and mouse ES cell maintenance. *Cell Death Differ.* (In press)
3. Xu, X., Blackwell, S., Lin, A., Li, F., Qin, Z. and **Xiao, W**. (2015) Error-free DNA-damage tolerance in *Saccharomyces cerevisiae*. *Mutat. Res. - Rev*. **764**: 43-50. [Text]
4. Li, J., Biss, M., Fu, Y., Xu, X., Moore, S. and **Xiao, W**. (2015) Two duplicated genes *DDI2* and *DDI3* in budding yeast encode a cyanamide hydratase and are induced by cyanamide. *J. Biol. Chem*. **290**: 12664-12675. [Text]
5. Xue, C., Liang, K., Liu, Z., Wen, R. and **Xiao, W**. (2015) Similarities and differences between Arabidopsis *PCNA1* and *PCNA2* in complementing the yeast DNA damage tolerance defect. *DNA Repair* **28**: 28-36. [Text]
6. Rout, M.K., Hodge, C.D., Markin, C.J., Xu, X., Glover, J.N.M., **Xiao, W**. and Spyracopoulos, L. (2014) Stochastic gate dynamics regulate the catalytic activity of ubiquitination enzymes. *J. Am. Chem. Soc*. **136**: 17446-17458. [Text]
7. Ball, L.G., Hanna, M.D., Lambrecht, A.D., Mitchell, B., Ziola, B., Cobb, J.A. and **Xiao, W**. (2014) The Mre11-Rad50-Xrs2 complex is required for yeast DNA postreplication repair. *PLoS One*. **9**: e109292. [Text]
8. Wen, R., Wang, S., Xiang, D., Venglat, P., Shi, X., Zang, Y., Datla, R., **Xiao, W**. and Wang, H. (2014) UBC13, an E2 enzyme for Lys63-linked ubiquitination, functions in root development by affecting auxin signaling and Aux/IAA protein stability. *Plant J.* **80**: 424-436. [Text]
9. Wu, Z., Shen, S., Zhang, Z., Zhang, W. and **Xiao, W**. (2014) Ubiquitin-conjugating enzyme complex Uev1A-Ubc13 promotes breast cancer metastasis through nuclear factor-□B mediated matrix metalloproteinase-1 gene regulation. *Breast Cancer Res.* **16**: R75. [Text]
10. Cao, L., Tang, X., Zhang, X., Zhang, J., Tian, X., Wang, J., Xiong, M. and **Xiao, W**. (2014) Two-stage transcriptional reprogramming in *Saccharomyces cerevisiae* for optimizing ethanol production from xylose. *Metab. Eng.* **24**: 150-159. [Text]
11. Ball, L.G., Xu, X., Blackwell, S., Hanna, M.D., Lambrecht, A.D. and **Xiao, W**. (2014) The Rad5 helicase activity is dispensable for error-free DNA post-replication repair. *DNA Repair* **16**: 74-83. [Text]

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Dr. Jiong Yan, MD, PhD

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Dr. Jiong Yan obtained her doctoral degree in Medicine in Peking Union Medical College in China and received her PhD and post-doctoral training in molecular and human Genetics at Baylor College of Medicine. She then completed her Pathology residency and Hematopathology fellowship training at New York-Presbyterian Hospital/Weill Cornell Medical Center. She has published about 20 peer-reviewed papers in reputed journals. Currently, she is an assistant professor in the Department of Pathology and Laboratory Medicine at the University of Saskatchewan.

Her research interests are molecular mechanisms of hematopoietic neoplasms, especially lymphomas. She is interested in characterizing morphologic and immunophenotypic features of different types of lymphomas as well as identification of novel molecular pathways that are suitable for targeted therapy.

Selected Publications:

1. Zhang T, Ma J, Nie K, **Yan J**, Liu Y, Bacchi CE, Queiroga EM, Gualco G, Sample JT, Orazi A, Knowles DM, Tam W. 2014. Hypermethylation of the tumor suppressor gene PRDM1/Blimp-1 supports a pathogenetic role in EBV-positive Burkitt lymphoma. Blood Cancer J. 4:e261. doi: 10.1038/bcj.2014.75.
2. Hasserjian RP, Campigotto F, Klepeis V, Fu B, Wang SA, Bueso-Ramos C, Cascio MJ, Rogers HJ, Hsi ED, Soderquist C, Bagg A, **Yan J**, Ochs R, Orazi A, Moore F, Mahmoud A, George TI, Foucar K, Odem J, Booth C, Morice W, DeAngelo DJ, Steensma D, Stone RM, Neuberg D, Arber DA. 2014. De novo acute myeloid leukemia with 20-29% blasts is less aggressive than acute myeloid leukemia with ≥30% blasts in older adults: a Bone Marrow Pathology Group study. Am J. Hematol. 89:E193-199.
3. **Yan J**, Nie K, Mathew S, Tam Y, Cheng S, Knowles DM, Orazi A, Tam W. 2014. Inactivation of BANK1 in a novel IGH-associated translocation t(4;14)(q24;q32) suggests a tumor suppressor role in B-cell lymphoma. Blood Cancer J. 4:e215. doi: 10.1038/bcj.2014.36.
4. **Yan J**, Rennert H. 2013. Chapter 152. Molecular testing for factor V Leiden and prothrombin gene mutations. 2nd ed. Transfusion Medicine and Hemostasis: Clinical and Laboratory Aspects. Edited by Shaz BH, Hillyer CD, Abrams CS and Roshal M. Elsevier, NY.
5. Lacaria M, Saha P, Potocki L, Bi W, **Yan J**, Girirajan S, Burns B, Elsea S, Walz K, Chan L, Lupski JR, Gu W. 2012. A duplication CNV that conveys traits reciprocal to metabolic syndrome and protects against diet induced obesity in mouse and human. PLoS Genet. 8(5):e1002713.
6. Schuetz AN, Pisapia D, **Yan J**, Hoda RS. 2012. An atypical morphologic presentation of Coccidioides spp. in fine-needle aspiration of lung. Diagn Cytopathol. 40:163-167.
7. Elizondo LI, Cho KS, Zhang W, **Yan J**, Huang C, Huang Y, Choi K, Sloan EA, Deguchi K, Lou S, Baradaran-Heravi A, Takashima H, Lücke T, Quiocho FA, Boerkoel CF. 2009. Schimke immuno-osseous dysplasia: SMARCAL1 loss-of-function and phenotypic correlation. J Med Genet. 46:49-59.
8. **Yan J**, Zhang F, Brundage E, Scheuerle A, Lanpher B, Erickson RP, Powis Z, Robinson HB, Trapane PL, Stachiw-Hietpas D, Keppler-Noreuil KM, Lalani SR, Sahoo T, Chinault AC, Patel A, Cheung SW, Lupski JR. 2009. Genomic duplication resulting in increased copy number of genes encoding the sister chromatid cohesion complex conveys clinical consequences distinct from Cornelia de Lange. J Med Genet. 46:626-634.

Dr. Jian Yang, PhD

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Dr. Jian Yang received his B.Sc. degree from Peking University in P.R. of China and Ph.D. degree from the University of Saskatchewan. His post-doctoral training in the area of protein chemistry and protein crystallography was done in the lab of Dr. Wayne G. Zhou at University of Massachusetts Medical School and in the lab of Drs. Gregory A. Petsko and Dagmar Ringe at Brandeis University. Dr. Yang is presently an associate professor in the College of Pharmacy and Nutrition at the University of Saskatchewan.

Sphingosine-1-phosphate (S1P) is a bioactive sphingolipid metabolite. It forms a rheostat with ceramide and regulates important physiological and pathophysiological processes in human. The intracellular level of S1P is predominately controlled by sphingosine kinase (SK) and sphingosine-1-phosphate lyase (SPL), which catalyze the phosphorylation of sphingosine to form S1P and irreversible degradation of S1P to produce ethanolamine and hexadecanol, respectively. Two isoforms of SK have been identified with SK1 distributed mainly in the cytoplasm and SK2 primarily located in the nucleus or perinuclear region. When S1P is synthesized by SK1, it follows an "Inside-Out" model to be translocated out of the cell to exert its extracellular functions *via* binding to a family of five G protein-coupled receptors ($S1PR_{1\text{-}5}$) distributed in various tissues. Binding to $S1PR_1$ promotes cell proliferation, survival, motility and migration; whereas binging to $S1PR_2$ inhibits cell proliferation, survival, motility and migration and induces cell apoptosis. For S1P synthesized by SK2 inside the nucleus, it is incorporated into co-repressor complexes containing SK2, histone deacetylase1 and histone deacetylase 2, which, in turn, upregulates the expression of tumor suppressor gene *p21* and proto-oncogene *c-fos.*

With recent advances in chemotherapy and targeted therapy, survival rate has significantly increased for early-stage breast cancer patients. However, prognosis for late-stage and recurrent breast cancer remains poor. Many patients seek integrative medical treatments during chemotherapy or after developing resistance towards thermotherapy drugs. Unfortunately, there is no guideline for oncologists on whether, when and how to apply integrative medical treatments. Establishing a preclinical database is important for both oncologists and cancer patients to correctly practice integrative medical treatments.

Dr. Yang's research program has three research themes designed to identify novel combination therapies for human breast cancer: i) to characterize effects of S1P concentration on human breast cancer cells especially basal-like triple negative breast cancer cells; ii) to investigate the therapeutic efficacy of chemotherapy drugs in combination with S1P; iii) to establish a preclinical integrative medicine database for human breast cancer.

Selected Publications:

1. D.P. Okinyo-Owiti, Q. Dong, B. Ling, P.D. Jadhav, R. Bauer, J.M. Maley, M.J.T. Reaney, **J. Yang** and R. Sammynaiken, 2015. Evaluating the cytotoxicity of flaxseed orbitides for potential cancer treatment. *Toxicology Reports*, 2, 1014-1018.
2. B. Ling, L. Chen, Q. Liu and **J. Yang**, 2014. Gene expression correlation for cancer diagnosis? A pilot study. *Biomed Research International*, Article ID 253804.
3. Q. Dong, B. Ling, B. Gao, J. Maley, R. Sammynaiken and **J. Yang**, 2014. Hedyotis diffusa water extract diminished the cytotoxic effects of chemotherapy drugs against human breast cancer MCF7 cells. *Natural Product Communications*, 9, 699-700.
4. A. Sultan, B. Ling, H. Zhang, B. Ma, D. Michel, J. Alcorn and **J. Yang**, 2013. Synergistic effect between sphingosine-1-phosphate and chemotherapy drugs against human brain-metastasized breast cancer MDA-MB-361 cells. *Journal of Cancer*, 4, 315-319.
5. W. Sun, R. Sammynaiken, L. Chen, J. Maley, G. Schatte, Y. Zhou and **J. Yang**, 2011. Sphingobium chlorophenolicum dichlorohydroquinone dioxygenase (PcpA) is alkaline resistant and thermally stable. *International Journal of Biological Sciences*, 7, 1171-1179.
6. W. Sun, L. Qiao, Q. Liu, L. Chen, B. Ling, R. Sammynaiken and **J. Yang**, 2011. Anticancer activity of the PR domain of tumor suppressor RIZ1. *International Journal of Medical Sciences*, 8, 156-160.
7. B. Ling, L. Chen, J. Alcorn, B. Ma and **J. Yang**, 2011. Sphingosine-1-phosphate: a potential therapeutic agent against human breast cancer. *Investigational New Drugs*, 29, 396-399.

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Clinical Trials Platform at The George and Fay Yee Centre for Healthcare Innovation

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Dr. Salah Mahmud is the Director of the Clinical Trials Platform at The George and Fay Yee Centre for Healthcare Innovation.

The George and Fay Yee Centre for Healthcare Innovation is a partnership between the University of Manitoba and the Winnipeg Regional Health Authority. The centre houses seven unique platforms, each staffed with experts and leaders from all disciplines in academia and practice.

At CHI, we are committed to ensuring that the latest research and evidence are translated into improved patient outcomes, enhanced patient experiences and improved access to care for Manitobans.

Who we work with:

- Patients
- Healthcare Leadership
- Clinicians
- Researchers
- Policy Makers

Our commitment to Manitobans:

- Engaging patients as full partners in care
- Providing healthcare professions and policy makers with the best available evidence to make informed decisions
- Supporting the development of innovative and cutting edge research
- Supporting strengthened clinical care, process improvements and better delivery of health care services
- Making crucial knowledge and research findings accessible

The Clinical Trials Platform supports Manitoban researchers to engage in high quality, practice changing, patient-oriented research by supporting the implementation of clinical trials in Manitoba. We define a clinical trial as any health related research study involving human participants. Therefore besides interventional studies, we also support researchers to conduct qualitative studies, non-interventional studies and restrospective reviews.

In partnership with key institutions, the Clinical Trials platform offers the following core services:

- Methodological input into investigator-driven clinical research
- Project Management support for large investigator-driven clinical trials
- Protocol and source documents/case report form templates
- A detailed road-map, outlining the steps required to conduct clinical trials in Manitoba
- Clinical research mentorship and orientation
- Services and staff to assist with planning and conduct of clinical trials

The support provided by the Clinical Trials platform has been determined in consultation with administrative leaders, investigators and research nurses responsible for supporting and carrying out clinical trials in Manitoba.

The Clinical Trials Platform at George and Fay Yee Centre for Healthcare Innovation website can be viewed at the following URL: http://chimb.ca/clinicaltrials

Clinical Trials Research at CancerCare Manitoba
Your Vehicle to Leading-Edge Care

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Kathryn is the Manager of the Clinical Investigations Office and has worked within the Clinical Investigations Office (CIO) at CancerCare Manitoba for the past 19 years, taking on various roles within the department. First, working as a Clinical Research Professional at the MacCharles and St. Boniface Units, followed by a position in the newly created Ethics & Regulatory Affairs section, then promoted to Supervisor of the section and eventually taking on the role of Manager which she has held for the past 9 years. Kathryn has her Bachelor of Arts Degree, majoring in Administrative Studies, her Health Information Management Diploma and Certification with the Society of Clinical Research Associates.

The Clinical Investigations Office (CIO) at CancerCare Manitoba (CCMB) is legislated by provincial law to facilitate and coordinate clinical research in the areas of prevention, treatment, palliation and quality of life. Our vision is that every patient would have the opportunity to participate in a research study.

Under the direction of the fifteen disease site groups, the CIO has been the facilitator of clinical trials at CCMB since the late 1960's. Data collected from our participation in national and international research has influenced the standard treatments used today, thus benefiting all patients. Through clinical trials, patients are provided with the opportunity to access state-of-the-art treatments and to raise the profile of CCMB as a significant contributor to the research being done worldwide. This, in turn, assists CCMB with the retention and recruitment of key researchers, physicians and professional staff to the organization.

Of the approximately 120 adult and pediatric clinical trials open to participation each year, the CIO enters an average of 300 new patients while continuing to follow thousands of participants in long-term follow up. Clinical research conducted at CCMB incorporates studies offered through cooperative groups, pharmaceutical companies and in-house research. Patients participating in these studies have access to some of the most innovative and cutting edge treatments, tests or prevention tools available.

The CIO has extensive experience across a spectrum of clinical trial activities, and offers the following services:

- protocol and consent development
- case report form design
- budget and contract negotiation
- management of ethics documentation, including initial submissions, amendments and safety reports
- completion of regulatory documentation
- screening patients for eligibility
- obtaining patient consent
- conducting patient evaluations
- case report form completion, data management

The clinical research conducted at CCMB plays a vital role in lessening the growing burden of cancer and benign hematological disorders.

The Clinical Trials Research website can be viewed at the following URL:
http://www.cancercare.mb.ca/home/cancer_research/clinical_investigations_office/

Epidemiology & the Manitoba Cancer Registry Fact Sheet

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CancerCare Manitoba's Department of Epidemiology & Cancer Registry consists of a dedicated team of experts highly skilled in transforming raw data into useful information. By collecting, organizing, and analyzing a variety of population-based cancer data, we can drive the development of programs to prevent cancer, detect it earlier or improve how we treat it. This work is frequently done in collaboration with clinical, basic, and other health researchers.

Main functions of the department include:

- Maintaining and constantly improving the Manitoba Cancer Registry's database with current up-to-date standards and coding classification systems
- Providing cancer data and consultation on statistical analysis and cancer epidemiology to CancerCare Manitoba, Manitoba Health, the University of Manitoba, provincial, national and international agencies and to the private sector
- Providing knowledge, data collection support, and analytical expertise to Manitoba Health, the Regional Health Authorities, and chronic disease stakeholders on cancer (and chronic disease) risk factors
- Undertaking surveillance, analytical, and evaluative epidemiological research
- Collaborating with health service providers and researchers in studies of: risk factors, screening, diagnosis, treatment, and outcome evaluations, as well as in other health-related research
- Participating in the education and training of graduate students and residents

Epidemiology Unit

Epidemiologists study the occurrence of diseases in human populations and investigate the causes, distribution, and outcomes of diseases in a given population. Our team studies patterns of cancer in the population and try to determine what factors distinguish people who develop or die from cancer and those who don't. The Epidemiology Unit has become a leader in the area of risk factor surveillance in Manitoba. Much of our work uses population-based information from the Manitoba Cancer Registry (see below) and other health databases and surveys. Current projects span the cancer spectrum including: identification of risk factors, the benefits of cancer screening, and the patterns and outcomes of various treatments.

Manitoba Cancer Registry

Much of what we know about cancer today comes from cancer registry data. Recognized as a leader in North America and the first province capturing stage data on all cancer sites, the Manitoba Cancer Registry is an essential tool for evidence-based, data-driven decision-making. Every day, physicians, researchers, health care administrators and standard setters rely on accurate cancer data because this vital information is used in research, treatment, health care planning and delivery and prevention initiatives.

The Epidemiology and Cancer Registry website can be viewed at the following URL:
http://www.cancercare.mb.ca/home/cancer_research/epidemiology_and_cancer_registry/

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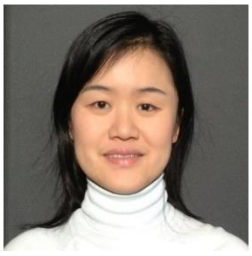

The University of Manitoba Flow Cytometry Core is located is a multi-user facility that provides a wide range of flow cytometry-based services, including training, access to multiple analysis instruments and cell sorting.

Flow cytometry is a laser-based technology that allows for simultaneous multiparametric analysis of physical and/or chemical characteristics of cells at the single-cell level. Fluorescence-labeled cells are carried to sensing area in sheath fluid and cross laser beam one a time. Information about the properties of cells, including cell size, granularity by scattered light and relative fluorescence intensity, are transmitted to light detectors after passing through a series of optical filters. This information is then converted into digital electronic signals and collected by specialized computer programs for further analysis.

Flow cytometry technique can be used in a wide range of research applications such as immunophenotyping, simultaneous analysis of levels of surface and intracellular markers (e.g. intracellular cell viability, apoptosis and proliferation,DNA content and cell cycle analysis, gene expression and transfer (e.g. transfection efficiency), intracellular Calcium flux activation states and oxidative burst.

Fluorescence-activated cell sorting is a specialized type of flow cytometry where a heterogeneous mixture of cell suspension can be sorted into up to four populations of interest based on specific light scattering and fluorescent characteristics. Cells are sorted one a time into single-cell-containing droplets that are broken off from the stream by a vibrating mechanism. As droplets flow pass laser beam and light detectors, those with cell of interest that meets the pre-set criteria are placed with an electrical charge and deflected to different angles before entering designated collection tubes. Fluorescence-activated cell sorting purification of rare populations such as cancer stem cells.

With our hands-on training program, you will quickly be able to perform flow cytometry analysis techniques on your own using our flow cytometry instruments and specialized analytical software. Our dedicated personnel are always here to offer you full-time technical support on experimental setup, troubleshooting and project design. Instruments available in the Core include 8 colour FACS Canto-II and 14 colour LSR-II instruments, as well as a 15 colour FACS Aria-III cell sorter housed within a custom BSL2/3 cabinet.

The University of Manitoba Flow Cytometry Core website can be viewed at the following URL:
http://www.umanitobaflow.ca/index.html

Genomic Centre of Cancer Research and Diagnosis

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Dr. Ludger Klewes received his first in-depth training in the field of fluorescence microscopy during the workshop offered by the GCCRD. In 2009 he moved on to work in Dr. Sabine Mai's lab where he validated the automated platform for the three-dimensional detection of fluorescent signals. During a visit of the ASI-software development team in Israel he received training on the newly released software platform for the automated signal detection. In June 2014 he accepted the position as facility manager. The team members are Landon Wark (part-time technician) and Daniel Lichtenzstejn (full-time computer technician). Together they train new personnel, assist in imaging and maintain and/or upgrade the GCCRD equipment, software and data (back-ups, networking and archiving).

The Genomic Centre for Cancer Research and Diagnosis was created as a Regional/National Facility for all cutting edge imaging applications. The objectives are focused on research in early detection of cancer and novel cancer treatments as well as teaching and training of highly qualified personnel.

The GCCRD is equipped with state-of-the-art equipment and the technical capabilities of the GCCRD are diverse, but complementary, enabling the researchers to perform microscopy and imaging of live cells, the study of relative nuclear and cytosolic protein levels by quantitative fluorescent immuno-staining, as well as the analysis of chromosomal changes by Spectral karyotyping (SKY), spectral imaging, Fluorescent in situ hybridization (FISH) such as multicolour-FISH (M-FISH), quantitative-FISH (Q-FISH), and multicolour-Banding (m-Banding). Furthermore, the facility offers the technology to perform Comparative genomic hybridization (CGH).

The automation is an important step to move new diagnostic tools based on fluorescent techniques into clinical trials. Therefore the imaging capability was extended by the purchase of an automated platform that allows for the fully automated data acquisition and analysis of fluorescent signals. A laser micro-dissection microscope enables researchers to identify and isolate cells for single cell sequencing, linking fluorescent microscopy with Next generation sequencing.

Cutting edge research requires imaging beyond the diffraction limit of 200nm. In order to address this need the GCCRD-platform extended it's imaging capabilities with a new array of methodologies collectively termed superresolution microscopy. The need for super-resolution microscopy is met with the Zeiss ELYRA PS.1 module and software modules to perform LSM, SR-SIM, PALM in 2- and 3D high-resolution (20 nm) fluorescence imaging,

Training at the GCCRD: The GCCRD serves as the training base for innovative technologies as outlined in the grant and in our training website (http://www.itmhrt.ca). Dr. Ludger Klewes and Mrs. Nikki Ryan coordinate the workshops and all educational aspects that are part of the training program. The GCCRD provides imaging workshops twice a year, one in the summer and another in the fall, attracting participants from various institutions in Canada, the United States and other countries from around the world. The workshop cover areas such as various fluorescence and microscopy techniques applicable to the biomedical field. Throughout the year, the GCCRD is involved in tours through the facility. In addition, the training of high school and undergraduate students, as well as the education of teachers and the public, is a firm foundation of the training program. Please see our training program website for more details. The GCCRD team, which includes Mr. Lichtenzstejn (full-time computer technician), Mr. Landon Wark (part-time technician) and Dr. Klewes (manager) participate in organizing these tours with MICB staff. Tours generally involve high school students from, as well as representatives from the industry, the government and the interested public.

Funding: The GCCRD is funded by the CancerCare Manitoba Foundation and the University of Manitoba. The workshops are kindly supported by Zeiss Canada, Applied Spectral Imaging (USA) and MetaSystems (USA).

The GCCRD is a member of Canadian Cytometry and Microscopy Association.

The GCCRD website can be viewed at the following URL:
https://www.umanitoba.ca/institutes/manitoba_institute_cell_biology/MICB/Platforms/GCCRD.html

Mammalian Functional Genomics Centre

The Research Institute in Oncology and Hematology is an international leader and major innovator in Functional and Cancer Genomics. With the recent completion of the human genome, the next major hurdle for the Human Genome Project will be to discover what these genes do. Given that we know there are as many as 5,000 human diseases with a genetic determinant, this new field of functional genomics will have a tremendous impact on health care and prevention. Our disease focus is clearly cancer.

The Research Institute in Oncology and Hematology has been leading the field by establishing the first Mammalian Functional Genomics Centre in Canada. The approach combines the wealth of sequence information available from the Genome Project with powerful cutting-edge genetic technologies in mice. The result is a national resource that will provide over 40,000 genetic "knock-out" mutations in mouse stem cells. Each mouse stem cell has a single gene missing as well as the capacity to actually form an intact mouse. Because mice are genetically 95% similar to humans they provide an ideal experimental model system for human disease. The mice that the Functional Genomics Centre can generate are 100% genetically identical to their mouse littermates - except for the one missing gene of interest. As such, any deficiency, defect or disease that might appear in the mutant mouse will be directly linked to the function of the single gene in question. The importance of discovering gene function in the context of the whole animal cannot be said too strongly for this is the context of disease itself - it cannot be modeled or predicted any other way. In this regard, the mutant mice themselves will not only provide insights into the genetic basis for the development of human diseases, but will also provide an experimental model to study the treatment and potential cures for human disease. On a practical note, development of the mice themselves initiates a chain of propriety that would be considered in all future discoveries as a result of the mice.

Programs:

The MICB Mammalian Functional Genomics Centre, directed by Dr. Geoff Hicks, continues to provide international leadership in what is currently being dubbed as the next *Human Genome Project*. The centre has established a high throughput technology for the genome-wide creation of a library of transgenic knockout mice. Knockout mice are considered to be one of the most powerful approaches to discovering gene function and can be used to reveal how disease-related genes, like cancer-causing genes, work. It's a critical first piece of the puzzle towards understanding what causes diseases in humans, and more importantly, how medicine can intervene or prevent the ensuing disease processes.

Dr. Hicks' Knockout program aims to generate a knockout mouse for every single gene in the genome. The mice are freely available to the scientific community at large, thereby providing this powerful tool directly to the hands of every disease expert in the world. The impact of this project is considered to be so important that it has led to a worldwide effort to achieve the mouse resource as soon as possible, the *International Mouse Knockout Project*. Major funding for the centre was recently renewed by CIHR will provide the centre with an additional $2.0 M in operating funds over four years. Most notably, Dr. Hicks is also the lead investigator for a $23 Million Genome Canada application that will provide funding to support the Canadian initiatives related to the International Knockout Mouse Project.

This Canadian led initiative is now recognized as one of the cornerstone international programs in Mammalian Functional Genomics. The next step in the overall strategy is to generate and functionally analyze knockout mice.

Dr. Hicks has established a leading edge Transgenics program located in both the MFGC and a state of the art transgenic mouse barrier facility located in the Faculty of Medicine's Brodie Building. The later, known as the University of Manitoba Genetic Modeling of Disease Centre (GMC, Dr. Geoff Hicks is the Scientific Director), provides both the faculty and the province with a full suite of transgenic services. GMC services are provided in a cost-recovery fee basis to ensure all members of the Institute and Faculty can have ready access to this powerful approach to study disease genes and mouse models of human disease. Services provided include the generation of mice from ES cells, cryopreservation of ES cells, germ cells, and the rederivation of mouse models brought into the faculty from around the world.

Dr. Hicks has also established the Canadian Mouse Consortium (www.MouseCanada.ca). The CMC integrates all the major mouse centres across Canada and will provide essential transgenic services to any Canadian disease-focused research program. Finally, the MFGC also provides additional key service platforms to the Institute. These include a high throughput DNA sequencing facility, a flow-cytometry facility and a long term cryogenic cell storage facility. Once again, these are provided to MICB members as cost-recovery services that significantly reduce the operating costs of MICB research programs. As these services are used by all member of MICB, the Institute provides support for the on-going maintenance of the key instruments.

In summary, the MICB Mammalian Functional Genomics Centre is currently a leader in the field and creating an invaluable genetic resource. The Centre's goal is to develop this resource to its fullest potential by focusing its efforts on the functional analysis of genes that are known, or suspected to be, determinants of cancer and human disease. We are hopeful that the true impact of the project will be to discover experimental mouse models of human disease that would greatly accelerate the development of pharmaceutical therapies, or even cures, for human cancer.

The Mammalian Functional Genomics Centre website can be viewed at the following URL:
http://www.umanitoba.ca/institutes/manitoba_institute_cell_biology/MICB/Platforms/MFG.html

Manitoba Breast Tumor Bank / Manitoba Tumor Bank

The Manitoba Breast Tumor Bank is a collection of tissue and related clinical data. The Bank is situated in the Research Institute in Oncology and Hematology and operates within the Faculty of Medicine of the University of Manitoba and CancerCare Manitoba. The Bank operates with the approval of the University of Manitoba Research Ethics Board. The bank was originally established by the National Cancer Institute of Canada in 1993 with funds from the Canadian Cancer Society and is now supported by CancerCare Manitoba Foundation in partnership with the University of Manitoba. The Bank provides an important resource both for breast cancer research at the University of Manitoba and for researchers across Canada and internationally.

During the assessment of each breast biopsy specimen small tissue samples are taken by Pathologists to process and examine under a microscope and these samples are then stored as a 'clinical archive'. After all diagnosis has been completed the Bank organizes these tissues and related clinical data into 'cases' for both future research and future clinical purposes and stores these 'cases' in CancerCare Manitoba. Researchers can apply to study these cases only through a review process and if they obtain approval for their research project from an institutional ethics review board. If approved, researchers are provided with tissue sections and the related clinical information from a set of typically 100 or more 'cases'. These cases are carefully selected from the computer database on the basis of selection criteria such as size and type of tumor that are relevant to the research question under study. All cases are distinguished by a Tumor Bank number but are anonymous due to the absence of any tag that might allow it to be traced to an individual patient. Researchers are charged to cover the costs of storage and release but no tissue or information is sold. The Bank has supported hundreds of research studies on breast cancer across North America, Europe and Australia.

The Bank stores three types of information on each case within a secure location in CancerCare Manitoba. This information relates to the tissue, clinical, and follow-up information. Tissue information includes the composition of the tissue, the size and type of tumor. Clinical information includes the patient age, clinical symptoms and the results of clinical tests such as x-rays. Follow-up information includes the type of treatment after surgery and the response to this treatment. Information is never released from the Bank with any label that might allow it to be traced to an individual. Information is only released as part of a set of anonymized cases, where each case is labeled by an anonymous tumor bank number and consists of a section of tissue with related information. We are a founding member of the Canadian Tissue Repository Network, (CTRNet, www.ctrnet.ca) and have CTRNet certification.

Since 2006 the MBTB has expanded to collect from other cancer disease sites, as described below. As well the MBTB has merged with the Manitoba Blood and Marrow Disorders Research Biobank, to form the Manitoba Tumour Bank (MTB). The Blood and Marrow Disorders component of the MTB, largely consists of samples (blood, bone marrow, buccal swabs) from Chronic Lymphocytic Leukemia (CLL) patients, although other blood & marrow disorders (ALL, AML, MM) in smaller numbers are being collected.

Inventory Update

The Breast Tumour Bank has over 5400 cases of frozen and/or formal fixed breast tumours, with long term patient follow-up >10 years in most cases. The Tumour Bank has also developed standard operating protocols for collection and banking of prostate cancers, normal breast tissues from reduction mammoplasties in 2009, ovarian cancers in 2012 and lung cancers 2010. To date the bank has accrued 304 prostate cases, 199 normal breast cases, 88 ovarian cases (35 ascites) and 210 lung cases. We have matched normal tissue samples for some cases. As well in some cases we have blood samples i.e. lung, ovarian, prostate. The bank has constructed and re-constructed several breast cancer tissue microarrays, two lung cancer tissue microarrays and a colon cancer tissue microarray; and has recently built a new lung cancer tissue microarray. The CLL inventory consists of over 2000 blood samples representing over 800 patients.

Operations: Consent. Informed consent continues to be obtained for use of samples and data for research. Potential clients are first asked by the clinic staff if they are willing and interested in being approached to participate in a Tissue Bank research study. Those clients who sign a preliminary invitation to participate form are then contacted by the consent nurse to discuss and consider participation in the MTB project.

Operations: Access, Release, and Revenue. Over the years we have released thousands of cases in the form of hundreds of thousands of very thin tissue sections. (FFPE and frozen) to support hundreds of research projects for local, national and international researchers. Over the last year we have released breast cases in support of research studies to 7 local laboratories, 2 national laboratories and 1 international laboratory. We have also provided lab services to 3 U of M researchers to help facilitate their research projects. Three lung cancer projects and 2 colon cancer projects have been supported for local researchers. We also generate around $18000 per year for the cost recovery of laboratory materials used in the process of release of breast cases and other services provided. Over the past year the Manitoba Blood and Marrow Disorders part of MTB has supported over 12 projects for local researchers as well as another project for a national researcher. Access to the MTB resources is via application and peer review. Application forms and process can be obtained from the website. *http://www.umanitoba.ca/institutes/manitoba_institute_cell_biology/MBTB/Index4.htm.*

Operations: Personnel. The overall operation of the MBTB is now directed by Dr. Leigh Murphy and Co-directed by Dr. Peter Watson; he remains directly involved with the MBTB and CTRNet. The director and co-director have been assisted by the MTB coordinator, Michelle Parisien, and the following personnel: Pathologist Dr. Carla Penner (0.1 FTE), Lab Technician, Andrea Fristensky (1 FTE), and Clinical consent nurse, Diane McAlpine (0.5 FTE), Data assistant Nicole Wozny (1FTE) and Data Coordinator Shannon Kornelsen (1 FTE). The MTB Blood and Marrow Disorder section has the following personnel: Lab technicians Michelle Queau, Kristin Hunt and Laurie Lange (2. 3 FTE,); research nurse and consent co-ordinator Donna Hewitt (1 FTE); all data managers associated with the MBTB also have data management responsibilities within the Blood and Marrow Disorders section.

Services. Tissue processing, fixation and paraffin-embedding. Tissue block and frozen tissue sectioning. The unit contains an automated tissue processing unit, cytostats and microtomes. A variety of fridges, -90C freezers and liquid nitrogen freezers and other storage equipment is also present in the MTB. The unit contains an auto-staining machine for high through-put immunohistochemistry (IHC) and in situ hybridization (ISH) analyses of multi-tissue sections; and Imaging Systems to capture and document high resolution images of the contents of the tumour sections that have been processed on the Ventana. IHC services and/or advice are regularly provided. The unit has the hardware for tissue micro-array construction and cooperates with other platforms within the Breast Cancer Research Centre and MICB generally; performing molecular profiling when required by the research programs within and associated with the MICB. MTB also has equipment for the processing and storage of blood and bone marrow samples.

The MTB website can be reviewed at: http://www.umanitoba.ca/institutes/manitoba_institute_cell_biology/MBTB/Index4.htm.

Medical Physics: Diagnostic and Therapeutic Cancer Imaging Research Program

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Microwave imaging is a novel non ionizing breast imaging technique that promises to increase sensitivity and specificity of breast cancer detection. We are working on integrating two distinct approaches (tomography and radar techniques) together with advanced solid-state microwave sensors to enable breast lesions to be detected with greater accuracy than existing methods. This research will contribute to the development of a novel breast imaging modality that will be accurate, comfortable, and safe. Such systems could be used for screening in remote and developing areas and for improving the accuracy of breast cancer diagnosis, thereby improving the quality of life for all women.

We are developing: Quantitative, 3D estimation of in vivo patient radiation dose received during therapeutic treatment via transit imaging, for off-line and on-line verification as well as adaptive radiation therapy applications. Fast methods of radiation scatter estimation for both diagnostic and therapeutic x-ray applications. Tumour tracking in lung SBRT. Multi-objective optimization for advanced treatment planning. 3D printer technology for custom patient treatment accessories.

X- and γ-ray scatter Imaging and Correction. All x- and gamma-ray imaging systems are negatively affected by the presence of scattered radiation which results in increased patient dose and image degradation, and which in turn can lead to misdiagnosis. We have shown that these scattered photons can be used to characterize tissues with greater detail and accuracy than can current systems. We are currently examining the application of these approaches to breast computed tomography and to dose reduction, attenuation correction and anatomical imaging in 3D PET imaging systems.

Real-time Adaptive Intensity-modulated radiotherapy Dosimetry (RAID). This research program uses three-dimensional reconstructions of in vivo patient dosimetry to adapt radiation treatment delivery to account for deficiencies in delivered dose as well as daily and real-time changes in patient anatomy. A significant fraction of patients experience short and long term changes in anatomy that can result in dangerous (>5%) changes in delivered dose leading to loss of local control (underdose) or increased complications (overdose). Our aim is to develop and optimize clinical tools including the ability to automatically track patient and organ motion and 3D dose, which will allow us to optimize and adapt the radiation treatments in real time to remove or significantly reduce these errors.

Other Research: We also support a number of smaller research projects into improved applications of MRI for radiation oncology, Virtual Reality for Brachytherapy Optimization and Training, Ultrasound imaging and the use of GPU programming for enhancing image processing and reconstruction performance.

Funding for these projects is provided by: Natural Sciences and Engineering Research Council (NSERC), Manitoba Health Research Council (MHRC), CancerCare Manitoba Foundation (CCMF), University of Manitoba Graduate Fellowship (UMGF), Canadian Foundation for Innovation (CFI), Canadian Breast Cancer Foundation (CBCF), Grand Challenges Canada – Stars in Global Health, Mathematics of Information Technology and Complex Systems Inc, (MITACS), American Society for Radiation Oncology, Varian Medical Systems and Manitoba Hydro.

Major Research Equipment includes: Linear Accelerators (Varian Trilogy and Edge), CT, MRI and PET scanners, Vector Network Analysers, Signal Generators and Oscilloscopes, Transmission Detectors, Anthropomorphic Breathing Phantom, 0.2T Open Bore MRI, Mammography and Ultrasound Units, Linux and GPU based servers.

Collaborators and Partners on these projects includes: EU-COST Consortium (Medical Microwave Imaging), Electromagnetic Imaging Group (ECE-UM), Spintronics Group (P&A-UM), Ultrasonics Research Laboratory (P&A-UM), Department of Radiology (UM), University of Cape Town, South Africa, Abuja National Hospital, Nigeria, University of Calgary, Calvary Mater Newcastle Hospital (Radiation Oncology Department), University of Newcastle (Australia), Vancouver Cancer Centre.

Next Generation Sequencing Platform

Dr. Deborah Tsuyuki, PhD

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Following the sequencing of the Human Genome, Next Generation sequencing was developed to produce genome sequencing at a reasonable cost. Rather than sequencing long, linear fragments as in traditional Sanger sequencing, small parallel and overlapping fragments are sequenced and recombined into genomic sequence using powerful computer servers. The first human genome was estimated to cost several billion dollars, now genomes can be sequenced for under $10,000. In additional to whole genomes, these NGS machines are being used for many different sequencing applications including Exome sequencing, Transcriptome sequencing, ChIP-Seq, RNA-Seq, targeted reSeq, and DNA methylation analysis and variations.

To that end, we have established a Next Generation Sequencing platform which will be available to U of M and other researchers. Our platform will consist of three different sequencing technologies. The Life Technologies SOLID 5500xl which uses clonally amplified DNA on beads and sequences by detection by ligation. The Ion Torrent Personal Genome Machine which sequences using semiconductor detection of the hydrogen ions released during nucleotide incorporation. Finally, the Illumina MiSeq which uses reversible dye terminators to sequence bridge-amplified query DNA by fluorescence detection. It has become accepted that due to inherent biases within the different technologies, discoveries made on one instrument should be validated on another instrument. This is a requirement to publish in the top journals. Our platform has the advantage of three disparate technologies which will compliment and validate each other.

The NGS platform allows UM researchers to have access to state-of-the-art technology to participate in epigenetic and genetic networks both in Canada and internationally. Our goal is to create a facility that will meet the needs of U of M researchers, from the initial experimental design, to reagent QC through sequencing and bioinformatics analysis, all at a reasonable cost.

Dr. Deborah Tsuyuki was introduced to DNA sequencing during her PhD in the Dept of Physiology at the University of Manitoba with Dr. R.P.C. Shiu. Sanger sequencing was a relatively new technology, using gel electrophoresis of radioactively labeled DNA fragments. She used it to sequence and characterize androgen, estrogen, and retinoic acid response elements in the 5' flanking region of the PIP/GCDFP-15 gene. Her post-doctoral studies were conducted at Mount Sinai Hospital at the University of Toronto. The development of fluorescently labeled nucleotides allowed her to sequence mutations in the PSA (Prostate Specific Antigen) gene. Subsequent work included research into methods for developing microsatellite markers for genotyping of domestic and wild animals using an early single column automated DNA sequencer. The following years were spent with Dr. G. Hicks (MICB, University of Manitoba) using an 8 column automated DNA sequencer to characterize the 5' insertion sites of genes disrupted by a retroviral gene trap vector in embryonic stem cell clones and sequence confirmations of targeted knockout genes in ESC clones. During this time, Dr. Tsuyuki has had the opportunity to gain experience with pyrosequencing and a large assortment of robotic workstations. Currently, Dr. Tsuyuki is the manager of the newly created Next Generation Sequencing facility at the University of Manitoba.

The Next Generation Sequencing Platform website can be viewed at the following URL:
http://chrim.ca/research/ngs/

Dr. Gilbert Arthur, PhD

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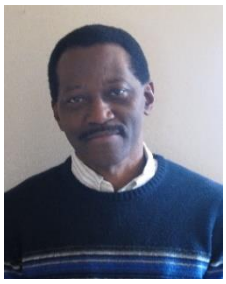

Dr. Gilbert Arthur received his B.Sc. degree from the University of Ghana in Accra, Ghana, and his Ph.D. degree from the University of Leeds in England. He moved to Winnipeg to do his post-doctoral training with Dr. P. C. Choy at the University of Manitoba in the area of phospholipid metabolism in the heart with special emphasis on plasmalogens. Dr. Arthur is currently a Professor in the Department of Biochemistry and Medical Genetics at the University of Manitoba.

Dr. Arthur's research focus is developing novel anticancer drugs via synthetic approaches or isolating novel compounds from plants. The goal is to develop new drugs that are effective against advanced and hard to treat cancers. We have successfully developed a number of synthetic compounds, glycosylated antitumor ether lipids, that are very effective against drug resistant cancer cells and cancer stem cells derived from a variety of human tumors. These compounds have the potential to prevent cancer recurrence and significantly prolong overall survival.

Dr. Arthur's research program seeks to **(a)** develop more effective analogs of the existing compounds; **(b)** investigate their efficacy in animal models of human tumors and **(c)** investigate the mechanism of action of these compounds.

Selected Publications:

1. Idowu T, Samadder P, **Arthur G**, Schweizer F. Design, synthesis and antitumor properties of glycosylated antitumor ether lipid (GAEL)- chlorambucil-hybrids. Chem. Phys. Lipids **2015**, http://dx.doi.org/10.1016/j.chemphyslip.2015.07.003
2. **Arthur G**, Bittman R. Glycosylated antitumor ether lipids: activity and mechanism of action. Anticancer Agents Med Chem. **2014**, 14, 592-596
3. Samadder P, Xu Y, Schweizer F, **Arthur G**. Cytotoxic properties of D-gluco-, D-galacto- and D-manno-configured 2-amino-2-deoxy-glycerolipids against epithelial cancer cell lines and BT-474 breast cancer stem cells.Eur J Med Chem, **2014**, 78,225-235
4. Xu Y, Ogunsina M, Samadder P, **Arthur G**, Schweizer F. Structure-activity relationships of glucosamine-derived glycerolipids: the role of the anomeric linkage, the cationic charge and the glycero moiety on the antitumor activity, ChemMedChem, **2013,** 8, 511–520
5. Samadder, P., Byun, H. S., Bittman, R. & **Arthur, G**. An active endocytosis pathway is required for the cytotoxic effects of glycosylated antitumor ether lipids. Anticancer Res. **2011**, 31, 3809–3818 (2011).
6. Samadder, P., Bittman, R., Byun, H. & **Arthur, G**. A glycosylated antitumor ether lipid kills cells via paraptosis-like cell death. Biochem. Cell Biol. **2009,** 414**,** 401–414.

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Structural changes or mutations in cancer genes have been identified as one of the causes of cancer. Common examples include gene amplification of the ERBB2 gene in 30% of breast cancers, EGFR gene mutations in 10% of North American lung cancer cases, and KIT mutations in occurring in over 70% of cases of a particular sarcoma subtype known as gastrointestinal stromal cancer. These mutations are particularly significant because they have led to the development of 'targeted' therapies, where a drug is designed to stop the growth of cancer cells with the specific gene abnormality, while sparing normal cells. This leads to therapy that not only prolongs survival, but reduces the toxicity of therapy.

After completing my clinical training, I conducted a research fellowship in Boston where I helped discover new potentially targetable genes in breast cancer including mutations in ERBB2 and a gene rearrangement involving AKT3 and MAGI3. The latter is the first example of a targetable fusion gene in breast cancer.

The goal of my laboratory at the Research Institute of Oncology and Hematology is to identify new gene targets in cancer using next generation DNA sequencing technology. We aim to characterize the rates of specific cancer associated mutations in the Manitoba population using resources like the Manitoba breast cancer and lung cancer tissue repositories. We also analyze cancer tissue obtained from patients being treated at CancerCare Manitoba to try and identify targeted therapies that may be more effective for their cancer treatment. This is essential as we move towards more personalized therapy for all patients with cancer.

Selected Publications:

1. Imielinski M, Berger AH, Hammerman PS, Hernandez B, Pugh TJ, Hodis E, Cho J, Suh J, Capelletti M, Sivachenko A, Sougnez C, Auclair D, Lawrence MS, Stojanov P, Cibulskis K, Choi K, de Waal L, Sharifnia T, Brooks A, Greulich H, **Banerji S**, Zander T, Seidel D, Leenders F, Ansen S, Ludwig C, Engel-Riedel W, Stoelben E, Wolf J, Goparju C, Thompson K, Winckler W, Kwiatkowski D, Johnson BE, Janne PA, Miller VA, Pao W, Travis WD, Pass HI, Gabriel SB, Lander ES, Thomas RK, Garraway LA, Getz G, Meyerson M. Mapping the hallmarks of lung adenocarcinoma with massively parallel sequencing. Cell. 2012 Sep 14;150(6):1107-20. doi: 10.1016/j.cell.2012.08.029.

2. Peifer M, Fernandez-Cuesta L, Seidel D, Leenders F, Sun R, Sos ML, Zander T, Menon R, Koker M, Dahmen I, Muller C, Altmuller J, Plenker D, Baessmann I, Becker C, de Wilde B, Vandesompele J, Bohm D, Ansen S, Gabler F, Wilkening I, Heuckmann J, Lu X, Cibulskis K, **Banerji S**, Getz G, Rauh D, Grutter C, Wright G, Wainer Z, Russell P, Petersen I, Chen Y, Stoelben E, Ludwig C, Schnabel P, Hoffmann H, Brockmann M, Engel-Riedel W, Muscarella LA, Groen H, Timens W, Sietsma H, Thunnissen E, Smit E, Heideman D, Snijders P, Cappuzzo F, Ligorio C, Damiani S, Field J, Sollberg S, Brustugun OT, Singer J, Clement J, Soltermann A, Moch H, Solomon B, Soria JC, Besse B, Brambilla E, Brambilla C, Lorimier P, Schneider PM, Hallek M, Meyerson M, Buttner R, Wolf J, Perner S, Heukamp L, Nurnberg P, Haas S, Thomas RK. Small cell lung cancer: identification of relevant mutated genes in a highly mutated genome by integrative genome analyses. Nat Genet. 2012 Sep 2. doi: 10.1038/ng.2396. [Epub ahead of print]

3. **Banerji S**, Cibulskis K, Rangel-Escareno C, Brown KK, Carter SL, Frederick AM, Lawrence MS, Sivachenko AY, Sougnez C, Zou L, Cortes ML, Fernandez-Lopez JC, Peng S, Ardlie KG, Auclair D, Bautista-Piña V, Duke F, Francis J, Jung J, Maffuz-Aziz A, Onofrio RC, Parkin M, Pho NH, Quintanar-Jurado V, Ramos AH, Rebollar-Vega R, Rodriguez-Cuevas S, Romero-Cordoba SL, Schumacher SE, Stransky N, Thompson KM, Uribe-Figueroa L, Baselga J, Beroukhim R, Polyak K, Sgroi DC, Richardson AL, Jimenez-Sanchez G, Lander ES, Gabriel SB, Garraway LA, Golub TR, Melendez-Zajgla J, Toker A, Getz G, Hidalgo-Miranda A, Meyerson M. Sequence analysis of mutations and translocations across breast cancer subtypes. Nature. 2012 Jun 20;486(7403):405-9. doi: 10.1038/nature11154.

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My research program focuses on metabolic deregulation in hematologic malignancies in the hopes to develop biomarkers for diagnostic and prognostic use, understanding of drug resistance and finally the identification of novel targets and development of targeted therapies.

Chronic Lymphocytic Leukemia (CLL) is an incurable disease with the exception of allogeneic bone marrow transplantation. Most patients requiring treatment do not meet the criteria for transplantation. To date, conventional modalities used in CLL therapy include nucleoside analogues, alkylating agents and are therefore rather nonspecific. Although monoclonal antibodies are currently being used, patients continue to relapse with treatment. Hence, the development of novel targeted therapeutic approaches remains a critical goal of CLL research. Banerji et al. investigated the role of a metabolic enzyme glycogen synthase kinase -3 alpha in acute myeloid leukemia.1 This implicated metabolic signaling as potential targets in leukemia therapy. Currently we are investigating the role of targeting metabolic signaling on CLL cells and their microenvironment.

Selected Publications:

1. Gefitinib targets ZAP-70-expressing chronic lymphocytic leukemia cells and inhibits B-cell receptor signaling. Dielschneider RF, Xiao W, Yoon JY, Noh E, **Banerji V**, Li H, Marshall AJ, Johnston JB, Gibson SB. Cell Death Dis. 2014 Oct 2;5:e1439. doi: 10.1038/cddis.2014.391.
2. On-target effect of FK866, a nicotinamide phosphoribosyl transferase inhibitor, by apoptosis-mediated death in chronic lymphocytic leukemia cells. Gehrke I, Bouchard ED, Beiggi S, Poeppl AG, Johnston JB, Gibson SB, **Banerji V**. Clin Cancer Res. 2014 Sep 15;20(18):4861-72. doi: 10.1158/1078-0432.CCR-14-0624. Epub 2014 Aug 29.
3. Increased risk of second malignancies in chronic lymphocytic leukaemia patients as compared with follicular lymphoma patients: a Canadian population-based study. Beiggi S, Johnston JB, Seftel MD, Pitz MW, Kumar R, **Banerji V**, J Griffith E, Gibson SB. Br J Cancer. 2013 Jul 16. doi: 10.1038/bjc.2013.381. [Epub ahead of print]
4. SYK regulates mTOR signaling in AML. Carnevale J, Ross L, Puissant A, **Banerji V**, Stone RM, Deangelo DJ, Ross KN, Stegmaier K. Leukemia. 2013 Mar 28. doi: 10.1038/leu.2013.89. [Epub ahead of print]
5. Targeting metabolism and autophagy in the context of haematologic malignancies. **Banerji V**, Gibson SB.Int J Cell Biol. 2012;2012:595976. Epub 2012 Jul 8.
6. The intersection of genetic and chemical genomic screens identifies GSK-3a as a target in human acute myeloid leukemia. **Banerji V**, Frumm SM, Ross KN, Li LS, Schinzel AC, Hahn CK, Kakoza RM, Chow KT, Ross L, Alexe G, Tolliday N, Inguilizian H, Galinsky I, Stone RM, DeAngelo DJ, Roti G, Aster JC, Hahn WC, Kung AL, Stegmaier K.J Clin Invest. 2012 Mar 1;122(3):935-47. doi: 10.1172/JCI46465. Epub 2012 Feb 13.
7. High incidence of chronic lymphocytic leukemia (CLL) diagnosed by immunophenotyping: a population-based Canadian cohort.Seftel MD, Demers AA, **Banerji V**, Gibson SB, Morales C, Musto G, Pitz MW, Johnston JB.Leuk Res. 2009 Nov;33(11):1463-8. Epub 2009 Jul 5.

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Dr. Beiko was born and raised in Winnipeg, Manitoba. He attended the University of Winnipeg where he completed a BA (Hons.) degree in psychology. An interest in learning and memory lead him to pursue graduate work at the University of Western Ontario. While working in Dr. Peter Cain's laboratory he obtained a MSc. for his work in developing a biochemical model of Alzheimer's disease and a PhD. for his work on the electrophysiological basis of learning and memory.

Dr. Beiko received his medical degree from the University of Ottawa prior to returning home to complete a neurosurgical residency at the University of Manitoba. After residency Dr. Beiko completed a Neurosurgical Oncology Fellowship at MD Anderson Cancer Center in Houston Texas before joining the Neurosurgery Department at the Health Sciences Centre.

Dr. Beiko's main clinical focus is treating patients with brain, spine, and peripheral nervous system cancer. While at MD Anderson he studied under the supervision of Dr. D. Cahill and examined the role that the IDH1 mutation has in predicting patient outcomes in patients with brain glioma. His current research is aimed at understanding the factors that influence survival outcomes in patients with brain gliomas. In particular, understanding the role of surgery, molecular tumour variables, chemotherapy, and radiation therapy contribute to overall and progression free survival.

Selected Publications:

1. Diagnostic discrepancies in malignant astrocytoma due to limited small pathological tumor sample can be overcome by IDH1 testing. Kim BY, Jiang W, **Beiko J**, Prabhu SS, DeMonte F, Gilbert MR, Sawaya R, Aldape KD, Cahill DP, McCutcheon IE. J Neurooncol. 2014 Jun;118(2):405-12.
2. IDH1 mutant malignant astrocytomas are more amenable to surgical resection and have a survival benefit associated with maximal surgical resection. **Beiko J**, Suki D, Hess KR, Fox BD, Cheung V, Cabral M, Shonka N, Gilbert MR, Sawaya R, Prabhu SS, Weinberg J, Lang FF, Aldape KD, Sulman EP, Rao G, McCutcheon IE, Cahill DP. Neuro Oncol. 2014 Jan;16(1):81-91.
3. Surgical resection of low-grade gliomas. **Beiko, J** & Cahill, DP. The Evidence for Neurosurgery. Eds. Benzel, et al. 2012, tfm Publishing Limited.

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Dr. Hugo Bergen, PhD

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Dr. Hugo Bergen is an Associate Professor in the Dept. of Human Anatomy and Cell Science. He received his B.Sc. (Hons.) from the University of Manitoba and his Ph.D. from the University of British Columbia. This was followed by post-doctoral studies at The Rockefeller University before coming to the University of Manitoba.

I have an interest in understanding the basis for chemoresistance in glioblastoma and developing strategies to overcome the chemoresistance that occurs with many chemotherapeutics. In addition it is critical to provide specific targeting of drugs to cancer cells while minimizing the exposure of non-cancerous cells to toxic drugs. We have recently explored novel strategies using protein nanotubes as carriers for different types of chemotherapeutic compounds. Our studies have revealed these compounds have the potential to serve as a novel and stable drug delivery system in brain cancer. Using my expertise in small animal stereotactic surgery I am working to develop in vivo models of glioblastoma that can be used to test the efficacy of new treatments for glioblastoma.

Selected Publications:

1. Thanasupawat T*, **Bergen HT***, Hombach-Klonisch S*, Krcek J, Ghavami S, Del Bigio MR, Krawitz S, Stelmack G, Halayko A, McDougall M, Meier M, Stetefeld J, Klonisch T. 2015. Platinum (IV) coiled coil nanotubes selectively kill human glioblastoma cells. Nanomedicine 11: 913-925.
2. Chen X, Li S, Li Y, Lin Z, **Bergen HT**, Vrontakis ME, Kirouac GJ. 2014. Orexins (Hypocretins) are involved in fear and anxiety in rats exposed to a single episode of footshocks. Brain Structure and Function 219: 2103-2118.
3. Thanasupawat T, Hombach-Klonisch S, Ogbomo EK, **Bergen HT**, Krawitz S, Del Bigio M, Stetefeld J, Krcek JP, Klonisch T. 2012. Tetrameric Right Handed Coiled Coil (RHCC) protein nanotubes as a modular delivery system of chemotherapeutics for effective killing of glioblastoma cells. 15th Biennial Canadian Neuro-Oncology Meeting 2012.

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Dr. Kevin Coombs received his B.A.s in Biology and English from the State University of New York in Geneseo, N.Y., and his M.A. and Ph.D degrees from the University of Texas in Austin, TX. His post-doctoral training in molecular and structural virology was done in the labs of Dr. Bernard Fields at Harvard Medical School and Dr. Steven Harrison at Harvard University. Dr. Coombs is presently a Professor in the Department of Medical Microbiology with cross-appointments in the Departments of Physiology and Pathophysiology and Microbiology, and is Assistant Dean of Research for the College of Medicine in the Faculty of Health Sciences. He serves on several Editorial Boards of journals publishing in Cell Biology, Molecular Biology and Virology. He has served as a panel member on NIH and AHFMR Peer Review Committees and as Scientific Officer and panel member on the CIHR Virology and Viral Pathogenesis Committee. His research interests include delineation of the protein and nucleic acid interactions in nucleoprotein complexes, using a variety of RNA viruses as models. His lab studies how these interactions change as a result of, and in turn, are modulated by, conformational transitions that occur during macromolecular assembly and disassembly, how these processes can be attenuated by anti-viral compounds, and how these processes in virus infections contribute to pathogenesis in the host. This work is in general areas of:

* Generation and molecular characterization of assembly-defective virus mutants
* Inhibition of virus replication using pharmacologic inhibitors
* Mass spectrometry- and Systems-based analyses of virus and host protein alterations
* Development of non-pathogenic viruses as "bio-indicators" for wastewater and medical instrument disinfection

Viruses are obligate intracellular pathogens that are intimately dependent upon host cells for replication and thus make extensive usage of host processes. By understanding how viruses and hosts interact we can gain fundamental knowledge about cellular processes and how to mitigate diseases caused by them. For example, several viruses require signaling pathways that are also involved in cancer and transformation for their replication. In addition, one of our viruses, mammalian reovirus, is an efficient oncolytic (cancer-killing) agent.

Selected Recent Publications:

1. Berard, A.R., A. Severini, and **K.M. Coombs**. (2015). Differential reovirus-specific and herpesvirus-specific AP-1 activation of secretogranin II leads to altered virus secretion. *J. Virol.* In press. PMID:26378181.
2. Berard, A.R., **K.M. Coombs**, and A. Severini. (2015). Comparative proteomic analyses of two reovirus T3D subtypes and comparison to T1L identifies multiple novel proteins in key cellular pathogenic pathways. (Invited). *Proteomics.* **15:**2113-2135. (Invited; Spotlight article). PMID:25900405.
3. Berard, A.R., **K.M. Coombs**, and A. Severini. (2015). Quantification of the host response proteome after Herpes Simplex 1 virus infection. *J. Proteome Res.* **14:**2121-2142. PMID:25815715.
4. Yeganeh, B., S. Ghavami, A. Kroeker, T. Mahoud, G.L. Stelmack, T. Klonisch, **K.M. Coombs**, and A.J. Halayko. (2014). Suppression of influenza A virus replication in human lung epithelial cells by noncytotoxic concentrations bafilomycin A1. *Am J. Physiol. Lung Cell Mol. Physiol.* **308:**L270-L286. PMID: 25361566
5. Shahiduzzaman, M., P. Ezatti, G. Xin, and **K.M. Coombs**. (2014). Proteasomal serine hydrolases are up-regulated by and required for influenza virus infection. *J. Proteome Res.***13:**2223-2238. PMID:24669782.
6. Tran, A.T., M.N. Rahim, C. Ranadheera, A. Kroeker, J.P. Cortens, K.J. Opanubi, J.A. Wilkins, and **K.M. Coombs.** (2013). Knockdown of specific host factors protects against Influenza virus-induced cell death. *Cell Death & Disease.* **4:**e769. (Highlighted by *LeadDiscovery's DailyUpdates*, http://www.leaddiscovery.co.uk/articles/23949218). PMID:23949218.
7. Kroeker, A., P. Ezzati, **K.M. Coombs** and A. Halayko. (2013). Influenza A infection of primary human airway epithelial cells up-regulates proteins related to purine metabolism and ubiquitin-related signaling. *J. Proteome Res.* **12:**3139-3151. PMID:23750822.
8. Rahim, M.N., M. Selman, P.J. Sauder, N.E. Forbes, W. Stecho, W. Xu, M. Lebar, E.G. Brown, and **K.M. Coombs.** (2013). Generation and characterization of a new panel of broadly reactive anti-NS1 mAbs for detection of Influenza A virus. *J. Gen. Virol.* **94:**592-604. [Cover illustration]. PMID:23223621
9. F1000 Prime Tran, A.T., J.P. Cortens, Q. Du, J.A. Wilkins, and **K.M. Coombs.** (2013). Influenza virus induces apoptosis via BAD-mediated mitochondria dysregulation. *J. Virol.* **87:**1049-1060. (Recommended by Faculty of 1000). PMID:23135712.
10. Kroeker, A., P. Ezzati, A. Halayko, and **K.M. Coombs.** (2012). Response of primary human airway epithelial cells to Influenza infection: A quantitative proteomic study. *J. Proteome Res.* **11:**4132-4146. PMID:22694362.
11. **Coombs, K.M.**, A. Berard, W. Xu, O. Krokhin, X. Meng, J.P. Cortens, D. Kobasa, J. Wilkins, and E.G. Brown. (2010). Quantitative proteomic analyses of influenza virus-infected cultured human lung cells. *J. Virol.* **84:**10888-10906. (Spotlight article). PMID:20702633.

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Dr. Jim Davie received his B.Sc. and Ph.D. degrees from the University of British Columbia. His post-doctoral training in the area of chromatin structure and function was done in the lab of Dr. Ken van Holde at Oregon State University. Dr. Davie is presently the Leader of the Terry Fox Research Institute Prairie Node, and Professor in the Department of Biochemistry and Medical Genetics at the University of Manitoba. He serves on several Editorial Boards of journals publishing in Biochemistry, Cell Biology and Molecular Biology and is Editor of the journal Biochemistry and Cell Biology. He has served as a Chair and panel member on CIHR and NCIC/CCSRI Peer Review Committees. His research interests include epigenetic regulation of gene expression in normal and cancer cells, nuclear matrix structure and function, sub-cellular trafficking of transcription factors and chromatin remodeling complexes, signal transduction pathways, chromatin structure and function, and biomarkers in the early detection of cancer. He currently holds a Canada Research Chair in Chromatin Dynamics (Tier 1). Jim was recently elected as a fellow in the Royal Society of Canada.

Epigenetic is a term used to describe changes in gene expression that are stable between cell divisions. Chromatin modifying enzymes including lysine acetytransferases (KATs), histone deacetylases (HDACs), histone kinases, histone phosphatases, lysine/arginine methyltransferases, lysine/arginine demethylases, ATP-dependent chromatin remodeling complexes and DNA methyltransferases mediate chromatin remodeling and are components of a complex epigenetic network regulating gene expression during development, differentiation and disease. Multistep tumorigenesis is a progression of events resulting from alterations in the processing of the genetic information. These alterations result from stable genetic changes (mutations) in tumor suppressor genes and oncogenes (e.g. *RAS*) and potentially reversible epigenetic changes. DNA methylation and histone post-translational modifications (PTMs) are two epigenetic mechanisms that are altered in cancer cells.

The mammalian cell's nucleus is highly organized, with transcription factors and factories, chromatin modifying enzymes, and chromosomes having defined sites. Altered nuclear structure and function (gene expression) underlie the development and progression of cancer and other disease states.

Dr. Davie's research program has three research themes designed to understand the roles of chromatin dynamics and nuclear structure in gene expression in normal and disease cell states: **i)** to characterize histone PTMs and chromatin modifying enzymes associated with transcribed chromatin; **ii)** to investigate the mechanisms by which signal transduction pathways control chromatin dynamics; **iii)** to explore the roles of the nuclear matrix and nuclear organization in chromatin dynamics in normal and disease cell states.

Selected Publications: (total citations 15,487; H-index 59)

1. Khan DH, Gonzalez C, Cooper C, Sun JM, Chen HY, Healy S, Xu W, Smith KT, Workman JL, Leygue E, **Davie JR**. RNA-dependent dynamic histone acetylation regulates MCL1 alternative splicing. Nucleic Acids Res. 2014 Feb;42(3):1656-70. doi: 10.1093/nar/gkt1134. Epub 2013 Nov 14. PMID: 24234443
2. Wang X, He S, Sun JM, Delcuve GP, **Davie JR**. Selective association of peroxiredoxin 1 with genomic DNA and COX-2 upstream promoter elements in estrogen receptor negative breast cancer cells. Mol Biol Cell. 2010 Sep 1;21(17):2987-95. doi: 10.1091/mbc.E10-02-0160. Epub 2010 Jul 14. PMID: 20631257
3. Drobic B, Pérez-Cadahía B, Yu J, Kung SK, **Davie JR**. Promoter chromatin remodelling of immediate-early genes is mediated through H3 phosphorylation at either serine 28 or 10 by the MSK1 multi-protein complex. Nucleic Acids Res. 2010 Jun;38(10):3196-208. doi: 10.1093/nar/gkq030. Epub 2010 Feb 3. PMID: 20129940
4. Shogren-Knaak M, Ishii H, Sun JM, Pazin MJ, **Davie JR**, Peterson CL. Histone H4-K16 acetylation controls chromatin structure and protein interactions. Science. 2006 Feb 10;311(5762):844-7. PMID: 16469925
5. **Davie JR**. Inhibition of histone deacetylase by butyrate. J Nutr. 2003 Jul;133(7 Suppl):2485S-2493S. PMID: 12840228
6. Chadee DN, Hendzel MJ, Tylipski CP, Allis CD, Bazett-Jones DP, Wright JA, **Davie JR**. Increased Ser-10 phosphorylation of histone H3 in mitogen-stimulated and oncogene-transformed mouse fibroblasts. J Biol Chem. 1999 Aug 27;274(35):24914-20. PMID: 10455166
7. **Davie JR**, Murphy LC. Level of ubiquitinated histone H2B in chromatin is coupled to ongoing transcription. Biochemistry. 1990 May 22;29(20):4752-7. PMID: 2163669

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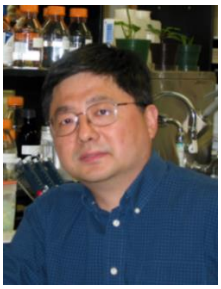

Dr. Hao Ding graduated with a Bachelor of Medicine from Shanghai Medical University in China on 1987. He received a Ph.D degree on Molecular Biology from University of Leuven, Belgium on 1997. He did his postdoctoral training (between 1997 and 2004) with Drs. Andras Nagy and Abhijit Guha at Samuel Lunenfeld Research Institute, Toronto. On 2004, he was awarded a Canada Research Chair and established his research laboratory at the Department of Biochemistry and Medical Genetics, University of Manitoba. He currently holds associate professor position. His research program focuses on mouse modeling of gene's function and human genetic diseases.

Now that the genomes of many organisms have been sequenced, the emphasis in genetics research has moved on to determining the gene functions encoded by these sequences. As the genomes of mice are 99 per cent identical to those of humans, one of the most powerful ways to model a genetic disease in humans is to manipulate the level or properties of that gene's product in a mouse.

In the past, Dr. Ding made important contributions in the fields of neuro-oncology and developmental biology, using transgenic approaches. He made several mouse brain tumour models that have been recognized as vital tools in understanding the development of brain tumours and characterizing new therapeutics for these diseases. He also made important discoveries regarding the functions of several genes-PDGF-C and two DNA helicase proteins. His lab is currently applying mouse transgenic approaches to characterize several specific genetic alterations in the development of human genetic diseases and cancers.

Selected publications:

1. Fu, B., Wang, L., **Ding, H.**, Schwamborn, JC., Li, S., Dorf, ME. TRIM32 Senses and Restricts Influenza A Virus by Ubiquitination of PB1 Polymerase. PLoS Pathog. 2015 Jun 9;11(6):e1004960
2. Armistead, J., Patel, N., Wu, X., Hemming, R., Chowdhury, B., Basra, GS., Del Bigio, MR., **Ding, H.**, Triggs-Raine, B. Growth arrest in the ribosomopathy, Bowen-Conradi syndrome, is due to dramatically reduced cell proliferation and a defect in mitotic progression. Biochim Biophys Acta. 2015 May;1852(5):1029-37
3. He, C., Zhao, C., Kumar, A., Lee, C., Chen, M., Huang, L., Wang, J., Ren, X., Jiang, Y., Chen, W., Wang, B., Gao, Z., Zhong, Z., Huang, Z., Zhang, F., Huang, B., **Ding, H.**, Ju, R., Tang, Z., Liu, Y., Cao, Y., Li, X., Liu, X. Vasoprotective effect of PDGF-CC mediated by HMOX1 rescues retinal degeneration. PNAS, 2014, Oct 14; 111(41):14806-11
4. Vannier, J.B., Sandhu, S., Petalcorin, M., Wu, X., Nabi, Z., **Ding, H*.**, Boulton, S.J*. RTEL1 is a replisome-associated helicase that promotes telomere and genome-wide replication. Science, 2013, 342(6155):239-242 (*shared corresponding authorship)
5. Andrae, J., Ehrencrona, H., Galini, R., Lai, M., **Ding, H.**, Betsholtz, C. Analysis of mice lacking the heparin-binding splice isoform of platelet-derived growth factor a. Mol Cell Biol, 2013, 33920):4030-40
6. Vannier, J.B., Pavicic-Kaltenbrunner, V., Petalcorin, M., **Ding, H.**, Boulton, S.J. RTEL1 dismantles T Loops and counteracts telomeric D4-DNA to maintain telomeric Integrity. Cell, 2012, 149 (4):795-806
7. Sandhu, S., Wu, X., Nabi, Z., Rastegar, M., Kung, S., Mai, S., **Ding, H.** Loss of HLTF promotes intestinal carcinogenesis. Molecular Cancer, 2012, 11(1):18
8. Nicklas, S., Otto, A., Wu, X., Miller, P., Stelzer, S., Wen, Y., Kung, S., Wrogemann, K., Patel, K., **Ding, H*.**, Schwamborn, J.C*. TRIM32 regulates skeletal muscle stem cell differentiation and is necessary for normal adult muscle regeneration. Plos One, 2012, 7(1): e30445 (* shared corresponding authorship)
9. Wu, X., Sandhu, S., Nabi, Z., **Ding, H.** Generation of a mouse model for studying the role of upregulated RTEL1 activity in tumorigenesis. Transgenic Res., 2012, Jan 12 (Epub ahead of print)
10. Fredriksson, L., Nilsson, I., Su, E.J., Andrae, J., **Ding, H.**, Betsholtz, C., Eriksson, U., Lawrence, D.A. Platelet-derived growth factor C deficiency in C57BL/6 mice leads to abnormal cerebral vascularization, loss of neuroependymal integrity and ventricular abnormalities. Am. J. Pathol., 2012, 180(3):1136
11. Krijger, PH., Lee, KY., Wit, N., van den Berk, PC., Wu, X., Roest, HP., Maas, A., **Ding, H.**, Hoeijmakers, JH., Myung, K., Jacobs, H. HLTF and SHPRH are not essential for PCNA polyubiquitination, survival and somatic hypermutation: existence of an alternative E3 ligase. DNA Repair, 2011, 10(4):438
12. Wu, X., Sandhu, S., Patel, N., Triggs-Raine, B., **Ding, H.** EMG1 is essential for mouse preimplantation embryo development. BMC Dev Biol, 2010, 10:99
13. Tang, Z., Arjunan, P., Lee, C., Li, Y., Kumar, A., Hou, X., Wang, B., Wardega, P., Zhang F., Dong, L., Zhang, Y., Zhang, S., **Ding, H.**, Becker K.G., Cao Y., Lennartsson J., Nagai, N., Li, X. Survival effect of PDGF-CC rescues neurons from apoptosis in both retina and brain by regulating GSK3beta phosphorylation. J Exp Med, 2010, 207(4):867

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Dr. Brenda Elias received her BA (Honours), MA and PhD from the University of Manitoba. Her first two degrees are in Sociology (Law) and has a PhD in community health sciences. Her doctoral and post-doctoral training focused on indigenous health and the social determinants of health. Dr. Elias is an Associate Professor in Community Health Sciences at the University of Manitoba, and former co-director and founding member of the Manitoba First Nations Centre for Aboriginal Health Research. She is the Director of the CHS Bold Ideas Colloquium Series.

Her research interests encapsulate population and public health, gender health, chronic disease, social determinants, health info-structures, Indigenous and interdisciplinary research, and research ethics. She conducts multilevel quantitative and mixed-method studies into the social, cultural, biological, economic, legal, political and historical determinants of health. Dr. Elias is a strong advocate of team collaborations, and has contributed as a principal, co-principal and co-investigator to over 44 grants exceeding $20 million. She is a research affiliate with the U of Manitoba Centre for Human Rights Research (CHRR) and is working to advance health rights of populations. Dr. Elias is a member of the CHRR water rights research consortium, which secured national funding from CIHR, NSERC and SSHRC to advance First Nations water rights in Canada. She has initiated and led three noteworthy national CIHR grants to understand, through data linkage, health disparities and health care rights for First Nations. The health disparity program involved linking the federal Indian Registry System to the provincial health and social administrative databases (via Manitoba Centre for Health Policy and CancerCare Manitoba) to make transparent health gaps pertaining to First Nations. She is a longstanding member of the International Group for Indigenous Health Measurement and is a founding member of the newly created Canadian Indigenous Research Network Against Cancer. Dr. Elias, in her affiliation with Regenerative Medicine, is the lead investigator of "Translating to the Community: A social epigenetic nutritional study of FASD". This study is linked to an international FASD consortium developing an early diagnostic biomarker tool for FASD and associated co-morbidities. This study is framed to advance the rights of children, adults and families living with FASD. Complimenting this study is a research group she leads to advance dignity for those living with neurodevelopmental disorders.

Selected Publications: (total citations 1489; H-Index 14)

1. **ELIAS B**, Busby K, Martens P. One little, too little: Counting Canada's Indigenous people for improved health reporting. Social Science & Medicine, 2015, Vol. 138, 179-86.
2. Decker K, Demers AA, Biswanger N, Musto G, Kliewer EV, **ELIAS B**, Griffeth, J, Turner D, Pap test use and cervical cancer incidence in First Nations women living in Manitoba, Cancer Prevention Research, 2015 January, 8(1): 49-55.
3. Demers AA, Decker K, Kliewer EV, Musto G, Shu E, Biswanger N, Fradette K, **ELIAS B**, Griffith J, Turner D, Mammography rates for breast Cancer screening: a comparison of First Nations and all other women living in Manitoba (Canada), Prevention and Chronic Disease, 2015 May 28; 12-E82.
4. Decker K, Demers A, Kliewer EV, Musto G, Shu E, Biswanger N, **ELIAS B**, Griffith J, Turner D, Colorectal cancer screening in First Nations people living Manitoba, Cancer Epidemiology, Biomarkers & Prevention, 2015 Jan 24,Vol. 24(1): 241-8.
5. **ELIAS B**, Moving beyond the historical quagmire of measuring infant mortality for the First Nations population in Canada, Social Science and Medicine, 2014, Vol. 123: 125-32.
6. **ELIAS B**, Hart L, Martens P, "Just get on with it": Linking data systems to report on infant mortality and the First Nations population in Manitoba (Canada), Statistical Journal of the International Association of Official Statistics, 2014, 30(3):285-295.
7. **ELIAS B**, Mignone J, Hall M, Hong S, Hart L, Sareen J, Trauma and suicide behaviour histories among a Canadian indigenous population: An empirical exploration of the potential role of Canada's residential school system, Social Science and Medicine, Vol. 74(10): 1560-9.
8. Shafer LA, Jeffrey I, **ELIAS B**, Shearer B, Canfell K, Kliewer E, Quantifying the impact of dissimilar HPV vaccination uptake among Manitoban school girls by ethnicity using a transmission dynamic model. Vaccine. 2013 Oct 1; 31(42): 4848-55.
9. **ELIAS B**, Hall M, Hong S, Kliewer E, "When the data does not match the story" Does trauma history and addiction predict poor cervical screening uptake among Manitoba Indigenous women, Journal of Aboriginal Health, March 2012, Vol. 8(1), 9-16.
10. **ELIAS B**, Kliewer E, Hall M, Demers A, Turner D, Martens PJ, Hong SP, Hart L, Chartrand C, Munro G, The Burden of cancer risk in Canada's indigenous population: A comparative study of known risks in a Canadian region, International Journal of General Medicine, October 2011, Vol. 4: 699-709.

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Marco Essig, MD, PhD, FRCPC is currently the Professor and Chair of the Radiology Department at the University of Manitoba, and Medical Director of the Diagnostic Imaging Program with the Winnipeg Regional Health Authority.

Dr. Essig received his medical degree from the University of Heidelberg and his doctorate in neurological sciences at the Medical Faculty of the University of Heidelberg. Dr. Essig did his internship and residency training in radiology at the German Cancer Research Center. He pursued two fellowships, one in Neuroradiology at the University of Iowa Hospitals and Clinics, Department of Radiology, in Iowa City and a second in Interventional Radiology at Brigham and Women's Hospital, Harvard Medical School, Department of Radiology and Neurosurgery, in Boston.

Upon completion of his fellowship at Harvard Medical School, Dr. Essig undertook three additional residencies: the first in the Department of Neurosurgery at the University of Heidelberg, the second in the Department of Radiology, German Cancer Research Center; and the third in Abteilung Radiodiagnostik also at the University of Heidelberg. After he completed these residencies, Dr. Essig earned Board Certification in Diagnostic Radiology, at which point he became assistant medical director of the Department of Radiology. He was appointed as a Professor of Radiology at Heidelberg Medical School and worked as assistant medical director of the Department of Radiology. In 2011 he worked as a full professor at the department of Neuroradiology of the University of Erlangen, Germany.

Dr. Essig is a valued member of numerous societies, including the Deutsche Rontgengesellschaft, the International Society for Magnetic Resonance in Medicine (ISMRM), the Radiological Society of North America (RSNA), the American Society of Neuroradiology, the European Society of Neuroradiology, the Deutsche Gesellschaft für Neuroradiologie, and the European Society of Radiology. He served in the scientific advisory board for the European Society and is founding member of the ESR subcommittee on imaging biomarkers. Since 2011 he is member of the neuroimaging subcommittee of the RSNA.

He is a member of the editorial board of European Radiology, Investigative Radiology, Insights into Imaging, Polish Journal of Radiology and Der Radiologe. Dr. Essig is debuty editor for Neuroimaging at the Journal of Magnetic Resonance Imaging (JMRI) and served as a reviewer of several non-radiological, radiological journals including Nature, Science and Academic institutions including the German Research foundation, the French Research Foundation, the Institute Cancer de France, the University of Bordeaux, France, the University of Leiden, Netherlands, the Mount Sinai School of Medicine, the University of California San Diego and the University of Southern California.

Dr. Essig is an author on more than 200 peer-reviewed articles and the author of more than 20 book chapters.

Selected Publications: (total citations 5,643, H-index 43)

1. Principles of T2 *-weighted dynamic susceptibility contrast MRI technique in brain tumor imaging.
   Shiroishi MS, Castellazzi G, Boxerman JL, D'Amore F, **Essig M**, Nguyen TB, Provenzale JM, Enterline DS, Anzalone N, Dörfler A, Rovira À, Wintermark M, Law M J Magn Reson Imaging. 2015 Feb;41(2):296-313. doi: 10.1002/jmri.24648. Epub 2014 May 12. PMID: 24817252 [PubMed - in process]. Similar articles
2. Principles of T2 *-weighted dynamic susceptibility contrast MRI technique in brain tumor imaging.
   Shiroishi MS, Castellazzi G, Boxerman JL, D'Amore F, **Essig M**, Nguyen TB, Provenzale JM, Enterline DS, Anzalone N, Dörfler A, Rovira À, Wintermark M, Law M. J Magn Reson Imaging. 2015 Feb;41(2):296-313. doi: 10.1002/jmri.24648. Epub 2014 May 12 PMID: 24817252 [PubMed - in process] Similar articles
3. Magnetic Resonance Imaging and Computed Tomography of the Brain-50 Years of Innovation, With a Focus on the Future.
   Runge VM, Aoki S, Bradley WG Jr, Chang KH, **Essig M**, Ma L, Ross JS, Valavanis A. Invest Radiol. 2015 Sep;50(9):551-6. doi: 10.1097/RLI.0000000000000170. PMID: 26050021 [PubMed - in process] Similar articles
4. Optimizing contrast-enhanced magnetic resonance imaging characterization of brain metastases: relevance to stereotactic radiosurgery.
   Anzalone N, **Essig M**, Lee SK, Dörfler A, Ganslandt O, Combs SE, Picozzi P.
   Neurosurgery. 2013 May;72(5):691-701. doi: 10.1227/NEU.0b013e3182889ddf. Review. Similar articles

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Dr. Gadji holds an Affiliate Senior Scientist position at Research Institute in Oncology and Haematology (RIOH), former Manitoba Institute of Cell Biology (MICB), at CancerCare Manitoba (CCMB). He is an Affiliate Researcher in the Department of Physiology and Pathophysiology at the University of Manitoba. And he is a Master-Assistant Professor in the Department of Biology at the University Cheikh Anta Diop of Dakar, Senegal, and at the National Centre of Blood Transfusion (NCBT or CNTS).

Dr. Gadji earned his pharmaceutical degree (Pharm.D.) and his internship (residency) at the University Cheikh Anta Diop of Dakar (UCAD). He moved to Quebec (Canada) at University Laval where he got his Master Sciences (M.Sc.) in molecular and cellular biology. He earned his Ph.D. at Sherbrooke University, Sherbrooke, Canada. Dr. Gadji obtained the Manitoba Health Research Council (MHRC) post-doctoral award and joined the MICB as a post-doctoral fellow (PDF) in Dr. Sabine Mai's lab, after completing his PhD degree. Dr. Gadji's research program has three main research themes designed to understand genetic, cellular and molecular biology of human diseases:

1) To evaluate genomic instability underlying any malignancy by quantitative measurement of nuclear telomere remodelling:
- in myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) in order to decipher the mechanisms of MDS transformation to AML;
- in gliomas to gain comprehension of the initiation of these diseases in order to establish nuclear telomere architecture as a novel and highly efficient biomarker of glioblastomas, olidendrogliomas and oligoastrocytomas.

2) To establish a non – invasive prenatal diagnosis by tracking foetal cells circulating in maternal blood and by using new techniques as "Primed *In Situ* Labelling" or PRINS technique.

3) To improve blood transfusion safety in Africa.

Selected Publications:

1. AYUB Seemi, **GADJI Macoura**, KRABCHI Kada, CÔTÉ Sylvie, GEKAS Jean, MARANDA Bruno, DROUIN Régen: Three New Cases of Terminal Deletion of the Long Arm of Chromosome 7 and Literature Review to Correlate Genotype and Phenotype Manifestation. (Accepted for publication in Am. J. Med. Genet. Part)
2. **Gadji M**, Crous-Tsanaclis A M, Mathieu D, Mai S, Fortin D, Drouin R. (2014). A new der(1;7)(q10;p10) leading to a singular 1p loss in a case of glioblastoma with oligodendroglioma component. Neuropathology. 2014 Apr ;34(2) : 170-178 ; PMID : 24118308
3. Tagny CT, Murphy EL, Lefrère JJ; Recherches Transfusionnelles en Afrique Francophone. (2014). The francophone Africa blood transfusion research network: a five-year report. Transfus Clin Biol. 2014 Mar;21(1):37-42. (I am a member of the group : Recherches Transfusionnelles en Afrique Frncophone : see listing membres in the paper) PMID : 24360798
4. **Gadji M**, Adebayo Awe J, Rodrigues P, Kumar R, Houston DS, Klewes L, Dièye TN, Rego EM, Passetto RF, de Oliveira FM, Mai S.. (2012). Profiling three-dimensional nuclear telomeric architecture of myelodysplastic syndromes and acute myeloid leukemia defines patient subgroups. Clin Cancer Res. 2012 Jun 15;18(12):3293-3304. *Highlighted in the journal* and Press release in *Hematopoiesis News* 3.18, May 8, 2012; PMID : 22539801
5. **Gadji M**, Krabchi K, Langis P, Aboura A, Périgny M, Côté S, Ferland M, Drouin R. (2011). Prenatal diagnosis and molecular characterization of two constitutional rings derived from one chromosome 22. Am J Med Genet A. 2011 Feb;155A(2):430-3. PMID : 21271667
6. **Gadji M**, Vallente R, Klewes L, Righolt C, Wark L, Kongruttanachok N, Knecht H, Mai S. (2011). Nuclear remodeling as a mechanism for genomic instability in cancer. (article and book chapter) (cover page of the issue) Adv Cancer Res. 2011;112:77-126. PMID : 21925302
7. Samassekou O, **Gadji M**, Drouin R, Yan J. (2010). Sizing the ends: normal length of human telomeres. Ann Anat. 2010 Sep 20;192(5):284-91. Review PMID : 20732797
8. **Gadji M**, Fortin D, Tsanaclis AM, Garini Y, Katzir N, Wienburg Y, Yan J, Klewes L, Klonisch T, Drouin R, Mai S. (2010). Three dimensional nuclear telomere architecture is associated with differential time to progression and overall survival in glioblastoma patients. Neoplasia. 2010 Feb;12(2):183-91. PMID : 20126476
9. **Gadji M**, Crous AM, Fortin D, Krcek J, Torchia M, Mai S, Drouin R, Klonisch T. (2009). EGF receptor inhibitors in the treatment of glioblastoma multiform: old clinical allies and newly emerging therapeutic concepts. Eur J Pharmacol. 2009 Dec 25;625(1-3):23-30. PMID : 19836372

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Dr. Saeid Ghavami, BSc, MSc, PhD

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Dr. Saeid Ghavami received his B.Sc. in Chemistry from Shiraz University (Iran) and later he received his MSc. and PhD in Clinical Biochemistry from Tarbiat Modarres University (Iran). He has done three post-doctoral training in the area of developing new therapeutic approach in cancer and cardiopulmonary disease focusing on modulation of cell fate regulating mechanisms (apoptosis, autophagy, unfolded protein response) in the lab of Dr. Marek J Los, Dr. Andrew J Halayko, and Dr. Ian M. Dixon. His research interests include the effect of autophagy and unfolded protein response in the modulation of cellular phenotype (especially lung) and characterization of the effect of cholesterol biosynthesis pathway in modulation different cancer therapy strategies.

Cellular phenotype plays an essential role in regulation of cellular response to different stimuli. My primary research interest focuses on the effect of autophagy and unfolded protein response on the cellular phenotype specially conversion epithelial to mesenchymal phenotype (EMT). As EMT plays an essential function in cancer cell metastasis, finding the mechanisms which are involved in its regulation would be beneficial for developing new cancer therapy. On the other hand cellular phenotype play an essential role in chemo-resistance and response to different chemotherapy agents therefore identifying the pathways which are involved in cellular pheno-conversion would be beneficial for cancer patients.

My second research interest focuses on cholesterol biosynthesis pathway and cancer therapy. Since their discovery, hydrophilic and lipophilic statins have significantly participated to improve the status of the health in human. They were initially used as an effective cholesterol-lowering drug which inhibit cholesterol biosynthesis rate limiting enzyme, hydroxymethylglutaryl coenzyme A reductase (HMGCR), and now they are considered as one of the most therapeutically effective and financially successful pharmaceuticals created in the history. Many of intermediate products of cholesterol biosynthesis pathway are involved in the regulation of cell fate because they are required for critical cellular functions such as maintenance of membrane integrity, signaling, protein synthesis, and cell-cycle progression. In past few years statins are being considered as a possible new approach in cancer treatment and epidemiologic studies have proved that statin use in patients with cancer was associated with reduced cancer-related mortality. I am currently identifying how cholesterol biosynthesis pathway might modulate different cancer therapy strategies to improve their effectiveness and avoid chemo-resistance.

Selected Publications: (Web of Knowledge: 2916 citations, *h*- index: 24, Google Scholar: 5745 citations, *h*-index:27)

1. Cieślar-Pobuda A, Vilas Jain M, Kratz G, Rzeszowska-Wolny J, Ebrahimi M, **Ghavami S**, Wiechec E. The expression pattern of PFKFB3 enzyme distinguishes between induced-pluripotent stem cells and cancer stem cells. *2015, Oncotarget, (In Press).*
2. **Ghavami S**, Cunnington RH, Yeganeh B, Bathe K, Shivika Gupta, Krista Filomeno, Shu-Ru Chen, Emma Ambrose, Ruhit Singal, Freed DH, Klonisch T, Halayko AJ, Dixon IMC. Autophagy is a regulator of TGF-β1-induced pro-fibrotic effect in primary human atrial myofibroblasts. *2015, Cell Death & Disease, doi: 10.1038/cddis.2015.36.*
3. Thanasupawat T, Bergen H, Hombach-Klonisch S, Krcek J, **Ghavami S**, Del Bigio M, Krawitz S, Stelmack G, Halayko AJ, Meier M, Stetefeld J, Klonisch T. Right Handed Coiled Coil (RHCC) Nonotubes for Effective Platinium Mediated Killing of Human Glioblastoma Cells. *2015, Nonomedicine, pii: S1549-9634(15)00038-6. doi: 10.1016/j.nano.2015.01.014. [Epub ahead of print].*
4. Chaabane W, Cieslar-Pobuda A, El-Gazzah M, Jain MW, Rzeszowska-Wolny J, Rafat M, Stettefeld J, **Ghavami S**, Los MJ., Human-Gyrovirus-Apoptin Triggers Mitochondrial Death Pathway-Nur77 is Required for Apoptosis Triggering. *2014, Neoplasia, 16(9):679-93.*
5. **Ghavami S**, Sharma P, Yeganeh B, Oluwaseun, O, Jha A, Mutawe MM, Kashani HH, Los M, Klonisch T, Unruh H, Halayko H. Airway Mesenchymsl Cell Death by Mevalonate Cascade Inhibition: Integration of Apoptosis, Autophagy, and ER Stress. 2014, *Biochim Biophys Acta., 843(7):1259-71.*
6. Gong C, Bauvy C, Tonelli G, Delomenie C, Nicolas V, Zhu Y, Domergue V, Marin-Esteban V, Delobos L, Gary H, Morel AP, **Ghavami S**, Song E, Codogno P, Mehrpour M. Self-renewal and tumorgenicity of Breast Cancer Stem Cells is Dependent on Beclin 1 and Autophagy. *2013, Oncogene, 32(18):2261-72.*
7. **Ghavami S**, Yeganeh B, Stelmack G, Kashani HH, Sharma P, Cunnington R, Ratan S, Bathe K, Klonisch T, Dixon I, Freed D, Halayko AJ. Apoptosis, Autophagy and ER Stress in Mevalonate Cascade Inhibition-Induced Cell Death of Human Atrial Fibroblasts. *2012, Cell Death Dis., 3:e330. Doi:10.1038/cddis.2012.61.*
8. Klionsky DJ, Abbadie C, Abdalla FC, ……., **Ghavami S**,…, Zucchini-Pasxcal N, Zuckerbraun B. Guidelines for the Use and Interpretation of Assays for Monitoring Autophagy. *2012, Autophagy, 8 (4): 445-554.*

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Discovering Signal Transduction Pathways Regulating Cell Death. In maintaining integrity and homeostasis of multicellular organisms, the balance between cell death and survival is fundamentally important. When this balance is altered diseases occur such as cancer. One protein important in regulation of cell death is the Bcl-2 BH-3 only member BNIP3. BNIP3 expression is induced under low oxygen (hypoxia) conditions and is over expressed in solid tumors in hypoxic regions. When BNIP3 is over expressed in cancer cells it induces cell death mediated by mitochondrial dysfunction. This cell death instead of being apoptotic is autophagic (a new form of programmed cell death). This paradox of BNIP3 killing cancer cells and being over expressed in live cells within tumors is a focus of our research. To date three explanations could account of these differences. The first difference is growth factors block BNIP3 cell death function and tumors have deregulated growth factor signaling leading to cell survival (see below). Secondly, BNIP3 is also localized in the nucleus of tumor cells prevent its interaction with the mitochondria blocking its cell death function. Finally, the BNIP3 gene is mutated to an inactive protein. This protein acts in a dominant negative fashion blocking hypoxia induced cell death. The importance of these mechanisms for cancer progression and treatment is under active investigation.

Cell survival is as important as cell death. The epidermal growth factor receptor (EGFR) is expressed at high levels in several cancers such as breast cancer. We discovered that pretreatment of breast cancer cell lines with epidermal growth factor (EGF) effectively blocked drug and death receptor induced apoptosis. This protection from apoptosis is mediated by a serine threonine kinase called AKT through up-regulation of the Bcl-2 anti-apoptotic family member Mcl-1. Besides breast cancer, we have found that a lipid, lysophosphatic acid (LPA) blocks apoptosis in chronic lymphocytic leukemia (CLL) cells using a similar mechanism. We are currently investigating the regulatory elements controlling Mcl-1 expression. Molecular-based therapies could alter the balance between cell death and survival towards killing cancer cells. Tumor necrosis factor related apoptosis-inducing ligand (TRAIL) selectively kills cancer cells while normal cells are resistant to TRIAL-induced apoptosis. In collaboration with Dr. James Johnston, we are investigating the potential of TRAIL as a therapy for chronic lymphocytic leukemia (CLL) alone or in combination with chemotherapy.

In addition, we previously discovered that chemotherapeutic drugs increase TRAIL death receptor (DR4/5) expression and this contributes to drug-induced apoptosis. We are defining the regulatory elements controlling DR4/5 expression in CLL cells to enhance the clinical effectiveness of TRAIL. The goal of this research is to define the signal transduction pathways leading to cell death or survival. This will elucidate pharmaceutical targets that could alter the cellular balance in favour of cell death. This research will be the foundation to establish clinical trials using molecular targeted therapies to increase effectiveness of chemotherapy in cancer.

Selected Publications:

1. Beiggi, S., Seftel, M.D., Pitz, M.W., Kumar, R., Banerji, V., Griffith, E.J., **Gibson, S.B** and Johnston, J.B. 2015 Referred patients to a specialized CLL clinic have increased overall survival compared to non-referred patients independent of patient's age. Cancer Medicine In press
2. Lafarge, S. T., Hou, S., Pauls, S. D. Johnston, J. B**., Gibson, S. B.** and Marshall, A. J. 2015 A novel role for CD27 in chronic lymphocytic leukemia interaction with stromal cells. Leukemia Research S0145-2126
3. Li, H., Wu, X**.,** Hou, S., Noh, E., Makondo, K**.,** Du, Q., Wilkins**,** JA, Johnston, JB**, Gibson, SB,** Lin, F. and Marshall, AJ 2015 Phosphatidylinositol-3,4-biphosphate and its binding protein lamellipodin regulate chemotaxis of malignant B lymphocytes. Submitted
4. Chen, Y., Henson, E.S., Huang, D. and **Gibson, S.B**. 2015 Tyrosine kinase receptor EGFR regulates the switch in cancer cells between cell survival and cell death induced by autophagy in hypoxia. Autophagy In press
5. Chen, Y., Henson, E.S., Xiao, W., Shome, E., Azad, M.B., Burton, T.R., Queau, M., Sathya, A., Eisenstat, D.D., and **Gibson, S.B**. 2015 Bcl-2 family member Mcl-1 expression is reduced under hypoxia by E3 ligase FBW7 contributing to BNIP3 induced cell death in glioma cells. Cancer Biology Therapy In press

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Dr. Aleksandra Glogowska is an Instructor at Department of Human Anatomy andCell Science at the University of Manitoba. She received her Ph.D. degree from University of Manitoba in Winnipeg working on function of EGF like ligands in cancer. She did her post-doctoral training at CancerCare Manitoba working on genomic instability in cancer. Thereafter, she joined Department of Human Anatomy and Cell Science, University of Manitoba, and continues to pursue research on the EGF system in brain cancer. She is a member of the Brain Tumor Research Alliance Manitoba (BTRAM).

Dr. Glogowska is interested in studying the effect of proEGF-like ligands on the ubiquitin-proteasome system in brain cancer. Knowledge of the regulatory mechanisms that control the function of ubiquitin-proteasome system is critical to designing innovative therapeutic strategies that target the ubiquitin-proteasome system and induce anticancer effects. Her PHD work demonstrated important functions of proEGF molecular domains in the regulation of proteolytic degradation of ErbB1/2 which affects the cell cycle process and leads to the inhibition of cancer cell proliferation and migration. EGFR gene amplifications and/or EGFR over-expression are frequently observed in oligodendrogliomas and glioblastomas and identify these brain tumors as targets for the actions of EGF-like ligands. ProEGF affects tumor cell growth, differentiation, and metastasis. Amplification and ligand-induced activation of EGFR correlate with increased tumor cell migration, matrix degradation, and enhanced tissue invasiveness.

Selected Publications:

1. Schulz H, Dahlhoff M, **Glogowska A**, Zhang L, Arnold GJ, Fröhlich T, . Schneider MR, Klonisch T (2015).'' Betacellulin transgenic mice develop urothelial hyperplasia and show sex-dependent reduction in urinary major urinary protein content. Experimental and Molecular Pathology2015 201599, (1): 33–38
2. Mathura S, **Glogowska A**, McAvoy E, Righolt C, Rutherford J, Willing C, Banik U, Ruthirakuhan M, Mai S, Garcia A (2014). Three-dimensional quantitative imaging of telomeres in buccal cells identifies mild, moderate, and severe Alzheimer's disease patients. J Alzheimers Dis. 2014; 39(1): 35-48.
3. Tian Y, **Glogowska A**, Zhong W, Klonisch T and Xing M (2013). Polymeric mesoporous silica nanoparticles as a ph—responsive switch to control doxorubicin intracellular delivery. J Materials Chemistry B. 2013, 1, 5264-5272
4. **Glogowska A**, Kunanuvat U, Stetefeld J, Patel TR, Thanasupawat T, Krcek J, Weber E, Wong GW, Del Bigio MR, Hoang-Vu C, Hombach-Klonisch S, Klonisch T (2013) C1q-tumour necrosis factor-related protein 8 (CTRP8) is a novel interaction partner of relaxin receptor RXFP1 in human brain cancer cells. J Pathol. 2013 Dec; 231(4): 466-79.
5. **Glogowska A**, Stetefeld J, Weber E, Ghavami S, Hoang-Vu C, Klonisch T (2012). Epidermal growth factor cytoplasmic domain affects ErbB protein degradation by the lysosomal and ubiquitin-proteasome pathway in human cancer cells. Neoplasia. 2012 May; 14(5): 396-409.
6. Klonisch T, **Glogowska A**, Gratao AA, Grzech M, Nistor A, Torchia M, Weber E, de Angelis MH, Rathkolb B, Cuong HV, Wolf E, Schneider MR. (2009) The C-terminal cytoplasmic domain of human proEGF is a negative modulator of body and organ weights in transgenic mice. FEBS Lett.583:1349-57.
7. **Glogowska A**, Pyka J , Kehlen A, Los M, Perumal P, Weber E, Dralle H, Hoang-Vu, Sheue –yann Cheng C, Klonisch T (2009) The cytoplasmic domain of proEGF negatively regulates motility and elastolytic activity in thyroid carcinoma cells. Neoplasia 10:1120-3

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Dr. Yuewen Gong received his B.M. degree from the Beijing University of Chinese Medicine and Ph.D. degree from the University of Manitoba. His post-doctoral training in the area of prostate cancer was done in the lab of Dr. Donald J. Tindall at Mayo Clinic/Foundation and training in the area of liver diseases was done in the lab of Dr. Gerald Y. Minuk at the University of Manitoba. Dr. Gong is a Professor in the College of Pharmacy and has a nil-salary appointment in the section of Hepatology of the Department of Internal Medicine at the University of Manitoba. He is currently the Associate Dean (Research) of the College of Pharmacy. He serves on several Editorial Boards of journals publishing in Gastroenterology, and Alternative and Complimentary Medicine. His research interests include understanding of the expression and regulation of bone morphogenetic proteins, signal transduction pathway of members of the transforming growth factor superfamily in liver cells such as hepatocytes and hepatic stellate cells, mechanism of liver fibrosis and hepatocellular carcinoma, hepatic cancer stem cells, differentiation and trans-differentiation of liver cells, development of therapeutic methods for liver fibrosis and hepatocellular carcinoma. In collaboration with Chinese researchers, he is also interested in investigation of traditional Chinese herbal medicine for treatment of kidney diseases.

Bone morphogenetic proteins (BMPs) are the largest sub-family of the transforming growth factor superfamily. Biological activities of BMPs are mediated by their binding to type I and type II BMP receptors and then activating intracellular signaling molecules – Smads and mitogen activated protein kinase (MAPK). Liver fibrosis is a wound healing process in the liver and involves in activation of hepatic stellate cells. Activation of hepatic stellate cells includes increased proliferation and trans-differentiation from quiescent phenotype to myofibroblast phenotype with increased expression alpha smooth muscle actin. BMP4 is a cellular factor that induces hepatic stellate cell trans-differentiation but does not stimulate cell proliferation. Hepatocellular carcinoma is one kind of cancers that chemotherapy does not have very successful effect. This could be due to presence of cancer stem cells, which can differentiated into either hepatocyte phenotype or cholangiocyte phenotype. Elevated level of BMP4 in hepatocellular carcinoma biopsy suggests a role of BMP4 in differentiation of cancer stem cells.

In collaboration with Chinese partners, several traditional Chinese herbal formulations were employed to investigate their efficacy in rat models of diabetic nephropathy. These herbal formulations were able to alleviate protein in urine and improve histology of the kidneys.

Dr. Gong's research program is designed to understand the roles of growth factors and signal transduction molecules in normal and disease liver cells through: **i)** to characterize biological activity of BMPs in hepatic stellate cell trans-differentiation; **ii)** to investigate the mechanisms of BMPs in cancer stem cell differentiation; **iii)** to develop possible therapeutics for liver fibrosis and hepatocellular carcinoma.

Selected Publications: (total citations 2,465; H-index 28)

1. Lanman Xu, **Yuewen Gong**, Benfu Wang, Keqing Shi, Yijun Hou, Liping Wang, Zuo Lin, Yixiang Han, Lu Lu, Dazhi Chen, Xiuli Lin, Qiqiang Zeng, Yongping Chen: A Randomized Trial of Autologous Bone Marrow Mesenchymal Stem Cells Transplantation for HBV Cirrhosis: Regulation of Treg/Th17 cells. J Gastroenterol Hepatol. 2014 Aug;29(8):1620-8. doi: 10.1111/jgh.12653
2. Jingai Fang, Hongkun Wei, Yanyan Sun, Xiaodong Zhang, Wenyuan Liu, Qintao Chang, Ruihua Wang, **Yuewen Gong**: Regulation of podocalyxin expression in the kidney of streptozotocin-induced diabetic rats with Chinese herbs (Yishen capsule). BMC Complementary and Alternative Medicine 2013, 13:76 doi:10.1186/1472-6882-13-76
3. **Yuewen Gong**.: Identifying the targets for treatment of liver fibrosis and hepatocellular carcinoma from both western medicine and traditional Chinese medicine, Chin J Integr Med. 2012 Apr;18(4):245-9. Epub 2012 Mar 30
4. Li Z, Zhang H, Dong X, Burczynski FJ, Choy P, Yang F, Liu H, Li P, **Gong Y**: Proteomic profile of primary isolated rat mesangial cells in high glucose culture condition and decreased expression of PSMA6 in renal cortex of diabetic rats. Biochem Cell Biol. 2010 Aug;88(4):635-648
5. Fan J, Shen H, Dai Q, Minuk GY, Burzynski FJ, **Gong Y**: Bone morphogenetic protein-4 induced rat hepatic progenitor cell (WB-F344 cell) differentiation toward hepatocyte lineage through Smad1, ERK1/2 and C/EBP alpha. J Cell Physiol. 2009 Jul;220(1):72-81. PMID: 19229878 [PubMed - indexed for MEDLINE]
6. Shen H, Fan J, Burczynski FJ, Minuk GY, Cattini P, **Gong Y**: Increases Smad1 expression and transcriptional activity enhances transdifferentiation of hepatic stellate cells J Cell Physiol. 2007 Sep:212(3):764-70. PMID: 17525996 [PubMed - indexed for MEDLINE]

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Dr. Tom Hack is Professor in the College of Nursing, Faculty of Health Sciences, at the University of Manitoba, and Director of the Psychosocial Oncology and Cancer Nursing Research Group (with Drs. Lobchuk, McClement, Schultz, Woodgate) in the College of Nursing, University of Manitoba. He holds a Chair in Psychosocial and Supportive Care Oncology Research from the Canadian Breast Cancer Foundation. He is a Visiting Professor at the University of Central Lancashire, Preston, UK, and Honorary Researcher at the Peter MacCallum Cancer Centre, Melbourne, Australia. Dr. Hack was the inaugural Dorothy J. Lamont Scientist with the Canadian Cancer Society Research Institute in partnership with the Canadian Institutes of Health Research. Dr. Hack is a recipient of the Queen's Golden Jubilee medal.

Dr. Hack's research interests include coping and adjustment to life-threatening cancer, and knowledge translation (KT). He has conducted the largest trials worldwide examining the utility and effectiveness of providing cancer patients with audio-recordings of primary treatment consultations, and has applied his KT expertise to assist CancerCare Manitoba in launching a consultation recording service as standard clinical practice. He recently completed a knowledge exchange operating grant to facilitate the transfer and uptake of consultation recording use in oncology, and has begun a new study to examine the use of consultation recordings in patients with brain tumors or neuroendocrine cancer. Dr. Hack is the Manitoba lead on CIHR study examining the implementation of a national online course to enhance oncology nurse therapeutic effectiveness in responding to cancer patient pain, fatigue, anxiety and depression. Dr. Hack is a member of KT Canada, and is collaborating on KT research projects with the Manitoba Palliative Care Research Unit and with colleagues in the UK and Australia.

Selected Publications:

1. Boquiren, V. M., **Hack, T. F.**, Beaver, K., & Williamson, S. (in press). What do measures of patient satisfaction with the doctor tell us? *Patient Education & Counseling*. doi:10.1016/j.pec.2015.05.020
2. Chochinov, H. M., McClement, S., **Hack, T.**, Thompson, G., Dufault, B., & Harlos, M. (2015). Eliciting personhood within clinical practice: Effects on patients, families and health care providers. *Journal of Pain and Symptom Management*. 49, 974-980. doi:10.1016/j.jpainsymman.2014.11.291
3. Wakefield, C. E., Butow, P.N., Aaronson, N.A., **Hack, T.F.**, Hulbert-Williams, N.J., Jacobsen, P.B., on behalf of the International Psycho-Oncology Society Research Committee. (2015). Patient-reported depression measures in cancer: A meta-review. *Lancet Psychiatry*, 2, 635-647. doi:10.1016/S2215-0366(15)00168-6
4. **Hack, T.F.**, Crooks, D., Plohman, J., & Kepron, E. (2014). Citation analysis of Canadian psycho-oncology and supportive care researchers. *Supportive Care in Cancer*, 22, 315-324. doi:10.1007/s00520-013-1966-5.
5. **Hack, T.F.**, Ruether, J.D., Weir, L. M., Grenier, D., & Degner, L.F. (2013). Promoting consultation recording practice in oncology: Identification of critical implementation factors and determination of patient benefit. *Psycho-Oncology*, 22, 1273-1282. doi:10.1002/pon.3135.
6. **Hack, T.F.**, Ruether, J.D., Pickles, T., Bultz, B.D., Chateau, D., & Degner, L.F. (2012). Behind closed doors II: Systematic analysis of prostate cancer patients' primary treatment consultations with radiation oncologists and predictors of satisfaction with communication. *Psycho-Oncology*, 21, 809-817. doi:10.1002/pon.1984.
7. **Hack, T.F.**, Carlson, L., Butler, L., Degner, L. F., Jakulj, F., Pickles, T., Ruether, D., & Weir, L. (2011). Facilitating the implementation of empirically valid interventions in psychosocial oncology and supportive care. *Supportive Care in Cancer*, 19, 1097-1105. doi:10.1007/s00520-011-1159-z.
8. **Hack, T.F.**, Kwan, W., Thomas-MacLean, R.L., Towers, A., Miedema, B., Tilley, A., Chateau, D. (2010). Predictors of arm morbidity following breast cancer surgery. *Psycho-Oncology*, 19, 1205-1212. doi:10.1002/pon.1685.
9. **Hack, T.F.**, Crooks, D., Plohman, J., & Kepron, E. (2010). Research citation analysis of nursing academics in Canada: identifying success indicators. J*ournal of Advanced Nursing*, 66, 2542-2549. doi:10.1111/j.1365-2648.2010.05429.x.
10. **Hack, T.F**., McClement, S.E., Chochinov, H. M., Cann, B., Hassard, T., Kristjanson, L.J., & Harlos, M. (2010). Learning from dying cancer patients during their final days: life reflections gleaned from dignity therapy. *Palliative Medicine,* 24, 715-723.doi: 10.1177/0269216310373164.
11. **Hack, T.F.**, Pickles, T., Ruether, J.D., Weir, L., Bultz, B.D., Mackey, J., & Degner, L.F. (2010). Predictors of distress and quality of life in patients undergoing cancer therapy: Impact of treatment type and decisional role. *Psycho-Oncology*, 19, 606-616. doi:10.1002/pon.1590.
12. **Hack, T.F.**, Pickles, T., Ruether, J.D., Weir, L., Bultz, B.D., & Degner, L.F. (2010). Behind closed doors: Systematic analysis of breast cancer consultation communication and predictors of satisfaction with communication. *Psycho-Oncology,* 19, 626-636. doi:10.1002/pon.1592.

Dr. Geoff Hicks, PhD

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Dr. Geoffrey G. Hicks received his undergraduate degree in Biochemistry from the University of Manitoba. His PhD thesis focused on p53 as a tumor suppressor where he studied in the lab of Dr. Michael Mowat at the Manitoba Institute of Cell Biology. Pursuing his interest in cancer biology, Dr Hicks held National Cancer Institute of Canada postdoctoral fellowships at the Massachusetts Institute of Technology and the Vanderbilt University School of Medicine. With Dr. H. Earl Ruley he developed a novel gene trapping technology as a genetic strategy to identify recessive gene in mammalian cells. This high throughput sequence-based screen is currently being applied to develop a library of knock-out mutations in mouse embryonic stem cells, and is an international resource provided by Dr. Hicks' Mammalian Functional Genomics Centre. Dr. Hicks is a founding member of the International Mouse Mutagenesis Consortium, the International Gene Trap Consortium, the Federation of International Mouse Resources and the International Knock-out Mouse Consortium. Dr. Hicks' research program focuses on the functional analysis of genetic determinants of cancer and leukemia. His research team is currently examining the related RNA binding proteins, TLS and EWS, to identify the transforming potential of these genes in acute myelogenous leukemia and Ewing sarcoma, respectively.

Dr. Geoff Hicks is a Canada Research Chair in Functional Genomics and is the Director of the Mammalian Functional Genomics Centre, a centre in the Manitoba Institute of Cell Biology which is a joint institute between CancerCare Manitoba and the University of Manitoba and the Genetics Modeling Centre in the University of Manitoba. He is currently leading the North American Conditional Mouse Mutagenesis Project (NorCOMM), the Canadian component of The International Knockout Mouse Project. NorCOMM is supported by Genome Prairie with funding of $13.5 million from Genome Canada and other partners. Dr. Hicks and his team are working with other scientists from around the world to create knockout mice lines for each of the approximately 20,000 mouse genes. Most recently, Dr. Hicks has been appointed Director of the Regenerative Medicine Program in the University of Manitoba's Faculty of Medicine. The eight Principal Investigators of the program will focus on stem cell-based applications for the treatment of human disease, including cardiovascular disease, cancer, and spinal cord injury repair.

International Leadership in Functional Genomics. Dr. Hicks' genomics program is now a major component of the International Mouse Mutagenesis Consortium, the International Genetrap Consortium (IGTC), the International Knock-out Mouse Project Consortium, and the International Mutant Mouse Federation. He is also a founding member of each consortium and contributed directly to several high profile papers. A letter was published in the Human Genome issue of Science and outlines the importance of developing functional resources that are integrally linked with the sequence data available in from the genome initiatives. The IGTC next published a combined analysis of gene trap targets, supporting role as the first major step in the proposed international Mouse Knockout Project. Dr. Hicks' program has also been highlighted in several recent high profile publications.

Functional Analysis of Genetic Determinants of Cancer. Identification of the TLS protooncogene function as regulating lymphocyte development, B cell activation the maintenance of genomic stability. This report has far reaching implications for both the role of this protein in tumor development and of the role of RNA binding proteins in general. It provides a powerful example of how the ES cell library will impact on rapidly identifying gene function in vivo as well as to highlight my research program. It should be noted that Dr Hicks initiated this project as an independent investigator and that the major discoveries were established in his lab at the Manitoba Institute of Cell Biology. Currently, the role of TLS in DNA damage and repair is the major research focus of the lab.

Selected Publications:

1. Lagier-Tourenne C, Polymenidou M, Hutt KR, Vu AQ, Baughn M, Huelga SC, Clutario KM, Ling SC, Liang TY, Mazur C, Wancewicz E, Kim AS, Watt A, Freier S, Hicks GG, Donohue JP, Shiue L, Bennett CF, Ravits J, Cleveland DW, Yeo GW. Divergent roles of ALS-linked proteins FUS/TLS and TDP-43 intersect in processing long pre-mRNAs. Nat Neurosci. 2012 Nov;15(11):1488-97. doi: 10.1038/nn.3230. Epub 2012 Sep 30.
2. Beaulieu CL, Samuels ME, Ekins S, McMaster CR, Edwards AM, Krainer AR, Hicks GG, Frey BJ, Boycott KM, Mackenzie AE. A generalizable pre-clinical research approach for orphan disease therapy. Orphanet J Rare Dis. 2012 Jun 15;7(1):39.
3. Lin CP, Choi YJ, Hicks GG, He L.The emerging functions of the p53-miRNA network in stem cell biology. Cell Cycle. 2012 Jun 1;11(11):2063-72. Epub 2012 Jun 1.
4. Choi YJ, Lin CP, Ho JJ, He X, Okada N, Bu P, Zhong Y, Kim SY, Bennett MJ, Chen C, Ozturk A, Hicks GG, Hannon GJ, He L. miR-34 miRNAs provide a barrier for somatic cell reprogramming. Nat Cell Biol. 2011 Oct 23;13(11):1353-60. doi: 10.1038/ncb2366.

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Dr. Sabine Hombach-Klonisch, MD, PhD

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Dr. Sabine Hombach-Klonisch is an Associate Professor at the Department of Human Anatomy and Cell Science at the University of Manitoba. Dr. Hombach is a member of the Brain Tumor Research Alliance Manitoba (BTRAM) and the Manitoba Breast Cancer Research Group. She completed her MD at the Justus-Liebig University in Giessen, Germany, and received her Ph.D. degree from the Martin-Luther University of Halle-Wittenberg, Germany. Her post-doctoral training focused on the functional role of Relaxin-like peptides in tumor biology. Dr. Hombach-Klonisch joined the University of Manitoba in 2004.

Dr. Hombach-Klonisch's research focuses on the investigation of the molecular and cellular mechanisms which drive tumor invasion and metastasis and cancer cell survival in different tumor microenvironments.

Her lab investigates the role of relaxin-like peptides and their G protein-coupled receptors (RXFP1+2) in promoting tumor invasion and metastasis. Her team discovered matrix metalloproteinases, lysosomal proteases of the cathepsin family and the Ca2+-binding protein S100A4 (metastasin) as mediators of the pro-migratory and pro-angiogenic responses of RXFP1 signaling and they recently discovered the C1q- tumor necrosis factor related protein 8 (CTRP8) as a novel ligand of RXFP1 and demonstrated its involvement in brain cancer migration. The Hombach lab investigates the signaling pathways and molecular mechanisms induced by RXFP1 activation which facilitate tumor cell survival and stem cell recruitment.

The stem cell protein and non-histone chromatin binding protein HMGA2 contributes to nuclear telomere architecture and resistance to DNA damage in cancer cells. HMGA2 promotes DNA damage repair and enhances cancer cell survival under chemotherapy. The research team investigates the HMGA2 interacting proteins in the nucleus under conditions of oxidative and chemotherapeutic stress to identify molecular mechanisms of HMGA2-mediated cancer cell survival and help design innovative therapeutic approaches for cancer patients.

Selected Publications: (*equal author contribution)

1. Medapati MR, Dahlmann M, Ghavami S, Pathak KA, Lucman L, Klonisch T, Hoang-Vu C, Stein U, **Hombach-Klonisch S**. RAGE mediates the pro-migratory response of extracellular S100A4 in human thyroid cancer cells. *Thyroid*. 2015 May;25(5):514-27.
2. Thanasupawat T*, Bergen H*, **Hombach-Klonisch S***, Krcek J, Ghavami S, Del Bigio M, Krawitz S, Stelmack G, Halayko A, McDougall M, Meier M, Stetefeld J, Klonisch T. Platinum (IV) coiled coil nanotubes selectively kill human glioblastoma cells. *Nanomedicine*. 2015 May;11(4):913-25.
3. **Hombach-Klonisch S**, Natarajan S, Thanasupawat T, Medapati M, Pathak A, Ghavami S, Klonisch T. Mechanisms of therapeutic resistance in cancer (stem) cells with emphasis on thyroid cancer cells. *Front Endocrinol (Lausanne*). 2014 Mar 25;5:37.
4. Glogowska A, Kunanuvat U, Stetefeld J, Patel TR, Thanasupawat T, Krcek J, Weber E, Wong GW, Del Bigio M, Hoang-Vu C, **Hombach-Klonisch S***, Klonisch T*. "C1q-tumor necrosis factor-related protein 8 (CTRP8) is a novel ligand of relaxin receptor RXFP1 in human brain cancer cells". *J Pathol*. 2013 Dec;231(4):466-79.
5. Danescu A, Herrero Gonzalez S, Di Cristofano A, Mai S, **Hombach-Klonisch S**. Three-dimensional (3D) Nuclear Telomere Architecture Changes during Endometrial Carcinoma Development, Accepted for Publication in *Genes, Chomosomes and Cancer* 2013 Aug;52(8):716-32.
6. Natarajan S, **Hombach-Klonisch S**, Dröge P, Klonisch T. HMGA2 inhibits apoptosis through interaction with ATR-CHK1 signaling complex in human cancer cells. *Neoplasia* 2013 Mar;15(3):263-80.
7. Bialek J, Kunanuvat U, **Hombach-Klonisch S**, Spens A, Stetefeld J, Sunley K, Lippert D, Wilkins JA, Hoang-Vu C, Klonisch T. Relaxin enhances the collagenolytic activity and in vitro invasiveness by upregulating matrix metalloproteinases in human thyroid carcinoma cells. *Mol Cancer Res*. 2011 Jun;9(6):673-87.
8. Radestock Y, Willing C, Kehlen A., Hoang-Vu C, **Hombach-Klonisch S**. (2010) Relaxin enhances S100A4 and promotes growth of human thyroid carcinoma cell xenografts. *Mol Cancer Res*; Apr;8(4):494-506.

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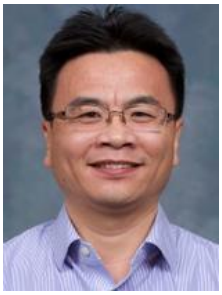

Dr. Pingzhao Hu received his Ph.D. degree in computer science from York University. He has worked as the Manager of Statistical Analysis Facility of The Centre for Applied Genomics (TCAG) in The Hospital for Sick Children for 10 years. During that time, the facility was used and accessed by more than 160 scientists from 7 countries, 13 research universities and their teaching hospitals from 8 provinces (BC, AB, SK, MB, ON, QC, NL and NS) in Canada. Dr. Hu is presently an Assistant Professor in the Department of Biochemistry and Medical Genetics and a member of Data Science Platform of **George and Fay Yee Centre for Healthcare Innovation** at the University of Manitoba **and an Assistant Professor (status) in** Division of Biostatistics, Dalla Lana School of Public Health in the University of Toronto. He is one of Review Editors of Statistical Genetics and Methodology in Frontiers in Genetics. His research interests include bioinformatics and statistical genetics.

Recent advances in high-throughput omics technologies have enabled biomedical researchers to collect large-scale multimodal genomic data for the same set of subjects and perform integrative and multi-level analyses. As a consequence, there has been growing interest in designing innovative algorithms to conduct the analyses in order to obtain deeper insights regarding the underlying biological system. The development of computational approaches and tools for handling the big multimodal data still lags behind the increasing complexity of the data produced, and many methodological challenges remain ahead. One of these is the heterogeneity present in the different multimodal data sources, which makes it difficult to discern the coordinated signal of interest from source-specific noise or extraneous effects. This creates a gap between the massive data being generated and the biological knowledge that could be gleaned from the data. Dr. Hu's research program focus on developing large-scale machine learning algorithms to combine different layers of multimodal data generated from high-throughput experimental methodologies computationally to form complex models, which incorporate expert biological knowledge and predict biological outcomes based on the models in a context-dependent way. The overarching goal is to help clinicians and biologists gain new insights on better understanding disease mechanisms, and improving diagnosis and treatment.

Dr. Hu's research program is funded by Natural Sciences and Engineering Research Council of Canada (NSERC), Canadian Breast Cancer Foundation (CBCF), Prostate Cancer Canada (PCC), Health Sciences Centre Foundation (HSCF), Research Manitoba (RM), Manitoba Medical Service Foundation (MMSF), Mitacs, Canadian Institutes of Health Research (CIHR) and University of Manitoba.

Selected Publications: (total citations 1,826; H-index 20)

1. KL Wright, JR Adams, J Liu, AJ Loch, RG Wong, C Jo, LA Beck, DR Santhanam, L Weiss, X Mei, TF Lane, S Koralov, SJ Done, JR. Woodgett, E Zacksenhaus, **P Hu**, SE Egan (2015). Ras signaling is a key determinant of metastatic dissemination and poor survival of luminal breast cancer patients. *Cancer Research*, In Press
2. R Johnson*, **P Hu***, C Fan, C Anders (2015). Gene expression analysis of "young adult type" breast cancer: a retrospective analysis. *Oncotarget* 6:13688-13702 (* equal contribution)
3. N Kanwar, **P Hu**, P Bedard, M Clemons, D McCready, SJ Done (2015) Identification of genomic signatures in circulating tumor cells from breast cancer. *International Journal of Cancer* 137:332-344
4. M Uddin, K Tammimies, G Pellecchia, B Alipanahi, **P Hu**, Z Wang, D Pinto, L Lau, T Nalpathamkalam, CR. Marshall, BJ Blencowe, BJ Frey, D Merico, R Yuen, SW Scherer (2014). Brain-expressed exons under purifying selection are enriched for *de novo* mutations in autism spectrum disorder. *Nature Genetics* 46: 742-747.
5. **P Hu**, S Bull, H Jiang (2012). Gene network modular-based classification of microarray samples. *BMC Bioinformatics*13: S17.
6. PC Havugimana, GT Hart, T Nepusz, H Yang, AL Turinsky, Z Li, PI Wang,, DR Boutz, V Fong , S Phanse, M Babu, SA Craig, **P Hu**, C Wan, J Vlasblom, V Dar, A Bezginov, GW Clark, GC Wu, SJ Wodak, ERM Tillier, A Paccanaro, EM Marcotte, A Emili (2012). A census of human soluble protein complexes. *Cell* 150:1068-1081.
7. D Picard, S Millar, CE Hawkins, E Bouffet, HA Rogers, TSY Chan, SK Kim, YS Ra, J Fangusaro, A Korshunov, H Toledano, H Nakamura, JT Hayden, J Chan, L Lafay-Cousin, **P Hu**, X Fan, KM Muraszko, SL Pomeroy, CC Lau, HK Ng, C Jones, TV Meter, SC Clifford, C Eberhart, A Gajjar, SM Pfister, RG Grundy, A Huang (2012). Markers of survival and metastatic potential in childhood CNS primitive neuro-ectodermal brain tumors: an integrative genomic analysis. *Lancet Oncology* 13:838-848.
8. Z Wei, W Wang, **P Hu**, GJ Lyon, H Hakonarson (2011). SNVer: a statistical tool for variant calling in analysis of pooling or individual next-generation sequencing data. *Nucleic Acids Research* 39:e132.
9. SD Molyneux, MD Grappa, AG Beristain, TD McKee, DH Wai, J Paderova, M Kashyap, **P Hu**, T Maiuri, SP Narala, V Stambolic, J Squire, J Penninger, O Sanchez, TJ Triche, GA Wood, LS Kirschner, R Khokha (2010). PRKAR1A is an Osteosarcoma tumor suppressor and defines a molecular subclass in mice. *Journal of Clinical Investigation* 120:3310-3325.
10. **P Hu**, G Bader, DA Wigle, A Emili (2007). Computational Prediction of cancer gene function. *Nature Reviews Cancer* 7:23-34.

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Dr. Israels received her MD degree from the University of Manitoba and trained in Pediatrics at Stanford University Medical Center. She received her clinical Pediatric Hematology/Oncology training at the Hospital for Sick Children and her research training at the Manitoba Institute of Cell Biology and Scripps Research Institute. She joined the faculty in 1986.

Dr. Israels is a Professor in the Section of Pediatric Hematology/Oncology, Department of Pediatrics and Child Health. She is the director of the Haemostasis Laboratory at Health Sciences Centre, co-director of the Manitoba Pediatric Bleeding Disorders Program and a Senior Scientist in the Research Institute in Oncology and Hematology. She serves as Vice Dean (Academic Affairs) for the Faculty of Health Sciences.

The platelet research laboratory studies basic mechanisms of platelet function and dysfunction with a particular focus on platelet function in the fetus and newborn. We are also interested in the investigation of patients with inherited platelet function abnormalities, in conjunction with the clinical Haemostasis Laboratory. The laboratory is involved in evaluating new methodology for laboratory testing of platelet function and developing best practices for clinical laboratory testing.

On-going projects include:

1. Studies of patients with inherited platelet function disorders, with a particular focus on families with a congenital deficiency of platelet granules.
2. Investigation of in vivo platelet activation in boys with severe Hemophilia A and its relationship to bleeding phenotype.
3. Investigation the defects in the collagen signaling pathway in neonatal platelets.
4. Initiatives to improve and standardize platelet function testing and quality assurance.

Selected Publications:

1. Langley AR, Stain AM, Chan AKC, McLimont M, Chait S, John K. Wu, Poon MC, Card R, **Israels SJ**, Laferriere N, Klaassen RJ, Rivard GE, Cloutier S, Hawes S, Feldman B, Blanchette V. Experience with central venous access devices (CVADs) in the Canadian Hemophilia Primary Prophylaxis Study (CHPS). Haemophilia 2015; 21(4): 469-76.

2. Torabi M, Singh H, Galloway K, **Israels SJ**. Geographical variation in the incidence of childhood leukemia in Manitoba. J Pediatrics & Child Health 2015.

3. **Israels SJ**. Laboratory testing for platelet function disorders. Int J Lab Hematol 2015; 37(Suppl 1):18-24.

4. Kulkarni K, Halton J, Spavor M, **Israels SJ**, Abish S, Yong J, Yasui Y, Mitchell LG. Increased requirement for central venous catheter replacement in pediatric oncology patients with deep venous thrombosis: A multicentre study. Thromb Haemost 2015; 113:434-5.

5. **Israels SJ**, McNicol A, Dean HJ, Cognasse F, Sellers, EAC. Markers of platelet activation are increased in adolescents with type 2 diabetes. Diabetes Care 2014; 37:2400-3

6. Stammers DM, **Israels SJ**, Lambert PJ, Cuvelier GDE. Cancer incidence, morbidity, and mortality in Canadian First Nation Children: a Manitoba population-based study from the Cancer in Young People in Canada (CYP-C) Registry. Pediatr Blood Cancer 2014; 61:2164-9.

7. Bush JW, Hancock BJ, **Israels SJ**, Ellison DW, Stefanovici C, Krawitz S. Intracranial atypical teratoid/rhabdoid tumour presenting as an axillary mass: A case report and review of literature. Pediatr Dev Pathol 2014; 17:122-5.

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Born and raised in Thompson, Manitoba, Dr. Davinder S. Jassal attended the University of Manitoba where he obtained his BSc in Microbiology, MD, and residency in Internal Medicine in 2001. Subsequently, he completed a residency in Adult Cardiology at Dalhousie University, followed by a fellowship in Advanced Cardiovascular Imaging at Massachusetts General Hospital, Harvard Medical School in Boston, Massachusetts, US from 2004-2006. After joining the Section of Cardiology, Department of Internal Medicine in 2006 at the University of Manitoba as a Clinician Scientist, Dr. Jassal is currently Associate Professor of Cardiology, Oncology, Radiology, and Physiology and is the Principal Investigator of the Cardiovascular Imaging Laboratory at the Albrechetsen Research Institute.

Cardio-Oncology is a novel discipline that focuses on the prevention, diagnosis, and management of cancer patients who are at risk of developing cardiovascular complications as a result of their cancer treatment. Despite the beneficial effects of chemotherapy agents in increasing overall survival of cancer patients, cardiotoxicity remains a serious complication of many anti-cancer therapies. Two types of targeted therapy currently in use for colorectal (CRC) and renal cell cancer (RCC), respectively, are the monoclonal antibody Bevacizumab (BVZ; Avastin) and the tyrosine kinase inhibitor Sunitinib (SNT; Sutent). Although both anti-cancer drugs improve overall morbidity and mortality in the CRC and RCC settings, an unexpected side effect is the risk of developing cardiotoxicity in nearly 1 in 4 patients, affecting over 8000 Canadians on an annual basis. Early detection of cardiac dysfunction and preventative therapies would be useful for addressing the cardiac safety profile of anti-cancer drugs. As leading experts in this field, our recent basic science and clinical investigations have confirmed the utility of novel imaging techniques for the early detection of left ventricular (LV) systolic dysfunction due to Doxorubicin and Trastuzumab therapy in the breast cancer setting. Our laboratory was the first to demonstrate that tissue velocity imaging (TVI) using echocardiography could detect early evidence of cardiac dysfunction prior to a decrease in conventional LV ejection fraction (LVEF) parameters in both a murine model of chemotherapy induced cardiotoxicity and in women with breast cancer. A number of Cardio-Oncology sites worldwide have incorporated serial TVI parameters as part of their routine surveillance for monitoring cardiac function in the breast cancer population based on our seminal findings.

Although heart failure medications including renin-angiotensin system (RAS) antagonists are commonly used after cardiac dysfunction develops in the cancer setting, it raises the question of whether these agents can be used prophylactically to prevent BVZ and SNT mediated cardiotoxicity. In experimental models of cardiac injury due to BVZ or SNT, cardiac angiotensin II (Ang-II) levels are increased with a concomitant up-regulation of the RAS, which leads to increased OS, apoptosis, and ultimately heart failure as demonstrated by our group and others. We are currently exploring whether the prophylactic administration of RAS antagonists will prevent both BVZ and/or SNT mediated cardiotoxicity. The anticipated goal of our Cardio-Oncology research program is to improve the overall morbidity and mortality in cancer patients treated with either BVZ or SNT, while at the same time, preventing the detrimental side effects of these two drugs on cardiac health.

Selected Publications:

1. Bordun KA, Premecz S, daSilva M, Mandal S, Goyal V, Glavinovic T, Cheung M, Cheung D, White CW, Chaudhary R, Freed DH, Villaraga HR, Herrmann J, Kohli M, Ravandi A, Thilveris J, Pitz M, Singal PK, Mulvagh SL, **Jassal DS.** The utility of cardiac biomarkers and echocardiography for the early detection of Bevacizumab and Sunitinib mediated cardiotoxicity. ***Am J Physiol Heart Circ Physiol***. 2015 Jun 19:ajpheart:00172.2015.
2. Zeglinski M, Premecz S, Lerner J, Wtorek J, daSilva M, Hasanally D, Chaudhary R, Sharma A, Thliveris J, Ravandi A, Singal PK, **Jassal DS.** Congenital absence of nitric oxide synthase 3 potentiates cardiac dysfunction and reduces survival in Doxorubicin- and Trastuzumab-mediated cardiomyopathy. ***Can J Cardiol.*** 2014. Mar;30(3):359-67.
3. Fallah-Rad N, Walker JR, Wassef A, Lytwyn M, Bohonis S, Fang T, Tian G, Kirkpatrick ID, Singal PK, Krahn M, Grenier D, **Jassal DS**. The utility of cardiac biomarkers, tissue velocity and strain imaging, and cardiac magnetic resonance imaging in predicting early left ventricular dysfunction in patients with human epidermal growth factor receptor II-positive breast cancer treated with adjuvant trastuzumab therapy***. J Am Coll Cardiol*** 2011; 57(22): 2263-70.
4. Walker J, Bhullar N, Fallah-Rad N, Lytwyn M, Golian M, Fang T, Summers AR, Singal PK, Barac I, Kirkpatrick ID, **Jassal DS.** Role of three-dimensional echocardiography in breast cancer: comparison with two-dimensional echocardiography, multiple-gated acquisition scans, and cardiac magnetic resonance imaging. ***J Clin Oncol.*** 2010 Jul 20;28(21):3429-26.

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Distinguished Professor Dr. Digvir Jayas was educated at the G.B. Pant University of Agriculture and Technology in Pantnagar, India; the University of Manitoba, and the University of Saskatchewan. Before assuming the position of Vice-President (Research and International), he held the position of Vice-President (Research) for two years and Associate Vice-President (Research) for eight years. Prior to his appointment as Associate Vice-President (Research), he was Associate Dean (Research) in the Faculty of Agricultural and Food Sciences, Department Head of Biosystems Engineering, and Interim Director of the Richardson Centre for Functional Foods and Nutraceuticals. He is a Registered Professional Engineer and a Registered Professional Agrologist.

Dr. Jayas held a Canada Research Chair in Stored-Grain Ecosystems, and he conducts research related to drying, handling and storing grains and oilseeds and digital image processing for grading and processing operations in the Agri-Food industry. He has authored or co-authored over 800 technical articles in scientific journals, conference proceedings and books dealing with issues of storing, drying, handling and quality monitoring of grains. He has collaborated with researchers in several countries but has had significant impact on development of efficient grain storage, handling and drying systems in Canada, China, India, Ukraine and USA.

Selected Publications:

1. Senthilkumar*, T., **D.S. Jayas** and N.D.G. White. 2015. Detection of different stages of fungal infection in stored canola using near-infrared hyperspectral imaging. *Journal of Stored Products Research*, **63**:80-88.
2. Jian*, F., V. Chelladurai*, **D.S. Jayas** and N.D.G. White. 2015. Three-dimensional transient heat, mass, and momentum transfer model to predict conditions of canola stored inside silo bags under Canadian Prairie conditions: Part I - soil temperature model. *Transactions of the ASABE*, **58**(4):1127-1134.
3. Jian*, F., V. Chelladurai*, **D.S. Jayas** and N.D.G. White. 2015. Three-dimensional transient heat, mass, and momentum transfer model to predict conditions of canola stored inside silo bags under Canadian Prairie conditions: Part II B model of canola bulk temperature and moisture content. *Transactions of the ASABE*, **58**(4):1135-1144.
4. Jian*, F., **D.S. Jayas**, P.G. Fields and N.D.G. White. 2015. A new method to rapidly detect rusty grain beetle, *Cryptolestes ferrugineus* (Stephens), in stored grain. *Journal of Stored Products Research*, **63**:1-5.
5. Vadivambal*, R., V. Chelladurai*, F. Jian* and **D.S. Jayas**. 2015. Tensile strength and elongation of hemp and sisal ropes at different temperatures. *Canadian Biosystems Engineering*, **57**:3.9-3.12.
6. Ravikanth*, L., C.B. Singh, **D.S. Jayas** and N.D.G. White. 2015. Classification of contaminants from wheat using near-infrared hyperspectral imaging. *Biosystems Engineering*, **135**:73-86.
7. Amudhasurabi*, A., **D.S. Jayas** and K. Alagusundaram. 2015. Assessment of effectiveness of subsidized food grain distribution in India with respect to rice and wheat. *Indian Journal of Marketing*, **45**(1):49-59.
8. Amudhasurabi*, A., J. Carlberg, **D.S. Jayas** and L. Ravikanth*. 2015. Impacts of grain handling and transportation system deregulation on farm profitability in Manitoba Province of Canada. *International Journal of Business Management & Research*, **5**(2):37-44.
9. Singh, C.B., **D.S. Jayas** and R. Larson. 2015. Assessment of fan control strategies for in-bin natural air drying of wheat in western Canada. *Canadian Biosystems Engineering*, **56**:3.25-3.36.
10. Moses*, J.A., **D.S. Jayas** and K. Alagusundaram. 2015. Climate change and its implications on stored food grains. *Agricultural Research*, **4**(1):21-30.
11. Mahesh*, S., **D.S. Jayas**, J. Paliwal and N.D.G. White. 2015. Hyperspectral imaging to classify and monitor quality of agricultural materials. *Journal of Stored Products Research*, **61**:17-26.
12. Moses*, J.A., **D.S. Jayas** and K. Alagusundaram. 2015. Simulation and validation of airflow distribution patterns in hopper-bottom bins filled with canola (accepted in December 2014 for publication in *Applied Engineering in Agriculture*, **31**(2):303-311.
13. Jian*, F., **D.S. Jayas**, N.D.G. White, P.G. Fields and N. Howe*. 2015. An evaluation of insect expulsion from wheat samples by microwave treatment for disinfestation. *Biosystems Engineering*, **130**:1-12.
14. Mahesh*, S., **D.S. Jayas**, J. Paliwal and N.D.G. White. 2015. Comparison of partial least squares regression (PLSR) and principal components regression (PCR) methods for protein and hardness predictions using the near-infrared (NIR) hyperspectral images of bulk samples of Canadian wheat. *Food and Bioprocess Technology*, **8**:31-40.

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Dr Johnston is a Professor of Internal Medicine, Section of Hematology/Oncology, University of Manitoba. He is a clinical hematologist and a Senior Investigator in the Research Institute for Oncology and Hematology at the University of Manitoba. His primary research interest is in chronic lymphocytic leukemia (CLL) and he is involved in a number of translational research projects supported by the Manitoba CLL Cluster. To further these activities, Dr Johnston has developed the CLL Clinic at CancerCare Manitoba, the CLL Clinical Data base and is the Clinical Director of the Manitoba CLL Tumor Bank. Ongoing research projects are related to the epidemiology of CLL in Manitoba, second malignancies and infections in CLL, and the development of new agents for the treatment of CLL.

Selected Publications:

1. Dielschneider RF, Eisenstat H, Mi S, Curtis JM, Xiao W, **Johnston JB**, and Gibson SB. Lysosomotropic Agents Selectively Target Chronic Lymphocytic Leukemia Cells Due to Altered Sphingolipid Metabolism. Leukemia (in press)
2. Li H, Wu X, Hou S, Malek M, Kielkowska A, Noh E, Makondo KJ, Du Q, Wilkins HA, **Johnston JB**, Gibson SB, Lin F, and Marshall A. Phosphatidylinositol-3,4-biphosphate and its binding protein lamellipodin regulate chemotaxis of malignant B lymphocytes. J Immunol 2015 Dec 22 [Epub]
3. Beiggi S, Banerji V, Deneka A, Griffith EJ, Gibson SB and **Johnston JB**. Comparison of outcome between referred and non-referred chronic lymphocytic leukemia patients to a specialized clinic: A Canadian population-based study. Cancer Medicine (in press)
4. Quest G, and **Johnston JB**. Clinical features and diagnosis of hairy cell leukemia. Best Practice & Research Clinical Haematology, 28(4)180-192, 2015.
5. **Johnston JB**. Enhancing monoclonal antibody activity in chronic lymphocytic leukemia. Leuk Lymph. 2015 Aug;56(8):2231-2232.
6. Beauchemin C, **Johnston JB**, Lapierre ME, Aissa F, Lachaine J. The relationship between progression-free survival and overall survival in chronic lymphocytic leukemia: a literature-based analysis. Current Oncology 2015 June;22(3)e148-56.
7. Lafarge ST, Li H, Pauls SD, Hou S, **Johnston JB**, Gibson SB, and Marshall AJ. ZAP-70 expression directly promotes chronic lymphocytic leukaemia cell adhesion to bone marrow stromal cells. Br J Haematol, 168:139-159, 2015.
8. Lafarge ST, Hou S, Pauls SD, **Johnston JB**, Gibson SB, and Marshall AJ. Differential expressin and function of CD27 in chronic lymphocytic leukemia cells expressing ZAP-70. Leuk Res 2015 May 2 [Epub].
9. Ye, X, Mneina A, **Johnston JB**, and Mahmud SM. Associations between statin use and non-Hodgkin lymphoma (NHL) Risk and Survival: A meta-analysis". Hematological Oncology 2015 Oct 20 [Epub].
10. Kouroukis CT, Crump M, MacDonald D, Larouche JF, Stewart D, **Johnston JB**, Sauvageau S, Beausoleil E, Sage P, Dubois S, Christofides A, Di Clemente S, and Sehn L. An open-label expanded access trial for bendamustine in patients with refractory iNHL or previously untreated CLL (BEND-ACT). Current Oncology 2015 Aug;22(4):e260-71.
11. Kriangkum J, Motz SN, Mack T, Beiggi S, Baigorri E, Kuppusamy H, Belch AR, **Johnston JB**, and Pilarski LM. Oligoclonal expansions defined by IGH rearrangements persist in patients with chronic lymphocytic leukemia: single-cell analysis and next-generation immuno-sequencing. PLoS One, 2015 Sep 9:e0137232
12. Gehrke I, Bouchard ED, **Johnston JB**, Gibson SB and Banerji V. NAMPT-inhibition by FK866 efficiently induces apoptosis in leukemic cells from high-risk chronic lymphocytic leukemia (CLL) patients. Clin Cancer Res, 20:4861-4872, 2014.
13. Lafarge ST, **Johnston JB**, Gibson SB, and Marshall AJ. Adhesion of ZAP-70+ chronic lymphocytic leukemia cells to stromal cells is enhanced by cytokines and blocked by inhibitors of the P13-kinase pathway. Leuk Res, 38:109-115, 2014.
14. Dielschneider RF, Xiao W, Yoon Ju-Yoon, Noh E, **Johnston JB**, and Gibson SB. Gefitinib targets ZAP70+ chronic lymphocytic leukemia cells and inhibits B cell receptor signaling. Cell Death Dis, 2014 Oct 2;5:e1439
15. Kuppusamy H, Ogmundsdottir HM, Baigorri E, Warkentin AM, Steingrimsdottir H, Haraldsdottir V, Mant MJ, Mackey J, Adamia S, **Johnston JB**, Belch AR and Pilarski LM. Inherited polymorphisms in *Hyaluronan Synthase I* predict risk of B-cell malignancies but not of breast cancer. PLoS One, 20:9e100691, 2014.
16. Minuk GY, Lerner B, Gibson S, **Johnston JB**, Uhanova J, Andonov A, and Wu J. Hepatitis B and C viral infections in patients with chronic lymphocytic leukemia. Can J Gastroenterology, 28:131-134, 2014.
17. Yoon J-Y, Ishdorj G, Graham BA, Johnston JB, Gibson SB. Valproic acid enhances fludarabine-induced apoptosis mediated by ROS and involving decreased AKT and ATM activation in B-cell-lymphoid neoplastic cells. Apoptosis, 19:191-200, 2014.

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Dr. Elissavet Kardami is the Director of the Muscle Biochemistry Laboratory, at the Institute of Cardiovascular Sciences at St. Boniface Albrechtsen Research Centre, and a Professor of HACS, cross-appointed in Physiology & Pathophysiology, University of Manitoba. She obtained her B.Sc. from the University of Athens, Greece, and her Ph.D. from King's College, Biophysics Department London, U.K., where she studied the biophysical properties of muscle proteins. She conducted post-doctoral studies at the Pasteur Institute, Paris, France, and then at Berkeley, University of California, on the cell and molecular biology of muscle. She started her independent career at the University of Manitoba in 1987.

Dr. Kardami's research interests revolve around signaling pathways controlling cell growth (hyperplastic and hypertrophic) and cell resistance to ischemic or drug-induced injury. She is a recognized expert in FGF-2 (fibroblast growth factor-2) growth factors and their downstream targets such as the membrane-channel forming protein Connexin-43 (Cx43) and mitochondrial populations.

Current laboratory projects address:

a) Production of, and differential signaling by, FGF-2 isoforms, in cardiac muscle and non-muscle cells, leading to growth stimulation or inhibition and modulation of vulnerability to injury by ischemia or chemotherapeutic drugs
b) Direct growth-factor-mediated intra-mitochondrial signaling, protecting or promoting permeability transition pore formation
c) The role of Connexin-43 and its phosphorylation downstream of growth factor pathways in growth regulation.

Selected Publications:

1. Santiago JJ, McNaughton LJ, Koleini N, Ma X, Nickel BE, Fandrich RR, Wigle J, Freed DH, Arora RC, **Kardami E.**(2014). High molecular weight FGF-2 released by human heart cells is a potential target for prevention of cardiac remodelling. PLoS One.9(5): e97281.
2. Srisakuldee W, Makazan Z, Nickel BE, Zhang F, Thliveris JA, Pasumarthi KB, **Kardami E.** (2014).The FGF-2-triggered protection of cardiac subsarcolemmal mitochondria from calcium overload is mitochondrial connexin43-dependent.Cardiovascular Research. 103(1): 72-80.
3. Thandapilly SJ, Louis XL, Behbahani J, Movahed A, Yu L, Fandrich R, **Kardami E**, Netticadan T. (2013).Reduced hemodynamic load aids low-dose resveratrol in reversing cardiovascular defects inhypertensive rats. Hypertension Research. 36(10): 866-72.
4. Sontag DP, Wang J, **Kardami E**, Cattini PA. (2013). FGF-2 and FGF-16 Protect Isolated Perfused Mouse Hearts from Acute Doxorubicin-Induced Contractile Dysfunction.Cardiovascular Toxicology. 13(3): 244-53.
5. Wang J, Nachtigal MW, **Kardami E**, Cattini PA. (2013). FGF-2 protects cardiomyocytes from doxorubicin damage via protein kinase C-dependent effects on efflux transporters.Cardiovascular Research. 98(1): 56-63.
6. Jeyaraman MM, Fandrich RR, **Kardami E.** (2013). Together and apart: inhibition of DNA synthesis by connexin-43 and its relationship to transforming growth factor β. Front Pharmacol. 19;4:90(1-9)
7. Jeyaraman MM, Srisakuldee W, Nickel BE, **Kardami E.** (2012). Connexin-43 phosphorylation and cytoprotection in the heart. Biochimica et Biophysica Acta. 1818(8): 2009-13.

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Dr. Sachin Katyal received his B.Sc. (Biochemistry) degree from the University of Alberta and received his Ph.D. (Oncology) degree at the Cross Cancer Institute at the University of Alberta. His post-doctoral training in the area of DNA damage and repair in neurodevelopment and neuro-oncology was done in the lab of Dr. Peter McKinnon at the prestigious St. Jude Children's Research Hospital; work that led to numerous publications in internationally-renowned journals such as Nature, Nature Neuroscience and EMBO J. Dr. Katyal's research is CIHR-funded and he is the recipient of the CIHR Institute of Cancer Research *Early Career Award in Cancer Research* and a CIHR New Investigator award. He serves on several scientific review committees for international academic journals and grant review panels.

Modulating DNA Damage repair mechanisms to enhance brain tumour treatment success

DNA strand breaks occur on a daily basis in cells due to cell stress, environmental factors, oxidation and metabolism. Damaged DNA is resolved by dedicated DNA damage response (DDR) and repair mechanisms in order to preserve genomic integrity and cell function. The goal of conventional chemotherapeutic drugs and radiotherapy is to elicit DNA damage to overwhelm the tumour's innate DDR and induce cell death. However, tumour cells have remarkable ability to respond to DNA damage, repair and adapt thus allowing survival and eventual drug resistance. It is predicted that >90% of all tumours incur at least one defect in the DNA damage response (DDR), thus tumour cell survival relies upon enhanced activity of other compensatory DNA repair pathways. The aggressive and deadly brain tumour, glioblastoma multiforme (GBM) shows a very high level of recurrence due to emergence of chemo/radio-resistant tumour cell populations; patients usually live about 1 yr from their date of diagnosis. We are identifying the "back-up" DNA repair pathways in these deadly brain tumours so that we can enhance the patients' treatment success and their quality-of-life.

Selected Publications:

1. Heo, J., Li, J., Summerlin, M., Hayes, A., **KATYAL, S.**, McKinnon, P., Nitiss, K., Nitiss, J. and Hanakahi, L. (2015). Tdp1 promotes assembly of non-homologous end joining protein complexes on DNA. *DNA Repair* **30**: 28-37.
2. **KATYAL, S.**, Lee, Y., Nitiss, K., Downing, S., Zhao, J., Li, Y., Russell, H.R., Petrini, J.H.J, Nitiss, J.L., #McKinnon, P.J. (2014). Aberrant topoisomerase-1 DNA lesions are pathogenic in neurodegenerative genome instability syndromes. *Nat. Neurosci*. **17**: 813-21. ***# denotes co-corresponding***
3. Shokolenko, I.N., Fayzulin, R., **KATYAL, S.**, McKinnon, P.J., Wilson, G.L., Alexeyev, M.F. (2013). Mitochondrial DNA ligase activity is dispensable for viability, but is essential for mtDNA maintenance. *J. Biol. Chem.* Epub 23884459.
4. Lee, Y., **KATYAL, S.**, Downing, S., Zhao, J., Russell, H.R., McKinnon, P.J. (2012). Neurogenesis requires TopBP1 to prevent catastrophic replication-associated DNA damage in early progenitors. *Nat. Neurosci.* **15**: 829-826.
5. Lee, Y., Shull, E.R.P., Frappart, P.-O., **KATYAL, S.**, Enriquez-Rios, V., Zhao, J., Russell, H.R., Brown, E.J., McKinnon, P.J. (2011). ATR maintains select progenitors during nervous system development. *EMBO J.*, **31**: 1177-1189.
6. **KATYAL, S.**, Glubrecht, D.D., Guo, Z., Li., L. and Godbout, R. (2011). Disabled-1 alternative splicing in human fetal retina and neural tumours. *PLoS One,* **6**: e28579.
7. **KATYAL, S.** and McKinnon, P.J. (2011). Disconnecting XRCC1 and DNA ligase III. *Cell Cycle.* **10**: 2269-2275.
8. Simsek, D., Brunet, E., Wong, Y.-W., **KATYAL, S.**, Gao, Y., McKinnon, P.J., Lou, J., Zhang, L., Li, J., Rebar, E., Gregory, P., Holmes, M. and Jasin, M. (2011). DNA ligase III promotes alternative nonhomologous end-joining during chromosomal translocation formation. *PLoS Genet.* **7**: e1002080.
9. *Gao, Y., ****KATYAL, S.***, Lee, Y., Zhao, J., Rehg, J.E., Russell, H.R. and McKinnon, P.J. (2011). Ligase III is critical for mtDNA integrity but not Xrcc1-mediated nuclear DNA repair. *Nature.* **471**: 240-244. ****denotes Equal Contribution***
10. Becherel, O.J., Jacob, B., Cherry, A.L., Gueven, N., Fusser, M., Kijas, A.W., Peng, C., **KATYAL, S.**, McKinnon, P.J., Chen, J., Epe, B., Smerdon, S.J., Taucher-Scholz, G. and Lavin, M.F. (2009). CK2 phosphorylation-dependent interaction between aprataxin and MDC1 in the DNA damage response. *Nucl. Acids Res.* **38**: 1489-1503.
11. Lee, Y., **KATYAL, S.**, Li, Y., El-Khamisy, S.F., Russell, H.R., Caldecott, K.W. and McKinnon, P.J. (2009). Genesis of cerebellar interneurons and the prevention of neural DNA damage require Xrcc1. *Nat. Neurosci.* **12**: 973-980
12. El-Khamisy, S.F., **KATYAL, S.**, Patel, P., Ju, L., McKinnon, P.J. and Caldecott, K.W. (2009). Synergistic decrease of DNA single-strand break repair rates in mouse neural cells lacking both Tdp1 and aprataxin. *DNA Repair* **8**: 760-766.
13. Reynolds, J.J., El-Khamisy, S.F., **KATYAL, S.**, Clements, P., McKinnon, P.J. and Caldecott, K.W. (2009). Defective DNA ligation during short-patch single-strand break repair in ataxia oculomotor apraxia-1. *Mol. Cell. Biol.* **29**: 1354-1362.
14. **KATYAL, S.** and McKinnon, P.J. (2009). 'Mouse Models of DNA Double Strand Break Repair Deficiency and Cancer', in K.K. Khanna and Y. Shiloh (eds.), *The DNA Damage Response: Implications on Cancer Formation and Treatment*, Springer Press, New York, 285-305.

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Dr. Kauppinen received her M.Sc. in Biotechnology and Ph.D. in Biotechnology and Molecular Neuroscience from the University of Kuopio, Finland. Her Ph.D. studies (published in her maiden name, Tikka) discovered the neuroprotective potential of minocycline, an antibiotic that has several anti-inflammatory functions unrelated to its anti-microbial mechanisms. Dr. Kauppinen did her postdoctoral training at the University of California, San Francisco. After which she became an Adjunct Assistant Professor in the Department of Neurology at University of California, San Francisco. Currently Dr. Kauppinen is a principle investigator in the Neuroscience Research Program at Kleysen Institute for Advanced Medicine, Health Sciences Centre, an assistant professor in the Department of Pharmacology and Therapeutics at the University of Manitoba and researcher in Children's Hospital Research Institute of Manitoba.

Dr. Kauppinen's research centers on the role of microglia and neuroinflammation in central nervous system (CNS) disorders and pathologies. Microglia are brain immune cells and believed to be the drivers of neuroinflammation, a nervous system-specific inflammatory-like responses to injury. These responses are characterized by production and interplay of different cytokines, chemokines, adhesion molecules, free radicals, and destructive enzymes produced and released by microglia, astroglia, endothelial cells and infiltrating peripheral immune lineage cells. While immune responses are meant to protect tissue from pathogens, microglia and neuroinflammation can contribute to neurodegeneration, jeopardice neurogenesis, healing and promote tumour progression.

Dr. Kauppinen's research laboratory is investigating how microglial functions are regulated and how to harness them to promote brain health and recovery in CNS tumour (glioblastoma multiform), neurodegenerative disorders (Azheimer's disease, stroke), and neurodevelopmental disturbances (caused by gestational diabetes). Her research program is built around the novel hypothesis that PARP-1 is the key regulator of microglial functions, and that PARP-1 inhibition allows microglial responses to be directed towards neuroprotective actions. She has developed unique molecular tools that allow microglia specific manipulation of PARP-1 activity and expression.

The overall goals of Dr. Kauppinen's research program are to **1)** understand how microglial functions affect neuroinflammation, neurodegeneration, neurogenesis, neuronal functions and brain tumour growth, **2)** establish approaches to modulate microglial responses, and **3)** develop new therapeutic strategies with multiple disease relevance.

Selected Publications: (total citations 3,466; H-index 22)

1. **Kauppinen TM***, Gan L, Swanson RA. Poly(ADP-ribose)polymerase-1 regulates NF-κB activity via SIRT1/sirtuins. *Biochim Biophys Acta*. 2013; 1833(8):1985-91.
2. **Kauppinen TM*,** Suh SW, Higashi Y, Berman AR, Escarten C, Won SJ, Wang C, Cho SH, Gan L and Swanson RA. Poly(ADP-ribose)polymerase-1 modulates microglial responses to amyloid β. ***J Neuroinflam.*** 2011; 8:152.
3. **Kauppinen TM*,** SW Suh SW, Berman A, Hamby A, Swanson RA. Inhibition of poly(ADP-ribose)-polymerase suppress inflammation and promotes recovery after ischemia injury. *J. Cereb. Blood Flow Metab.* 2009; 29(4):820-829.
4. Brennan AM, Suh SW, Won SJ, Narasimhan P, **Kauppinen TM**, Lee H, Edling Y, Chan PH, Swanson RA. NADPH oxidase is the primary source of superoxide induced by NMDA receptor activation. ***Nat. Neurosci.*** 2009; 12(7):857-863
5. **Kauppinen TM**, Chan WY, Suh SW, Wiggins AK, Huang EJ and Swanson RA. Direct phosphorylation and regulation of poly(ADP-ribose) polymerase-1 by extracellular signal-regulated proteins 1/2. ***Proc. Natl. Acad. Sci. U S A.*** 2006; 103(18): 7136-7141.
6. Alano CC, **Kauppinen TM**, Vall AV, Swanson RA. Minocycline inhibits poly(ADP-ribose) polymerase-1 at nanomolar concentrations. ***Proc. Natl. Acad. Sci. U S A.*** 2006; 103(25):9685-90.
7. **Kauppinen TM**, Swanson RA. Poly(ADP-ribose)polymerase-1 promotes microglial activation, proliferation,and matrix metalloproteinase-9 - mediated neuron death. ***J. Immunology.*** 2005; 174: 2288-2296.

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Dr. Lorrie Kirshenbaum, PhD

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Dr. Lorrie Kirshenbaum's laboratory is focused on understanding the molecular mechanisms that underlie the cell death in the heart. "There are certain genes that are highly regulated in the body that tell cells when to live and when to die and we are just beginning to understand why this takes place," he explains. "We want to learn how these genes become turned on or turned off in disease processes." We are interested in understanding how these genes impinge upon mitochondrial quality control and cellular processes such as mitophagy during hypoxia as well as in response to chemotherapeutic agents. Employing advanced techniques in molecular biology and gene delivery to this largely uncharted area of research, this laboratory is helping to set the stage for the use of gene therapy in the treatment of cardiovascular diseases. Another component of Dr. Kirshenbaum's studies is to assess the relationship between cell metabolism and cell death. After birth, when heart cells lose their ability to divide, they begin to increase in their metabolic capacity to allow the heart to grow in size to support organ growth. A number of disease conditions such as hypertension and diabetes have adverse effects on cell metabolism that sets in motion pathological changes that result in cardiac cell death and heart failure. The laboratory is investigating stimuli that cause heart cells to die during disease conditions and whether these pathways can be manipulated genetically with novel therapies for preventing heart failure.

Selected Publications:

1. Sassone F, Margulets V, Maraschi A, Rodighiero S, Silani V, Ciammola A, Sassone J and **Kirshenbaum LA**. Bcl-2/adenovirus E1B 19-kDa interacting protein (BNip3) has a key role in the mitochondrial dysfunction induced by mutant Huntington. Human Molecular Genetics. Epub ahead of print; 2015.
2. Dhingra R, Lin J and **Kirshenbaum LA**. Disruption of RIP1-FADD Complexes by MicroRNA-103/107 Provokes Necrotic Cardiac Cell Death**.** Circulation Research 117(4):314-6; 2015.
3. Biala AK, Dhingra R and **Kirshenbaum LA**. Mitochondrial Dynamics: Orchestrating the Journey to Advanced Age. J Mol Cell Cardiol. 83:37-43; 2015.
4. Li Y, Müller A, Ngo MA, Sran K, Bellan D, Arora RC, **Kirshenbaum LA** and Freed DH. Statins Impair Survival of Primary Human Mesenchymal Progenitor Cells via Mevalonate Depletion, NF-κB Signaling, and Bnip3. J Cardiovasc Transl Res. (2):96-105; 2015.
5. Dhingra R, Margulets V, Chowdhury SR, Thliveris J, Jassal D, Fernyhough P, Dorn II G and **Kirshenbaum LA**. Bnip3 Mediates Doxorubicin-induced Cardiac Myocyte Necrosis and Mortality Through Changes in Mitochondrial Signaling. Proc Natl Acad Sci. 111(51):5537-44; 2014.
6. Lin J and **Kirshenbaum LA**. Wnt-1 Dishevelled Signaling Functionally Links CAMKII and Cardiac Dysfunction. Hypertension. 65(2):287-8:2014.
7. Barbato E, Lara-Pezzi E, Stolen C, Taylor A, Barton PJ, Bartunek J, Iaizzo DP, Judge DP, **Kirshenbaum LA**, Blaxall BC, Terzic A and Hall JL. Advances in Induced Pluripotent Stem Cells, Genomics, Biomarkers, and Antiplatelet Therapy Highlights of the Year in JCTR 2013. J Cardiovasc Transl Res. 7(5):518-25; 2014.
8. Biala AK and **Kirshenbaum LA**. The Interplay between Cell Death Signaling Pathways in the Heart. Trends Cardiovasc Med. 24(8):325-331; 2014.
9. Dhingra R and **Kirshenbaum LA**. Regulation of Mitochondrial Dynamics and Cell Fate, Circulation Journal; 78:(4)803-810; 2014.

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Dr. Thomas Klonisch is a Full Professor at the Department of Human Anatomy and Cell Science at the University of Manitoba. Dr. Klonisch is the founder of the Brain Tumor Research Alliance Manitoba (BTRAM) and a member of the Manitoba Breast Cancer Research Group. He completed his MD and PhD degree at the Justus-Liebig University Giessen, Germany, and did his habilitation at the Martin-Luther University of Halle-Wittenberg, Germany. He did post-doctoral training at the University of Guelph, Ontario, Canada, and was a Senior Research Fellow at the University College London, London, UK. He was a faculty member at the Dept. of Anatomy and Cell Biology, Martin-Luther University of Halle-Wittenberg, Germany, and in 2004 was appointed head of the Dept. of Human Anatomy and Cell Science, University of Manitoba, Winnipeg.

The research focus in the Klonisch lab is on mechanisms and inter-connections between genomic stability, cell death, therapeutic resistance in cancer (stem) cells. These are key cellular responses shaped by the impact of the tumor microenvironment which modulates the ability of these cancer (stem) cells to undergo epithelial-mesenchymal transition (EMT) and tissue invasion/metastasis.

His lab discovered new roles for the G protein coupled relaxin receptor RXFP1 in brain cancer and the research team is exploring novel and clinically relevant signaling effects by this receptor system in glioblastoma. To study patient brain tumor cells, the Klonisch lab has established a brain tumor cell resource from patient brain tumor tissues.

Protection of the genome is pivotal to stem cells and a key element for cell survival. The Klonisch lab studies the nuclear stem cell factor and non-histone chromatin binding protein HMGA2 (High Mobility Group A2) which they found to be an important protein for genome protection. HMGA2 can facilitate more efficient DNA damage repair and promotes cancer (stem) cell survival. His research team discovered novel HMGA2 interacting proteins under conditions of oxidative and chemotherapeutic stress and is elucidating the molecular mechanisms by which HMGA2 mediates cell survival in different cancer models.
The overarching goal of these studies is to identify novel innovative therapeutic strategies for more effective treatment of cancer patients.

Selected Publications: (*equal authorship)

1. Thanasupawat T, Glogowska A, Burg M, Wong GW, Hoang-Vu C, Hombach-Klonisch S**, KlonischT**. RXFP1 is targeted by Complement C1q Tumor Necrosis Factor-Related Factor 8 in Brain Cancer. Front Endocrinol (Lausanne). 2015; 6:127-133.
2. Thanasupawat T, Bergen H, Hombach-Klonisch S, Krcek J, Ghavami S, Del Bigio M, Krawitz S, Stelmack G, Halayko A, McDougall M, Meier M, Stetefeld J, **Klonisch T**. Platinum (IV) coiled coil nanotubes selectively kill human glioblastoma cells. *Nanomedicine*. 2015; 11:913-925.
3. Yu H, Lim HH, Tjokro NO, Sathiyanathan P, Natarajan S, Chew TW, **Klonisch T**, Goodman SD, Surana U, Dröge P. Chaperoning HMGA2 protein protects stalled replication forks in stem and cancer cells. Cell Rep. 2014; 6:684-697.
4. Glogowska A, Kunanuvat U, Stetefeld J, Patel TR, Thanasupawat T, Krcek J, Weber E, Wong GW, Del Bigio M, Hoang-Vu C, Hombach-Klonisch S*, **Klonisch T***. "C1q-tumor necrosis factor-related protein 8 (CTRP8) is a novel ligand of relaxin receptor RXFP1 in human brain cancer cells". *J Pathol*. 2013;231: 466-479.
5. Natarajan S, Hombach-Klonisch S, Dröge P, **Klonisch T**. HMGA2 inhibits apoptosis through interaction with ATR-CHK1 signaling complex in human cancer cells. *Neoplasia* 2013; 15:263-280.
6. Bialek J, Kunanuvat U, Hombach-Klonisch S, Spens A, Stetefeld J, Sunley K, Lippert D, Wilkins JA, Hoang-Vu C, **Klonisch T**. Relaxin enhances the collagenolytic activity and in vitro invasiveness by upregulating matrix metalloproteinases in human thyroid carcinoma cells. *Mol Cancer Res*. 2011;9: 673-687.
7. Hombach-Klonisch S, Bialek J, Radestock Y, Truong A, Agoulnik AI, Fiebig B, Willing C, Weber E, Hoang-Vu C, **Klonisch T**. INSL3 has tumor-promoting activity in thyroid cancer. Int J Cancer 2010; 127:521-531.

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Dr. Jay Kormish received her B.Sc. at the University of Alberta and completed her Ph.D. at the University of Calgary with Dr. James MgGhee focusing on intestine development in the nematode *C. elegans*. Continuing her research in the area of GI tract development, Dr. Kormish continued her post-doctoral training at the Fox Chase Cancer Center in Philadelphia with Dr. Kenneth Zaret. This research focused on the role of forkhead transcription factors and epigenetic marks during endoderm and liver progenitor cell specification in the mouse embryo. Through this research Dr. Kormish pioneered a methodology for performing Chromatin Immunoprecipitation (ChIP) from small amounts of embryo tissue. Dr. Kormish continued a similar line of research with Dr. Aaron Zorn at the Cincinnati Children's Hospital using the *Xenopus* embryo as a platform to study regionalized differential binding of transcription factors *in vivo* during early patterning of the digestive tract. Returning to *C. elegans* research, Dr. Kormish received a CIHR Genetics, Child Development and Health Fellowship for her post-doctoral research with Dr. Jeb Gaudet at the University of Calgary. This research focussed on the signalling mechanisms regulating cell migration during foregut organ development. In 2012, Dr. Jay Kormish became an Assistant Professor within the Department of Biological Sciences at the University of Manitoba. Her areas of research include molecular genetics, live-imaging studies of the developing embryo and signalling pathways that regulate the establishment of epithelial layers and migration of cells through organ primordium during *C. elegans* embryo digestive tract development.

Dr. Kormish's lab takes advantage the low genetic redundancy in *C. elegans* to study three key signalling receptors regulating cell migration in the developing foregut. CAM-1, the single ROR2-like receptor tyrosine kinase, provides a positive cue for migration using a kinase-dependent activity and non-canonical Wnt pathway. Loss of function mutations in EGL-15, the single Fibroblast Growth Factor Receptor, and INA-1, one of two α-integrin receptors, in *C. elegans* causes a penetrant over-migration phenotype where cells of the foregut over migrate their developmental target and invade the intestinal tissue. A combination of forward genetic screens, transgenic rescue assays and cellular imaging of protein localization are being used to define the molecular details of how these three pathways are co-ordinating cell adhesion and migration through an epithelial structure. Deregulation of these signalling pathways and uncontrolled migration are hallmarks of cancer metastasis in humans. New insight into these pathway are expected to generate new molecular targets, hence potential therapeutic targets, for the development of new drug therapies for the treatment of epithelial human cancers.

Selected Publications:

1. Lagha M, Mayeuf-Louchart A, Chang T, Montarras D, Rocancourt D, Zalc A, **Kormish J**, Zaret KS, Buckingham ME, Relaix F. (2013). *Itm2a* is a Pax3 target gene, expressed at sites of skeletal muscle formation *in vivo*. PLoS One.;8(5):e63143. Epub 2013 May 1.
2. Cha SW, McAdams M, **Kormish J**, Wylie C, Kofron M. (2012). *Foxi2* is an animally localized maternal mRNA in *Xenopus*, and an activator of the zygotic ectoderm activator *foxi1e*. PLoS One 7(7):e41782. Epub 2012 July 27.
3. Watts JA, Zhang C, Klein-Szanto AJ, **Kormish JD**, Fu J, Zhang MQ, Zaret KS. (2011). Study of FoxA Pioneer Factor at Silent Genes Reveals Rfx-Repressed Enhancer at *Cdx2* and a Potential Indicator of Esophageal Adenocarcinoma Development. PLOS Genetics 7(9):e1002277 Epub 2011 Sept 15.
4. Xu C, Cole PA, Meyers DJ, **Kormish J**, Dent S, Zaret KS. (2011) Chromatin "prepattern" and histone modifiers in a fate choice for liver and pancreas. Science 332:963-966.
5. Rankin SA, **Kormish J**, Kofron M, Jegga A, Zorn AM. (2011) A gene regulatory network controlling hhex transcription in the anterior endoderm of the organizer. Developmental Biology 351:297-310.
6. **Kormish JD**, Gaudet JG and McGhee JD. (2010) The *C. elegans* endoderm. Current Opinion in Genetics and Development 20:346-354.
7. **Kormish JD**, Sinner D, Zorn AM. (2010) Interactions between Sox factors and Wnt/β-catenin signaling in development and disease. Developmental Dynamics 239:56-68.
8. Lagha M*, **Kormish JD***, Rocancourt D, .Epstein JA, Zaret KS, Relaix F and Buckingham ME. *These authors contributed equally to this work. (2008) Pax3 regulation of FGF signaling affects the progression of embryonic progenitor cells into the myogenic program. Genes and Development 22:1828-1837.

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Dr. Krcek's post-secondary education began at the University of Western Ontario where he received a BA from the Faculty of Science and an MSc in Anatomy. In 1982 he completed a PhD in Medical Science at the University of Calgary. He was awarded an Alberta Heritage Foundation for Medical Research Fellowship and went to McMaster University to carry out post-doctoral research in Immunology. He returned to Calgary where he attended Medical School while continuing with further post-doctoral research in Immunology. He received his MD degree in 1986. After an internship year in Internal Medicine he completed his residency in Neurosurgery in Calgary in 1992.

He became a member of the staff of the Calgary General and Alberta Children's Hospitals. After closure of the General Hospital he joined the Foothills Neurosurgeons and the Calgary Regional Health Authority. While at Foothills Hospital his focus turned to Stereotactic Neurosurgery and Neuro-oncology. After further training in Functional Stereotactic surgery with Drs. Tasker and Lozano in Toronto he developed the Surgical Movement Disorders Program in Calgary. He also taught Anatomy at the University of Calgary Medical School and was Director of Neuroscience Undergraduate Medical Education.

In July 2003 Dr. Krcek joined the Neurosurgery Section of the Department of Surgery, University of Manitoba. His main focus is Stereotactic/Functional Neurosurgery and Neuro-Oncology. He is involved in collaborative Basic Science and Translational Research with members of the Department of Human Anatomy and Cell Science, where he has a cross-appointment. The research involves investigations of the biological characteristics, behaviour and treatment of primary, metastatic and recurrent brain tumours. Studies regarding mechanisms of brain tumour resistance to Radiotherapy and Chemotherapy as well as novel ways of delivering Chemotherapy into brain tumours using nano-technology are currently being done. He also established the Brain Tumor Data Base and helps to maintain it. He and Dr. Thomas Klonisch are co-founders of the Brain Tumor Research Alliance of Manitoba (BTRAM), a collaborative forum for brain tumor researchers in Manitoba who share research and plan new initiatives.

Selected Publications:

1. Thanasupawat T, Bergen H, Hombach-Klonisch S, **Krcek J**, Ghavami S, Del Bigio MR, KrawitzS, Stelmack G, Halayko A, McDougall M, Meier M, Stetefeld J, Klonisch T. (2015) Platinum (IV) coiled coil nanotubes selectively kill human glioblastoma cells. Nanomedicine (4):913-25.
2. Glogowska,A, Kunanuvat,U, Stetefeld,J, Patel,T R, Thanasupawat,T, **Krcek,J.P.**, Weber,E, Wong,GW, Del Bigio,MR, Hoang-Vu,C, Hombach-Klonisch,S, Klonisch,T. (2013) C1q-tumor necrosis factor-related protein 8 (CTRP8) is a novel interaction partner of relaxin receptor RXFP1 in human brain cancer cells. J. Pathol 231: 466-479.
3. Zeiler FA, Wilkinson M, **Krcek J.P.** (2013) Subthalamic nucleus deep brain stimulation: defining an invaluable role for MER. Can J Neurol Sci. 40(4):572-5.
4. Chowdhury, T., MD, Wilkinson, M. F., **Krcek, J.P.** (2013) A transient acute neurological event in a patient undergoing GPi microelectrode mapping: Diagnostic dilemma. Journal of Neurosurgical Anesthesiology 25(2):212.
5. Thanasupawat,T, Hammje, K, Adham, I, Ghia, J, Del Bigio, M, **Krcek, J.P.**, Hoang-Vu, C, Klonisch, T, Hombach- Klonisch, S. (2012) INSL5 is a novel marker for human enteroendocrine cells (EEC) of the large intestine and neuroendocrine tumours. Oncology Reports 29(1):149-54.
6. Zeiler, FA, **Krcek, J.P.** (2012) Lithium Induced Diabetes Insipidus, Trauma and the Shrunken Brain. Can J Neurol Sci. 39 (5): 681-2
7. Zeiler, F, **Krcek, J.P.** (2011) Plaque-Type Blue Nevus with Meningeal Melanocytomas: Case Report and Review. Can J Neurol Sci. 39(1): 117-20
8. Hughes, P.S., **Krcek, J.P.**, Hobson, D.E., Del Bigio, M.R. (2011). An unusual inflammatory response to implanted deep-brain electrodes. Canadian Journal of Neurological Sciences 38:168-170.
9. Gadji, M., Crous, A. Fortin, D., **Krcek J.P.**, Torchia, M, Klonish, T. (2009). EGFR inhibitors in anti-cancer therapy of Glioblastoma multiforme: old clinical allies and newly emerging therapeutic concepts. European Journal of Pharmacology 625: 23-30.

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Dr. Sam Kung received his B.Sc and M.Phil degrees from University of Hong Kong. His Ph.D. work, under supervision of Dr. Richard Miller at University of Toronto studied receptor recognition of natural killer cells. His post-doctoral training in the area of lentiviruses and gene therapy was done in the lab of Dr. Irvin S.Y. Chen at UCLA. Dr. Kung is presently Associate Professor in the Department of Immunology at the University of Manitoba. At University of Manitoba, Dr. Kung established a CFI-funded laboratory which focused on genetic manipulation of primary natural killer cells and dendritic cells. He is currently the Director of two core platforms of shRNA libraires and lentiviral vector production at U Manitoba. His research interests include natural killer cell biology, natural killer-dendritic cell crosstalk and immunotherapy of cancer.

Improper regulation of immune system accounts for a large number of immune disorders. Innate immunity is the host's first line of defense, and is critically involved in determining the magnitude and nature of subsequent T cell and antibody mediated immune responses. The ability to regulate these processes either positively or negatively would have important clinical implications in infection, autoimmunity, transplantation and allergic diseases. His laboratory at University of Manitoba studies two major cellular components of innate immunity- natural killer cells and dendritic cells. These two cell types exert their immunological functions independently. In addition, they can interact to regulate the cellular activities of each other. Current work includes identifying factors that (**i**) define dendritic cell development and functions; (**ii**) regulate natural killer cell differentiation and functions, and also (**iii**) natural killer cell-dendritic cell crosstalk in cancers.

Selected Publications:

1. Sohail M, Zhang M, Litchfield D, Wang L, **Kung S**, Xie J. (2015). Differential expression, distinct localization and opposite effect on Golgi structure and cell differentiation by a novel splice variant of human PRMT5. Biochim Biophys Acta. 1853(10 Pt A):2444-2452
2. Deepak, Upreti, Pathak, A., and **Sam K.P. Kung**. (2015). Development of a standardized flow cytometric method to conduct longitudinal analyses of intracellular CD3z expressions in Head and Neck cancer patients. (Oncology letters, in press).
3. Wang HM, Yan Q, Yang T, Cheng H, Du J, Yoshioka K, **Kung SK**, Ding GH. (2015) Scaffold protein JLP is critical for CD40 signaling in B lymphocytes. J Biol Chem. 290(9):5256-66
4. Mahmood S, Deepak Upreti, Ibrahim Sow, Abdulaziz Amari, Saravanan Nandagopal, and **Sam K.P. Kung**. (2015). Bidirectional interactions of natural killer cells and dendritic cells in immunotherapy: current and future perspectives. Immunotherapy 7(3):301-8.
5. Liu G, Lei L, Yu J, **Kung S**, Xie J. (2014). Refinement of the spectra of exon usage by combined effects of extracellular stimulus and intracellular factors. Biochim Biophys Acta. 1839(7): 537-45.
6. Mahmood, S*, Nandagopal, S*, Sow, Ibrahim*, Francis Lin and **Sam K.P. Kung**. (2014). A microfluidic based, real-time analysis of natural killer cell migratory properties in natural killer-dendritic cells crosstalk.. European Journal of Immunology. 2014 Sep;44(9):2737-48.
7. Upreti D *, Pathak A , **Kung SK**. (2014). Lentiviral vector-based therapy in head and neck cancer (Review).. Oncology letters. 7(1): 3-9.
8. Wang H*, Zhao C*, Zhang M*, Lee CM , Reddy EP , **Kung SK**. (2013). A novel role of the scaffolding protein JLP in tuning CD40-induced activation of dendritic cells.. Immunobiology. 218(6): 835-843.
9. Li H , Hou S , Wu X , Nandagopal S , Lin F , **Kung S** , Marshall AJ. (2013). The tandem PH domaincontaining protein 2 (TAPP2) regulates chemokine-induced cytoskeletal reorganization and malignant B cell migration.. PloS one. 8(2): e57809.
10. Liu G , Razanau A , Hai Y , Yu J , Sohail M , Lobo VG , Chu J , **Kung SK** , Xie J. (2012). A conserved serine of heterogeneous nuclear ribonucleoprotein L (hnRNP L) mediates depolarization-regulated alternative splicing of potassium channels.. The Journal of biological chemistry. 287(27): 22709-16.
11. Patel A , Dong JC , Trost B , Richardson JS , Tohme S , Babiuk S , Kusalik A , **Kung SK** , Kobinger GP. (2012). Pentamers not found in the universal proteome can enhance antigen specific immune responses and adjuvant vaccines.. PloS one. 7(8): e43802.
12. Mahmood S*, Kanwar N , Tran J*, Zhang ML*, **Kung SK**. (2012). SHP-1 phosphatase is a critical regulator in preventing natural killer cell self-killing.. PloS one. 7(8): e44244.
13. Emilie Narni-Mancinelli, Baptiste N. Jaeger, Claire Bernat, Aurore Fenis, **Sam Kung**, Aude De Gassart, Sajid Mahmood, Marta Gut, Simon C. Heath, Jordi Estellé, Elodie Bertosio, Louis N. Gastinel, Bruce Beutler, Bernard Malissen, Marie Malissen, Ivo G. Gut, Eric Vivier1, and Sophie Ugolini. Tuning of natural killer cell reactivity by NKp46 and Helios calibrates T cell responses. Science (2012) 335, 344 – 348. [funded by NSERC]
14. Huiming Wang, Liang Zhang and **Sam K.P. Kung**. Emerging applications of lentiviral vectors in dendritic cell-based immunotherapy. Immunotherapy, 2010 Sep;2(5):685-95. [funded by MHRC/CIHR]

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Dr. Ted M. Lakowski, PhD

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Dr. Ted Lakowski received his B.Sc. (Pharm) and Ph.D. degrees from the University of British Columbia. His post-doctoral training was in the area of the enzymology of protein arginine methyltransferases (PRMT) and was conducted under the supervision of Dr. Adam Frankel at the University of British Columbia. Dr. Lakowski is an Assistant Professor in the College of Pharmacy in the Faculty of Health Sciences at the University of Manitoba. He runs the mass spectrometers and other analytical equipment within the Pharmaceutical Analysis Laboratory at the College of Pharmacy. His research interests include anti-cancer drugs targeting epigenetic enzymes and the mechanisms of enzymes adding or removing post-translational modifications to histones.

Dr. Lakowski's laboratory utilizes liquid chromatography tandem mass spectrometry (LC-MS/MS) to develop validated methods to quantify epigenetic modifications on histones *in vitro,* in animal tissue and in cells. These methods are utilized to measure the effects of epigenetic enzyme inhibitors on modifications to histones. His laboratory also measures the *in vitro* activity of histone modifying enzymes including histone lysine methyltransferases (HKMT), demethylases (HDM), acetyltransferases (HAT) and deacetlyases (HDAC) as well as arginine methyltransferases (PRMT). The knowledge gained by studying epigenetic enzymatic activity is being used to produce inhibitors of epigenetic enzymes as potential therapeutics for cancer. In addition, his laboratory is attempting to produce epigenetic enzyme inhibitors that are targeted to particular genes to produce gene specific reductions in expression as potential therapeutics for leukemia.

Dr. Lakowski's research is organized into 5 areas, development of advanced mass spectrometry techniques to study post-translational modifications to histones, development of gene specific inhibitors of epigenetic enzymes, determining the kinetic mechanism of epigenetic enzymes, utilizing chemical biological techniques to probe epigenetic enzyme catalysis, and development of techniques to measure epigenetic modifications within cells and animal tissues.

Selected Publications: (total citations 205; H-index 8)

1. **Lakowski TM**, Pak ML, Szeitz A, Thomas D, Vhuiyan MI, Clement B, Frankel A. Arginine methylation in yeast proteins during stationary phase growth and heat shock. Amino Acids. 2015, Dec;47(12):2561-71
2. Thomas D, Koopmans T, **Lakowski TM**, Kreinin H, Vhuiyan MI, Sedlock SA, Bui JM, Martin NI, Frankel A. Protein arginine N-methyltransferase substrate preferences for different N-substituted arginyl peptides. ChemBioChem. 2014, Jul 21;15(11):1607-13.
3. **Lakowski TM**, Szeitz A, Pak ML, Thomas D, Vhuiyan MI, Kotthaus J, Clement B, Frankel A. MS^3 fragmentation patterns of monomethylarginine species and the quantification of all methylarginine species in yeast using MRM^3. Journal of Proteomics. 2013 Jan 17;80C:43-54.
4. 't Hart P, Thomas D, van Ommeren R, **Lakowski TM**, Frankel A, Martin NI. Analogues of the HIV-Tat peptide containing N^{η}modified arginines as potent inhibitors of the Protein Arginine N-Methyltransferases. MedChemComm. 2012, Jul 20; 3(10):1235-1244.
5. Pak ML, **Lakowski TM**, Thomas D, Vhuiyan MI, Hüsecken K, Frankel A. A protein arginine N-methyltransferase 1 (PRMT1) and 2 heteromeric interaction increases PRMT1 enzymatic activity. Biochemistry. 2011 Sep 27;50(38):8226-40.
6. 't Hart P, **Lakowski TM**, Thomas D, Frankel A, and Martin NI. Peptidic Partial Bisubstrates as Inhibitors of the Protein Arginine N-Methyltransferases. Chembiochem, 2011 Jun 14;12(9):1427-32.
7. **Lakowski TM**, 't Hart P, Ahern CA, Martin NI, Frankel A. N^{η}-Substituted Arginyl Peptide Inhibitors of Protein Arginine N-Methyltransferases. ACS Chemical Biology, 2010 Nov 19; 5 (11):1053–63.

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Dr. Etienne Leygue, PhD

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Dr. Etienne Leygue was educated in France where he obtained his Master (Biology of Organisms and Populations, with Distinctions) at the University Paul Sabatier in Toulouse in 1989. He got his Post-graduate Diploma (Diplome d'Etudes Approfondies, DEA, with distinctions, Head of the 1990 Class) specializing in Reproductive Physiology at the University Pierre et Marie Curie in Paris. Awarded multiple grants from the Minister of Research and Technology, the "Ligue Nationale Francaise Contre le Cancer" and the Institute National de la Sante et de la Recherche Medical (INSERM), he obtained his Ph.D with distinctions from the same University in 1994. He moved to Winnipeg in 1995 as a Post-doctoral Fellow under the supervision of Dr. LC Murphy and Dr. PH Watson. He became an Assistant Professor in the Departmental of Biochemistry & Medical Genetics in 2000 and a Senior Scientist at the Manitoba Institute of Cell Biology in 2004. During his career, Dr. Leygue has obtained several National and International Awards including the Ken Hughes Young Investigator Award in Medical Research (2006), the Sanofi-Aventis Biotech Challenge, Mentor Award (2006), an US Army Medical Research and Materiel Command Career Development Award, (2001) and a Canadian Breast cancer Research Initiative New Investigator Award (2001). He has served for many years as a Chair and panel member of the Canadian Research Society Peer Review Committees.

His research interests include hormone regulation of gene expression in normal and cancer cells, role and biology of non-coding RNAs, and alternative splicing events and their impact on breast tumorigenesis and tumor progression.

Dr. Leygue is presently an Associate Professor in the Department of Biochemistry and Medical Genetics at the University of Manitoba and a Senior investigator in the Research Institute in Oncology and Hematology.

His recent research efforts have been focused on the study of a very peculiar system consisting of a functional RNA, the steroid receptor RNA activator (SRA) able to code for a protein (SRAP). His laboratory was the first to identify the protein aspect of this system and to establish that this protein could be a prognostic or a predictive indicator in breast cancer. His laboratory currently investigates the potential roles and mechanisms of action of this protein in tumorigenesis and breast cancer progression.

Selected Publications: (total citations 2,978; H-index 33)

1. Gang, H., Dhingra, R., Lin, J., Hai, Y., Aviv, Y., Margulets, V., Hamedani, M., Thanasupawat, T., **Leygue, E.**, Klonisch, T., Davie, J.R., Kirschenbaum, L.A. PDK2 Mediated Alternative Splicing Switches Bnip3 From Cell Death to Cell Survival. J Cell Biol. 210 (7): 1101-1115, 2015
2. Khan, D.H., Gonzalez, C., Cooper, C., Sun, J.M., Chen, H.Y., Healy, S., Xu, W., Smith, K.T., Workman, J., **Leygue, E.**, Davie, J.R. RNA-Directed Dynamic Histone Acetylation Regulates *MCL1* Alternative Splicing. Nucl. Acids Res. 42 (3): 1656-1670, 2014.
3. Yan, Y., Penner, C., Skliris, G., Cooper, C., Nugent, Z., Blanchard, A., Hamedani, M., Wang, X., Myal, Y., Murphy, L. C., **Leygue, E.** Steroid Receptor RNA Activator Protein (SRAP) expression as a prognostic factor in ER+ human breast tumor. J. Cancer Res. Clin. Oncol. 139 (10): 1637-1647, 2013.
4. Cooper, C., Guo, J., Yan, Y., Chooniedass-Kothari, K.S., Hube, F., Hamedani, M.K., Murphy, L.C., Myal, Y., **Leygue, E.** Increasing endogenous relative expression of non-coding Steroid Receptor RNA Activator (SRA) in human breast cancer cells using modified oligonucleotides. Nuc. Acids Res. 37 (13): 4518-4531, 2009.
5. Chooniedass-Kothari, S., Emberley, E., Hamedani, M., Troup, S., Wang, X., Czosnek, A., Hube, F., Mutawe, M., Watson, P.H., and Leygue, E. The steroid receptor RNA activator (SRA) is the first functional RNA encoding a protein. Febs Letters, 566: 43-47, 2004.
6. Emberley, E., Huang, G-J., Hamedani, M. K., Czosnek, A., Ali, D., Grolla, A., Lu, B., Watson, P. H., Murphy L. C., Leygue, E. Identification of new human coding steroid receptor RNA activator isoforms. Biochem Biophys Res Com, 301: 509-515, 2003.
7. Miksicek, R.J, Myal, Y., Watson, P.H., Walker, C., Murphy, L.C., and Leygue, E. Identification of a novel breast- and salivary gland-specific, mucin-like gene strongly expressed in normal and tumor human mammary epithelium. Cancer Res, 62: 2736-2740, 2002.

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Dr. Michelle Lobchuk, RN, PhD

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Dr. Michelle Lobchuk received her Ph.D. degree from the University of Manitoba, Individual Interdisciplinary Studies Program (Nursing, Medicine, Psychology, and Sociology). She obtained post-doctoral training (quasi) in the area of evidence-based practice in cancer control under the supervision of Dr. Lesley Degner. Dr. Lobchuk is presently an Associate Professor at the College of Nursing, University of Manitoba and holds a Research Manitoba Chair in Caregiver Communication (2011 to 2016). She and Dr. Alan Katz are co-principal users of the CFI-funded Caregiver Communication Research Environment (aka CAre lab) at the Grace Hospital in Winnipeg. She is currently a researcher-in-residence at Grace Hospital, a Research Affiliate with Riverview Health Centre, Manitoba Centre for Nursing and Health Research, University of Manitoba Centre on Aging, Victoria General Hospital, and CancerCare Manitoba. She is also a member of the newly formed SPOR PIHCI Network (aka CIHR-funded Manitoba Primary and Integrated Health Care Innovation Network). Dr. Lobchuk's research interests include family caregiving, patient-caregiver communication, empathic processes, perceptual understanding, family role in health promotion, caregiver wellbeing, and symptom experiences. She has expertise in quantitative and qualitative methodologies, as well as video-feedback and video-analysis techniques.

Dr. Lobchuk's research program is designed to develop an empathy-based video-feedback intervention for caregivers (professional and family) to boost communication competence skills in cancer and non-cancer patient- and family-centred care. Much of her communication research is being conducted in CAre that is housed in a renovated 943 square foot space at Grace Hospital. CAre reflects a distinctive interface between human factors and dialogue, video-feedback, web-/videoconferenced learning, and knowledge translation. The flexible infrastructure of CAre is essential to the research that requires either visual recording cameras to capture dialogue or a one-way mirror to observe dialogue in the kitchen area. CAre is a multipurpose space for engaging in observational techniques in the control room, conducting studies in two conversation areas, and using portable equipment for video-feedback anywhere in CAre. CAre features a system of technology that is comprised of commercial off-the-shelf computer and video-recording devices and sophisticated Studiocode® video-tagging and -analysis software used by video coaches with NHL hockey players. Dr. Lobchuk's aim is to build research capacity to support highly qualified personnel and strengthen inter-professional partnerships that focus on testing innovative empathy-related training interventions for immediate impact on clinicians, students, families, and patients. The setting and video-recording, -feedback, and -editing infrastructure allow Lobchuk, Katz, and highly qualified personnel to conduct observational studies to test communication interventions and capture dialogue for training effects and interventions for open access and quick dissemination and uptake by clinicians, students and family caregivers (on-line resources). The infrastructure has live, interactive video-conferencing technology to test immediate effects of communication interventions, and rapid knowledge exchange and dissemination activities within (remote/northern communities) and outside Manitoba.

Selected Publications:

1. Seenandan-Sookdea, K-A, Hack, T., **Lobchuk, M.**, Murphy, L., & Marles, S. (May 2015). BRCA 1 / 2 and minors. Manuscript accepted for publication in Oncology Nursing Forum.
2. Ahmed, N, **Lobchuk, M.**, Hunter, W., Johnston, P., Nugent, Z., Sharma, A., & Sisler, J. (2015). Perceptions and preferences of the patients with terminal lung cancer and family caregivers about DNR. Cureus, 7(5): e271. doi 10.7759/cureus.271
3. Ahmed, N., **Lobchuk, M.**, Hunter, W., Johnson, P., & Sisler, J. (2015). Pilot study on end of life discussion with patients with lung and esophageal cancer and their families. Cureus, 7(3):e257. doi 10.7759/cureus.257.
4. **Lobchuk, M**, McClement, S., Rigney, M., Copeland, A., & Bayrampour, H. (2014). A qualitative analysis of 'naturalistic' conversations in a peer-led online support community for lung cancer. Cancer Nursing, 38(5). doi 10.1097/NCC.0000000000000207
5. Clouston K, Katz A, Martens PJ, Sisler J, Turner D, **Lobchuk M**, McClement S, Crow G, and the CIHR/CCMB Team in Primary Care Oncology (PCO-NET). (2014). Does access to a colorectal cancer screening website and/or a nurse-managed telephone help line provided to patients by their family physician increase fecal occult blood test uptake?: Results from a pragmatic cluster randomized controlled trial. BMC Cancer, 14: 263. doi 10.1186/1471-2407-14-263
6. McPherson, C., Hadjistavropoulos, T., **Lobchuk, M.**, & Kilgour, K. (2013). Cancer related pain in older adults receiving palliative care: Patient and family caregiver perspectives on the experience of pain. Pain Research and Management, 18(6), 293-300.
7. **Lobchuk, M.M.**, Bapuji, S., McClement, S.E., Sisler, J.J., Katz, A., Marten, P., Turner, D., & Clouston, K. (2012). What is the role of family in promoting recommended faecal occult blood test screening? Exploring physician, average-risk individual, and family perceptions. Cancer Epidemiology. doi 10.1016/j.canep.2012.01.002
8. **Lobchuk, M.**, McPherson, C., & McClement, S.E., & Cheang, M. (2012). Impact of patient smoking behavior on empathic helping by family caregivers in lung cancer. Oncology Nursing Forum, 39(2), E112-121. doi 10.1188/12.ONF.E112-E121

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Dr. Joe LoVetri received his B.Sc. and M.Sc. degrees from the University of Manitoba (UofM), and the Ph.D. from the University of Ottawa (1991), all in Electrical Engineering. His academic career began in 1991 when he joined the Dept. of Electrical and Computer Engineering at The University of Western Ontario where he remained until 1999. In 1999 he joined the University of Manitoba where he is currently Professor and Head of the Dept. of Electrical and Computer Engineering. He's a registered Professional Engineer in the province of Ontario (since 1994). He is currently the Director of the Electromagnetic Imaging Laboratory (EIL) at the UofM.

The EIL has been working on Microwave Imaging (MWI) techniques for close to ten years. The research has evolved from the creation of novel algorithms for the solution of the electromagnetic inverse problems to the development of complete imaging systems for biomedical applications. Microwave imaging creates quantitative maps of the dielectric properties (e.g., permittivity and conductivity) of tissues. The Lab's major focus has been the use of MWI for breast cancer where, working with CancerCare Manitoba and other research partners, several advances have been made on the use of MWI for breast cancer detection as well as for treatment monitoring.

An on-going effort during the past two years has been a joint project with researchers at the University of Calgary (UofC) that is funded by the Canadian Breast Cancer Foundation. The UofC researchers perform ultra-wideband radar measurements to obtain coarsely defined tissue-type regions which are then used as prior information in the EIL's non-linear inversion algorithms. The two groups have shown quite an improvement in imaging performance using this combined algorithm. The goal of this work is the creation of a combined Radar/Tomography breast imaging system. In addition to the MWI research, researchers in the EIL are developing quantitative ultrasound (US) imaging techniques using similar inversion algorithms to those used in the MWI work. In addition to stand-alone US imaging systems, a goal of this work is to combine the US and MW imaging techniques so that the property images arising from both techniques can be used to create tissue-type images. Such tissue-type images provide better diagnostic information to radiologists because the inference from physical properties to tissue-types is more certain and can be quatified.

Selected Publications:

1. Baran, A., Kurrant, D., Zakaria, A., Fear, E., **LoVetri, J.** (2014) Breast Imaging Using Microwave Tomography with Radar-Based Tissue-Regions Estimation, Progress In Electromagnetics Research, Vol. 149, pp. 161–171.
2. Asefi, M., OstadRahimi, M., Zakaria, A., **LoVetri, J.** (2014) A Three-Dimensional Dual-Polarized Near-field Microwave Imaging System, IEEE Transactions on Microwave Theory and Techniques, Vol. 62, No. 8, Aug., pp. 1790-1797.
3. Gilmore, C., Zakaria, A., Pistorius, S., **LoVetri, J.** (2013) Microwave Imaging of Human Forearms: Pilot Study and Image Enhancement, International Journal of Biomedical Imaging, Vol. 2013, Article ID 673027, 17 pages, doi:10.1155/2013/673027.
4. OstadRahimi, M., Mojabi, P., Zakaria, A., **LoVetri, J.**, Shafai, L. (2013) Enhancement of Gauss-Newton Inversion Method for Biological Tissue Imaging, IEEE Transactions on Microwave Theory and Techniques, Vol. 61, No. 9, Sept., pp. 3424-3434.
5. Gilmore, C., Zakaria, A., **LoVetri, J.**, Pistorius, S. (2013) A Study of Matching Fluid Loss in a Biomedical Microwave Tomography System, Medical Physics, Vol. 40, No. 2, February, 14 pages.
6. Zakaria, A., Baran, A., **LoVetri, J.** (2012) Estimation and Use of Prior Information in FEM-CSI for Biomedical Microwave Tomography, IEEE Antennas and Wireless Propagation Letters, Vol. 11, pp. 1606-1609 (Invited Paper, Special Cluster on Microwave Imaging)
7. Gilmore, C., Mojabi, P., Zakaria, A., Ostadrahimi, M., Kaye, C., Noghanian, S., Shafai, L., Pistorius, S., **LoVetri, J.** (2010) A Wideband Microwave Tomography System with a Novel Frequency Selection Procedure, IEEE Trans. on Biomedical Engineering, Vol. 57, No. 4, pp. 894-904.
8. Mojabi, P., **LoVetri, J.** (2009) Enhancement of the Krylov Subspace Regularization for Microwave Biomedical Imaging, IEEE Trans. on Medical Imaging, Vol. 28, No. 12, pp. 2015-2019, December.

See Joe LoVetri's other publications

Dr. Salah Mahmud, MD, PhD, FRCPC

Canada Research Chair in Pharmacoepidemiology and Vaccine Evaluation;
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Dr. Mahmud is a preventive medicine specialist with postgraduate training in cancer epidemiology and pharmacoepidemiology from London University (UK) and the University of Manitoba (Canada). His PhD thesis investigated the use of non-steroidal anti-inflammatory drugs (NSAIDs) in prostate cancer prevention. As a post-doctoral fellow at McGill's Division of Cancer Epidemiology, he worked on many projects related to the prevention of prostate and cervical cancers. He is currently an Associate Professor at the Department of Community Health Sciences-University of Manitoba (UM), where he holds a Canada Research Chair in Pharmacoepidemiology and Vaccine Evaluation. He is also a practicing physician working as a Medical Officer of Health at Manitoba Health and has served on many provincial and national advisory committees including Manitoba's Vaccine Advisory Committee and the National Immunization Strategy Workgroup.

In 2012, he founded the University of Manitoba Vaccine and Drug Evaluation Centre with funding from the Canadian Foundation for Innovation and the Canada Research Chairs Program. In 2014, he became the Director of the Clinical Trials Platform of the George and Fay Yee Centre for Healthcare Innovation and a member of CIHR's Founders Group of Canada's new registry-based clinical trials platform. He is also the Associate Editor of the journal Preventive Medicine.

For his work, he was received several awards including the Governor General's Gold Medal, the Mona and Allen Copp Award and the Aubie Angel Young Clinical Investigator Award. He has been the principal investigator on 29 grants totaling $6.7 million, with an additional $6 million obtained as a co-principal investigator and another $33 million obtained as a co-investigator in collaboration with partners across Canada and internationally.

His research interests include pharmacoepidemiology, specifically the use of pharmaceuticals to prevent or reverse carcinogenic progression to invasive cancer, cancer epidemiology and the role of infections and inflammation in cancer development, and evaluating safety and effectiveness of commonly used vaccines including the influenza and HPV vaccines. Dr. Mahmud is also interested in mathematical modeling of infectious disease as well as the practical applications of pharmacoepidemiology such as post-marketing surveillance for drug and vaccine adverse events.

Selected Publications: (total citations 2600; H-index 27)

1. Hinds, M Aynslie, Bozat-Emre, Songul, Van Caeseele, Paul, **Mahmud, M Salaheddin** (2015). Comparison of the epidemiology of laboratory-confirmed influenza A and influenza B cases in Manitoba, Canada. BMC Public Health.
2. Songul Bozat-Emre, Malcolm Doupe, PhD, Anita L. Kozyrskyj, Ruby Grymonpre, **Salaheddin M. Mahmud** (2014). Atypical Antipsychotic Drug Use and Falls among Nursing Home Residents in Winnipeg, Canada. International Journal of Geriatric Psychiatry. 29(11): 4223.
3. Ye X, Casaclang N, **Mahmud SM** (2014). Use of non-steroidal anti-inflammatory drugs and risk of non- Hodgkin lymphoma: a systematic review and meta-analysis.. Hematological oncology.
4. Schillberg E, Isaac M, Deng X, Peirano G, Wylie JL, Van Caeseele P, Pillai DR, Sinnock H, **Mahmud SM** (2014). Outbreak of invasive Streptococcus pneumoniae Serotype 12F among a marginalized inner-city population in Winnipeg, Canada (2009-2011). Clinical Infectious Diseases. 59(5): 651-657.
5. **Mahmud SM**, Kliewer EV, Lambert P, Bozat-Emre S, Demers AA. (2014). Effectiveness of the quadrivalent human papillomavirus vaccine against cervical dysplasia in Manitoba, Canada. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 32(5): 438-43.
6. Thompson LH‡, Malik MT, Gumel A, Strome T, **Mahmud SM** (2014). Emergency department and 'Google flu trends' data as syndromic surveillance indicators for seasonal influenza.. Epidemiology and Infection. 142(11): 2397-2405.
7. **Mahmud SM**, Thompson LH‡ , Nowicki DL , Plourde PJ. (2013). Outbreaks of influenza-like illness in long-term care facilities in Winnipeg, Canada.. Influenza and Other Respiratory Viruses. 7(6): 1055-61.

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Dr. Mai is a Senior Investigator at the Manitoba Institute of Cell Biology in CancerCare Manitoba and the Director of the Genomic Centre for Cancer Research and Diagnosis. She obtained her M.Sc. at the University of Cologne (Germany) and her Ph.D. in Molecular Biology at the University of Karlsruhe (Germany), did her post-doctoral training at the Basel Institute for Immunology (Basel, Switzerland). Research training included collaborative studies at the National Institutes of Health/National Cancer Institute (NIH/NCI) in Bethesda, MD, USA. Dr. Mai joined the Manitoba Institute of Cell Biology in 1995. Her international research activities include research at the German Cancer Research Center (Heidelberg, Germany) and at the Karolinska Institute (Stockholm, Sweden) as well as courses and workshops taught at Chiang Mai University (Thailand) and at Naresuan University (Thailand). Through CFI-funding, Dr. Mai initiated the Genomic Centre for Cancer Research and Diagnosis in 1999, has trained >1000 HQPs world-wide in new imaging technologies, has established a national 3D imaging node and was awarded a CFI LEF for new 3D super resolution imaging in 2009.

Research Projects - Overview.
Dr. Mai's research focuses on mechanisms of c-Myc-dependent locus-specific and karyotypic instability, c-Myc-dependent tumor development *in vivo* (using the mouse model of plasmacytoma) and on understanding the three-dimensional (3D) nuclear three-dimensional (3D) nuclear organization of the mammalian genome in normal, immortalized and tumor cells.

1) c-Myc-dependent locus-specific and karyotypic instability. We were the first to demonstrate that the deregulated expression of the proto-oncogene c-Myc induces dynamic karyotypic alterations (Mai *et al.*, 1996a), and mediates rearrangements, chromosomal and extrachromosomal amplification of specific genes. Among these genes are *dihydrofolate reductase* (*DHFR*), (Mai, 1994; Mai *et al.*, 1996b), *CCND2* (*cyclin D2*) (Mai *et al.*, 1999), *ribonucleotide reductase R2* (*R2*) (Kuschak *et al.*, 1999), and the *carbamoyl-phosphate synthetase-aspartate transcarbamoyl-dihydroorotase* (*CAD*) (Fukasawa *et al.*, 1997) gene. Other genes, such as *syndecan-1* and *2*, *glyceraldehyde-3-phosphate-dehydrogenase*, *ribonucleotide reductase R1*, and *cyclin C*, remain unaffected irrespective of c-Myc protein levels (Mai *et al.*, 1996b). c-Myc-dependent illegitimate locus-specific *de novo* replication initiation induces *R2* gene amplification (Kuschak *et al.*, 2002). An additional mechanism of c-Myc activation involves c-Myc transcription from extrachromosomal elements (Wiener *et al.*, 1999). Analyses into the functions of EEs have demonstrated that they carry modified histones and are transcriptional competent. Furthermore, they are able to replicate their DNA (Smith *et al.*, 2002). c-Myc-induced EEs therefore are functional mini-chromosomes with the ability to actively contribute to cellular transformation. Our work on c-Myc and genomic instability was presented as a textbook chapter in CSH Perspectives in Medicine. "MYC and the Pathway to Cancer". 2014 (eds. Dang and Eisenman).

2) c-Myc-dependent tumor development *in vivo*. Mouse plasmacytomas (PCTs) develop in susceptible mice. The traditional model uses pristane as inducing agent, and all PCTs that develop subsequently display the constitutive deregulation of c-Myc due to its translocation to one of the immunoglobulin (Ig) loci. The c-*myc/IgH* translocation is the most frequent one in pristane-induced plasmacytomas of BALB/c mice (Potter and Wiener, 1992). Pristane-induced PCTs develop over a long latency period (up to 300 days). If pristane is combined with v-*abl* or with v-*abl/myc*, the latency periods drop significantly (Potter and Wiener, 1992). Such short latency tumors develop within 45 days after v-*abl/myc* and display chromosomal aberrations of chromosome 11. We have recently identified the critical region of chromosome 11 involved in the promotion of accelerated plasmacytoma development (Wiener et al., 2010). This region is chromosome 11 cytoband 11E2, and it is syntenic to human 17q25 and rat 10q32. The evolutionarily conserved region undergoes frequent rearrangements in lymphoid and non-lymphoid tumors of all three species.

3) The three-dimensional (3D) nuclear organization of the mammalian genome in normal, immortalized and tumor cells. We have examined the spatial organization of telomeres, centromeres and chromosomes and obtained specific 3D signatures that were significantly different in normal, immortalized and tumor cell nuclei. In collaboration with colleagues at Delft University of Technology, we developed software [TeloView™] that enabled the measurements the 3D nuclear organization of telomeres (Vermolen *et al*., 2005). This program has allowed us to determine significant differences between normal and tumor cells (Mai and Garini, 2005), after c-Myc deregulation (Louis *et al*., 2005; Mai and Garini, 2005), after Epstein-Barr virus-infection (Lacoste *et al*., 2010), during the transition of mono-nucleated to multi-nucleated Hodgkin cells (Knecht *et al*., 2009), and in glioblastoma (Gadji *et al*., 2010). We have automated TeloView™ (Gadji *et al*., 2010), for cancer cell detection and analysis. Our sensitivity of detection is one cancer cell in one thousand normal cells (Klewes *et al*., 2010). Ongoing studies focus on Hodgkin's lymphoma (with and without recurrent disease), multiple myeloma, monoclonal gammopathies with unknown significance, myelodysplatic syndrome and acute myeloid leukemia, ependymoma, breast and thyroid cancer as well as cholangiocarcinoma. In summary, the 3D nuclear telomeric organization of normal and tumor cells, irrespective of their origin, is significantly different. It is our goal to introduce the 3D telomeric signatures into the clinic, as an essential added tool for cancer diagnosis, cancer cell detection, treatment decisions and monitoring. Co-founder of 3D Signatures Inc (2014) www.3dsigantures.com

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Dr. Aaron Marshall obtained his B.Sc. in Microbiology from University of Saskatchewan in and Ph.D. in Immunology in from the Department of Immunology at the University of Toronto. After a post-doctoral fellowship at the University of Washington, he established a research program in the Department of Immunology at the University of Manitoba. He is a Professor of Immunology and hold a Canada Research Chair in Molecular Immunology. He serves on the Editorial Boards of Frontiers in Immunology and as scientific reviewer for Immunology, Cell Biology and Hematology Journals. He has served as a panel member on CIHR and NCIC/CCSRI Peer Review Committees.

Dr. Marshall's research program centres on the intracellular signalling network that controls lymphocyte activation and differentiation. The goals of Dr. Marshall's research program include mapping new signalling mechanisms controlling normal immune responses and identifying the abnormalities in signalling networks that can transform normal B lymphocytes into leukemia or lymphoma cells. A particular focus is on understanding the signalling events linked to a family of enzymes that phosphorylate membrane phosphoinositide lipids, the PI 3-kinases. These enzymes are critical for a number of aspects of normal cell biology including i) metabolic activation, ii) cytoskeletal reorganization and cell motility, iii) cell survival. As such, dysregulation of this signalling pathway at various levels is a common feature of malignancy, including B cell malignancies. Dr. Marshall has uncovered functions of PI 3-kinase enzymes in lymphocytes linked to novel phosphoinositide-binding proteins which he discovered.

In conjunction with the Manitoba CLL clinic and the provincial Research Cluster in CLL, Dr. Marshall is defining the roles of different PI 3-kinase enzymes in CLL and assessing the impact of new kinase inhibitor therapeutics. He is applying innovative technologies for assessing cell migration behaviours to provide i) new insight into control of these behaviours by signalling networks, and ii) new insights into the therapeutic mechanisms of action of kinase inhibitors.

Selected Publications:

1. Lafarge ST, Li H, Pauls SD, Hou S, Johnston JB, Gibson SB, **Marshall AJ**. (2015) ZAP-70 expression directly promotes chronic lymphocytic leukemia cell adhesion to bone marrow stromal cells. Br J Haematol. 168(1):139-42.
2. Lafarge ST, Johnston JB, Gibson SB, **Marshall AJ**. (2014) Adhesion of ZAP-70+ chronic lymphocytic leukemia cells to stromal cells is enhanced by cytokines and blocked by inhibitors of the PI 3-kinase pathway. Leuk Res. 38:109-15.
3. Jennifer Costantini, Samuel M.S. Cheung, Sen Hou, Hongzhao Li, Sam Kung, James Johnston, John Wilkins, Spencer Gibson and **Aaron J. Marshall**. (2009) TAPP2 links phosphoinositide 3-kinase signaling to B cell adhesion through interaction with the cytoskeletal protein utrophin: expression of a novel cell adhesion-promoting complex in B cell leukemia. Blood Journal, 114:4703-12.
4. **Marshall, A.J.**, A.K. Krahn, K. Ma, V. Duronio and S. Hou. (2002). TAPP1 and TAPP2 are novel targets of phosphatidylinositol 3-kinase signaling: Sustained plasma membrane recruitment triggered by the B cell antigen receptor. Mol. Cell. Biol. 22: 5479-91
5. **Marshall, A.J.**, H. Niiro, C.G. Lerner, T.Y. Yun, S. Thomas, C.M. Disteche, and E.A. Clark. (2000). A novel B lymphocyte-associated adaptor protein, Bam32, regulates antigen receptor signaling downstream of phosphatidylinositol 3-kinase. J. Exp. Med. 191:1319

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Dr. Boyd McCurdy, PhD, FCCPM

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Dr. Boyd McCurdy is the Radiation Oncology Physics Lead in the Medical Physics Division at CancerCare Manitoba, and holds academic appointments as an associate professor in the Department of Physics and Astronomy as well as the Department of Radiology at the University of Manitoba. He completed a B.Sc. in Physics (Honours) at the University of Waterloo in 1993, and both a M.Sc. (Physics – Nuclear Medicine, 1996) and Ph.D. (Physics – Radiation Therapy, 2001) degrees at the University of Manitoba. In 2007 he was designated a Fellow of the Canadian College of Physicists in Medicine.

Dr. McCurdy has been a clinical medical physicist (radiation oncology physics) at CancerCare Manitoba since 2000, where he has played key roles in implementing several advanced clinical programs and treatment techniques, including various improvements in prostate, breast, and brain treatments, as well as imaging, targeting and process improvements. In 2007 he led the implementation of intensity modulated radiation therapy (IMRT), an advanced and complex radiation treatment technique. He is active in teaching graduate courses in the CAMPEP-accredited Medical Physics graduate program, supervising graduate students, and also training and supervising radiation oncology physics residents (another CAMPEP-accredited program). He is an active reviewer for several research journals and a panel reviewer for several provincial and national research grant committees. Dr. McCurdy was asked to lead the radiation oncology physics group at CancerCare Manitoba in 2012, and since then has been helping to strengthen both the clinical and research performance of the radiation oncology program.

Dr. McCurdy has several research interests aimed at improving the diagnosis and treatment of cancer. His research is focused in three areas: **1)** Radiation treatment verification using live transit imaging, which includes in vivo dosimetry, adaptive radiation therapy, and real-time error detection (these being pursued in collaboration with Dr. Peter Greer's research group at the Calvary Mater Newcastle Hospital in Newcastle Australia. These techniques will significantly improve the quality of radiation treatment for many patients. **2)** The use of evolutionary algorithms to solve the multi-objective radiation therapy treatment planning problem. This work is pursued in collaboration with University of Manitoba astrophysicist Dr. Jason Fiege. 3) Developing functional magnetic resonance imaging techniques for diagnosing and better targeting prostate cancer, collaboratively investigated with MRI imaging physicist Dr. Lawrence Ryner, also with CancerCare Manitoba.

Selected Publications (total of over 165 publications and presentations):

1. H.C. Woodruff, T. Fuangrod, **B.M.C. McCurdy**, J. Siebers, M. Lovelock, P. Keall, and P.B. Greer, "First experience with real-time EPID based delivery verification during IMRT and VMAT treatments", accepted in *International Journal of Radiation Oncology, Biology, and Physics*.
2. E. van Uytven, T. van Beek, K. Chytyk-Praznik, P.M. McCowan, P.B. Greer, and **B.M.C. McCurdy**, "In vivo 3D delivered dose reconstruction for IMRT and VMAT treatments using on-treatment EPID images and a model-based forward-calculation algorithm", accepted in *Medical Physics*.
3. **B.M.C. McCurdy**, "Dosimetry in radiotherapy using a-Si EPIDs:Systems, methods, and applications focusing on 3D patient dose estimation", *Journal of Physics: Conference Series,* 444, 012002, 2013.
4. N. Venugopal, **B.M.C. McCurdy**, D. Drachenberg, S. A. Mehairi, A. Alamri, G.S. Sandhu, S. Sivalingam, and L. Ryner, "Short echo time in vivo prostate 1H-MRSI", *Magn. Reson. Imaging*, 30(2):195-204, 2012.
5. J. Fiege, **B.M.C. McCurdy**, P. Potrebko, H. Champion, and A. Cull "PARETO: A Novel Evolutionary Algorithm Approach to Multi-Objective IMRT Planning", under review in *Medical Physics*, September, 2010.
6. J. Hatton, **B.M.C. McCurdy**, and P.B. Greer, "Cone beam computerized tomography: effect of calibration of Hounsfield unit number to electron density on dose calculation accuracy for adaptive radiation therapy", *Phys. Med. Biol.*, 54:N329-N346, 2009.
7. **B.M.C. McCurdy**, and P.B. Greer "Dosimetric properties of an amorphous-silicon EPID used in continuous acquisition mode for application to dynamic and arc IMRT", *Med. Phys*., 36(7):3028-3039, 2009.
8. K. Chytyk and **B.M.C. McCurdy**, "Comprehensive fluence model for absolute portal dose image prediction", *Med. Phys*. 36(4):1389-1398, 2009.
9. **B.M.C. McCurdy**, K. Luchka, and S. Pistorius, "Dosimetric investigation and portal dose image prediction using an amorphous silicon electronic portal imaging device", Med. Phys., 28(6):911-24, 2001.

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Dr. Sean McKenna, PhD

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Dr. Sean McKenna received his B.Sc. in Biochemistry from Queen's University (1998), and Ph.D. from the University of Alberta (2003) where he studied structural aspects of the protein ubiquitination machinery. His post-doctoral training in the investigation of RNA-protein complexes was done in the laboratory of Dr. Jody Puglisi at Stanford University in the Department of Structural Biology, Faculty of Medicine. Dr. McKenna began his faculty position at the University of Manitoba in 2008, where he is currently an Associate Professor. Dr. McKenna has served as a grant review panel member at CIHR, NSERC, Research Manitoba, and Fonds de Recherche du Quebec. His research is currently or has been recently been funded by CIHR, NSERC, Canadian Cancer Society, Cancer Research Society, Research Manitoba and CFI.

Originally thought to be only an intermediary between DNA and proteins, RNA has now emerged as key regulatory molecule in diverse cellular processes, many of which are mediated through interactions with proteins. Not surprisingly, aberrant RNA-protein interactions play a key role in a number of disease states. Dr. McKenna's laboratory provides an understanding of the structural features required for RNA recognition by cellular proteins, and correlates this information with biological function.

Dr. McKenna's research interests are as follows:
1) In cancerous cells the enzyme telomerase ensures maintenance of stable telomere length and enables indefinite growth characteristic of malignant tumour formation. Dr. McKenna investigates helicase enzymes that regulate telomerase activity via unwinding of an unusual RNA structure known as a G-quadruplex. This work is aimed to develop therapeutic interventions that exploit weaknesses in the interaction and thereby influence tumour cell viability.

2) Human cells recognize foreign viral RNA molecules and use them as triggers to mount an immune response. Dr. McKenna focuses on understanding the recognition of viral RNA by two separate immunity proteins (PKR and OAS) which both improve our understanding of how human cells combat viral infection but may also serve as the foundation for the design of novel antivirals.

Selected Publications: (total citations 1,106; H-index 17)

1. Deo, S., Patel, T.R., Koul, A., Dzananovic, K., Chojnowski, G., McEleney, Bujnicki, J.M., and **McKenna, S.A.** (2015) "Activation of 2' 5'-Oligoadenylate Synthetase by the 3'-Terminal Region and 3'-5'-Terminal Region RNA complex of the West Nile Virus Genome". *Journal of Structural Biology.* 19(2): 236-249
2. Booy, E.P., McRae, E.K.S., and **McKenna, S.A.** (2015) "Biochemical characterization of G4 quadruplex telomerase RNA unwinding by the RNA helicase RHAU." *Methods in Molecular Biology*. (Walker, J.M., Ed.). Humana Press. 1259: 125-35.
3. Deo, S., Patel, T.R., Dzananovic, E., Booy, E.P., Zeid, K., McEleney, K., Harding, S.E., and **McKenna, S.A.** (2014) "Activation of 2' 5'-oligoadenylate synthetase by stem loops at the 5'-end of the West Nile virus genome". *PLosOne*. 9(3):e92545.
4. Booy, E.P., Howard, R., Ariyo, E.O., Deo, S.R., Meier, M., Marushchak, O., Dzananovic, E., Stetefeld, J., and **McKenna, S.A.** (2014) "The RNA Helicase RHAU (*DHX36*) suppresses translation of PITX1 through quadruplex binding in the 3' untranslated region of the messenger RNA." *Nucleic Acids Research*. 42(5): 3346-3361.
5. Dzananovic, E., Patel, T.R., Chojnowski, G., Boniecki, M.J., Deo, S., McEleney, K., Harding, S.E., Bujnicki, J.M., and **McKenna, S.A.** (2014) "Solution Conformation of Adenovirus Associated RNA-I and its interaction with PKR". *Journal of Structural Biology*. 185(1):48-57.
6. Meier, M., Patel, T.R., Booy, E.P., Maruschak, O., Okun, N., Deo, S., Howard, R., McEleney, K., Harding, S.E., Stetefeld, J., and **McKenna, S.A.** (2013) "Binding of G-quadruplexes to the N-terminal Recognition Domain of the RNA Helicase Associated with AU-rich Element (RHAU)". *Journal of Biological Chemistry.* 288(49):35014-27.
7. Dzananovic, E., Patel, T.R., Deo, S., McEleney, K., Stetefeld, J., and **McKenna, S.A.** (2013) "Recognition of Viral RNA Stem Loops by the Tandem Double-Stranded RNA Binding Domains of PKR". *RNA*. 19(3): 333-344.
8. Meng, H., Deo, S., Xiong, S., Dzananovic, E., Donald, L.J., van Dijk, C.W., and **McKenna, S.A.** (2012) "Regulation of the interferon inducible 2'-5'-oligoadenylate synthetases by adenovirus VA_I RNA." *Journal of Molecular Biology.* 422: 635-649.
9. Booy, E.P., Meier, M., Okun, N., Novakowski, S.K., Xiong, S., Stetefeld, J., and **McKenna, S.A.** (2012) "The RNA helicase RHAU (*DHX36)* unwinds a G4 quadruplex in human telomerase RNA and promotes the formation of the P1 helix template boundary." *Nucleic Acids Research*. 40(9): 4011-4024.

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Dr. Kirk McManus is an Associate Professor in the Department of Biochemistry and Medical Genetics at the University of Manitoba. He is also a Senior Scientist in Research Institute in Oncology & Hematology housed within CancerCare Manitoba. He received his BSc (1995) and MSc (1999) from the University of Manitoba before moving to Edmonton, Alberta to conduct his PhD studies (1999) in Oncology under the supervision of Dr. Michael Hendzel. There he studied the regulation and dynamics of post-translational histone modifications and their influence on chromosome segregation. His post-doctoral studies were performed with Dr. Phil Hieter at the Michael Smith Laboratories in Vancouver, BC, where he utilized cross-species approaches to identify genes that regulate chromosome stability and characterize their impact on cancer development. Dr. McManus joined the University of Manitoba and the Manitoba Institute of Cell Biology in June 2009.

Dr. McManus' research focuses on defining the molecular constituents and defective biological processes that contribute to the development of colorectal cancer, and seeks to exploit this information to develop novel strategies designed to better combat cancer. He currently supervises two research technicians, six graduate students and two undergraduate students. Collectively, their research goal is to identify and characterize human genes involved in chromosome stability, which represent candidate genes for subsequent tumor sequencing and gene expression analysis projects. The ultimate goal of their research is to exploit this information using a synthetic lethal paradigm to identify and develop the next generation of therapeutic targets designed to specifically target and kill cancer cells relative to normal surrounding tissues. His research projects couple innovative approaches involving mammalian tissue culture, bioinformatics, cross-species analyses, reverse genetics (RNA-interference), cytogenetics and digital imaging microscopy with standard biochemical approaches to identify and characterize gene involved in genome and chromosome stability. Using state-of-the-art and high-throughput imaging approaches, they seek to uncover new and highly selective drug targets that represent lead compounds for the development of novel therapeutic strategies designed to better combat cancer. The ultimate goal of his research program is to positively impact the future development of cancer therapies, by increasing the specificity and efficacy of cancer treatments while minimizing the adverse side effects so commonly associated with current chemotherapeutic approaches.

Selected Publications:

1. Sajesh, B.V., and **McManus, K.J.** Targeting SOD1 induces synthetic lethal killing in *BLM*- and *CHEK2*-deficient colorectal cancer cells. *Oncotarget* 2015 (Accepted).
2. Thompson, L.L. and **McManus, K.J.** A novel multiplexed and image-based approach to identify chromosome instability genes in human cells. *PLoS ONE* 2015;10:e0123200.
3. Cisyk, A.L., Penner-Goeke, S., Lichtensztejn, Z., Nugent, Z., Wightman, R., Singh, H., and **McManus, K.J.** Chromosome instability is correlated with interval colorectal cancers. *Neoplasia* 2015;17:306-16.
4. Guppy, B.J. and **McManus, K.J.** Mitotic Accumulation of di-methylated Lysine 79 of Histone H3 Is important for maintaining genome integrity during mitosis in human cells. *Genetics* 2015;199:423-33.
5. Cisyk, A.L., Singh, H., and **McManus, K.J.** Establishing a biological profile for interval colorectal cancers. *Dig Dis Sci* 2014;59:2390-402.
6. Sajesh, B.V., Guppy, B.J., and **McManus, K.J.** Synthetic genetic targeting of genome instability in cancer. *Cancers* 2013;5:739-61.
7. Sajesh, B.V., Bailey, M.L., Lichtensztejn, Z., Hieter, P., and **McManus, K.J.** Synthetic lethal targeting of superoxide dismutase 1 selectively kills *RAD54B-deficient cells. Genetics*. 2013;195:757-67.
8. Thompson, L.L., Guppy, B.J., Sawchuk, L., Davie, J.R., and **McManus, K.J.** Regulation of chromatin structure via histone post-translational modification and the link to carcinogenesis. *Cancer Metast Rev.* 2013; 32:363-73.
9. Price, J.C., Pollock, L.M., Rudd, M.L., Fogoros, S.K., Mohamed, H., Hanigan, C.L., NISC Comparative Sequencing Program, Zhang, S., Cruz, P., Hansen, N.F., Cherukuri, P.F., **McManus, K.J.**, Godwin, A.K., Sgroi, D.C., Mullikin, J.C., Wolfsberg, T.G., Merino, M.J., Hieter, P., and Bell, D.W. Sequencing of candidate chromosome instability genes in endometrial cancers reveals somatic mutations in *ESCO1*, *CHTF18*, and *MRE11A*. *PLoS ONE*. 2013;8:e63313.
10. van Pel, D.M., Barrett, I.J., Shimizu, Y., Sajesh, B.V., Guppy, B.J., Pfeifer, T., **McManus, K.J.**, and Hieter, P. An evolutionarily conserved synthetic lethal interaction network identifies FEN1 as a broad-spectrum target for anticancer therapeutic development. *PLoS Genetics*. 2013;9:e10003254.

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Dr. Donald Miller received his B.Sc. in Chemistry from Bethel College, Newton, Kansas, and his PhD in Pharmacology and Toxicology from the University of Kansas. He was a Marion Merrell Dow Postdoctoral Research Fellow in Dr. Ronald Borchardt's laboratory at the University of Kansas where he studied biological approaches for enhancing drug delivery and drug absorption. Dr. Miller is presently a Professor in the Department of Pharmacology and Therapeutics at the University of Manitoba. He is an internationally recognized expert in drug transporters and blood-brain barrier function, having served on both NIH and CIHR grant and fellowship review panels, as well as reviewer and site visit examiner for Austrian and European Union based program grant initiatives. He has participated on External Scientific Advisory Boards for Vireo Systems Inc. (US based nutraceutical company) and SFB35 –Transporters in Health and Disease – a multiple researcher project scheme type grant from the University of Vienna. His research interests include understanding cellular and molecular mechanisms regulating blood-brain barrier function under normal and pathological conditions and identification of methods for enhancing drug delivery to the brain.

Dr. Miller's research program includes examination of blood-brain barrier changes during brain tumor development and identification of methods for increasing the delivery of chemotherapeutic agents brain tumor; identification and characterization of drug efflux transport proteins in the blood-brain barrier and the molecular mechanisms influencing activity and expression; and the design and development of nanoparticle drug delivery platforms for CNS applications.

Selected Publications (80 total publications; 5 issued patents; H-index 34)

1. Laksitorini, M., Kiptoo, P.K., On, N.H. Thliveris, J.A., ***Miller, D.W.*** and Siahaan, T.J. Modulation of intercellular junctions by cyclic ADT peptides as a method to reversibly increase blood-brain barrier permeability. J. Pharm. Sci. 104:1065-1075, 2015. PMID:25640479
2. On, N.H. and ***Miller, D.W***. Transporter-Based Delivery of Anticancer Drugs to the Brain: Improving Brain Penetration by Minimizing Drug Efflux at the Blood-Brain Barrier. Curr. Pharm. Design 20:1499-1509, 2014. PMID:23789953
3. Dalvi, S. Mitchell, R.W., On, N.H., Aukema, H.M., ***Miller, D.W***., and Hatch, G.M. Exogenous arachidonic acid mediates permeability of human brain microvessel endothelial cells. J. Neurochem.
4. Sun, Z., Worden, M., Wroczynskyj, Y., Yathindranath, V., van Lierop, J., Hegmann, T., and ***Miller, D.W.*** Magnetic field enhanced convective diffusion (MFECD) of iron oxide nanoparticles in an osmotically disrupted cell culture model of the blood-brain barrier. Int. J. Nanomed. 9:3013-3026, 2014. PMID:25018630
5. Sun, Z., Yathindranath, V., Worden, M., Thliveris, J.A., Chu, S., Parkinson, F.E., Hegmann, T., and ***Miller, D.W.*** Characterization of cellular uptake and toxicity of aminosilane coated iron oxide nanoparticles with different surface charge in CNS relevant cell culture models. Intl J. Nanomedicine 8:1-10, 2013. PMID:23494517
6. On, N., Mitchell, R., Savant, S., Bachmeier, C., Hatch, G. M. and ***Miller, D.W***. Examination of blood-brain barrier (BBB) integrity in a mouse brain tumor model. J. Neuro-oncol. 111:133-143, 2013. PMID:23184143
7. On N., Chen F., Hinton, M. and ***Miller, D.W***. A near infrared fluorescent probe for monitoring P-glycoprotein activity in both in vitro and in vivo applications. Pharm. Res. 28:2505-2515, 2011. PMID:21598079
8. Chakravarthi, S.S., De, S., Miller, D.W., and Robinson, D.H. Comparison of anti-tumor efficacy of paclitaxel delivered in PLGA nanospheres and microspheres. Intl. J. Pharm. 383:37-44, 2010. PMID:19747969
9. Zhang, Y., Elmquist, W.F., Schuetz, J., and ***Miller, D.W.*** Plasma membrane localization of multidrug resistance-associated protein (MRP) homologues in brain capillary endothelial cells. J. Pharmacol. Exp. Ther. 311:449-455, 2004. PMID:15218051
10. Batrakova, E.V., Shu, L., Elmquist, W.F., ***Miller, D.W***., Alakhov, V.Y., and Kabanov, A.V. Mechanism of sensitization of MDR cancer cells by pluronic block copolymers: Selective energy depletion. Br. J. Cancer 85:1987-97, 2001. PMID:11747344

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Dr. Suresh Mishra received his M.Sc. and Ph.D. degrees in Biochemistry and Endocrinology from the University of Delhi, and his post-doctoral training at the University of Louisville and University of Manitoba. Dr. Mishra is currently an Associate Professor in the Department of Internal Medicine and an Adjunct Professor in the Department of Physiology and Pathophysiology, University of Manitoba. He serves as a reviewer of journals publishing in Endocrinology, Obesity, Biochemistry, Cell Biology and Molecular Biology. He also serves as a reviewer of NSERC Discovery Grant, Canadian Breast Cancer Foundation and UK Diabetes. His research interests include **(1)** biological and pathological mechanisms that links metabolism and cancer in general with special interest in the relationship between obesity and different types of cancer, and **(2)** the mechanisms involved in the regulation of commonly occurring post-translational modifications in proteins at the systemic level in health and disease processes with special interest in cancer metabolism.

A number of studies have been done to address the connection between obesity and cancer using commonly used obese rodent models. In the majority of the studies either genetically obese (ob/ob, db/db) or diet-induced obese (DIO) rodent models have been used to investigate transgenic and carcinogen induced tumor development. To study tumor progression the major focus has been on allograft studies in mice with either genetic or diet-induced obesity. In general, obesity has been demonstrated to shorten tumor latency and to impact tumor pathology. However, in genetic models with a defect in leptin or leptin receptor, the impact of obesity is not as straightforward. This is also the case with diet-induced obese rodent models and it is difficult to discern the effect of diet from overweight and other confounding factors. Similarly, it is very difficult to prove causal associations between diabetes and cancer due to the host of confounding factors. The hypothesis that hyperinsulinemia and IGF-I receptor activation promote cancer is strong, but confounded by the association of hyperinsulinemia with obesity, which separately promotes malignancy. Thus, there is lack of apt translational models to study the relationship between obesity, insulin resistance and cancer. Future studies using more physiologically relevant obesity models and clearly distinguishing the diet component from body weight and obesity from insulin resistance effects will be important in continuing to understand the factors associated with body weight's impact on cancer development, progression and cancer associated mortality.

To this end, Dr. Mishra has used an innovative approach and developed novel transgenic obese mice models that spontaneously developed obesity-linked cancer in a progressive manner, independent of diet and carcinogen. Now his research plans are to capitalize on these opportunities to answer some of the fundamental questions in this field such as:

1. How obesity and obesity-associated abnormalities facilitate cancer development and progression?
2. What are the similarities and differences exist between obesity-linked different types of cancer?
3. How obesity and obesity-associated abnormalities lead to different types of cancer in humans? Are obesity-linked different types of cancer interrelated?

He hope that research outcomes will help

- **I.** To develop effective strategies to prevent or reduce the impact of obesity on different types of cancer,
- **II.** May lead to discovery of novel therapeutic targets and
- **III.** Create new knowledge that will allow us to predict the likelihood of cancer development in obese/type 2 diabetic patients.

Selected Publications:

1. Ande SR, Nguyen KH, Nyomba BLG, **Mishra**. Prohibitin-induced obesity associated insulin resistance and accompanying inflammation is sufficient to cause NASH and HCC. Hepatology. 2015 (submitted)
2. Ande SR, Nguyen KH, Padilla-Meier GP, Nyomba BLG, **Mishra**. Expression of a mutant prohibitin from the aP2 gene promoter leads to obesity-linked tumor development in insulin resistance dependent manner. Oncogene 2015 (Under revision).
3. Ande SR, Nguyen KH, Padilla-Meier GP, Nyomba BLG, **Mishra**. Prohibitin overexpression in adipocytes induces mitochondrial biogenesis, leads to obesity development, and affects glucose homeostasis in a sex-specific manner. Diabetes 63 (2014)3734-41.
4. Wang Y, Ande SR, **Mishra S**. Phosphorylation of transglutaminase 2 (TG2) at serine-216 plays a role in TG2 mediated activation of nuclear factor-kappa B and in the down regulation of PTEN. BMC Cancer (2012) 12(1).
5. Wang Y, Ande SR, **Mishra S**. Overexpression of phospho mutant forms of transglutaminase 2 downregulates epidermal growth factor receptor. Biochem Biophys Res Commun (2012) 417(1)
6. **Mishra S**, Ande SR, Salter NW. O-GlcNAc modification: Why so intimately associated with phosphorylation? Cell Commun Signal 9 (2011) 1.
7. **Mishra S**, Ande SR, Nyomba BLG. The role of prohibitin in cell signaling. FEBS Journal, 277 (2010) 3937–3946.
8. Ande SR, Moulik S, **Mishra S**. Interaction between O-GlcNAc modification and tyrosine phosphorylation of prohibitin: implication for a novel binary switch. PLoS One. 2009;4(2):e4586.

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Dr. Michael Mowat received his B.Sc. from York University and Ph.D. from the University of Alberta. His post-doctoral training in the area of molecular biology of Tetrahymena was done in the lab of Ron Pearlman at York University. Dr. Mowat was a research associate at the Ontario Cancer Institute with Alan Bernstein working on Friend Virus-Induced Erythroleukemia and TP53 tumor suppressor gene. Dr. Mowat is presently a senior scientist at the Research Institute in Oncology and Hematology CancerCare Manitoba and Professor in the Department of Biochemistry and Medical Genetics, University of Manitoba. He served as an associate editor of the Canadian Journal of Physiology & Pharmacology. He has served as on several review panels for CIHR, NCIC/CCSRI, NIH, CRS and CBCF. His research interests include the genetics of cancer, mechanisms of drug resistance and mouse models of cancer.

One area of research in my laboratory is the study of programmed cell death or apoptosis, a form of cell suicide. As a result of genetic changes, cancer cells have a reduced or slowed ability to undergo apoptosis, which can also make tumor cells more resistant to anti-cancer drug treatment. To better understand programmed cell death, we have taken a genetic approach. Several mutant cell lines have been isolated that are defective in apoptosis. This was done by using a specially constructed virus that, after it infects a cell, integrates into genes and interferes with their function. After selection for drug resistant cells, the underlying genes disrupted by the virus are studied for their role in programmed cell death and drug resistance. By understanding the genetic basis of resistance to cell death, completely new treatments can be devised.

A gene that came out of these screens was the Dlc-2 (Deleted in liver cancer two) tumor suppressor gene. We are now studying the role this gene plays, along with the closely related Dlc-1 gene, in tumor cell progression and drug response.

The Dlc-1 gene is found deleted in over 50 percent of breast, lung, liver and colon cancers. Also, the other normal copy of the gene is frequently silenced by promoter methylation. To study the role these genes play in the body, we have developed conditional knockout mouse models. With these mouse models, we can study the role the Dlc genes play in lung, and breast cancer spread through the body and anti-cancer drug response.

Selected Publications:

1. Basak P, Dillon R, Leslie H, Raouf A, **Mowat MR**. The Deleted in Liver Cancer 1 (Dlc1) tumor suppressor is haploinsufficient for mammary gland development and epithelial cell polarity. BMC Cancer. Sep 9;15(1):630. (2015)
2. Sabbir MG, Prieditis H, Ravinsky E, **Mowat MR**. The Role of Dlc1 Isoform 2 in K-Ras2(G12D) Induced Thymic Cancer. PLoS One.;7(7):e40302. Epub 2012 Jul 5. (2012)
3. Sabbir, M.G., Wigle, N., Shauna Loewen, S., Gu. Y., Buse C., Hicks G.G., **Mowat M.R.** Identification and characterization of Dlc1isoforms in the mouse and study of the biological function of a single gene trapped isoform. BMC Biology 8(1): 17-38 (2010).
4. Hatch, G., Gy Y., Xu, F.Y., Cizeau, J., Park, J.-S.,Neumann, S., Loewen, S., and **Mowat, M**. StARD13 (Dlc-2) StARD13 (Dlc-2) RhoGap Mediates Ceramide Activation of Phosphatidylglycerolphosphate Synthase and Drug Response in Chinese Hamster Ovary Cells. Molecular Biology of the Cell, 19(3):1083-92 (2008).
5. Stewart, N., G. Hicks, F. Paraskevas and **M. Mowat**. Evidence for a second cell cycle block at G2/M by p53. Oncogene 10: 109-115 (1995).
6. **M. Mowat**, A. Cheng, N. Kimura, A. Bernstein and S. Benchimol. Rearrangements of the cellular p53 gene in erythroleukemic cells transformed by Friend virus. Nature 314: 633-636 (1985).

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Dr. Leigh C. Murphy, PhD

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Dr. Leigh Murphy is a senior scientist in the Manitoba Institute of Cell Biology, and holds an academic appointment as a full professor in the Department of Biochemistry & Medical Genetics at the University of Manitoba. She was educated in Australia and majored in Biochemistry at the University of Sydney, Australia in 1972. This was followed by graduate studies leading to a Ph.D. (Reproductive Endocrinology) from the University of Sydney, 1976. She undertook postdoctoral fellowships at the Ludwig Institute of Cancer Research, Sydney University and then the Department of Physiology at the University of Manitoba

In 1987 she went on Faculty as an Assistant Professor in the Department of Biochemistry & Molecular Biology, University of Manitoba, obtained tenure and was promoted to full professor in 1995. She became a Senior Scientist at the Manitoba institute of Cell Biology in 2000, Associate Director in 2006 and Interim Director in 2009.

Since estrogen is a major driver of human breast cancer, and the action of estrogen changes during breast tumorigenesis and breast cancer progression, the overall aim of her research program is to elucidate the mechanisms by which estrogen action changes during the development of breast cancer and how breast cancers develop resistance to endocrine therapies and progress from hormone dependence to independence. To do this her group is identifying the molecular players involved in the estrogen receptor signaling pathways in human breast tissues, how they are altered during tumorigenesis, and breast cancer progression to hormone independence. Specifically her research is determining the types and putative function of estrogen receptor isoforms, i.e. estrogen receptor alpha and beta and phosphorylated forms of estrogen receptor alpha, that are expressed in human breast tissues *in vivo*, using tissues obtained from the Manitoba Breast Tumor Bank/Clinical Database. She is pursuing the hypothesis that the profiling of estrogen receptor isoforms is a more precise biomarker of prognosis and treatment outcome in human breast cancer. She was the first to identify a phosphorylation code for estrogen receptor alpha in breast tumors *in vivo* again using the tissues from the Manitoba Breast Tumor Bank. This code is a strong prognostic marker in breast cancer. She is working to identify the enzymes called kinases that regulate the estrogen receptor alpha phosphorylation code, since some of these kinases may be excellent targets for drug development. In collaboration with Dr. Afshin Raouf they are investigating alterations of the estrogen receptor alpha phosphorylation code and kinases in Dr. Raouf's novel model of normal human breast epithelial cells that are estrogen receptor alpha positive. In collaboration with Dr. Wayne Xu, they are investigating prognostic molecular signatures in models of beast cancer and large data sets from human breast tumor samples. In collaboration with Drs G Qing, S Banerji and M Pitz, they are investigating how steroid hormones such as estrogen and androgen affect some lung cancers. In collaboration with Dr Peter Watson and the Manitoba Tumorbank, they are also investigating tissue collection issues that may affect detection of various gene products in banked tissues. She is the author of 204 publications and has received nationally competitive career awards and operating funds for her research.

Selected Publications:

1. Yingfeng Zheng, **Leigh Murphy**. (2015) Regulation of Steroid Hormone Receptors and Coregulators During the Cell Cycle Highlights Potential Novel Function in Addition to Roles as Transcription Factors. Nuclear Receptor Signaling (invited review) in press
2. Basak P, Bruce MC, Weger S, **Murphy LC**, Raouf A.Estrogen signaling regulates proliferation and differentiation of ERα+luminal progenitors through H19 gene. 2015 Endocrine Related Cancer Aug;22(4):505-17
3. Jill I. Murray, Nathan R. West, **Leigh C. Murphy**, Peter H. Watson. (2015) Intratumoral inflammation and endocrine resistance in breast cancer. Endocrine Related Cancer. 2015 Feb;22(1):R51-R67 (invited review)
4. M Chrissie Bruce, Danielle McAllister, **Leigh C Murphy**. (2014) The Kinome Associated with Estrogen Receptor Positive Status in Human Breast Cancer. Invited review Endocrine Related Cancer Oct;21(5):R357-70.
5. Anuraag Shrivastav, M Chrissie Bruce, Danira Jaksic, Tarek Bader, Sri Seekallu, Carla Penner, Zoann Nugent, Peter Watson, **Leigh Murphy**. The Mammalian Target for Rapamycin Pathway is Associated with the Phosphorylation Score (P7) for Estrogen Receptor-a in Human Breast Tumors, *in vivo*. (2014) Breast Cancer Res 16(3):R49 IF 5.9.
6. Yan Y, Li X, Blanchard A, Bramwell VH, Pritchard KI, Tu D, Shepherd L, Myal Y, Penner C, Watson PH, Leygue E, **Murphy LC**. Expression of both Estrogen Receptor-beta 1 (ER-b1) and its co-regulator Steroid Receptor RNA Activator Protein (SRAP) are predictive for benefit from tamoxifen therapy in patients with Estrogen Receptor-alpha (ER-a)-Negative Early Breast Cancer (EBC). Ann Oncol. 2013 Aug;24(8):1986-93. doi: 10.1093/annonc/mdt132. Epub 2013 Apr 11.
7. Curtis C, Shah SP, Chin SF, Turashvili G, Rueda OM, Dunning MJ, Speed D, Lynch AG, Samarajiwa S, Yuan Y, Gräf S, Ha G, Haffari G, Bashashati A, Russell R, McKinney S; METABRIC Group, Langerød A, Green A, Provenzano E, Wishart G, Pinder S, Watson P, Markowetz F, **Murphy L**, Ellis I, Purushotham A, Børresen-Dale AL, Brenton JD, Tavaré S, Caldas C, Aparicio S. (2012) Nature. Apr 18;486(7403):346-52.

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Dr. Yvonne Myal, PhD

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Dr. Yvonne Myal is a professor in the departments of Pathology and Physiology. She received her B.Sc. (Hons) from the University of Winnipeg and her MSc/ PhD from the University of Manitoba. Her post-doctoral training was in the area of molecular biology/ transgenic and knockout mouse technology in the laboratory of Dr. Robert Shiu in the Department of Physiology at the University of Manitoba, Faculty of Medicine. Dr. Myal has served as a panel member on NCIC and CIHR Peer Review Committees, reviewer for NSERC, CIHR, Department of foreign Affairs and International trade (DFAIT**)** Global Partnership Program and the Norway Research Council. She has served as chair on many University committees and Provincial operating grant committees including the Manitoba Health Research Council. Dr Myal is currently the Director of Research for Diagnostic Services of Manitoba. She received a YWCA/YMCA Woman of Distinction Award in 2011.

My long term research program is based on identifying breast/breast cancer specific biomarkers and understanding the biological role of these markers in the progression of breast cancer from a localized disease to metastases. Our research efforts over the last few years have been focused on two molecules, claudin 1, and the human prolactin inducible protein/gross cystic disease fluid protein, PIP/GCDFP-15.

PIP/GCDFP-15: PIP/GCDFP-15 is an established biomarker for abnormal breast function. PIP/GCDFP-15 is abundantly found in the fluid of benign cysts of the breast and its gene expression has been detected in more than 90% of breast cancers. Currently, its role in breast cancer as well as in normal breast development is presently not known. Our laboratory generated the first transgenic and knockout mouse model to address the function of this protein. Recent studies from our laboratory show that the role of the PIP/GCDFP-15 protein is multifunctional and may have an immunomodulatory role.

Claudin 1: We are studying the role of the tight junction protein claudin 1 in breast cancer progression and metastasis. Tight junction proteins are localized in the membrane of epithelial cells, including mammary epithelial cells which are the milk secreting cells of the breast. Most breast cancers develop from this cell type. Tight junction proteins are important for cell-cell interaction, regulating the transport of ions and nutrients between these cells. Furthermore, the claudins are indispensible for maintenance of the apical polarity and the epithelial cell structure. The breakdown of cell-cell interaction and a loss of tight junction proteins have long been associated with the progression of several cancers. However, such an involvement of claudin 1 in breast cancer has not been delineated. Our laboratory and others have shown that in invasive human breast cancers, claudin 1 is down regulated or absent, suggestive of a tumor suppressor role. However, paradoxically, we have also shown a close association with claudin 1 and a particularly aggressive subtype of breast cancer, the basal like subtype, for which there are no current effective treatment. We are focusing on several in vitro and in vivo approaches to address the role of claudin 1 in breast cancer, as well as examining the relationship between claudin 1 expression, tumor aggressiveness and patient survival.

Selected Publications:

1. Zhou J, Blanchard A, Wang N, Ma X, Han J, Schroedter I**,** Leygue E, and **Myal, Y.** Claudin 1 promotes migration and increases sensitivity to tamoxifen and anticancer drugs in luminal-like human breast cancer cells MCF7. Cancer Investigation 1–11, 2015.
2. Blanchard A., Ezzati P., Shamshurin D., Nistor A., Leygue E., Wilkins J., **Myal Y**. Towards further defining the proteome of mouse saliva. Proteome Sci. 2015 Feb 25;13:10. doi: 10.1186/s12953-015-0068-3. eCollection 2015.
3. Cheung K, Cole LK, Ma X, Xiang B, **Myal Y**, Hatch GM, Tong Q, Dolinsky VW. SIRT3 attenuates doxorubicin-induced oxidative stress and improves mitochondrial respiration in H9c2 cardiomyocytes. J Biol Chem. Apr 24;290(17):10981-93. doi: 10.1074/jbc.M114.607960. Epub 2015 Mar 10. 2015.
4. Li J, Liu D, Mou Z, Ihedioha OC, Blanchard A, Jia P, **Myal Y**, Uzonna JE. Deficiency of prolactin-inducible protein leads to impaired Th1 immune response and susceptibility to Leishmania major in mice. Eur J Immunol. 2015 Apr;45(4):1082-91. doi: 10.1002/eji.201445078. Epub 2015 Feb 12.
5. Umadat Vivake, Ihedioha Olivia, Shiu Robert, Uzonna Jude, **Myal Yvonne.** The prolactin-inducible-protein (PIP): A regulatory molecule in adaptive and innate immunity. Open Journal of Immunology. Vol.3, No.4, 210-217. (2013). http://dx.doi.org/10.4236/oji.2013.34026.
6. Yan Y, Li X, Blanchard A, Bramwell VH, Pritchard KI, Tu D, Shepherd L, **Myal Y**, Penner C, Watson PH, Leygue E, Murphy LC. Expression of both Estrogen Receptor-beta 1 (ER-b1) and its co-regulator Steroid Receptor RNA Activator Protein (SRAP) are predictive for benefit from tamoxifen therapy in patients with Estrogen Receptor-alpha (ER-a)-Negative Early Breast Cancer (EBC). Ann Oncol. 2013 Aug;24(8):1986-93. doi: 10.1093/annonc/mdt132. Epub 2013 Apr 11.

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Dr. Mark Nachtigal received his B.Sc. (Biology) and Ph.D. (Molecular Endocrinology) degrees from the University of Manitoba. His post-doctoral research was conducted in Dr. Holly Ingraham's laboratory at the University of California, San Francisco in the area of mammalian reproductive tract development. Throughout his graduate and post-graduate training his research projects retained a link to human reproductive cancer biology. In 1998 Dr. Nachtigal was recruited to Dalhousie University as the Rossetti Scholar for Cancer Research to study human epithelial ovarian cancer (EOC). While at Dalhousie University he served as the co-chair of the Nova Scotia Cancer Research Training Program (2006-08) and as a member of the CIHR Institute of Cancer Research Advisory Board. Dr. Nachtigal returned to Manitoba in 2010 to continue his research on EOC. He is currently an Associate Professor in the Departments of Biochemistry & Medical Genetics, and Obstetrics, Gynecology, and Reproductive Sciences, as well as being a Senior Scientist in the Research Institute in Oncology & Hematology at CancerCare Manitoba.

EOC is the fifth leading cause of death by cancer amongst women. Approximately 95 women in Manitoba will be diagnosed with EOC this year. If detected at early stages of the disease, the cure rate approaches 90%; however, >70% of women are diagnosed with advanced disease when rates of survival are closer to 30%. Even after initial successful responses to therapy, EOC recurs in ~85% of patients. Dr. Nachtigal's laboratory uses a combination of cellular and molecular approaches to investigate human EOC biology with a special interest in recurrent, chemotherapy-resistant disease. With the formation of the Manitoba Ovarian Biobanking Program (MOBP) and cooperation with national programs such as the Canadian Ovarian Cancer Research Consortium (COCRC), his lab will be able to more readily translate data obtained with EOC patient samples to clinically relevant results. The ability to isolate and use patient donated EOC cells in 3-dimensional primary culture provides a more relevant model to assess cell responses. In particular he, in collaboration with other University of Manitoba scientists, is focusing on investigating aspects of ovarian cancer stem cell biology and chromosomal instability, in addition to evaluating novel lipid-based therapeutics for treatment of chemoresistant EOC. This laboratory-based research is being complemented by epidemiologic studies to evaluate whether recent changes in clinical management have produced positive outcomes for the EOC population.

Selected Publications:

1. Ali J, BJ Lagasse, AJ Minuk, AJ Love, AI Moraya, L Lam G Arthur, SB Gibson, LC Morrison, TE Werbowetski-Ogilvie, Y Fu, **MW Nachtigal**. 2015. Differential cellular responses induced by dorsomorphin and LDN-193189 in chemotherapy-sensitive and –resistant human epithelial ovarian cancer cells. *International Journal of Cancer* 136: E455-E469. doi: 10.1002/ijc.29220
2. Wang, J, **MW Nachtigal**, E. Kardami and PA Cattini. 2013. FGF-2 protects cardiomyocytes from doxorubicin damage via protein kinase C-dependent effects on efflux transporters. *Cardiovascular Research*. 98: 56-63. Doi:10..1093/cvr/cvt011
3. Thériault BL, Portelance L, Mes-Masson AM, **Nachtigal MW**. Establishment of primary cultures from ovarian tumor tissue and ascites fluid. Methods Mol Biol. 2013;1049:323-36. doi: 10.1007/978-1-62703-547-7_24.
4. Thériault BL, **Nachtigal MW**. December 2012. BMP4 (bone morphogenetic protein 4). *Atlas Genet Cytogenet Oncol Haematol.* URL: http://AtlasGeneticsOncology.org/Genes/BMP4ID811ch14q22.html
5. Thériault BL, **Nachtigal MW**. Human ovarian cancer cell morphology, motility, and proliferation are differentially influenced by autocrine TGFB superfamily signalling. Cancer Lett. 2011 Dec 26;313(1):108-21. Epub 2011 Sep 10.
6. Mujoomdar, ML, LM Hogan, AL Parlow and **MW Nachtigal**. Pcsk6 mutant mice exhibit progressive loss of ovarian function, altered gene expression, and formation of ovarian pathology. 2011. Reproduction 141(3): 343-355.
7. Fu Y and **MW Nachtigal**. 2011. Epigenetic analysis of proprotein convertase regulation in Human Cancer. In *Proprotein Convertases*, M Mbikay and NG Seidah, Eds., Humana Press. Invited article. *Methods in Molecular Biology* **768:** 231-245. doi: 10.1007/978-1-61779-204-5_12

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Richard Nason completed his medical training at Dalhousie University, Halifax, Nova Scotia; a residency in General Surgery at the University of Alberta, Edmonton, Alberta; an MSc in Experimental Surgery, University of Alberta, Edmonton, Alberta; and a fellowship in Head and Neck Surgical Oncology at Roswell Park Memorial Institute, Buffalo, New York.

He has practiced as a Head and Neck Surgical Oncologist at CancerCare Manitoba since 1993. Past appointments have included Head of Surgical Oncology CCMB; Chair Head and Neck Disease Site Group CCMB; Regional Medical Director, Surgery Program, Winnipeg Regional Health Authority and Head, Department of Surgery, University of Manitoba; Chair Examination Board General Surgery RCPS, President Canadian Society of Surgical Oncology. He is currently the lead for Synoptic Reporting in Manitoba.

Research interests have focused on outcomes in head and neck surgery, sentinel lymph node biopsy in head and neck cancer, and implementation of synoptic reporting for cancer surgery as a tool for knowledge management.

Selected Publications:

1. PathakKA, Mazurat A, Lambert P,Klonisch T,Nason RW.Prognosticnonmgramsto predictoncologicaloutcome of thyroid cancer. J Clin Endocrinol Metab. 2013 Dec;98(12):4768-75. doi: 10.1210/jc.2013-2318. Epub 2013 Oct 23.
2. Brandwein-Gensler M, Smith RV, Wang B, Penner C, Theilken A, Broughel D, Schiff B, Owen RP, Smith J, Sarta C, Hebert T, Nason R, Ramer M, DeLacure M, Hirsch D, Myssiorek D, Heller K, Prystowsky M, Schlecht NF, Negassa . Validation of the histologic risk model in a new cohort of patients with head and neck squamous cell carcinoma**.** A. Am J Surg Pathol. 2010 May;34(5):676-88.
3. Civantos FJ, Zitsch RP, Schuller DE, Agrawal A, Smith RB, Nason R, Petruzelli G, Gourin CG, Wong RJ, Ferris RL, El Naggar A, Ridge JA, Paniello RC, Owzar K, McCall L, Chepeha DB, Yarbrough WG, Myers JN. Sentinel lymph node biopsy accurately stages the regional lymph nodes for T1-T2 oral squamous cell carcinomas: results of a prospective multi-institutional trial. Clin Oncol. 2010 Mar 10;28(8):1395-400. Epub 2010 Feb 8
4. Nason R, Binahmed A, Abdoh A . What is the adequate margin of surgical resection in oral cancer. Oral SurgOral Med Oral Pathol Oral Radiol Endod. 2009;105(5):625-9.
5. Koul R, Dubey A, Butler J, Cooke A, Abdoh A, Nason R. Prognostic factors predicting disease specific survival in parotid gland tumors. Int J Radiation Oncol Biol Phys 2007;1:68(3):714-718
6. Nason R, Binahmed A, Torchia M, Thliveris J. Clinical observations of the anatomy and function of the marginal mandibular nerve. Int J Oral Maxillofac Surg 2007;36(8):712-5.
7. Nason RW, Torchia MG, Morales CM,Thliveris J. Dynamic MR lymphangiography and carbon dye for sentinel lymph node biopsy in mucosal head and neck cancer. Head Neck. 2005 Apr;27(4): 333-8.
8. Nason R, Abdulrauf B, Stranc M. The anatomy of the accessory nerve and cervical lymph node biopsy. Am J Surg 2000;180:241243.
9. Ash C, Nason R, Abdoh A, Cohen M. Prognostic implications of mandibular invasion in oral cancer. Head Neck 2000;8:794-799.

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Dr. K. Alok Pathak is Professor of Surgery, Director, Surgical Fellowships, and Program Director of Head & Neck Surgical Oncology Fellowship at the University of Manitoba. He is the current President Elect of Canadian Society of Surgical Oncology 2015-16. Dr Pathak completed his medical training and general surgical residency at the Banaras Hindu University in India (MBBS 1991, MS-1994). He is a Diplomate of National Board (1995) and a member of National Academy of Medical Sciences, India. Subsequently, he trained in Surgical Oncology at Tata Memorial Hospital, India and in Head and Neck Oncology research at Memorial Sloan Kettering Cancer Centre, USA. He is also a fellow of the Royal College of Physicians and Surgeons of Glasgow (1998), the Royal College of Surgeons of Edinburgh (1998) and the Royal College of Surgeons of Canada.

Dr Pathak has received several research grant awards and published over 75 peer reviewed papers, editorials, book chapters, invited articles and expert columns. He has delivered over two dozen keynote addresses, orations & invited lectures and presented over 125 papers. He has co-edited a volume of Head and Neck Clinics on "Controversies in oral cancer", and a second volume on "Special considerations in management of thyroid cancer" is currently in press. He is an avid reader and technology enthusiast with a keen interest in gardening and landscaping.

The core of Dr. Pathak's research has been cancers of Head and Neck particularly those of thyroid and oral cavity. His research interests spans both clinical and translational research. He is following the oncological outcome of a population based cohort of about 2300 thyroid cancer patients of thyroid cancer over 27000 patient-years. His recent paper on the changing face of thyroid cancer (Cancer Medicine 2013) challenges the hypothesis that the recent rise in thyroid cancer is due to over diagnosis This paper shows that the increase in age standardized incidence was not restricted to smaller thyroid cancers (micro-carcinomas) as has been thought of earlier. The significant improvement in thyroid cancer specific survival in this cohort was found to be independent of changes in patient characteristics; tumor stage or treatment practices and was due to the declining proportion of anaplastic thyroid cancers. His recent publication (Endocrine Connections 2013) questions the appropriateness of age threshold of 45 years in risk stratification of thyroid cancer. Dr. Pathak is currently involved in developing a mathematical model for individualized prediction oncological outcome of thyroid cancer patients. This paper on prognostic nomogram is an important milestone in this endeavor.

Peer Reviewed Publications:

1. Hombach-Klonisch S, Natarajan S, Thanasupawat T, Medapati M, **Pathak KA**, Ghavami S, Klonisch T. Mechanisms of therapeutic resistance in cancer (stem) cells with emphasis on thyroid cancer cells.Front Endocrinol (Lausanne). 2014 Mar 25;5:37
2. Upreti D, **Pathak KA**, Kung SK. Lentiviral vector-based therapy in head and neck cancer (Review).Oncol Lett. 2014 Jan;7(1):3-
3. **Pathak KA**, Mazurat A, Lambert P, Klonisch TC, Nason RW Prognostic nomograms to predict treatment outcomes of thyroid cancer.J Clin Endocrinol Metab. 2013 Dec;98(12):4768-75
4. **Pathak KA**, Leslie WD, Klonisch TC, Nason RW. The changing face of thyroid cancer in a population based cohort. Cancer Medicine 2013; 2:537–544.
5. Mazurat A, Torroni A, Hendrickson-Rebizant J, Benning H, Nason RW, **Pathak KA**.The age factor in survival of a population cohort of well-differentiated thyroid cancer. Endocr Connect. 2013 Sep 23;2(3):154-60
6. Aljabab AS, Nason RW, Kazi R, **Pathak KA**. Head and neck soft tissue sarcoma. Indian J Surg Oncol. Indian J Surg Oncol. 2011 Dec;2(4):286-90.
7. Le T, Aljabab A, Battistuzzi S, Nason RW, **Pathak KA**. Branchial cleft cyst masquerading as a laryngocele.J Otolaryngol Head Neck Surg. 2011 Aug;40(4):E35-8.
8. Pathare SM, Gerstung M, Beerenwinkel N, Schäffer AA, Kannan S, Pai P, **Pathak KA**, Borges AM, Mahimkar MB.Clinicopathological and prognostic implications of genetic alterations in oral cancers.Oncol Lett. 2011 May;2(3):445-451.
9. Sayed SI, Dwivedi RC, Katna R, Garg A, **Pathak KA**, Nutting CM, Rhys-Evans P, Harrington KJ, Kazi R. Implications of understanding cancer stem cell (CSC) biology in head and neck squamous cell cancer.Oral Oncol. 2011 Apr;47(4):237-43. Epub 2011 Mar 5.
10. **Pathak KA**, Aljabab AS, Kazi R, Nason RW. Lateral approach to central compartment of neck. Journal of Surgical Oncology 2011 Jan 1;103(1):101-2
11. Garg A, Dwivedi R, Sayed S; Katna R, Komorowski A, **Pathak KA** ,Rhys-Evans P, Kazi R. Robotics in head and neck cancer: is it the future? Oral Oncology 2010; 46(8):571-6.
12. Kazi R. Manikanthan K, **Pathak KA**, Dwivedi R. Head and neck squamous cell cancer: need for an organised time-bound surveillance plan. Eur Arch Otorhinolaryngol. 2010 Dec;267(12):1969-71

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Dr. Pelka obtained his degrees from McMaster University where he studied molecular biology, *Drosophila* development, and later the role of mammalian kinase, Nek9, in adenovirus replication. After obtaining his MSc in biology, Dr. Pelka worked for a biotechnology company in San Diego, California, as a research scientist before undertaking PhD studies at McMaster University under Dr. Peter Whyte. Following completion of his PhD, Dr. Pelka trained as a post-doctoral fellow under Dr. Joe S. Mymryk at Western University in London, Ontario, studying the biology of adenovirus E1A oncoprotein in cellular transformation and viral replication. Lastly, Dr. Pelka worked as a post-doctoral fellow in the lab of Dr. Bowdish at McMaster University studying host-pathogen interactions and effects on the immune system.

Dr. Pelka's research interests center on how a virus is able to reprogram an infected cell in order to replicate itself. The human adenovirus is a small DNA tumour virus that infects differentiated cells and causes mild illnesses such as conjunctivitis, cold, or gastro-intestinal problems. However, in 1962 it was shown that infection of rodent cells with the virus led to development of nodular tumours. This resulted in intense studies of the mechanism of tumour formation by adenovirus. It was discovered that the viral immediate early gene, E1A, was essential for cellular transformation and tumour formation. E1A induces cellular reprogramming on a massive scale, affecting more than 10,000 cellular genes and promoters in order to drive cells into S-phase to enable for virus replication. This property of E1A is extremely useful as many of the pathways that it affects are the same ones that become deregulated during the oncogenic process. Therefore, the Pelka lab is interested in using E1A as a tool to study the earliest events in cancer formation.

Dr. Pelka's research program has three major areas of focus that are designed to understand how a viral oncoprotein is reprogramming an infected cell in order to drive the cell cycle and support viral replication: **i)** to identify and characterize novel E1A-binding proteins during cellular transformation; **ii)** to investigate the mechanism of cell cycle induction by a mutant of E1A that is unable to interact with cell cycle regulators thought essential to the ability of E1A to drive S-phase; **iii)** to explore transcriptomic reprogramming of the infected cell during the course of adenovirus infection with a focus on how the virus is manipulating the cellular microRNA and long non-coding RNA regulatory network.

Selected Publications:

1. Radko S, Jung R, Olanubi O, **Pelka P** "Effects of adenovirus type 5 E1A isoforms on viral replication in arrested human cells." *PLOS ONE*, in press, 2015.
2. Radko S, Koleva M, James K, Jung R, Mymryk JS, **Pelka P** "Adenovirus E1A targets the DREF nuclear factor to regulate virus gene expression, DNA replication and growth." *J Virol,* 88(22): 13469-81, 2014.
3. Arulsundaram VD, Webb P, Yousef AF, **Pelka P**, Fonseca GJ, Baxter JD, Walfish PG, Mymryk JS. "The adenovirus 55 residue E1A protein is a transcriptional activator and binds the unliganded thyroid hormone receptor." *J Gen Virol* 95(1): 142-52, 2013.
4. Cohen MJ, Yousef AF, Massimi P, Fonseca GJ, Todorovic B, **Pelka P**, Turnell AS, Banks L, Mymryk JS. "Dissection of the C-terminal region of E1A re-defines the roles of CtBP and other cellular targets in oncogenic transformation." *J Virol* 87: 10348-55, 2013.
5. Ablack JA, Cohen M, Thillainadesan G, Fonseca GJ, **Pelka P**, Torchia J, Mymryk JS. "Cellular GCN5 is a Novel Regulator of Human Adenovirus E1A-Conserved Region 3 Transactivation." *J Virol* 86**:**8198-209, 2012.
6. Miller MS, **Pelka P**, Fonseca GJ, Cohen M, Kelly JN, Barr SD, Turnell AS, Grand RJ, Whyte P, Mymryk JS. "Characterization of the 55 residue E1A protein encoded by species C adenovirus." *J Virol* 86:4222-33, 2012.
7. **Pelka P*,** Miller MS, Cecchini M, Yousef AF, Bowdish DM, Dick F, Whyte P, Mymryk JS. "Adenovirus E1A directly targets the E2F/DP-1 complex." *J Virol* 85: 8841-51*,* 2011. *Corresponding author.
8. Ablack JNG, **Pelka P**, Yousef AF, Turnell AS, Grand RJ, Mymryk JS. "Comparison of E1A CR3 Dependent Transcriptional Activation Across Six Different Human Adenovirus Subgroups" *J Virol* 84:12771-81, 2010
9. Yousef AF, Fonseca GJ*, **Pelka P*,** Ablack JNG, Walsh C, Shaw GS, Bazett-Jones DP, Mymryk JS. "Identification of a molecular recognition feature in the E1A oncoprotein that confers binding to the SUMO conjugase Ubc9." *Oncogene* **29:**4693-704, 2010. *Shared authorship.

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Dr. Stephen Pistorius is a Senior Scientist at CancerCare Manitoba (CCMB) and at the Research Institute for Oncology and Hematology (RIOH). He serves as the Director of the Medical Physics Graduate Program and the Vice Director of the Biomedical Engineering Program at the University of Manitoba where he is a Professor of Physics and Astronomy and Associate Professor of Radiology. Educated in South Africa, he majored in Physics & Geography at the University of Natal, South Africa in 1977, before being conscripted into the Engineering Corps. Following a 2 year tour of duty he worked in industry where he had responsibility for the installation and commissioning of the first industrial linear accelerator in the country. This was followed by graduate studies leading to a Hons. B.Sc. (Radiation Physics), M.Sc. (Medical Science)(cum-laude) and Ph.D. (Physics) from the University of Stellenbosch, South Africa in 1983, 1984 and 1991 respectively. Following a medical physics residency from 1984 to 1986 he was certified as a medical physicist and in 2002 obtained a P.Phys. designation. He also holds a Post-graduate diploma in Business Management from the Edinburgh Business School, Heriot Watt University, UK.

In 1992 he moved to Canada as a Senior Medical Physicist (Radiotherapy Planning) at the Manitoba Cancer Treatment and Research Foundation, now CancerCare Manitoba. In 1995 he was appointed Director of Medical Physics and in 2000 was promoted to Provincial Director, responsible for more than 70 professional, technical and administrative staff in Radiotherapy Physics, Diagnostic Imaging, Radiation Protection, Clinical Engineering, Teaching and Research. He held this position until 2010 when he took on a full time academic role. He served as the Treasurer (1999-2002) and President (2006-2008) of the Canadian Organization of Medical Physics (COMP) and as the Director of Professional Affairs for the Canadian Association of Physicists (CAP) and is currently Vice President Elect for CAP. He has served as a Section Chair of the NSERC Physics Evaluation Group, and on the College of Reviewers for the Canada Research Chairs Program. As a founding member of the Canadian Light Source's (CLS) Biomedical Beamline steering committee, he continues to serve as a reviewer for the CLS as well as for other grant funding agencies and journals.

Prof. Pistorius has a particular interest in improving, optimizing and quantifying various diagnostic and therapeutic techniques and in understanding the radiation transport of clinically useful imaging and treatment modalities. He currently supervises one Research Associate and seven Graduate Students carrying out research in cancer imaging, specifically, in developing improved systems for cancer diagnosis which use scatter enhanced x- and γ-ray techniques and microwaves; as well as on-line megavoltage portal imaging, aimed at real time in-vivo tracking of motion and optimization of complex radiotherapy treatments. He is the author of over 200 publications and presentations, has received over $3.3M in grant funding in the last 5 years, is a Fellow of COMP, and he and his students have received numerous national and international awards for their research.

Selected Publications:

1. Y.S. Gui, A.M. Mehrabani, D. Flores-Tapia, L. Fu. L.H. Bai, **S. Pistorius**, L. Shafai, C.-M. Hu, "New Horizons for Microwave Applications Using Spin Caloritronics", Solid State Communications, 198(2014), pp 45-51, October 2014
2. L. Fu, W. Lu, D. Rodriguez-Herrera, D. Flores-Tapia, Y.S. Gui, **S. Pistorius**, C.-M. Hu, "Microwave Radar Imaging using a Solid State Spintronic Microwave Sensor", Applied Physics Letters 105(12):122406, Doi: 10.1063/1.4896691, Sept 2014
3. T. Chighvinadze, **S. Pistorius**, "The Effect of Detector Size and Energy Resolution on Image Quality in Multi-Projection Compton Scatter Tomography", Journal of X-Ray Science and Technology, 22(1) pp 113-128, January 2014
4. A. Sabouni, A. Ashtari, S. Noghanian, G. Thomas, **S. Pistorius**, "Hybrid Binary-Real GA Optimization Approach for Breast Microwave Tomography", ACES Journal, Vol. 28(11), pp 1005-1016, November 2013
5. C. Gilmore, A. Zakaria, **S. Pistorius**, Joe LoVetri, "Microwave Imaging of Human Forearms: Pilot Study and Image Enhancement", International Journal of Biomedical Imaging, Vol. 2013, Article ID 673027, 17 pgs, August 2013
6. T. Teo, R. Crow, S. Van Nest, D. Sasaki, **S. Pistorius**, "Tracking Lung Tumour Motion Using a Dynamically Weighted Optical Flow Algorithm and Electronic Portal Imaging Device", Measurement Science and Technology 24(2013) 074012(15pp), June 2013
7. C. Gilmore, A. Zakaria, J. LoVetri, **S. Pistorius**, "A Study of Matching Fluid Loss in a Biomedical Microwave Tomography System", Medical Physics, Vol. 40 (2), pp 023101-1 - 023101-14, February 2013
8. H. Sun, **S. Pistorius**, "Evaluation of the Feasibility and Quantitative Accuracy of a Generalized Scatter 2D PET Reconstruction Method", ISRN Biomedical Imaging, Vol. 2013, Article ID 943051, 11 pgs, January 2013
9. L. Fu, Z.X. Cao, S. Hemour, K. Wu, D. Houssameddine, W. Lu, **S. Pistorius**, Y.S. Gui, C.-M. Hu, "Microwave Reflection Imaging Using a Magnetic Tunnel Junction Based Spintronic Microwave Sensor", Applied Physics Letters, 101 (232406), doi: 10.1063/1.4769837, December 2012
10. D. Flores-Tapia, C. Alabaster. **S. Pistorius**, "Real-time Reconstruction of Three-Dimensional Cylindrical Near-Field Radar Images Using a Single Instruction Multiple Data Interpolation Approach", IET Radar Sonar & Navigation, Vol 6(6), pp. 494-506, July 2012

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Dr. Marshall Pitz is a medical oncologist at CancerCare Manitoba. His clinical training in Internal Medicine and Medical Oncology was at the University of Manitoba. He then went to Baltimore, MD, for special training in brain tumours at the Johns Hopkins Sidney Kimmel Cancer Center, and also obtained a Master's degree in Clinical Investigation at the Johns Hopkins Bloomberg School of Public Health. Dr. Pitz then returned to CancerCare Manitoba where he treats breast cancer and brain tumours and is Chair of the CNS Disease Site Group. He is also the Chief Medical Information Officer at CancerCare Manitoba, working to improve the use of the electronic record and of cancer informatics.

Dr. Pitz is working on three main areas of research. His independent research program is evaluating the role of the androgen pathway in lung cancer. This work includes pharmaco-epidemiological research into the association between medications affecting the sex hormone pathways and outcomes in lung cancer as well as an ongoing systematic review and an investigator initiated clinical trial of finasteride in lung cancer.

He was the Study Chair in a recently completed clinical trial of a novel PI3-kinase inhibitor in patients with recurrent glioblastoma, run through the National Cancer Institute of Canada – Clinical Trials Group. He is working to develop more therapeutic trials in his role in the Brain Disease Site Committee and Investigational New Drug Committee through that group. He also runs two investigator-initiated clinical trials through his breast cancer clinic at CancerCare Manitoba evaluating physical therapy and acupuncture as treatment modalities for chemotherapy-induced peripheral neuropathy.

As Chief Medical Information Officer at CancerCare Manitoba, Dr. Pitz is also funded to evaluate the role of mobile devices in the clinical environment as a way to improve care and improve the discrete data captured in the electronic health record. He continues to work on improving data capture in all Disease Sites at CancerCare Manitoba and is pursuing the development of a Pan-Canadian Brain Tumour Clinical Database.

Selected Publications:

1. Harlos CH, Musto G, **Pitz MW**. Androgen pathway manipulation and survival in patients with lung cancer. Hormones and Cancer. 2015 Jun;6(2-3):120-7. doi: 10.1007/s12672-015-0218-1. Epub 2015 Mar 20.
2. **Pitz MW**, Eisenhauer EA, MacNeil EA, Thiessen B, Easaw JC, Macdonald DR, Eisenstat DD, Kakumanu AS, Salim M, Chalchal H, Squire J, Tsao MS, Kamel-Reid S, Banerji S, Tu D, Powers J, Hausman DF, Mason WP. Phase II study of PX-866 in recurrent glioblastoma. Neuro-Oncology 2015 Jan 20; doi: 10.1093/neuonc/nou365
3. Beiggi S, Johnston JB, Seftel MD, **Pitz MW**, Kumar R, Banerji V, Griffith EJ, Gibson SB. Increased risk of second malignancies in chronic lymphocytic leukaemia patients as compared with follicular lymphoma patients: a Canadian population-based study. Br J Cancer. 2013 Sep 3;109(5):1287-90. doi: 10.1038/bjc.2013.381. Epub 2013 Jul 16.
4. Lother SA, Harding GA, Musto G, **Pitz MW**. Anti-Estrogen Use and Survival of Women with Non-Small-Cell Lung Cancer in Manitoba, Canada. Horm Cancer. 2013 Oct;4(5):270-6. doi: 10.1007/s12672-013-0149-7. Epub 2013 May 29.
5. **Pitz MW**, Musto G, Navaratnam SN. Sex as an independent prognostic factor in a population-based non-small cell lung cancer cohort. Canadian Respiratory Journal 2013;20(1):30-34.
6. **Pitz MW**, Lipson M, Hosseini B, Guilbert K, Lister D, Huszar S, Schroeder G, Jones K,Mihalcioiu C, Eisenstat DD. Extended duration adjuvant temozolomide with cis-retinoic acid for adult glioblastoma. Current Oncology 2012;19(6):308-314.
7. **Pitz MW**, Desai A, Grossman SA, Blakeley JO. Tissue concentration of systemically administered antineoplastic agents in human brain tumors. Journal of Neuro-Oncology 2011;104(3):629-638.

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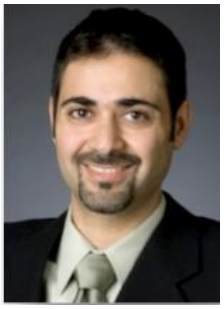

Dr. Afshin Raouf holds an academic appointment as an assistant professor in the Department of Immunology as well he is a senior scientist at the Research Institute in Oncology and Hematology (RIOH) in CancerCare Manitoba and is a member of the Regenerative Medicine Program at the Faculty of Health Sciences, University of Manitoba. He received an Hons. B.Sc. in Pharmacology and Toxicology from the University of Toronto in 1992. In 1996 he joined the Ph.D. training program at the same university where he made seminal contributions toward elucidating the molecular determinants of osteoblast differentiation and bone development. He then pursued his postdoctoral training in 2002 at the B.C. Cancer agency, Terry Fox Laboratories, in the field of normal and cancer stem cell biology. During this time he was able to demonstrate, for the first time, that primitive human breast cells can be isolated at near 50% purity. Using this purity, he was able to elucidate a new role for the Notch 3 receptor in determining the luminal cell fate.

In 2009, Dr. Raouf moved to CancerCare Manitoba to establish a research program that is focused on the application of the cancer stem cell concept to the development of new and more effective cancer therapeutics and diagnosis. He is a member of a number of international research societies and serves as a grant panel reviewer for the Canadian Health Research Institute, Canadian Cancer Research Institute, Canadian Breast Cancer Foundation and Manitoba Health Research Institute. As well, Dr. Raouf serves as ad hoc reviewer for a number of scientific journals such as Cell Stem cells and PLos Biology.

Dr. Raouf's overall research objective is to apply the cancer stem cell concept to translation research. Recent research efforts have demonstrated that tumors are initiated and maintained by a small subpopulation of cells with stem cell properties. Therefore, understanding the unique biology of these cells and their relationship to the normal primitive cells is of extreme interest towards the identification of new diagnostic markers to diagnose cancer at an early premalignant stage. As well, knowledge about the biology of cancer stem cells provides a framework to discover new therapies to specifically eliminate these rare but biologically relevant cells.
He is the author of over 52 journal article, abstracts, and presentations and has received national and international awards for his research.

Dr. Raouf's laboratory utilizes the mammary gland as a model system and his research activities are focused on 3 major themes:

1. Identify primitive cell programs that regulate the normal functions of the mammary stem and progenitor cells.
2. Establish how the inappropriate execution of these programs causes the normal stem and progenitor cells to acquire a cancer stem cell phenotype.
3. Examine how this information can be leveraged to develop new diagnostic markers as well as new therapies against breast cancer stem cells.

Selected Publications:

1. Basak P, Chatterjee S, Weger S, Bruce MC, Murphy LC, **Raouf A**, Estrogen regulates luminal porgenitors through H19 gene. Endocr Relat Cancer, 2015 22(4):505-17. Epub 2015 May 5
2. Chatterjee S, Laliberte M, Blellock S, Ratanshi I, Safneck J, Buchel E, **Raouf A**, Adipose-derived stromal vascular fraction differentially expands breast progenitors in tissue adjacent to tumors compared to the healthy breast tissue. Plast Reconstr Surg., 2015 136(4):414e-25e
3. Basak P, Dillon R, Leslie H, **Raouf A**, Mowat MR, The deleted in liver cancer 1 9Dlc1) tumor suppressor is haploinsufficient for mammary gland development and epithelial cell polarity. BMC Cancer, 2015 9(15):630, PMID: 26353792
4. Chatterjee S, Bacopulos S, Yang W, Amemiya Y, Spyropolous D, **Raouf A**, Seth A. Plos One 2014, 9(2):e87858 (Raouf and Seth are co-senior authors but Raouf is the corresponding)
5. Bautista W, Perez-Alvarez V, Burczynski F, **Raouf A**, Klonich T, Minuk G., Membrane potential differences and GABAA receptor expression in hepatic tumor and non-tumor stem cells. 2014, 92(1):85-91. Epub 2013 Nov 1
6. **Raouf A**, Sun YJ., In vitro methods to culture primary human breast epithelial cells. Methods Mol Biol. 2013, 946:363-81, PMID: 24383877
7. **Raouf A**, Sun Y, Chatterjee S, Basak P. The biology of human breast epithelial progenitors. Semin Cell Dev Biol. 2012 Jul;23(5):606-12. Epub 2012 May 17.
8. **Raouf A**. Basal-like breast cancers: the phenotypic disparity between the cancer-initiating cells and tumor histology. Breast Cancer Res. 2010;12(6):316. Epub 2010 Dec 16.
9. To K., Fotovati A., Reipas K.M., Law J.H., Hu K., Wang J., Astanehe A., Davies A.H., Lee L., Stratford A.L., **Raouf A**., Johnson P., Berquin I.M., Royer H.D., Eaves C.J., and Dunn S.E. (2010) YB-1 induces expression of CD44 and CD49f leading to enhanced self-renewal, mammosphere growth and drug resistance. Cancer Research 70(7), 2840-2851.

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Dr. Mojgan Rastegar received her PhD and DEA (Diplôme d'Etudes Approfondies) from the Université Catholique de Louvain (UCL) Brussels, Belgium; and her MSc and BSc from Tehran University of Medical Sciences, and Tehran University, Tehran, Iran. Her first post-doctoral training was in the area of Epigenetic Control of Multi-Drug Resistance in Breast Cancer and Leukemia which was done in Indiana University Cancer Center, IUPUI, IN, USA. In Canada, Dr. Rastegar further studied the Regulatory role of Epigenetics and Chromatin Remodelling in Stem Cell Differentiation, Mammalian Development, and Brain Disorders in McGill University in Montreal, Quebec with Professor Mark Featherstone; and Hospital for Sick Children, Toronto, Ontario with Professor James Ellis. Dr. Rastegar is currently an Associate Professor in the Department of Biochemistry and Medical Genetics, and a member of the Regenerative Medicine Program at the University of Manitoba. She serves as an editor of Frontiers in Genetics (Epigenetics) and reviewer of Acta Neuropathologica, Journal of Biological Chemistry, PLOS ONE, Molecular Pathology, Molecular cancer, and Current Genomics among others. She serves as a provincial, national and international grant reviews and has served on provincial and national review panels. Her lab applies molecular and stem cell biology techniques along with gene therapy strategies to investigate the underlying pathobiology of human disease. Dr. Rastegar research is focused on the epigenetic control of cell fate determination in stem cells and how deregulation of such processes cause human disease and cancer. Since joining the University of Manitoba in 2009, she has published 16 peer-reviewed original research and review articles, 3 book chapters; and over 60 international, national and provincial-local abstracts and oral presentations. Dr. Rastegar has been actively involved in mentoring and instructing trainees and students at all levels, including high school students, basic science undergraduate, graduate and medical students, and her research program has been continuously supported by national (NSERC, CIHR, CFI, SRCFC) and provincial funding.

Selected Publications:

1. Liyanage VRB, Zachariah RM, Davie JR, and **Rastegar M**. Ethanol Deregulate MeCP2 *via* Interplay Between 5-methylcytosine and 5-hydroxymethylcytosine at its Regulatory Elements During Neural Stem Cell Differentiation. **Experimental Neurology 2015**; *265 102-117. Doi: 10.1016/j.expneurol.2015.01.006.*
2. Olson CO, Zachariah RM, Ezeonwuka CD, Liyanage VRB, and **Rastegar M.** Brain Region-Specific Expression of MeCP2 Isoforms Correlates with DNA Methylation within *Mecp2* Regulatory Elements. **PLOS ONE 2014**; 9(3) 1-16: e90645. Doi: 10.1371/journal.pone.0090645
3. Liyanage VRB, Jarmasz J, Murugeshan N, Del Bigio MR, **Rastegar M**, and Davie JR. DNA Modifications: Function and Applications in Normal and Disease States. **Biology**. **2014**; 22;3(4):670-723. Doi: 10.3390/biology3040670.
4. Yasui DH, Aflatooni AO, Gonzales ML, Hu DJ, Gavino BJ, Golub MS, Vincent JB, Schanen NC, Olson CO, **Rastegar M,** and LaSalle JM. Mice with an Isoform-ablating *Mecp2*-exon 1 Mutation Recapitulates the Neurologic Deficits of Rett syndrome. **Human Molecular Genetics 2014;** 23(9):2447-58. Doi: 10.1093/hmg/ddt640.
5. Liyanage VRB, Zachariah RM, and **Rastegar M**. Decitabine Alters the Expression of *Mecp2* Isoforms *via* Dynamic DNA Methylation at the *Mecp2* Regulatory Elements in Neural Stem Cells. **Molecular Autism 2013**; 4:46. 1-21. Doi:10.1186/2040-2392-4-46
6. Sandhu S, Wu X, Nabi Z, **Rastegar M,** Kung S, Mai S, and Ding H. Loss of HLTF Promotes Intestinal Carcingogenesis. **Molecular Cancer 2012**; 27; 11(1): 18: 1-16.
7. Ellis J, Hotta A, and **Rastegar M.** Retrovirus silencing by an epigenetic TRIM. **Cell 2007;** 131(1), 13-14
8. **Rastegar M**, Kobrossy L, Nagy Kovàcs E, Rambaldi I, and Featherstone M. Sequential histone modifications at *Hoxd4* regulatory regions distinguish anterior from posterior embryonic compartments. **Molecular and Cellular Biology 2004**; 24: 8090-8103
9. Gordon J, Wu CH, **Rastegar M**, and Safa AR. *ß*2-microglobulin induces caspase-dependent apoptosis in CCRF-HBS-2 human leukemia cell line independently of caspase-3, -8, and -9 pathways but through increased reactive oxygen species. **International Journal of Cancer 2003**; 103: 316-327
10. Wu CH, Gordon J, **Rastegar M**, Ogretmen B, and Safa AR. Proteinase-3, a serine protease which mediates doxorubicin-induced apoptosis in the HL-60 leukemia cell line is down-regulated in its doxorubicin-resistant variant. **Oncogene 2002**; 21: 5160-5174
11. Wu CH, **Rastegar M**, Gordon J, and Safa AR. *ß*2-microglobulin induces apoptosis in HL-60 human leukemia cells and its multidrug resistant variants overexpressing MRP1 but lacking Bax or overexpressing P- glycoprotein. **Oncogene 2001**; 25: 7006-7020
12. **Rastegar M**, Rousseau GG, and Lemaigre FP. CCAAT/Enhancer Binding Protein alpha (C/EBP α) is a mediator of growth hormone action in the liver and controls the expression of Hepatocyte Nuclear Factor-6 (HNF-6). **Endocrinology 2000**; 141: 1686-92
13. **Rastegar M**, Szpirer C, Rousseau GG, and Lemaigre FP. Hepatocyte nuclear factor 6: organization and chromosomal assignment of the rat gene and characterization of its promoter. **Biochemical Journal 1998**; 334: 565-569

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Dr. Schacter is a Professor in the Department of Internal Medicine of the University of Manitoba and member of the Department of Medical Oncology and Hematology at CancerCare Manitoba. He practices Malignant Hematology at CancerCare Manitoba. He was the Chief Executive Officer of the Canadian Association of Provincial Cancer Agencies (CAPCA) from 2003 until 2008. Preceding that, he was the President and Chief Executive Officer of CancerCare Manitoba in Winnipeg from January 1993 to August 2003. For over 20 years, he was a Senior Scientist in the Manitoba Institute of Cell Biology, which is the basic research arm of CancerCare Manitoba. In his research role he published over 70 scientific papers and has participated in over 35 invited and guest lectureships. He was a member of the Board of the National Cancer Institute of Canada (NCIC) from 2000 until 2007. He was a member of the NCIC/CCS Steering Committee for Canadian Cancer Statistics from 2001 to 2008.

He was a member and then co-chair of the Steering Committee of the Canadian Strategy for Cancer Control (CSCC) from 1999 to 2002 and co-Vice-Chair of the Council for the Canadian Strategy for Cancer Control from 2004 to 2006. As the Canadian Partnership Against Cancer was being formed, he was a member of the Provisional Board of CPAC from December 2006 to April 2007, chair of the Standards Action Group of CSCC/CPAC from its inception to its dissolution in 2008, and a member of the CPAC Action Council and Advisory Councils during that period of time. He was a member of the Health Human Resources Action Group of CPAC and Chaired the HHRAG Service Delivery Models Project, He co-chairs the Canadian AYA Task Force which is funded by CPAC/C17.

Dr. Schacter was the principal investigator on a program grant from the Canadian Institutes of Health Research-Institute of Cancer Research to further support and sustain the Canadian Tumour Repository Network (CTRNet) (www.ctrnet.ca).

Selected Publications:

1. Albert M, Bartlett J, Johnston RN, **Schacter B**, Watson P. Biobank bootstrapping: is biobank sustainability possible through cost recovery? Biopreserv Biobank. 2014 Dec;12(6):374-80. doi: 10.1089/bio.2014.0051. PMID: 25496148
2. Barnes RO, **Schacter B**, Kodeeswaran S, CTRNET Management Committee, Watson PH. Funding Sources for Canadian Biorepositories: The Role of User Fees and Strategies to Help Fill the Gap. Biopreserv Biobank. 2014 Oct;12(5):300-5. doi: 10.1089/bio.2014.0052. Epub 2014 Oct 14. PMID: 25314324
3. Matzke L, Dee S, Bartlett J, Damaraju S, Graham K, Johnston R, Mes-Masson AM, Murphy L, Shepherd L, **Schacter B**, Watson PH. A Practical Tool for Modeling Biospecimen User Fees. Biopreserv Biobank. 2014 Aug;12(4):234-9. doi: 10.1089/bio.2014.0008. PMID: 25162459
4. Watson PH, Nussbeck SY, Carter C, O'Donoghue S, Cheah S, Matzke LA, Barnes RO, Bartlett J, Carpenter J, Grizzle WE, Johnston RN, Mes-Masson AM, Murphy L, Sexton K, Shepherd L, Simeon-Dubach D, Zeps N, **Schacter B**. A Framework for Biobank Sustainability. Biopreserv Biobank. 2014 Feb;12(1):60-8. doi: 10.1089/bio.2013.0064. PMID: 24620771
5. Barnes R, Albert M, Damaraju S, de Sousa-Hitzler J, Kodeeswaran S, Mes-Masson AM, Watson P, **Schacter B**. Generating a Comprehensive Set of Standard Operating Procedures for a Biorepository Network-The CTRNet Experience. Biopreserv Biobank. 2013 Dec;11(6):387-96. doi: 10.1089/bio.2013.0061. Epub 2013 Nov 22. PMID: 24835369
6. Rogers PC, De Pauw S, **Schacter B**, Barr RD. A Process for Change in the Care of Adolescents and Young Adults with Cancer in Canada. "Moving to Action": The Second Canadian International Workshop. International Perspectives on AYAO, Part 1. J Adolesc Young Adult Oncol. 2013 Jun;2(2):72-76. PMID: 23781404
7. Matzke EA, O'Donoghue S, Barnes RO, Daudt H, Cheah S, Suggitt A, Bartlett J, Damaraju S, Johnston R, Murphy L, Shepherd L, Mes-Masson AM, **Schacter B**, Watson PH. Certification for biobanks: the program developed by the Canadian Tumor Repository Network (CTRNet). Biopreserv Biobank. 2012 Oct;10(5):426-32. doi: 10.1089/bio.2012.0026. PMID: 24845043
8. Meir K, Gaffney EF, Simeon-Dubach D, Ravid R, Watson PH, **Schacter B**, Morente And The Marble Arch International Working Group on Biobanking MM. The Human Face of Biobank Networks for Translational Research. Biopreserv Biobank. 2011 Sep;9(3):279-85. doi: 10.1089/bio.2011.0018. PMID: 24850340
9. Ramphal R, Meyer R, **Schacter B**, Rogers P, Pinkerton R. Active therapy and models of care for adolescents and young adults with cancer. Cancer. 2011 May 15;117(10 Suppl):2316-22. doi: 10.1002/cncr.26048. PMID: 21523752
10. Fernandez C, Fraser GA, Freeman C, Grunfeld E, Gupta A, Mery LS, De Pauw S, **Schacter B**. Principles and Recommendations for the Provision of Healthcare in Canada to Adolescent and Young Adult-Aged Cancer Patients and Survivors. J Adolesc Young Adult Oncol. 2011 Apr;1(1):53-59. PMID: 23610731

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Dr. Alberto Severini obtained his medical degree from the University of Parma, Italy, and did his research training in biochemistry and molecular virology at the University of Alberta. He is currently the Chief of the Viral exanthemata and STD Section at the National Microbiology Laboratory, Public Health Agency of Canada. His laboratory conducts surveillance and reference activities for Human Papilloma and Polyoma Viruses, Herpesviruses, Chlamydia, Measles, Mumps and Rubella. Dr. Severini is on the editorial board of the Journal of Clinical Microbiology and of Antimicrobial Agents and Chemotherapy. His current research interests include molecular epidemiology of human papillomaviruses, mechanism of HPV carcinogenesis, herpesvirus genomics and measles molecular genetics. Dr. Severini's laboratory has developed and implemented a number of molecular tests for viral detection and genotyping, especially for HPV, which were used in a number of molecular epidemiology studies.

Molecular epidemiology of infectious agents is a powerful surveillance tool to map the spreading of infectious diseases. In addition, sequence comparison allows the identification of pathogenesis determinants and of risk factors, for example, the identification of high risk HPV types and their role in the causation of genital and extragenital malignancies. Sequencing analysis has also been instrumental in the investigation and diagnosis of antiviral and antibacterial drug resistance. Using molecular epidemiology techniques, we collaborated in a number of studies aimed at predicting HPV vaccine effectiveness in Canada and internationally. We also have studied the association of specific HPV variants with heightened risk of malignant transformation. We are now getting involved in HPV post-vaccine evaluation to see the effect of the HPV vaccine on the 4 covered types and the remaining HPV types.

We have also participated in numerous genomics studies on herpes simplex virus, Varicella-zooster viruses and simian simplexviruses. In depth genomic analysis has uncovered frequent recombination between HSV strains, with implications for diagnostics and epidemiology. We routinely genotype measles, rubella and mumps viruses as part of our duties as a WHO Regional Reference Laboratory for measles and rubella. In particular our lab, in collaboration with the NML's DNA and Bioinformatics core labs, specializes in whole genome sequencing and extended sequencing for measles.

In summary, we have developed a considerable capacity and know-how for pathogen sequence analysis and we continue leading and contributing to numerous studies aimed at the epidemiology and risk factors associated with infectious agents.

Selected Publications: (total citations 1,410; H-index 20)

1. Berard AR, **Severini A** and Coombs KM (2015) Differential reovirus-specific and herpesvirus-specific AP-1 activation of secretogranin II leads to altered virus secretion, J Virol (in press) JVI01639-15R2
2. Berard AR, Coombs KM, **Severini A.** (2015) Quantification of the host response proteome after herpes simplex virus type 1 infection. J Proteome Res. 14:2121-42
3. Maar M, Wakewich P, Wood B, **Severini A**, Little J, Burchell AN, Ogilvie G, Zehbe I. (2014) Strategies for Increasing Cervical Cancer Screening Amongst First Nations Communities in Northwest Ontario, Canada. Health Care Women Int. 6:1-18.
4. Jelen MM, et al. (2014) Global genomic diversity of human papillomavirus type 6 (HPV6) based on 724 isolates and 190 complete genome sequences. J Virol. 88:7307-7316
5. Jiang Y, Brassard P, **Severini A**, Chatwood S, Mao Y, Laroche JA, Chatwood S., Corriveau A, Kandola K, Hanley B, Sobol I, Ar-Rusdi M, Johnson G, Lo J, Ratnam S, Wong T, Demers A, Jayaraman G, Morrison H (2013) The Prevalence of Human Papillomavirus and Its Impact on Cervical Dysplasia in Northern Canada Infect Agent Cancer. 8:25.
6. Hosein F, Mohammed W, Zubach V, Legall G, **Severini A**. (2013) Human papillomavirus genotypes in invasive cervical squamous cell carcinoma in Trinidad. Rev Panam Salud Publica. 233:267–70.
7. **Severini A**, D. Tyler SD, Peters GA, Black D and Eberle R (2013) Genome Sequence of a Chimpanzee Herpesvirus and Its Relation to Other Primate Alpha-Herpesviruses. Arch Virol 158:1825-8.
8. **Severini A**, Jiang Y, Brassard P, Morrison H, Oguntuase E, Ar-Rushdi M, Preston F, Ratnam S, Jiang D and Mao Y (2013) Type-specific prevalence of Human Papillomavirus in women screened for cervical cancer in Labrador, Canada. Int J Circumpolar Health. 72:19743.
9. Berard AR, Cortens JP, Krokhin O, Wilkins JA, **Severini A**, Coombs KM. (2012) Quantification of the Host Response Proteome after Mammalian T1L Reovirus Infection. PloS One. 7:e51939
10. Zubach V, Smart G, Ratnam S and **Severini A** (2012) A Novel Microsphere-Based Method for the Detection and Typing of 46 Mucosal Human Papillomavirus Types, J Clin Microbiol. 50:460-464.
11. Norberg P, Tyler S, **Severini A**, Whitley R, Liljeqvist J and Bergstrom T (2011) A complete genome based comparative evolutionary analysis of herpes simplex virus type 1 and varicella zoster virus. PloS One. 6:e22527.

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Dr. Anuraag Shrivastav, PhD

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Dr. Anuraag Shrivastav is an Associate Professor at the Department of Biology, University of Winnipeg and Adjunct Professor at the Department of Biochemistry and Medical Genetics, University of Manitoba. He obtained his PhD from Banaras Hindu University, India and moved to Saskatchewan Cancer Agency and Department of Pathology, University of Saskatchewan, Canada to pursue postdoctoral training. He was awarded CIHR postdoctoral fellowship in 2004 to investigate the role of myristoylation in colorectal cancer.

Dr. Shrivastav's research program is dedicated to understanding alterations in signalling pathways leading to onset and progression of cancer. Cellular signalling mechanisms are intricately linked to homeostasis through events that control cell proliferation, survival and death. Aberrations in some of these mechanisms are often associated with oncogenic processes, which provide insights into the mechanisms that drive development and progression of different cancers. These may also lead to identification of novel biomarkers and potential targets of therapy. Because the evolution of cancer specific therapeutics is intricately linked to the understanding of the unique pathways involved in different cancers, Dr. Shrivastav laboratory is devoted to the study of cell signalling pathways linked to the onset and progression of colorectal cancer, prostate cancer and breast cancer. Member proteins of signalling pathways undergo various protein modifications that alter the signalling pathway. One such modification is myristoylation of proteins. Dr. Shrivastav's laboratory is especially interested in studying role of N-myristoyltransferase enzyme (NMT) in alteration of signalling pathways. The NMT enzyme catalyzes myristoylation of number of proteins involved in cancer onset, progression and pathogenesis.

Dr. Shrivastav in collaboration with Drs. Harminder Singh and Charles Bernstein of Health Sciences Centre, Winnipeg, is developing a simple cost effective highly sensitive and specific blood test for the screening of colorectal cancer.

In breast cancer area, Dr. Shrivastav in collaboration with Dr. Leigh Murphy is studying alterations of mitogenic pathways in estrogen receptor positive breast cancer, which may lead to discovery of novel prognostic/predictive biomarkers.
In collaboration with Drs. Arbind Dubey and Darryl Drachenberg, Dr. Shrivastav's team is investigating mechanistic interaction between Androgen Receptor, Mechanistic Target of Rapamycin and N-myristoyltransferase in prostate cancer.
Dr. Shrivastav holds number of patents on biomarkers and clinical studies are in progress to aid in commercialization of screening/predictive tests.

Patents:

U.S. Patent Number: 7,892,758 and three other patent applications are in process.

Selected Publications:

1. **Shrivastav A**, Seelkallu S, Troup S, Penner C, Nugent Z, Watson P, Murphy L. The Mammalian Target for Rapamycin Pathway is Related to the Phosphorylation Score (P7) for Estrogen Receptor-□ in Human Breast Tumors, in vivo. *Breast Cancer Research,* 2014 May 22;16 (3):R49. [Epub ahead of print].
2. **Shrivastav A**, Murphy L. Involvement of PI-3K/Akt/mTOR signalling in the activation of estrogen receptor in breast cancer. *Breast Cancer Management*, 2012;1;235-249.
3. **Shrivastav A,** Varma S, Senger A, Khandelwal RL, Carlsen, S, Sharma RK. Overexpression of Akt modulates N-myristoyltransferase activity. *Journal of Pathology*, 2009; 218:391-8.
4. **Shrivastav A**, Varma S, Lawman Z, Yang SH, Ritchie SA, Bonham K, Sharma RK. Requirement of N-myristoyltransferase in monocytic differentiation. *J. Immunol.* 2008;180:1019-1028.

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Dr. Pawan Singal, PhD, DSc

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Dr. Pawan Singal is a professor of Physiology and is Director of the Institute of Cardiovascular Sciences, St. Boniface Hospital and the University of Manitoba, Winnipeg, Canada. Dr. Singal completed his PhD in Physiology in 1974 from the University of Alberta. After three years in Saskatoon, Canada, as a Post-Doctoral Fellow of the Medical Research Council, Dr. Singal joined the Physiology Department at the University of Manitoba as a lecturer, rose through the ranks and has been a professor since 1990. He received DSc degree in 1994 in Cardiovascular Pathophysiology. He served as Associate Dean for the Faculty of Graduate Studies, University of Manitoba. Dr. Singal is also holder of the Naranjan S. Dhalla Chair established by the St. Boniface Hospital & Research Foundation.

Internationally known for his work on oxidative stress and heart failure, Dr. Singal has made significant contributions in our understanding of the role of cytokines in the sequeale of heart failure due to doxorubicin, chronic pressure overload as well as myocardial infarction. Dr. Singal is considered a pioneer and a world leader in the study of the role of oxygen radicals and oxidative stress in the pathogenesis of heart dysfunction and heart failure. Continuing with his pursuit, Dr. Singal has edited 30 books and monographs on different aspects of heart disease. He has a Citation Index of > 9000 and H-index 50. Dr. Singal has mainly used three different models of heart failure described below:

A) Oxidative Stress in Doxorubicin-induced Cardiomyopathy: The Therapeutic Potential of Combination Therapy with Antioxidants: Dr. Singal has researched and extensively published on Doxorubicin-induced heart failure. In a total of more than 265 papers published by Dr. Singal, more than 80 papers are focussed on this heart failure. He showed that this cardiomyopathy and heart failure are associated with an increase in myocardial oxidative stress. He reported that this was due to a molecular defect both in the production and activity of glutathione peroxidase – an enzyme responsible for the detoxification of oxidative stress. With this new understanding, Dr. Singal was able to completely prevent this cardiomyopathy and heart failure. These ground-breaking findings were summarized by Dr. Singal in his two papers published in the *New England Journal of Medicine* (1998, 1999) – one of these papers has been cited more than 900 times.

B) Endogenous Antioxidants as Putative Stabilizers of Cardiac Function in:

I. *Oxidative Stress in Heart Hypertrophy and Failure:* Dr. Singal was the first to discover that there is an increase in the endogenous antioxidant enzyme activities and a decrease in oxidative stress in hyperfunctional hypertrophied hearts and the converse was true in heart failure. For an *in vivo* testing of his hypothesis, Dr. Singal developed an animal model of hypertrophy and heart failure where these two stages of function are spatially separated by several weeks.

II. *Oxidative Stress Subsequent to Myocardial Infarction:* Using an animal model, Dr. Singal documented that heart failure subsequent to myocardial infarction was associated with an increase in oxidative stress and a decrease in antioxidants.

Selected Publications:

1. Akolkar, G., Bhullar. N., Bews. H., Shaikh. B., Premecz. S., Bordun. K.A., Cheung, D.Y., Goyal. V., Sharma. A.K., Garber. P., **Singal. P.K.**, Jassal. D.S. The role of renin angiotensin system antagonists in the prevention of Doxorubicin and Trastuzumab induced cardiotoxicity. Cardiovas.Ultraso. 13:18-28, 2015.
2. Bagchi, A.K., Sharma, A.K., Dhingra, S., Lüdke, A., Al-Shudiefat, A.A. and **Singal, P.K.** Interleukin-10 activates toll-like receptor 4 and requires MyD88 for the cardiomyocytes survival. Cytokine. 61: 304-314, 2013.
3. Dhingra, S., Sharma, A.K. Arora, R.C., Slezak, J. and **Singal, P.K.** IL-10 attenuates TNF-α-induced NFκB pathway activation and cardiomyocyte apoptosis. Cardiovas. Res. 82: 59-66, 2009.
4. Kaur, K., Sharma, A.K., and **Singal, P.K.** Significance of changes in TNF-α and IL-10 levels in the progression of heart failure subsequent to myocardial infarction. Am. J. Physiol., 291: 106-113, 2006.
5. Khaper, N. and **Singal, P.K.** Modulation of oxidative stress by a selective inhibition of angiotensin II type 1 receptors in MI-rats. J. Am. Coll. Cardiol. 37: 1461-1466, 2001.
6. Li, T. and Singal, P.K. Adriamycin-induced early changes in myocardial antioxidant enzymes and their modulation by probucol. Circulation. 102: 2105-2110, 2000.
7. **Singal, P.K.** and Iliskovic, N. Doxorubicin-induced cardiomyopathy. N. Engl. J. Med. 339: 900-905, 1998.

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Dr. Harminder Singh, MBBS, MD, MPH, FRCPC

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Dr. Harminder Singh received his MBBS and MD from All India Institute of Medical Sciences and MPH from the University of Manitoba. He received training in gastroenterology, gastrointestinal oncology and health outcomes research at University of Manitoba. He is currently an Associate Professor of Medicine and a member of the medical staff, Department of Medical Oncology and Hematology, CancerCare Manitoba. He is a member of the Canadian Task Force on Preventive Health Care, an organization developing and disseminating clinical practice guidelines for primary care. He is also a member of the University of Manitoba IBD Clinical and Research Centre. He is a clinician scientist, epidemiologist and practicing gastroenterologist.

Dr. Singh's research interests have been varied and include prevention and screening for cancers, clinical epidemiology, pharmaco-epidemiology and health services research. He is currently leading knowledge translation studies to improve processes around colonoscopy, an essential test to diagnosis colorectal cancer. His research group continues work on epidemiology and prevention of colorectal cancer, as well as IBD epidemiology and health care outcomes.

Selected Publications:

1. Dickinson J, Shane A, Tonelli M, Connor Gorber S, Joffres M, **Singh H**, Bell NR. Trends in prostate cancer incidence and mortality in Canada during the era of PSA screening. CMAJ Open 2015 (in press).
2. Decker KM, Demers AA, Nugent Z, Biswanger N, **Singh H**. Longitudinal rates of colon cancer screening use in Winnipeg, Canada: the experience of a universal health care system with an organized colon screening program. American Journal of Gastroenterology 2015 (in press).
3. Cisyk AL , Penner-Goeke S, Lichtensztejn Z, Nugent Z, Wightman RH, **Singh H**, McManus KJ. Characterizing the Prevalence of Chromosome Instability in Interval Colorectal Cancer. Neoplasia 2015 (in press).
4. **Singh H**, Bernstein C, Samadder N J, Ahmed R. Screening for Colorectal Cancer in Canada: a Cross-sectional study. CMAJ open April 8, 2015 vol. 3 no. 2 E149-E157
5. **Singh H**, Nugent Z, Demers AA, Czaykowski P, Mahmud SM. Risk of Colorectal Cancer after Diagnosis of Endometrial Cancers: A Population-Based Study. J Clin Oncol. 2013 Jun 1;31(16):2010-5.
6. **Singh H**, Bay D, Ip S, Bernstein C, Nugent Z, Gheorghe R, Wightman R. Pathological reassessment of hyperplastic colonic polyps in a city wide pathology practice: Implications for polyp surveillance recommendations. Gastrointest Endosc. 2012 Nov;76(5):1003-8
7. **Singh H**, Nugent, Z., Demers, A., Mahmud, S. and Bernstein, C. Exposure to bisphosphonates and risk of colorectal cancer. Cancer. 2012 Mar 1;118(5):1236-43.
8. **Singh H**, Nugent Z, Demers AA, Bernstein CN. Risk of Non-Melanoma Skin Cancer among individuals with Inflammatory Bowel Disease: A population-based study. Gastroenterology. 2011 Nov;141(5):1612-20.
9. **Singh H**, Nugent Z, Demers AA, Bernstein CN. Rate and predictors of early/missed colorectal cancers after colonoscopy in Manitoba: A population-based study. Am J Gastroenterol. 2010 Dec;105(12):2588-96.
10. **Singh H**, Nugent Z, Demers AA, Kliewer EV, Mahmud SM, Bernstein CN. The reduction in colorectal cancer mortality after colonoscopy varies by site of the cancer. Gastroenterology. 2010 Oct;139(4): 1128-1137.
11. **Singh H**, Nugent Z, Mahmud SM, Demers AA, Bernstein CN. Predictors of Colorectal Cancer after Negative Colonoscopy: A population-based study. Am J Gastroenterol. 2010 Mar;105(3):663-73.
12. **Singh H**, Mahmud SM, Turner D, Xue L, Demers A, Bernstein CN. Long term use of Statins and Risk of Colorectal Cancer: a Population- based Study. Am J Gastroenterol. 2009 Dec;104(12):3015-23.
13. **Singh H**, Demers AA, Nugent Z, Mahmud SM, Kliewer EV, Bernstein CN. Risk of cervical abnormalities in women with IBD: A population-based nested case-control study. Gastroenterology. 2009 Feb;136(2):451-8. Epub 2008 Oct 15.
14. **Singh H**, Demers AA, Xue L, Turner D, Bernstein CN. Time Trends in Colon Cancer Incidence and Distribution and Lower Gastrointestinal Endoscopy Utilization in Manitoba. Am J Gastroenterol. 2008 May;103(5):1249-56.
15. **Singh H**, Turner D, Xue L, Targownik LE, Bernstein CN. Risk of developing colorectal cancer following a negative colonoscopy examination: evidence for a 10-year interval between colonoscopies. JAMA. 2006 May 24;295(20):2366-73

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Geoffrey K. Tranmer, Ph.D., joined the College of Pharmacy as an Assistant Professor in July 2013. He has a B.Sc. (Hons.) degree from Brock University in Chemistry and a Doctor of Philosophy degree from the University of Guelph, specializing in Organic Chemistry. Following post-doctoral studies at Princeton University, he received an NSERC post-doctoral fellowship and continued his studies at the University of Cambridge under the supervision of Prof. Steven V. Ley, CBE, FRS, examining the application of new technologies in organic synthesis. His first industrial role was as a Senior Research Chemist at Merck Frosst in Montreal as a member of the Technology Enabled Synthesis group, integrating the application of automated synthesis and purification into medicinal chemistry programs. Following subsequent employment at McMaster University as the Synthesis and NMR Lab Manager in the Centre for Microbial Chemical Biology, and research at the Centre for Probe Development and Commercialization, he has accepted an appointment as Assistant Professor in the College of Pharmacy, with specialization in Medicinal Chemistry. His research interests are focused on the application of innovative technologies in the field of organic synthesis as applied to medicinal chemistry and new strategies for targeted cancer therapies. Specifically, he is interested in developing novel flow chemistry techniques that will aim at enhancing current synthetic organic methodologies, and focus on lead generation and optimization in drug discovery, while simultaneously focusing on the development of novel targeted cancer therapies, with particular focus on hypoxia. He has co-authored 21 papers in peer-reviewed international journals, and has been named as co-inventor on 6 published patent applications.

To date, synthetic organic chemistry has already had a significant impact on the fields of medicinal chemistry and cancer, with major advancements being applied towards development of new pharmaceutical therapies and for the study and manipulation of biological systems. Prof. Tranmer is a synthetic organic chemist by training, with industrial experience developing pre-clinical drug candidates and imaging agents. His area of research interest is centered within the broad field of medicinal chemistry, at the intersection of synthetic organic chemistry and pharmacology, and focused on understanding the state of hypoxia in cancer, developing targeting cancer therapies, and the imaging of hypoxia. Prof. Tranmer's research interests are largely focused on these main themes, and have an end goal of improving the process of drug discovery and facilitating innovation in drug discovery research.

"Geoff Tranmer, PhD – Taking the "ick" out of Organic Synthesis since 1998"

Selected Publications: (total citations 805; H-index 14)

1. Manansala, C.; **Tranmer, G. K.** Flow synthesis of 2-methylpyridines via α-methylation. *Molecules*, **2015**, 15797 – 15806.
2. Gverzdys, T.; Hart, M. K., Pimentel-Elardo, S.; Tranmer, G. K.; Nodwell, J. R. 13-Deoxytetrodecamycin, a new tetronate ring-containing antibiotic that is active against multi-drug-resistant *Staphyloccoccus aureus*. *J. Antibiot.*, **2015**, doi: 10.1038/ja.2015.60.
3. Bao, J.; **Tranmer, G. K.** The utilization of copper flow reactors in organic synthesis. *Chem. Commun.* **2015**, 3037-3044.
4. Lachance, N.; Gareau, Y.; Guiral, S.; Huang, Z.; Isabel, E.; Leclerc, J. P.; Leger, S.; Martins, E.; Nadeau, C.; Oballa, R. M.; Ouellet, S. G.; Powell, D. A.; Ramtohul, Y. K.; **Tranmer, G. K.**; Trinh, T.; Wang, H.; Zhang, Z. Discovery of potent and liver-targeted stearoyl-CoA desaturase (SCD) inhibitors in a bispyrrolidine series. *Bioorg. Med. Chem. Lett.* **2012**, *22*(2), 980 – 984.
5. Gauthier, J.; Belley, M.; Deschenes, D.; Fournier, J-F.; Gagne, S.; Gareau, Y.; Hamel, M.; Henault, M.; Hyjazie, H.; Kargman, S.; Lavallee, G.; Levesque, J-F.; Li, L.; Mamane, Y.; Morin, N.; Mancini, J.; Mulrooney, E.; Robichaud, J.; Therien, M.; **Tranmer, G. K.**; Wang, Z.; Wu, J.; Black, W. C. The identification of 4,7-disubstituted naphthoic acid derivatives as UDP-competitive antagonists of P2Y14. *Bioorg. Med. Chem. Lett.* **2011**, *21*(10), 2836 – 2839.
6. Guay, D.; Beaulieu, C.; Belley, M.; Crane, S.; DeLuca, J.; Gareau, Y.; Hamel, M.; Henault, M.; Hyjazie, H.; Kargman, S.; Chan, C. C.; Xu, L.; Gordon, R.; Li, L.; Mamane, Y.; Morin, N.; Mancini, J.; Therien, M.; **Tranmer, G. K.**; Truong, V. L.; Wang, Z.; Black, W. C. Synthesis and SAR of pyrimidine-based, non-nucleotide P2Y14 receptor antagonists. *Bioorg. Med. Chem. Lett.* **2011**, *21*(10), 2832 – 2835.
7. Fortin, R.; Lachance, N.; Li, C. S.; **Tranmer, G.** Preparation of novel spiro compounds useful as inhibitors of stearoyl-CoA delta-9 desaturase. *PCT Int. appl.* **2011**, pp. 77, WO 2011047481.
8. Powell, D.; **Tranmer, G. K.** Preparation of azetidine derivatives as inhibitors of stearoyl-coenzyme A delta-9 desaturase. *PCT Int. appl.* **2010**, pp. 55, WO 2010043052.

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Dr. Triggs-Raine received her B.Sc. and Ph.D. degrees from the University of Manitoba. Her post-doctoral training in the molecular basis of human genetic disease was done in the lab of Dr. Roy Gravel at The Hospital for Sick Children in Toronto and the McGill University-Montreal Children's Hospital Research Institute. Dr. Triggs-Raine is presently Associate Head and Professor in the Department of Biochemistry and Medical Genetics and cross-appointed in the Department of Pediatrics and Child Health at the University of Manitoba. She serves on the Chair of the Research Advisory Committee for Research Manitoba and is a member of the Board for Research Manitoba, the Board of the Children's Hospital Research Institute of Manitoba, and as a member of the CancerCare Manitoba Foundation's Program Grants and Awards Committee. Her research interests focus on the molecular basis of human disease and in particular on genome alterations that impact the metabolism of hyaluronan. She has studied mouse models with deficiencies in enzymes that break down hyaluronan and humans with disorders of hyaluronan degradation. More recently she has extended her work to include studies of the impact of hyaluronan levels on cancer resistance.

Hyaluronan is a large sugar that is present in the matrix that surrounds all cells in vertebrates. The interest in hyaluronan's role in conferring cancer resistance comes from studies of the naked mole rat. This rodent lives for approximately 30 years, and unlike other rodents, it does not get cancer. Studies by others to determine what conferred this cancer resistance to the naked mole rat led to the identification of very large-sized and abundant hyaluronan as a key feature. Interestingly, if a hyaluronan degrading enzyme called hyaluronidase 2 was used to remove the large-sized hyaluronan, it destroyed the cancer resistance of the naked mole rat cells. This led to the idea that hyaluronidase 2 could be a target for the prevention of cancer because its inhibition could lead to increased size and levels of hyaluronan.

Dr. Triggs-Raine's research laboratory has developed and utilized various tools to understand how hyaluronan is degraded and she is now applying these to determine if hyaluronidase 2 is a target for cancer prevention. Their program has three research themes designed to determine if hyaluronidase 2 is a target for cancer prevention: **i)** to determine if removing hyaluronidase 2 activity leads to increased size and levels of hyaluronan; **ii)** to determine if the removal of hyaluronidase 2 activity poses any health risk, and **iii)** to determine if the removal of hyaluronidase 2 activity alters the incidence or severity of basal cell carcinoma. All of this will be done using a mouse model deficient in the enzyme hyaluronidase 2.

Selected Publications:

1. **Triggs-Raine B**, Natowicz MR. Biology of hyaluronan: Insights from genetic disorders of hyaluronan metabolism. World J Biol Chem. 2015 Aug 26;6(3):110-20 PMID: 26322170
2. Feng D, Su RC, Zou L, **Triggs-Raine B**, Huang S, Xie J. Increase of a group of PTC(+) transcripts by curcumin through inhibition of the NMD pathway. Biochim Biophys Acta. 2015 Aug;1849(8):1104-15. PMID 25934542
3. Armistead J, Patel N, Wu X, Hemming R, Chowdhury B, Basra GS, Del Bigio MR, Ding H, **Triggs-Raine B**. Growth arrest in the ribosomopathy, Bowen-Conradi syndrome, is due to dramatically reduced cell proliferation and a defect in mitotic progression. Biochim Biophys Acta. 2015 May;1852(5):1029-37. PMID 25708872
4. Walia JS, Altaleb N, Bello A, Kruck C, LaFave MC, Varshney GK, Burgess SM, Chowdhury B, Hurlbut D, Hemming R, Kobinger GP, **Triggs-Raine B**. Long-term correction of Sandhoff disease following intravenous delivery of rAAV9 to mouse neonates. Mol Ther. 2014: 23(3):414-22. PMID: 25515709
5. Chowdhury B, Hemming R, Hombach-Klonisch S, Flamion B, **Triggs-Raine B**. Murine hyaluronidase 2 deficiency results in extracellular hyaluronan accumulation and severe cardiopulmonary dysfunction. J Biol Chem. 2013 Jan 4;288(1):520-8 PMID: 23172227
6. Gushulak L, Hemming R, Martin D, Seyrantepe V, Pshezhetsky A, **Triggs-Raine B**. Hyaluronidase 1 and β-hexosaminidase have redundant functions in hyaluronan and chondroitin sulfate degradation. J Biol Chem. 2012 May 11;287(20):16689-97. PMID: 22451654
7. Imundo L, Leduc CA, Guha S, Brown M, Perino G, Gushulak L, **Triggs-Raine B**, Chung WK. A complete deficiency of Hyaluronoglucosaminidase 1 (HYAL1) presenting as familial juvenile idiopathic arthritis. J Inherit Metab Dis. 2011 Oct;34(5):1013-22. PMID 21559944
8. Chatel A, Hemming R, Hobert J, Natowicz MR, **Triggs-Raine B**, Merz DC. The C. elegans hyaluronidase: a developmentally significant enzyme with chondroitin-degrading activity at both acidic and neutral pH. Matrix Biol. 2010 Jul;29(6):494-502 PMID 20576486

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Donna Turner is the Provincial Director of the Population Oncology portfolio at CancerCare Manitoba; she is also an Associate Professor in the Department of Community Health Sciences at the University of Manitoba. The Population Oncology portfolio consists of several programs including: Epidemiology, the Manitoba Cancer Registry, Screening Programs (Breast, Cervical and Colorectal) and Aboriginal Services.

Her path to this position began with training at the University of Victoria in Health Information Science (BSc 1988), followed by graduate work in epidemiology and oncology from the Universities of Calgary (MSc 1991) and Alberta (PhD 1997) and a postdoctoral fellowship at the Manitoba Centre for Health Policy. She further developed her interest in cancer epidemiology by working at two Canadian cancer agencies (the Alberta Cancer Board and CancerCare Manitoba).

As a result of these experiences, her research interests revolve around the use of population-based cancer registry data, particularly record linkage using cancer registries and administrative e data (information collected as part of the management of health care insurance plans or employment) as a means of informing cancer control activities. Her current position allows her to work in various aspects of cancer control research – from prevention/etiology to early detection to diagnosis/treatment to outcomes – using the population-based data resources of the provincial health department and the cancer agency in Manitoba.

Selected Publications:

1. Zakaria D, Trudeau R, Sanmartin C, Murison P, Carrière G, MacIntyre M, **Turner D**, Wagar B, King MJ, Vriends K, Woods R, Lockwood G, Louchini R. Using personal health insurance numbers to link the Canadian Cancer Registry and the Discharge Abstract Database. Health Rep. 2015 Jun 17;26(6):3-11. PMID: 26086334
2. Demers AA, Decker KM, Kliewer EV, Musto G, Shu E, Biswanger N, Fradette K, Elias B, Griffith J, **Turner D**. Mammography rates for breast cance r screening: a comparison of First Nations women and all other women living in Manitoba, Canada, 1999-2008. Prev Chronic Dis. 2015 May 28;12:E82. doi: 10.5888/pcd12.140571. PMID: 26020546
3. Decker K , Demers A , Kliewer E , Musto G , Shu E , Biswanger N , Elias B , Griffith J , **Turner D**. Colorectal cancer screening in First Nations people living in Manitoba. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 24(1): 241-8. DOI: 1055-9965. Cancer Epidemiol Biomarkers Prev; 24(1); 241–8. ©2014 AACR
4. McKay A, Donaleshen J, Helewa RM, Park J, Wirtzfeld D, Hochman D, Singh H, **Turner D**. Does young age influence the prognosis of colorectal cancer: a population-based analysis. World J Surg Oncol. 2014 Dec 2;12:370. doi: 10.1186/1477-7819-12-370. PMID: 25466394
5. Weir HK, Johnson CJ, Mariotto AB, **Turner D**, Wilson RJ, Nishri D, Ward KC. Evaluation of North American Association of Central Cancer Registries' (NAACCR) data for use in population-based cancer survival studies. J Natl Cancer Inst Monogr. 2014 Nov;2014(49):198-209. doi: 10.1093/jncimonographs/lgu018. PMID: 25417233
6. Decker KM, Demers AA, Kliewer EV, Biswanger N, Musto G, Elias B, Griffith J, **Turner D**. Pap test use and cervical cancer incidence in First Nations women living in Manitoba. Cancer Prev Res (Phila). 2015 Jan;8(1):49-55. doi: 10.1158/1940-6207.CAPR-14-0277. Epub 2014 Nov 17. PMID: 25403849
7. Decker KM, Demers AA, Kliewer EV, Musto G, Shu E, Biswanger N, Elias B, Griffith J, **Turner D**. Colorectal cancer screening in first nations people living in Manitoba. Cancer Epidemiol Biomarkers Prev. 2015 Jan;24(1):241-8. doi: 10.1158/1055-9965.EPI-14-1008. Epub 2014 Oct 21. PMID: 25336562
8. Weir HK, Johnson CJ, Mariotto AB, **Turner D**, Wilson RJ, Nishri D, Ward KC. Evaluation of North American Association of Central Cancer Registries' (NAACCR) Data for Use in Population-Based Cancer Survival Studies. J Natl Cancer Inst Monogr. 2014 Nov;2014(49):198-209. doi: 10.1093/jncimonographs/lgu018.
9. Clouston K, Katz A, Martens P, Sisler J, **Turner D**, Lobchuk M, McClement S, Crow G, et al. Does access to a colorectal cancer screening website and/or a nurse-managed telephone help line provided to patients by their family physician increase fecal occult blood test uptake?: Results from a pragmatic cluster randomized controlled trial. BMC Cancer. 2014; 14: 263. Published online 2014 April 16. doi: 10.1186/1471-2407-14-263 PMCID: PMC4023547
10. Elias B, Kliewer E, Hall M, Demers A, **Turner D**, Martens P, Hong S, Hart L, Chartrand C, Munro G . Pap test use and cervical cancer incidence in First Nations women living in Manitoba. Cancer Prevention Research, CAPR-14-0277. 2014 Nov 17. pii: canprevres.0277.2014. [Epub ahead of print]

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Dr. Issai Vanan is a Physician-Scientist and a Pediatric Neuro-Oncologist at RIOH / CCMB. Dr. Vanan received his basic medical education in India (BMC / PGIMER). He completed his Pediatric Hem-Onc and Pediatric Neuro-Oncology fellowships in New York (CCMCNY). His main research interests are in translational Neuro-Oncology with special emphasis on Radiation and Chemotherapy sensitization of Pediatric Brain tumors, Developmental Neurobiology as related to Brain tumors and Novel Neuro therapeutics (including BBB permeability and novel drug delivery methods). He is a PJ McKenna St Baldrick's Cancer research scholar and his research is also supported by CCMF, MMSF, HSCF and CCRS.

Radiation is an integral part of the therapeutic armamentarium in Pediatric Neuro-Oncology. The therapeutic benefits of radiotherapy are, however, accompanied by late toxicity that severely affects quality of life in children; deleterious effects include neurocognitive deficits, developmental problems and secondary malignancies in the majority of survivors (>90%). Identifying new approaches that would allow reduction of the total radiation dose in these treatments without compromising therapeutic efficacy is critical for improving tumor management and quality of life. Dr. Vanan's lab has identified several potential targets that mediate radiation and chemotherapy resistance in pediatric brain tumors. Validation of these targets using patient derived xenografts (PDX) in orthotopic murine brain tumor models will provide us with novel radio-sensitization drugs with larger therapeutic window; when used with current treatment protocols, this may lead to low dose therapeutic radiation and less long term side effects in survivors of childhood brain tumors.

Selected Publications (2014-2015):

1. Liang L, Aiken C, McClelland R, Morrison LC, Tatari N, Remke M, Ramaswamy V, **Issaivanan M** et.al. Characterization of novel biomarkers in selecting for subtype specific medulloblastoma phenotypes. Oncotarget. 2015 Oct 20. doi: 10.18632/oncotarget.6195. [Epub ahead of print]
2. Markowitz D, Powell C, Tran N, **Issaivanan M**, He M, Al-Abed Y, et.al. Pharmacological inhibition of the protein kinase MRK /ZAK radiosensitizes medulloblastoma (accepted). Molecular Cancer Therapeutics.
3. Miller IS, Didier S, Murray DW, Turner TH, **Issaivanan M**, Ruggieri R, Al-Abed Y, Symons M, "Semapimod sensitizes Glioblastoma tumors to ionizing radiation by targeting microglia", PLOS ONE 2014;9(5):e95885.
4. **Vanan MI**, Eisenstat DD (2015). DIPG in children-what can we learn from the past? Front. Oncol. 5:237. doi: 10.3389/fonc.2015.00237.
5. Woodgate RL, Tailor K, Yanofsky R, **Vanan MI**. Childhood brain cancer and its psychosocial impact on survivors and their parents: A qualitative thematic synthesis. Eur J Oncol Nurs. 2015 Jul 16. pii: S1462-3889(15)30012-0. doi: 10.1016/j.ejon.2015.07.004. [Epub ahead of print].
6. **Issaivanan M**, Mehta V, Eisenstat D. Diffuse Intrinsic Pontine Glioma, Pediatric Neuro-Oncology, Eds- Bouffet E, Scheinemann K, 1st Edition (2015).
7. **Issaivanan M**, Mehta V, Eisenstat D. High Grade Gliomas, Pediatric Neuro-Oncology, Eds- Bouffet E, Scheinemann K, 1st Edition (2015).
8. **Vanan MI**, Eisenstat DD. "Management of High Grade Gliomas in the Pediatric patient: (past), present and the future", Neuro-Oncology Practice 2014; 1(4):145-157.

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Dr. Werbowetski-Ogilvie received her HBSc of Science in Biology at the University Western Ontario in 2000. She completed her PhD in the Department of Neurology & Neurosurgery, Montreal Neurological Institute, McGill University in 2005. Dr. Werbowetski-Ogilvie completed her postdoctoral training at McMaster University in the area of human embryonic stem cells in 2010 under the supervision of Dr. Mick Bhatia following which she joined the University of Manitoba as a principal investigator in the Department of Biochemistry & Medical Genetics and the Regenerative Medicine Program in November, 2010. Werbowetski-Ogilvie currently holds a Tier II Canada Research Chair in Neuro-oncology and Human Stem Cells.

Central nervous system (CNS) tumors are among the most prevalent forms of childhood cancers accounting for nearly 20% of all new cases (Canadian Cancer Society Statistics, 2015). Medulloblastoma (MB) is the most common malignant primary pediatric brain tumor and is currently divided into 4 distinct molecular subtypes: WNT, SHH, Group 3 and Group 4. Extensive genetic, molecular and clinical heterogeneity between these subgroups has made it difficult to assess the functional relevance of genes to tumor progression.

The Werbowetski-Ogilvie lab employs high throughput flow cytometry-based screening platforms to identify and subsequently characterize novel roles for cell surface markers in regulating diverse medulloblastoma phenotypes both *in vitro* and *in vivo*. Utilizing a wide variety of functional assays including measures of self-renewal, differentiation, invasion and proliferation *in vitro* as well as tumor growth *in vivo* using xenograft models, the lab is currently investigating the role of CD271, also known as p75 neurotrophin receptor (p75NTR) or nerve growth factor receptor (NGFR), in regulating stem cell properties of SHH variant medulloblastoma cells.

In addition, the lab utilizes neural derivatives from human embryonic stem cells (hESCs) as a model system to study the mechanisms contributing to pediatric brain tumorigenesis. Using this powerful cell resource as both a complement to and surrogate for existing cell lines and heterogeneous patient samples, the goal is to better understand how genes such as the transcription factor orthodenticle homeobox 2 (OTX2) regulate the balance between self-renewal and differentiation to either prevent or sustain oncogenic properties.

Peer reviewed publication (last 5 years):

1. Kaur R, Coudière Morrison L, Aiken C, Rao R, Del Bigio MR, Rampalli S, **Werbowetski-Ogilvie TE**. 2015. OTX2 exhibits cell context-dependent effects on cellular and molecular properties of human embryonic neural precursors and medulloblastoma cells. **Disease Models & Mechanisms., Aug 6. pii: dmm.020594.**
2. Ali, JL, Lagasse BJ, Minuk AJ, Love AJ, Arthur G, Gibson SB, Coudière Morrison L, **Werbowetski-Ogilvie TE**, Fu Y, Nachtigal MW. 2015. Differential cellular responses induced by dorsomorphin and LDN-193189 in chemotherapy-sensitive and –resistant human epithelial ovarian cancer cells. ***International Journal of Cancer*, 136(5): E455-69.**
3. Coudière Morrison M *, McClelland R *, Aiken C, Bridges M, Wang X, Del Bigio MR, Taylor MD, **Werbowetski-Ogilvie TE.** 2013. Deconstruction of medulloblastoma cellular heterogeneity reveals differences between the most highly invasive and self-renewing phenotypes. ***Neoplasia,* 15(4): 384-398.**
4. Lee JB, **Werbowetski-Ogilvie TE**, Lee JH, McIntyre BAS, Schnerch A, Hong SH, Park IH, Daley GQ, Bernstein ID, Bhatia M. 2013. Notch-HES1 signaling axis controls hemato-endothelial fate decisions of human embryonic and induced pluripotent cells. ***Blood*, 122(7): 1162-1173.**
5. **Werbowetski-Ogilvie TE***, Coudière Morrison L, Fiebig-Comyn A, Bhatia M*. 2012. In vivo generation of neural tumors from neoplastic pluripotent stem cells models early human pediatric brain tumor formation. *Stem Cells*. 30(3): 392-404. * Denotes co-corresponding authorship.
6. **Werbowetski-Ogilvie TE**, Schnerch A, Rampalli S, Lee JB, Levadoux-Martin M, Mills CE, Bhatia M. 2011. Evidence for the transmission of neoplastic properties from transformed to normal human stem cells. *Oncogene,* 30(46): 4632-44.

Reviews and Book Chapters (last 5 years):

7. **Werbowetski-Ogilvie TE**. 2015. Using cell surface signatures to dissect neoplastic neural cell heterogeneity. Upcoming textbook entitled, Neural Surface Antigens: From Basic Biology Towards Biomedical Applications. Elsevier Press, Editor: Jan Pruszak. In press.
8. McClelland R, **Werbowetski-Ogilvie TE**. 2014: Human embryonic stem cells and disease modeling. Chapter 4. Cancer Stem Cells. Wiley Press, Editor: VJ Rajasekhar
9. Aiken C, **Werbowetski-Ogilvie TE**. 2013. Animal Models of Cancer Stem Cells: What are they really telling us? *Current Pathobiology Reports. 1(2):91-99.*

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Dr. Jeffrey Wigle received his B.Sc.(H) degree in Biochemistry from Queen's University and his PhD in Pharmacology from the University of Ottawa under the supervision of Dr. Balwant Tuana. He moved to St. Jude Children's Research Hospital in Memphis, TN for his postdoctoral studies under the mentorship of Dr. Guillermo Oliver. His PDF studies were on the developmental biology of the lymphatic system. Dr. Wigle is an Associate Professor in the Department of Biochemistry and Medical Genetics at the University of Manitoba and a Principal Investigator at the Institute of Cardiovascular Sciences. He is an associate editor of the Canadian Journal of Physiology and serves on the editorial board of the journal Molecular and Cellular Biochemistry. He has served as a Scientific Office and member on CIHR, HSF and AHA peer review Committees. Dr. Wigle's research program is focused on the induction and maintenance of cardiovascular cell phenotypes by transcription factors.

The lymphatic vasculature is a thin-walled, permeable system that functions to re-absorb protein rich extracellular fluid and returns this fluid to the circulatory system. Disruption of the lymphatic vasculature results in the accumulation of extracellular fluid and leads to diseases known as lymphedemas. Primary lymphedemas arise from a genetic cause and can vary in their onset and severity. In Canada, secondary lymphedema is a common, painful side effect that occurs when lymphatic nodes and vessels are destroyed during breast cancer therapy. In cancer, metastatic cells can enter the lymphatic circulation and escape the site of the original tumour. The degree of lymphatic vascularization has been correlated in both animal models and human studies with the tendency of tumour cells to spread.

Meox1/Meox2 are homeobox genes that are expressed early in the developing embryo. Meox2 (also known as Gax) was shown to be downregulated at both the mRNA and protein levels when vascular smooth muscle cells (VSMCs) are stimulated to proliferate with growth factors. Over expression of Meox2 protein halts VSMC growth by blocking proliferation and inducing cell death (apoptosis). In vivo, these effects lead to decreased vessel blockage (restenosis) in rodent models of balloon angioplasty. Recently, Meox2 expression was shown to be decreased in endothelial cells derived from blood vessels of Alzheimer disease patients and was required to maintain the ability of the endothelial cells to grow. Increased Meox2 expression has also been associated with diseases of accelerated ageing. In cell culture, Meox2 induces premature ageing (senescence) of cells. These genes are also potentially important in the control of the conversion of a cell from a fibroblast to a myofibroblast and are a target of the Zeb2 transcription factor, a positive regulator of epithelial to mesenchymal transition (EMT).

Selected Publications:

1. Cunnington, R.H., Northcott, J.M, Bathe, K.L, Jahan, F., Kavosh,M., Davies, J., **Wigle, J.T.**, and Dixon, I.M.C. The Ski/Zeb2/Meox2 pathway provides a novel mechanism for regulation of cardiac myofibroblast phenotype. Journal of Cell Science Cell Sci. 127:40-9, 2014.
2. Northcott, J.M., Yeganeh, A., Taylor, C.G., Zahradka, P., **Wigle, J.T.** Adipokines and the cardiovascular system: mechanisms mediating health and disease. Can. J. Physiol. and Pharm. 90(8):1029-5, 2012.
3. Douville, J.M., Cheung, D.Y., Herbert, K.L., Moffatt,T., and **Wigle, J.T.** Mechanisms of MEOX1 and MEOX2 regulation of the cyclin dependent kinase inhibitors p21CIP1/WAF1 and p16INK4a in vascular endothelial cells. PLoS One 6(12):e29099, 2011.
4. Baxter,S.A., Bocangel,P., Cheung,D.Y., Kim,H.K., Zhang, S., Douville, J.M., Jangamreddy, J., Herbert,K., Eisenstat,D.D., and **Wigle, J.T.** Regulation of the lymphatic endothelial cell cycle by the PROX1 homeodomain protein. Biochim Biophys Acta. 1813:201-12, 2011.
5. **Wigle, J.T.** and Oliver, G. Prox1 function is required for the development of the murine lymphatic system. Cell 98: 769-778, 1999
6. **Wigle, J.T.**, Chowdhury, K., Gruss, P., and Oliver, G. Prox1 function is crucial for mouse lens-fibre elongation. Nature Genetics 21: 318-322, 1999

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Dr. Roberta Woodgate's background is in pediatric nursing. In 2001, she received a Doctor of Philosophy from the University of Manitoba. Her PhD was interdisciplinary with a focus in the fields of sociology, psychology, and nursing. Dr. Woodgate is presently a Professor of Child Health and Illness at the University of Manitoba and a Research Scientist at the Children's Hospital Research Institute of Manitoba.

She has developed a strong foundation of research on children's (including adolescents) perspectives and experiences of health and illness that has contributed to advancing the improvement of health service delivery for Canada's children. The vision for her research program is to advance and translate pertinent knowledge regarding the experiences of children with complex care needs and conditions (CCNC) in order to design interventions that improves access and quality of health and related services, and quality of life for those children. Children with CCNC are those with multiple chronic physical and mental illnesses and disabilities, who require multiple services, from a variety of sectors, often at multiple locations. Children with CCNC include children living with cancer.

Improving health outcomes and the well-being of children living with cancer and their families requires a multilayered approach that addresses not only the deficits in health care management and the need for health and social services integration and system innovation, but also an approach that engages children living with cancer and their families to identify solutions to meet their complex care needs. Patient-engagement is the cornerstone of Dr. Woodgate's research program and participants in her research projects have described a sense of empowerment from their involvement. Engaging children living with cancer and their families in the research that affects them is fundamental to improving the delivery of health care services for them and key to developing effective interventions grounded in their experiences.

Dr. Woodgate has engaged children living with cancer and their families in studies that have yielded information about the challenges faced by them, their psychosocial and physical needs and coping behaviours, and how we can best support them throughout the cancer trajectory. The many challenging experiences faced by children impact how they feel. Dr. Woodgate's work with children with cancer challenged notions of how they conceptualized their health showing that while they have the capacity to articulate their feelings and needs, they may be unable to do so using traditional scales. Accordingly, Dr. Woodgate developed a prototype of an innovative psychosocial intervention to be used by children with cancer to help them understand, express, and manage how they feel during the course of their illness. With input from children, she created an interactive online virtual world called EMÜD (pronounced emood) that offers self-assessment of feelings and creative activities to help express those feelings (e.g., writing stories, drawing, creating music). Dr. Woodgate plans to test and evaluate the use of EMÜD with children with cancer.

Dr. Woodgate will also begin a new three-year CIHR funded research project, titled *The Journey for survivors of childhood brain tumours: From post-treatment into adulthood*. The project will explore the experiences and needs of survivors of childhood brain tumours and their families from five years post-treatment and into adolescence and adulthood. To better meet this group's needs, this research provides survivors of childhood brain tumours and their families the opportunity to describe, in their own words, what it's like to live with and manage the late-effects associated with survival. This project will integrate arts-based participatory methods of research allowing survivors of childhood brain tumours and their families to express their experiences of diagnoses, treatment, and remission in ways that standard research interviews do not. Ultimately, Dr. Woodgate would like for the project's outcomes to include the development of care interventions and support systems that reflect survivors' experiences of treatment, healing, and remission in ways that can better support incoming patients.

Other Research: Dr. Woodgate also studies children's understanding of cancer and cancer risk with the aim to inform and improve primary cancer prevention programmes and policies.

Selected Publications related to Children's Experiences with Cancer and Cancer Prevention:

1. **Woodgate, R. L.**, Tailor, K., Yanofsky, R., & Vanan, M. (In Press). Childhood brain cancer and its psychosocial impact on survivors and their parents: A qualitative thematic synthesis. European Journal of Oncology Nursing (2015), 1-10 pages.
2. **Woodgate, R. L.**, Safipour, J., & Tailor, K. (2014). Canadian adolescents' perspectives of cancer risks: A qualitative study. *Health Promotion International, 30(3)*684-694.
3. **Woodgate, R. L.**, West, C., & Tailor, K. (2014). Existential anxiety and growth: An exploration of computerized drawings and perspectives of children and adolescents with cancer. *Cancer Nursing, 37*(2), 146-159.
4. **Woodgate, R. L.** & Kreklewetz, C. (2012). "Youth's narratives about family members smoking: Parenting the parent- it's not fair!" *BMC Public Health,12*, 965 (13 pages). doi: 10.1186/1471-2458-12-965.

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Dr. Xie is currently Professor of Physiology & Pathophysiology at the College of Medicine, Faculty of Health Sciences, University of Manitoba. He graduated with a B.Sc. in Biology from Wuhan University in 1988 and with a Ph.D. in Genetics from the Peking Union Medical College & Chinese Academy of Medical Sciences in 1995. He then went to Cornell University in Ithaca, New York, and later to the Howard Hughes Medical Institute at the University of California, Los Angeles (UCLA) for postdoctoral trainings in neuroscience and molecular biology. He has been a faculty member in the Department of Physiology, University of Manitoba since 2003.

Dr. Xie's research interests has been on the control of alternative pre-mRNA splicing in cell function and diseases.

Alternative splicing is a common way of gene regulation that allows the generation of multiple mRNA and often protein isoforms from a single gene. Almost all human gene transcripts are alternatively spliced and some are known to generate extremely diverse protein isoforms. This greatly contributes to the proteomic complexity, particularly in neurons and endocrine cells. In experimental animals, genetic deficiencies in alternative splicing factors result in developmental defects or embryonic-lethal phenotypes. In humans, aberrant splicing accounts for the defect of about 30% of genetic mutations that cause diseases. However, it remains largely unclear how alternative splicing is controlled, particularly by cellular signals. With complex splicing patterns, widespread presence but unclear regulatory mechanisms, alternative splicing and its regulation in cell function and diseases pose a tremendous challenge in the post-genome era.

In Dr. Xie's lab, they study the regulation of alternative splicing by extracellular factors. Besides the signaling pathway they have delineated from cell membrane to the splicing regulatory elements/factors in neuroendocrine cells, their work has recently led to the identification in the human genome of a large group of genes that are related to cancer (*Sohail, et al, BMC Genomics'14*). These genes share splicing regulatory G tracts at the end of certain introns upstream of alternative exons. They have shown that one of the gene *PRMT5* evolved the G tracts in mammals and produces a novel shorter splice variant with an opposite effect on cell cycle from its original isoform (*Sohail, et al., MCB'15*). They are interested in collaboration with clinical cancer researchers on the distribution and role of these splice variants in the development and progression of cancers, as well as transcriptome-wide identification of stage-specific splice variants in cancer tissues.

Selected Publications:

1. Sohail, M., **Xie, J**. Diverse regulation of 3' splice site usage. Cell. Mol. Life Sci. (CMLS), 2015, DOI:10.1007/s00018-015-2037-5.
2. Sohail M., and **Xie, J**. Evolutionary emergence of a novel splice variant with an opposite effect on cell cycle. Molecular & Cellular Biology, 2015, 35(12): 2203-2214.
3. Sohail M., Cao, W.G., Mahmood, N., Myschyshyn, M., Hong, S.P., **Xie, J**. Evolutionarily emerged G tracts between the polypyrimidine tract and 3' AG are splicing silencers enriched in genes involved in cancer. BMC Genomics, 2014, 15:1143.
4. **Xie J**. Differential evolution of signal-responsive RNA elements and upstream factors that control alternative splicing. Cell. Mol. Life Sci. (CMLS), 2014, 71(22):4347-4360.
5. Feng D, and **Xie, J**. Aberrant splicing in neurological diseases. Wiley Inter-disciplinary Reviews (WIREs): RNA, 2013, 4:631-649.
6. Cao WG, Razanau, A., Feng, D.R., Lobo, V.G. and **Xie, J**. Control of alternative splicing by forskolin through hnRNP K during neuronal differentiation. Nucleic Acids Res. 2012, 40(16) 8059–8071.
7. Liu GD, Razanau, A., Hai, Y., Yu, J.K., Sohail, M., Lobo, VG, Chu, JY, Kung, S.K.P. and **Xie, J**. A conserved serine of hnRNP L mediates depolarization-regulated alternative splicing of potassium channels. J. Biol. Chem. 2012, 287:22709–22716.
8. Yu JK, Hai, Y., Liu, G.D., Fang, T.L., Kung, S.K.P., **Xie, J**. The heterogeneous nuclear ribonucleoprotein L is an essential component in the Ca++/calmodulin-dependent protein kinase IV-regulated alternative splicing through cytidine-adenosine repeats. J. Biol. Chem. 2009, 284:1505-1513.
9. Hai, Y., Cao, W.G., Liu, G.D., Hong, S., Abou Elela, S., Klinck, R., Chu, J.Y., **Xie, J**. A G-tract element in apoptotic agents-induced alternative splicing. Nucleic Acids Res. 2008, 36(10):3320-3331.

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Dr. Wayne Xu received his Ph.D. degree from the Nanjing Agricultural University in China. His post-doctoral training in the area of molecular biology and immunology was done at the University of Manitoba. He received his B.Sc in Computer Science from the University of Manitoba. Dr. Xu applies computer science into biology and genomics, and has worked as a Computational Genomics Specialist in the University of Minnesota, USA, for 10 years. Dr. Xu is presently a Senior Scientist in the Research Institute of Oncology and Hematology (RIOH) of CancerCare Manitoba, an Assistant Professor in the Department of Biochemistry and Medical Genetics, and Adjunct Professor in the College of Pharmacy at the University of Manitoba. His research focuses on cancer biomarker signatures development, especially the Yin Yang gene expression mean ratio (YMR) signature modeled around patient prognosis. Dr Xu has received Manitoba Medical Service Foundation (MMSF) to test YMR in lung cancer and Canadian Breast Cancer Foundation (CBCF) research funding for Breast cancer to test it in breast cancer. He currently collaborates with Dr Jim Davie, Dr. Leigh Murphy, and Dr. Shantanu Banerji.

Dr. Xu's research program has three research themes: **i)** To develop cancer gene signatures based on the Yin and Yang gene expression ratio (YMR). **ii)** To understand the pathways behind signatures' association with clinical outcome. **iii)** To modulate the Yin Yang gene expression ratio balance for new drug discovery. Dr. Xu hypothesized that two opposing effects, called Yin and Yang, determine the fate of cancer cell growth, thereby the cancer patients' prognosis. The expression of Yang genes dominates in normal cells compared to malignant cells (down-regulated in cancer), whereas Yin gene expression is greater in cancer cells (up-regulated in cancer) compared to normal cells. The Yin over Yang ratio of expression indicates the malignant potential of the cells, with a higher ratio more predictive of poor survival outcome. Dr. Xu has proofed his hypothesis using lung cancer data sets. He recently developed a 16-gene breast cancer YMR signature which can stratify breast cancer patients into four different risk levels. He is modeling the pathway that determines the four levels of tumor progression defined by YMR scores. The modeling will include the four risk group stratification, correlation of signature gene expression in each group, machine learning for connection edge enhancement or removal.

Selected Publications:

1. Davie JR, **Xu W**, Delcuve GP. Histone H3K4 trimethylation: dynamic interplay with pre-mRNA splicing. Biochem Cell Biol. 2015 Jul 15:1-11. PMID: 26352678
2. Skubitz KM, Skubitz AP, **Xu W**, Luo X, Lagarde P, Coindre JM, and Chibon F (2014). Gene expression identifies heterogeneity of metastatic behavior among high-grade non-translocation associated soft tissue sarcomas. J Transl Med. 2014 12:176.
3. **Xu W**, Banerji S, Davie JR, Kassie F, Yee D, Kratzke R (2013) Yin Yang gene expression ratio signature for lung cancer prognosis. PLoS One, 2013, 8(7): e68742
4. Lamont EA, **Xu W**, Sreevatsan S (2013). Host-Mycobacterium avium subsp. paratuberculosis interactome reveals a novel iron assimilation mechanism linked to nitric oxide stress during early infection. BMC Genomics. 2013, 14(1):694.
5. Li L, Petsch K, Shimizu R, Liu S, **Xu W**, Ying K, Yu J, Scanlon M, Schnable P, Timmermans M, Springer N, Muehlbauer G. (2012) Mendelian and non-Mendelian regulation of gene expression in the maize shoot apex. PLoS Genetics, 2013, 9(1):e1003202 (Impact factor =9.543).
6. Waters AJ, Makarevitch I, Eichten SR, Swanson-Wagner RA, Yeh CT, **Xu W**, Schnable PS, Vaughn MW, Gehring M, Springer NM. (2011) Parent-of-origin effects on gene expression and DNA methylation in the maize endosperm. Plant Cell, 2011, 23(12):4221-33. (Impact factor =9.396).
7. Yang SS, Tu Z, Cheung F, **Xu W**, Lamb JFS, Jung HJG, Vance CP, Gronwald JW (2011) Using RNA-Seq for gene identification, polymorphism detection and transcript profiling in two alfalfa genotypes with divergent cell wall composition in stems. BMC Genomics 2011, 12(1):199. P1-75 (Impact factor = 3.76).
8. Yang SS, **Xu W**, Tesfaye M, Lamb JF, Jung HJ, VandenBosch KA, Vance CP, Gronwald JW (2010) Transcript profiling of two alfalfa genotypes with contrasting cell wall composition in stems using a cross-species platform: optimizing analysis by masking biased probes. BMC Genomics, 11:323, p1-18. (Impact factor = 3.76).
9. **Xu W**, Carter CJ (2010) Parallel multiplicity and error discovery rate (EDR) in microarray experiments. BMC Bioinformatics. 2010, 11(1):465, p1-12.
10. **Xu W**, Cho S, Yang SS, Bolon YT, Bilgic H, Jia H, Xiong Y, Muehlbauer G (2009) Single-feature polymorphism discovery by computing probe affinity shape powers, BMC Genetics 10:48, p1-14. (Impact factor = 2.23).

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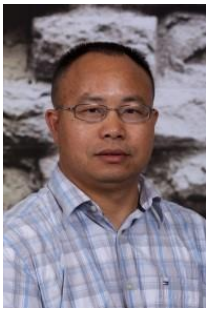

Dr. Xibiao Ye received his medical training and graduate degrees in public health and epidemiology in China and postdoctoral training at the National Institute of Environmental Health Sciences, the National Institutes of Health, USA. Dr. Ye is currently Epidemiologist at the George and Fay Yee Center for Healthcare Innovation, Assistant Professor, Department of Community Health Sciences, College of Medicine, and Research Scientist, Children's Hospital Research Institute of Manitoba, University of Manitoba.

Dr. Ye's research focuses on cancer epidemiology, particularly hematological malignancies. Main research activities include: temporal and spatial trends of cancer incidence, mortality, and survival; common drugs and lymphoma risk and survival; occupational and environmental exposures and cancer risk; and genetic susceptibility to cancer risk.

Selected Publications:

1. **Ye X,** Mneina A, Johnston J, Mahmud S.M. Associations between Statin Use and Non-Hodgkin Lymphoma (NHL) Risk and Survival: A Meta-analysis. Hematological Oncology (accepted).
2. **Ye X**, Casaclang N, Mahmud S. Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Risk of Non-Hodgkin's Lymphoma (NHL): A Systematic Review and Meta-Analysis. Hematological Oncology. 2014 Oct 23. doi: 10.1002/hon.2165.
3. **Ye X**, Fitzgerald EF, Gomez MI, Lambert GH, Longnecker MP. The ratio of specific polychlorinated biphenyls as a surrogate biomarker of CYP1A2 activity— a pharmaco-metabonomic study in humans. Cancer Epidemiology Biomarkers and Prevention, 2008, 17(4): 1013-6.
4. Lv L, Kerzic P, Lin G, Schnatter R, Bao L, Yang Y, Zou H, Fu H, **Ye X**, Gross SA, Armstrong TW, Irons RD. The TNF-a 238A polymorphism is associated with susceptibility to persistent bone marrow dysplasia following chronic exposure to benzene. Leuk Res, 2007, 31(11): 1479-85.
5. **Ye X**, Fu H. Epidemiology studies on associations between gene polymorphisms and non-Hodgkin's lymphoma. J Hyg Res, 2006, 35(3): 384-6.
6. Irons RD, Lv L, Gross SA, **Ye X**, Bao L, Wang XQ, Ryder J, Armstrong TW, Zhou Y, Miao L, Le AT, Kerzic PJ, Ni W, Fu H. Chronic exposure to benzene results in a unique form of dysplasia. Leuk Res, 2005, 29(12):1371-1380.
7. **Ye X**, Ni W, Song G, Zhou F, Wang H, Fu H. Cancer mortality among lead exposed workers: a retrospective cohort study in Shanghai. Chin J Occup Health Dis, 2001, (19 2 ; 108-111.
8. **Ye X**, Hu P, Fu H, Wu C. The Associations of Immunoregulation Genetic Variants and Risk of Non-Hodgkin's Lymphoma in Shanghai, China. (submitted)

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Dr. Ryan Zarychanski, MD, MSc, FRCPC

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Dr. Zarychanski received his B.Sc. and B.Sc (Med) degrees from the University of Manitoba and Doctorate of Medicine from the University of Manitoba. Following subspecialty fellowships Hematology and Critical Care Medicine, he obtained a Masters degree in Epidemiology and Community Medicine, and undertook a research fellowship at the University of Ottawa. He serves as the Director of Knowledge Synthesis at the Centre for Healthcare Innovation (University of Manitoba & Winnipeg Regional Health Authority, and the Director of clinical apheresis (Winnipeg Regional Health Authority). He receives salary support and operating grants as a New Investigator from the Canadian Institutes of Health Research (CIHR).

Dr. Zarychanski research focuses on the hematologic aspects of critical illness. One of his major research programs includes studies evaluating the efficacy and safety of unfractionated heparin in patients with life-threatening infection. He also has active research programs related to massive transfusion, blood conservation, and the use of immune globulin in patients with septic shock.

Dr. Zarychanski's methodological expertise includes clinical trials, meta-analysis, and propensity adjusted analyses. He teaches a graduate level course in Systematic Reviews & Meta-analysis at the University of Manitoba, and serves as the Director of Knowledge Synthesis at the Centre for Healthcare Innovation.

Selected Publications: (total citations 2401; H-index 22)

1. Carrier M, Lazo-Langner A, Shivakumar S, Tagalakis V, **Zarychanski R**, Solymoss S, Routhier N, Douketis J, Danovitch K, Lee AY, Le Gal G, Wells PS, Corsi D, Ramsay T, Coyle D, Chagnon I, Kassam Z, Tao H and Rodger MA for the SOME Investigators. Screening for occult cancer in unprovoked venous thromboembolism. *New England Journal of Medicine/NEJM.* 2015 Jun 22. [Epub ahead of print] PMID:26095467
2. **Zarychanski R**, Abou-Setta AM, Kanji S, Turgeon AF, Kumar A, Houston DS, Rimmer E, Houston BL, McIntyre L, Fox-Robichaud AE, Hébert P, Cook DJ, Fergusson DA. The efficacy and safety of heparin in patients with sepsis: A systematic review and meta-analysis. *Critical Care Medicine.* 2015 Mar;43(3):511-8. PMID:25493972
3. Gershengom HB, Wunsch H, Scales DC, **Zarychanski R**, Rubenfeld G, Garland A. Relationship between Arterial Catheter Use and Hospital Mortality in Intensive Care Units. *JAMA Internal Medicine*. 2014;174(11):1746-54. PMID: 25201069
4. **Zarychanski R**, Abou-Setta AM, Turgeon AF, Houston BL, McIntyre L, Marshall JC, Fergusson DA. Association of hydroxyethyl starch administration with mortality and acute kidney injury in critically ill patients requiring volume resuscitation: a systematic review and meta-analysis. *Journal of the American Medical Association/JAMA*. 2013 Feb 20;309(7):678-88. PMID: 23423413
5. Rimmer E, Kumar A, Doucette S, Marshall J, Dial S, Gurka D, Dellinger RP, Sharma S, Penner C, Kramer A, Wood K, Ronald J, Kumar A, Turgeon AF, Houston DS, **Zarychanski R**, and The Co-operative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group. Activated protein C and septic shock. A propensity matched cohort study. *Critical Care Medicine.* 2012;40:2974-2981. PMID: 22932397
6. **Zarychanski R**, Schulz VP, Houston BL, Maksimova Y, Houston DS, Smith B, Rinehart J, Gallagher PG. Mutations in the mechanotransduction protein PIEZO1 are associated with hereditary xerocytosis. *Blood.* 2012;120(9):1908-1915. PMID: 22529292
7. **Zarychanski R**, Stuart TL, Kumar A, Doucette S, Elliott L, Kettner J, Plummer FA. Correlates of severe disease in patients with 2009 pandemic influenza (H1N1) virus infection. *Canadian Medical Association Journal/CMAJ.* 2010;182(3):257-264. PMID: 20093297
8. Kumar A, **Zarychanski R,** Pinto R, Cook DJ, Marshall J, Lacroix J, Stelfox T, Bagshaw S, Choong K, Lamontagne F, Turgeon AF, Lapinsky S, Ahern S, Smith O, Siddiqui F, Jouvet P, Khwaja K, McIntyre L, Menon K, Hutchison J, Hornstein D, Joffe A, Lauzier F, Sing J, Karachi T, Wiebe K3, Olafson K, Ramsey C, Sharma S, Dodek P, Meade M, Hall R, Fowler R, Canadian Critical Care Trials Group H1N1 Collaborative, on behalf of the Canadian Critical Care Trials Group. Critically ill patients with 2009 influenza A (H1N1) infection in Canada. *Journal of the American Medical Association/JAMA.* 2009:302(17);1872-1879. PMID: 19822627
9. **Zarychanski R**, Doucette S, Fergusson D, Roberts D, Houston DS, Sharma S, Gulati H, Kumar A. Early intravenous unfractionated heparin and mortality in septic shock. *Critical Care Medicine.* 2008;36(11):2973-79. PMID: 18824906
10. **Zarychanski R**, Houston DS. Anemia of chronic disease: a harmful disorder or an adaptive, beneficial response? *Canadian Medical Association Journal/CMAJ.* 2008;179(4):333-7. PMID: 18695181

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