



UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

SURGICAL SCIENCE IN THE DIVISION OF GENERAL SURGERY (2012-13)



July 2012

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All entries in table above are hyperlinked.

Abbreviations

ICES – Institute of Clinical and Evaluative Sciences; HPME – Health, Policy, Management & Evaluation

IMS – Institute of Medical Sciences; OISE - Ontario Institute for Studies in Education

PDF – Postdoctoral Fellow

Boris Zevin, July 2012

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Dr. Sean Cleary, Surgeon Scientist
Dr. Marc de Perrot, Surgeon Scientist
Dr. David Hwang, Clinician Scientist
Dr. Andras Kapus, Non-Clinician Scientist
Dr. Shaf Keshavjee, Surgeon Scientist
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Dr. Carol Swallow, Surgeon Scientist
Dr. Thomas K. Waddell, Surgeon Scientist
Dr. Kazuhiro Yasufuku, Surgeon Investigator

CLINICAL EPIDEMIOLOGY/HEALTH SERVICES

Dr. Nancy Baxter, Surgeon Scientist
Dr. Priscilla Chiu, Surgeon Scientist
Dr. Tulin Cil, Surgeon Investigator
Dr. Natalie Coburn, Surgeon Scientist
Dr. Calvin Law, Surgeon Scientist
Dr. Anna R Gagliardi, Non-Clinician Scientist
Dr. Steven Gallinger, Surgeon Scientist
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Dr. Frances Wright, Surgeon Scientist

EDUCATION

Dr. Najma Ahmed, Surgeon Scientist
Dr. Ted Gerstle, Surgeon Scientist
Dr. Teodor Grantcharov, Surgeon Scientist
Dr. Carol-anne Moulton, Surgeon Scientist

Dr. Allan Okrainec, Surgeon Scientist
Dr. Ranil Sonnadara, Non-Clinician Scientist
Dr. Helen MacRae, Surgeon Scientist

TECHNOLOGY INNOVATION

Dr. Sharifa Himidan, Surgeon Scientist

Dr. Ranil Sonnadara, Non-Clinician Scientist

RESIDENTS

BASIC SCIENCE

Karineh Kazazian

Megha Suri

CLINICAL EPIDEMIOLOGY/HEALTH SERVICES

Andrea Covelli
Marvin Hsiao
Debbie Li
Charles de Mestral

Jennifer Muir
Lakho Sandhu
Chethan Sathya

EDUCATION

Marisa Louridas
Boris Zevin

Nathan Zilbert

RESEARCH SUPERVISORS

Dr. Najma Ahmed, Surgeon Scientist

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St. Michael's Hospital, member of Institute of Medical Science

Main Area of Interest

Dr. Ahmed's area of scholarship and research is in the area of curricular innovation in post graduate surgical education as well as career satisfaction and advancement in General Surgery.

Dr. Nancy Baxter, Surgeon Scientist

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St. Michael's Hospital, ICES

Main Area of Interest

Health Services Research and Non-experimental Design

Students under Supervision

Andrea Covelli, General Surgery Resident, PhD candidate (HPME); Corinne Daly, MSc candidate (IMS); Jennica Platt, Plastic Surgery Resident, MSc candidate (HPME)

Current Research

1) Young Adult Survivors of Cancer

Using linked data available through ICES, we are evaluating the long-term outcomes of young adults diagnosed with cancer. For all young adult patients diagnosed with cancer in Ontario from 1992 through 1999 who survived at least 5 years we will be evaluating health services utilization (including compliance with screening), fertility, development of second cancers and survival. Residents involved with this project will learn the about health services research, how to use large administrative databases to conduct cohort studies and will have excellent fundamentals for survivorship research.

2) Missed Cancers after Colonoscopy

A significant number of colorectal cancers develop in a short time frame after a normal colonoscopy. We are performing research to evaluate why cancers are missed or develop so quickly. We are evaluating this using large population based databases but are also performing a chart review study for 1000 patients (500 with missed cancers and 500 with detected cancers). We are obtaining pathological materials for these patients to determine if cancers developing through certain molecular pathways are more likely to present as a missed cancer. Residents involved in the project would learn how to use large administrative database and become involved in quality assessment at the population level. Residents would have the opportunity to be involved in studying molecular biology in conjunction with Dr Steve Gallinger.

3) Population-based Study of Cancer Incidence and Mortality in Patients with Solid Organ Transplants

In this CIHR funded study we will evaluate trends in incidence and mortality for cancer occurring in patients after Solid Organ Transplants in Canada and compare this to the general population. An indepth chart review study (chart reviews will be conducted by trained research assistants and not residents) of transplant patients who develop cancer and matched controls will be conducted to determine differences in presentation, treatment or comorbid conditions that may account for the worse outcome in this group of patients. Residents involved in this project will

learn about health services research, how to use large administrative databases and will gain confidence in the conduct of retrospective cohort studies.

Dr. Priscilla Chiu, Surgeon Scientist

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The Hospital for Sick Children Research Institute

Main Areas of Interest

Basic science research – developmental and stem cell biology, T cell development, thymic development, T cell-based malignancies

Clinical research – surgical and long-term health outcomes in diaphragmatic hernia and tracheal repair patients

Students under Supervision

Aunshu Goyal, medical student

Current Research

1) *T cell-based malignancies*

Using a xenograft model for human T-lymphoblastic leukemia (T-ALL), we have defined markers that allow us to isolate the engrafting subset of leukemia cells that are uniquely able to initiate and propagate the leukemia. These results provide the first evidence for a cancer stem cell basis to human T-ALL. Further experiments are in progress to elucidate the signaling pathways critical for leukemia-initiating cell (LIC) activity and to determine treatments that target the LIC in T-ALL, as current therapies may not target this subset and result in disease relapse that have contributed to poor T-ALL outcomes.

Publication: <http://bloodjournal.hematologylibrary.org/cgi/content/abstract/blood-2010-06-292300v1>

2) *Human thymic development*

Most of what is known about thymus development comes from murine studies. However, humans are born with a far more advanced and mature T cell immunity due to the earlier organogenesis and function of the human thymus during fetal development. One critical cellular population within the thymus for normal T cell development is the thymic epithelial cells (TEC) that comprise a component of the thymic stroma. These TEC are responsible for interactions with maturing T cells to regulate self-tolerance and self-MHC recognition. Our work is to focus on the identity and development of TEC to further our understanding the regenerative potential of these cells, as diseases caused by dysregulated TEC development (benign and malignant conditions such as DiGeorge syndrome, T cell-based autoimmunity, age-related immunodepression, thymic epithelial tumors) remain poorly understood.

Dr. Tulin Cil, Surgeon Investigator

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Princess Margaret & Women's College Hospitals

Main Areas of Interest

Surgical Education

Students under Supervision

Albert Fung, MSc candidate (Biomedical Communications)

Current Research

1) *The Sensitive Physical Exam*

Using video vignettes depicting clinical breast exams, we will be assessing the knowledge, skills and attitudes regarding sensitive physical exam skills among undergraduate medical students. Residents involved in this project will have the opportunity to learn mixed methods research skills including survey development, interviewing and statistical analysis of outcome measures.

2) *Visual Imagery in the Acquisition of Surgical Skills*

This is a mixed methods study looking at how surgical skills may be learned using innovative practices that are integral to other motor skills learning. Visual imagery and mental rehearsal have been used in sport and musical training for some time. This study will explore if and how surgeons can use these practices in acquiring their skill sets.

Dr. Sean Cleary, Surgeon Scientist

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UHN, Prosserman Center, Samuel Lunenfeld Research Institute

Main Areas of Interest

Genetic Epidemiology, Liver and Pancreas cancer

Current Research

1) *Molecular Pathogenesis of Hepatocellular Carcinoma*

Through studying a prospective registry of HCC patients with tumour and blood samples, our goal is to examine the role of DNA methylation and folate metabolism in the pathogenesis of HCC. Resident research projects could involve the study of methylation patterns in HCC and/or the influence of folate metabolism markers on tumour methylation.

2) *Genetic Epidemiology of Pancreatic Cancer*

Our aim is to study the influence of gene-environment interactions in the pathogenesis of pancreatic cancer. We are currently undertaking a study to examine the interaction of vitamin D levels and genetic variants in vitamin D-related genes as in modifying risk for pancreatic cancer.

Dr. Natalie Coburn, Surgeon Scientist

natalie.coburn@sunnybrook.ca

Sunnybrook Health Sciences Centre, ICES

Main Area of Interest

Health Services Research

Current Research

1) *Outcomes for gastric cancer patients*

Currently, I am conducting a RAND/UCLA appropriateness study for surgery for gastric cancer patients in Ontario. Data collection will begin October 2009 for 2000 gastric cancer cases 2005-2008. We will collect staging information and surgical details. In October 2010, we are holding a consensus conference to ascertain what 15 international experts consider appropriate and necessary care for gastric cancer patients (Does everyone need an EUS? Should you resect in non-curative situations?) The results of this panel will be compared to what occurred in the care given to the 2000 cases in the chart review.

Dr. Marc de Perrot, Surgeon Scientist

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Toronto General Hospital, Toronto Medical Discovery Tower

Main Area of Interest

Malignant pleural mesothelioma (MPM)

Students under Supervision

Tetsuzo Tagawa, PDF

Current Research

- 1) Malignant pleural mesothelioma (MPM) is a highly aggressive cancer with poor prognosis. However, current treatments only achieve very limited effect. Our overall goal is to improve the outcome of this disease through surgery followed by conventional chemotherapy and immunotherapy. This approach could open a new avenue in cancer treatment that could rapidly translate into clinical practice.
- 2) Pulmonary hypertension is a form of lung disease that leads to progressive right heart failure. The mechanisms of pulmonary hypertension and its treatment remains not well understood. We detected a gene expression profiling associated with the development of pulmonary hypertension. We are currently evaluating the specific roles of these genes in the development of pulmonary hypertension in animal models.

Dr. Anna Gagliardi, Non-Clinician Scientist

anna.gagliardi@uhnresearch.ca

Toronto General Research Institute, University Health Network

Main Area of Interest

Knowledge translation/implementation science with the aim to develop, implement and evaluate tools and interventions that improve the organization, delivery and outcomes of care.

Students under Supervision

Stephanie Hylmar, MSc candidate (HPME); Emily Pearsall, PhD candidate (HPME); Flavia Abdallah, PDF (UHN)

Current Research

1) Guideline implementation

Funded by the Canadian Institutes for Health Research, this series of studies investigates the impact and feasibility of approaches for promoting guideline use (syntheses of evidence on best practice), including improvements to the format and content of the products themselves such that they are easier to apply or accommodate, and development among organizations seeking to improve quality of care such that they more effectively implement those products. This work is undertaken in collaboration with an international group of guideline developers, implementers and researchers.

2) Establishing priorities for research on implementation of quality improvement/patient safety tools and practices

Funded by the Canadian Institutes of Health Research, this study will engage international experts in prioritizing and planning ongoing research on mechanisms for monitoring the safety of surgical devices, including assistive and implantable devices.

3) *Development and validation of a framework to guide the reporting, review and use of qualitative health research*

This series of studies will identify the publication rate of qualitative studies in top-ranked medical, health services and nursing journals; and examine how the reporting, publication rate, views about, and use of qualitative research in health care decision making could be improved.

Dr. Steven Gallinger, Surgeon Scientist

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Samuel Lunenfeld Research Institute, Mount Sinai Hospital (basic science research), Toronto General Hospital (clinical)

Main Area of Interest

GI Cancer Genetics

Students under Supervision

Wigdan Al-Sukhni, General Surgery Resident, PhD candidate (IMS); Frank Schwenter, PDF; Subani Selvarajah

Current Research

1) *Identification of the Familial Pancreas Cancer Gene(s)*

We are using our large infrastructure of family history, epidemiologic data, and germline DNA to identify novel genetic and genomic candidates. Both copy number variants and high penetrant germline mutations are being analysed in subjects identified in Toronto and in samples assembled by the NIH funded Pancreas Cancer Genetic Epidemiology consortium (PACGENE).

2) *Genetic variants in Hereditary and Sporadic Colorectal Cancer*

We are using both GWAS data of 1,200 cases and 1,200 controls to study the 'common disease/common variant' etiology hypothesis, and deep sequencing to identify rare highly penetrant variants. Clinicopathologic associations are also being investigated, as well as molecular somatic predictors of chemoresponsiveness

Dr. J. Ted Gerstle, Surgeon Investigator

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SickKids Hospital

Main Area of Interest

Surgical Education

Students under Supervision

None

Current Research

1) *Validation of the Pediatric Laparoscopic Surgery (PLS) simulator (joint project with Georges Azzie)*

The advent of minimal access surgery (MAS) has renewed the challenge of how best to teach and measure operative skills. Ever-growing constraints on training in surgery exist everywhere, including reduced trainee work hours, increased operating room costs, focus on medical error and ethics surrounding learning basic skills on patients. In response to this, more and more of the training is taking place outside the operating room. In the realm of MAS, this has triggered the development of simulators which provide the opportunity to learn and practice skills which can be transferred to the operating room.

While many adult simulators exist, there is only one validated model. There have been no pediatric counterparts. We have designed and built a Pediatric Laparoscopic Surgery (PLS) simulator at our own expense. We have also carried out preliminary validation, which sets us apart from all other centres embarking on this course (Published in *Journal of Pediatric Surgery*, May, 2011).

Further validation and development are required to establish this as a validated model. Once fully validated, this model has the potential to become the simulator for pediatric surgery, including teaching, training and assessment of basic MAS skills at an international level.

2) *Motion Analysis in Minimal Access Surgery (joint project with Georges Azzie)*

“Expertise”, regardless of the field, is difficult if not impossible to define. In sports, motion analysis has been one focus of study. In surgery, no data exists regarding differences in motion between novices, intermediates and experts.

We have developed equipment (software and hardware) and a methodology to track, measure and compare the movement of instruments in a laparoscopic simulator. Our current model allows us to track and measure movement in the “X”, “Y” and “Z” axes, with a resolution a 0.03 mm and a sample rate of 30 Hz and as well as “roticulation” (pronation/supination) with a resolution of 0.07 degrees and a sample rate of 15 Hz. We can also track range of motion, acceleration/deceleration and “stop/start” movements. We are able to compare computer-generated data to real-time video recordings of arbitrarily defined candidate groups (based on levels of experience). Examples of metrics that have been developed include Geometry of Path Length (the shape of the paths generated by the instruments for each task), Fluidity of Movement (the “smoothness” of the paths generate by the instruments for each task) and Volume of Motion (the volume of space in which each instruments moves for each task).

While methods for tracking motion have been described in the literature, no one has even begun to measure and log such data, much less apply it. This project puts us at the cutting edge of this technology.

We hope to define parameters related to motion that will help define levels of expertise and assist with surgical education. This will translate into a novel methodology for teaching and assessing surgical skills. Eventually, we hope to establish concurrent validity: that is, skills taught and assessed through analysis of motion do translate into better intra-operative performance and better surgical outcomes.

Dr. Anand Ghanekar, Surgeon Scientist

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Toronto General Hospital Research Institute

Main Area of Interest

Role of Stem Cells in Diseases of the Liver

My laboratory is located in the MaRS complex and has active collaborations with senior investigators in transplantation (G. Levy), stem cell biology (G. Keller), and cancer biology (J. Dick). We utilize state-of-the-art techniques in molecular and cellular biology, as well as small animal models.

Students under Supervision

There are currently 3 postdoctoral fellows and 1 technician participating in the research described below. My laboratory provides excellent opportunities for surgical residents interested in basic/translational research.

Current Research

1) *Elucidating the role of cancer stem cells in the pathogenesis of human hepatocellular carcinoma*

We are utilizing human HCC resection specimens to generate in vivo models of primary human HCC by generating tumor xenografts in immunodeficient mouse strains. We are also developing methods for stable in vitro culture of

primary human HCC cells. We anticipate that these resources will permit the identification and characterization of tumor initiating cells in human HCC.

2) *Studying the pathophysiology of a variety of human liver diseases through the use of induced pluripotent stem cells*

We are interested in studying the developmental biology of human liver cell populations (hepatocytes and cholangiocytes) through the use of embryonic and induced pluripotent stem cells. We are interested in studying the differentiation potential of induced pluripotent stem cell (iPS) lines generated from patients with diseases of liver development in order to elucidate the mechanisms by which liver development is affected.

Dr. Rebecca Gladdy, Surgeon Scientist

rgladdy@mtsinai.on.ca

Systems Biology Group, Samuel Lunenfeld Research Institute, Mount Sinai Hospital (Scientific meetings shared with Dan Durocher).

Main Area of Interest

My lab is working on Functional Genomics and the Development of Selective Therapeutics in cancer. At this time, our disease focus is sarcoma however we are a translational/basic science lab interested in fundamental mechanism of cancer genetics.

Students under Supervision

One graduate student, one research associate and a technician

Current Research

1) *Mouse models of sarcoma*

We are using a retroviral system to introduce novel and known oncogenes, so that we can create a novel model to functionally validate whether mutations found in genome-wide studies are oncogenic or not.

2) We have begun a high-throughput screening project to look for novel genes that may confirm; a) growth/survival advantage for cancers b) pathways of drug resistance. This is using an siRNA lentiviral library in collaboration with Jason Moffat at CCRB.

3) Using xenograft models, we are developing pre-clinical mouse models to test novel small molecules in collaboration with OICR medicinal chemistry. Our initial focus is to directly inhibit transcription factors that are commonly expressed in certain sarcomas, which would ideally target cancer cells more exclusively and thus mitigate patient toxicity.

4) Developing surface markers to solid tumours using monoclonal and phage libraries.

Dr. Teodor Grantcharov, Surgeon Scientist

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St. Michael's Hospital

Main Area of Interest

Surgical Education, Minimally Invasive Surgery

Students under Supervision

Vanessa Palter, General Surgery Resident, PhD candidate (IMS); Bharat Sharma, General Surgery Resident, MEd candidate; Boris Zevin, General Surgery Resident, MEd candidate

Current Research

- 1) *Design and validation of comprehensive training and assessment curricula in Minimally Invasive Surgery*
 - 2) *Design and validation of assessment tools in Basic and Advanced Laparoscopic procedures*
-

Dr. Anand Govindarajan, Surgeon Scientist

anand.govindarajan@utoronto.ca

Mount Sinai Hospital

Main areas of interest

Health services research, knowledge translation

Current research

- 1) *Assessment of the use of preoperative staging and use of neoadjuvant therapy in the treatment of rectal cancer across the province.*
 - 2) *Stage, presentation and treatment of colon cancers missed on screening.*
 - 3) *Natural history of relatives of high risk patients with non-CDH1 mutant gastric cancer.*
-

Dr. Robert Gryfe, Surgeon Scientist

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Mount Sinai Hospital, Princess Margaret Hospital

Main Area of Interest

Genetic determinants of inherited risk, survival and response to therapy in patients with colorectal cancer

Current Research

Using both genome-wide association (GWAS) and candidate gene approaches, we are currently pursuing international, multi-institutional studies of genetic and epigenetic prognostic determinants of survival in patients with colorectal cancer and the predictive association of genetic variation with response to current chemotherapy.

Dr. Sharifa Himidan, Surgeon Scientist

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Hospital for Sick Children, North York General Hospital

Main Area of Interest

Surgical and Imaging Technology Development and Innovation

Field of Study

Technology innovation

Current Research

- 1) Development of next generation surgical tools; real-time and image fusion technology; simulation technology and products in collaboration with front-running technology industry partners.
- 2) Development of disruptive technologies that will fundamentally change the current surgical paradigm such as NOAD, MIEMS and MR-HIFU.
- 3) In collaboration with U of Waterloo, development of specific technologies based on nanotechnology for surgical and imaging diagnostic and therapeutic applications.

Dr. Claire Holloway, Surgeon Scientist

claire.holloway@sunnybrook.ca

Sunnybrook Health Sciences Centre, Sunnybrook Research Institute

Main Area of Interest

Imaging technology development for surgical application and Health Services Research (Surgical Oncology)

Current Research

1) *Application of 3D Imaging and Pathological Evaluation Methods to Improve Accuracy of Breast Cancer Staging*

We have developed techniques for 3D assessment of lumpectomy and sentinel node specimens and are conducting studies to determine how 3D assessment affects assignment of tumour size, margin involvement and sentinel node involvement. Residents involved in this project will learn clinical study design, principles of technology development and evaluation, and computerized algorithm creation.

2) *Development of Supine Breast MRI for Intraoperative Applications*

Working with imaging scientists we are evaluating patients with breast cancer to determine optimal methods for acquiring therapeutic quality supine MRI images that can be co-registered to standard diagnostic prone images. Residents involved with this project should have a background/interest in engineering/physics/computer science.

3) *Improving Adoption of Core Needle Biopsy in Breast Diagnosis*

We will be conducting a systematic literature review to establish what is known about the indications for core needle biopsy and the target rate for its use. This review will inform an expert panel charged with developing core needle biopsy rate as a quality indicator in breast diagnosis using a consensus-based approach. Residents involved in this project will learn the techniques of systematic review and the modified Delphi approach to consensus-based quality indicator development.

Dr. David Hwang, Clinician Investigator (Lung Pathologist)

david.hwang@uhn.on.ca

Toronto General Hospital, Toronto Medical Discovery Tower

Main Area of Interest

Lung Pathology, Cystic Fibrosis

Students under Supervision

Shawn Clark, PhD candidate (Laboratory Medicine & Pathobiology); Yu Zhang (Technician)

Current Research

Studies involving the role of the pulmonary microbiota in lung transplantation for cystic fibrosis

Dr. Paul Karanicolas, Surgeon Scientist

paul.karanicolas@sunnybrook.ca

Sunnybrook Health Sciences Centre

Main Areas of Interest

Clinical Trials, Quality of Life, Systematic Reviews, and Health Services Research. Hepatobiliary, Pancreatic, and Gastrointestinal Surgical Oncology

Field of Study

Clinical Epidemiology

Current Research Projects

1) *Quality of Life Following Gastrointestinal Cancer Surgery*

We are currently implementing an infrastructure at the Odette Cancer Centre to prospectively capture data on Quality of Life among all patients who undergo surgery for gastrointestinal cancer. This database will be linked to a clinical database of outcomes. This will allow for several projects to be completed, including methodological studies (validating QOL instruments, establishing psychometric properties), observational studies (factors associated with QOL), and clinical trials (using QOL as an important outcome).

2) *Phase II Trial in patients with rectal adenocarcinoma and synchronous liver metastases*

We are currently beginning development a phase II trial in this patient population.

3) *Randomized Trials of surgical techniques in gastrointestinal cancer*

We have a series of single-center randomized trials in the early stages of development focused on specific techniques in gastrointestinal cancer surgery – e.g. pancreatic transection, anastomoses, etc.

Dr. Erin Kennedy, Surgeon Scientist

erin.kennedy@uhn.on.ca

Centre for the Evaluation of Health Services in Surgery (University Health Network)

Main Area of Interest

Erin is an internationally recognized expert in Patient Centred Care and Shared Decision Making in Surgery. Her other research interests include Quality of Life and Cancer Survivorship. She holds research grants from the Canadian Institutes of Health Research and the Cancer Services Innovation Partnership. Erin teaches a graduate course on measurement of patients' preferences in health care decision making in the Department of Health Policy, Management and Evaluation.

Students under Co-Supervision (in conjunction with Robin McLeod)

Elsar Al-Sukhni, General Surgery Resident, MSc candidate (HPME)

Dr. Andras Kapus, Non-Clinician Scientist

kapusa@smh.toronto.on.ca

St. Michael's Hospital (Office: Queen Wing 7-009, Lab: 9-014)

Main Area of Interest

Cell biology of fibrosis, cellular stress, osmoregulation

Students under Supervision

One graduate student, two PDFs

Current Research

1) Epithelial-mesenchymal transition in fibrogenesis

EMT is a key process in organ fibrosis and cancer, whereby epithelial cells lose their strong contacts and polygonal shape and transform into motile, contractile and often invasive fibroblasts and myofibroblast. We study the cell biology EMT; we aim to understand the cellular and molecular mechanisms whereby kidney and lung cells, exposed to pathogenic stimuli, reorganize their cytoskeleton and reprogram their gene expression to become myofibroblasts. We use a variety of techniques, including imaging of live and fixed cells (florescence microscopy), gene promoter assays, coimmunoprecipiation (for protein-protein interaction), RT-PCR and others.

2) Osmotic and volume regulation at the cellular level

Dehydration of cells, which occurs under various physiological and many pathological conditions initiates 3 major adaptive responses: a) activation of ion and other solute transporters to regain water and volume; 2) reinforcement of the cytoskeleton and 3) change in gene expression to serve 1) and 2). We study how the initial volume change leads to these vital adaptive responses. We use all the techniques described above, as well cell volume measurements and assays to follow signal transduction steps during osmotic stress.

Dr. Shaf Keshavjee, Surgeon Scientist

shaf.keshavjee@uhn.on.ca

Toronto General Hospital, Latner Thoracic Surgery Research Labs

Main Area of Interest

Clinical outcomes & Lung Injury & Gene Therapy in Lung Transplantation

Students under Supervision

Jonathan Yeung, General Surgery Resident, PhD candidate (IMS); Shin Hirayama, PDF; Terumoto Koike, PDF; Yasushi Matsuda, PDF

Current Research

1) Injured Donor Lung Repair

We have recently developed a method for stable normothermic ex vivo lung perfusion. Using this system, we are developing therapeutics to repair donor lungs currently deemed unsuitable for repair. Among others, we are currently developing IL-10 gene therapy as one such therapeutic technique using large animal models and rejected human lungs.

2) Mechanisms in bronchiolitis obliterans syndrome

Bronchiolitis obliterans syndrome is the major limitation to long term survival of lung transplant recipients. Using an intrapulmonary tracheal transplant model developed in this laboratory, we are studying the mechanisms which lead to the development of this syndrome. This model has recently been successfully performed in the mouse. We

anticipate that the use of knockout mice together with this system will further our understanding of the development of this syndrome.

3) *Identification of biomarkers for improved donor assessment*

Currently, assessment of the suitability of a donor lung for transplantation is a clinical judgment. Using microarray technology and our donor lung tissue bank, we seek to identify biomarkers which predict lung function and suitability for transplantation. Ultimately, we hope to use these biomarkers clinically to both identify suitable lungs and to recognize lung repair following therapeutics during ex vivo lung perfusion.

Dr. Jacob Langer, Surgeon Scientist

jacob.langer@sickkids.ca

The Hospital for Sick Children Research Institute

Main Area of Interest

Pediatric General Surgery

Students under Supervision

David Levin (University of Toronto Medical student), Nada Gawad (University of Toronto Medical student), multiple residents and fellows

Current Research

1) *Delivery of Pediatric Surgical Care in Ontario*

Using linked data available through ICES and OHIP, we have been examining the effect of sub-specialization on outcome for common pediatric surgical conditions. We have also examined the effect of wait times on outcome for infants with inguinal hernia.

2) *Management of Hirschsprung Disease*

We are looking at ways to improve the management of children with Hirschsprung disease, both surgically and post-operatively. This research has taken the form of retrospective reviews, prospective evaluation of innovative techniques, and involvement in randomized trials. We are also initiating several collaborative studies looking at the genetics of Hirschsprung disease and the influence of genetic mutations on surgical outcomes.

3) *Randomized Trials in Pediatric Surgery*

We are involved in a number of randomized trials in the field of pediatric surgery.

Dr. Calvin Law, Surgeon Scientist

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The Edmond Odette Cancer Centre at Sunnybrook Health Sciences, ICES

Main Area of Interest

Health Services Research (Surgical Oncology)

Current Research

- 1) Population Health Study on the delivery of care following colorectal cancer resection
- 2) Decision Analysis on the preferred approach to the elderly patient with colorectal liver metastases
- 3) Population Health Study on the surgical treatment of pancreatic neuroendocrine cancer
- 4) Gastric Cancer – co-investigator on studies of population health services delivery and development of an expert consensus panel

My questions revolve not around what is the ultimate treatment, but around what is the actual treatments delivered to a population, how consistent and how optimized is it? From this understanding, we can hope to identify and address barriers that prevent even the best of treatment protocols from reaching the people it was intended to help in the first place.

Dr. Mingyao Liu, Non-Clinician Scientist

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Toronto General Hospital, Toronto Medical Discovery Tower

Main Area of Interest

Cellular and molecular mechanisms of acute lung injury, Drug discovery for ischemia-reperfusion-induced lung injury in transplantation, Nano-drug delivery, XBI30 in intracellular signal transduction and tumorigenesis, Repair/regeneration of injured lung

Students under Supervision

Hyunhee Kim, PhD student (Physiology); Serisha Moodley, PhD student (IMS); Richard Gao, MSc student (Physiology); Daiyoon Lee, MSc student (IMS); Shaun Pacheco, MSc student (Physiology); Dr. Grace Shen-Tu, PDF; Dr. Jinbo Zhao, PDF; Dr. Hiroki Takeshita, PDF

Current Research

1) *Drug discovery for ischemia-reperfusion induced lung injury in transplantation*

We are focusing on lung injury induced by ischemia-reperfusion in lung transplantation. A cell culture model has been developed for high throughput screening of drugs. A rat lung transplantation model is used for in vivo therapeutic assessment. A pig lung transplantation model and Ex Vivo Lung Perfusion system are available through collaboration with Dr. Shaf Keshavjee, to test new therapeutic drugs.

2) *Nanoparticle-based drug delivery*

Another exciting research area in my lab is nano-particle-based drug delivery. We have used self-assembly peptide to formulate drugs that block signal transduction pathways related to inflammatory responses. A patent has been filed. We also developed a gold nanoparticle/peptide hybrid system for peptide based drug delivery.

3) *The role of XBI30 in repair/regeneration of injured lung, and in tumorigenesis*

XBI30, an adaptor protein cloned in my lab, is involved in regulation of cell proliferation, survival and migration via PI3K/Akt pathway. Knock down of XBI30 significantly inhibits tumor cell growth in vitro and in vivo. We have developed XBI30 deficient mice to systemically study its role in repair/regeneration of injured lung, and in tumorigenesis/metastasis.

Dr. John Marshall, Surgeon Scientist

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St. Michael's Hospital, Li Ka Shing Knowledge Institute

Main Area of Interest

The host response to life-threatening infection, trauma, and critical illness

Students under Supervision

Jennifer Tsang, PhD candidate (IMS); Zeenat Malam, PhD candidate (IMS)

Current Research

Mechanisms regulating neutrophil survival in sepsis: My CIHR-funded lab focuses on 3 novel themes:

1) *The role of PBEF/visfatin, a novel NAD-generating enzyme and insulin antagonist*

We have identified this highly conserved protein as a cardinal regulator of neutrophil survival and seek to characterize its divergent roles in NAD generation and as a ligand for the insulin receptor.

2) *The role of tyrosine phosphorylation of caspase-8*

We have found that phosphorylation of the key apoptotic enzyme, caspase-8, not only prevents its activation, but is also necessary for activation of the PI3 kinase survival pathway.

3) *The role of a novel natural anti-sense transcript, ILIP*

We have identified a novel gene that regulates a key earlier regulator of the MAP kinase cascade.

All of these are phenomena that are evident in neutrophils from septic critically ill patients. Participating residents would learn basic cell biology, flow cytometry, molecular biology, and imaging techniques, and have the opportunity to apply these to understanding persistent inflammation in septic critically ill patients.

Dr. Andrea McCart, Surgeon Scientist

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Mount Sinai Hospital, Toronto General Hospital Research Institute

Main Area of Interest

Oncolytic virotherapy for Cancer

Students under Supervision

Katherine Ottolino-Perry, PhD candidate (IMS); Sara Farshchi, MSc candidate (IMS)

Current Research

1) *Developing a novel virotherapy strategy for treatment and detection of peritoneal mesothelioma*

Using cell culture and animal models of peritoneal mesothelioma, we will evaluate a novel fluorescent virus for its ability to target, infect and kill peritoneal mesothelioma. Prospective student will gain experience in small animal handling and surgery, cell culture, and viral propagation.

2) *Development of a molecular assay of oncolytic virotherapy for colorectal carcinomatosis*

This project will use protein arrays to develop a unique viral signature for vaccinia virus and other oncolytic viruses to be used in the clinical setting. Prospective student will gain experience with cell culture, protein arrays, viral propagation and viral infection of cell lines and fresh tumour samples.

Dr. Ian McGilvray, Surgeon Scientist

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Toronto General Hospital

Main Areas of Interest

We have been studying gene expression in various liver diseases since 2003, using high-throughput technology to identify new aspects of liver pathology. More recently we have focused our attention on viral hepatitis, both before and after liver transplantation. We demonstrated that patients with chronic hepatitis C viral infection have two distinct patterns of gene and cellular activation: one pattern is highly associated with response to treatment. We are now studying how the genes that distinguish treatment responders from treatment nonresponders can be used to design new treatments for the infection.

Dr. Robin McLeod, Surgeon Scientist

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Mount Sinai Hospital, General Surgery

Main Areas of Interest

Evidence-based medicine, quality improvement in IBD and colorectal cancer

Students under Supervision

Elsar Al-Sukhni, General Surgery Resident, MSc candidate (HPME); Thomas Walters, Paediatric Gastroenterologist, PhD Candidate (HPME); David Messenger, Colorectal Research Fellow

Current Research

1) Best Practice in General Surgery

The aim of Best Practice in General Surgery is to standardize care across the seven adult teaching hospitals at the University of Toronto and North York General Hospital based on best evidence. The rationale for this is to improve patient care, improve resident education, and increase collaboration among the faculty and hospitals. Residents have an opportunity to work with the committee on an area of interest and develop and implement a clinical practice guideline and evaluate its outcome on patients.

2) Colorectal Cancer

All patients having surgery for colorectal cancer at Mount Sinai Hospital are entered into a database. Surgical pathology and outcome data are available on over 1,500 patients. Recent studies include assessing surgical technique as well as the effect of synoptic pathology reports. Because of our interest in hereditary colon cancer, we have a large cohort of patients with FAP and HNPCC and are performing studies in collaboration with Steve Gallinger and Rob Gryfe.

3) IBD

Mount Sinai Hospital is recognized for its expertise in managing IBD. We have a database of over 2,000 ulcerative colitis patients and 3,000 Crohn's disease patients who have had surgery. This facilitates studies assessing surgical outcome and recruitment of patients for prospective studies. We have completed a number of clinical trials as well as prospective evaluations of quality of life, patient preferences for different treatment options and surgical-pathological-genetic correlative studies. We are currently assessing the impact of laparoscopic surgery on outcome in IBD patients.

Dr. Carol-anne Moulton, Surgeon Scientist

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Toronto General Hospital, Wilson Centre for Research in Education

Main Area of Interest

The main research focus of this lab is to develop a more explicit understanding of surgical judgment by exploring how surgeons make decisions and judgments in the moments of practice. Using a variety of methodologies we are exploring what makes an expert surgeon 'expert' and the factors - both cognitive and socio-cultural - that influence surgeons' abilities to self-regulate in the moment of practice.

Students under Supervision

Nathan Zilbert, General Surgery Resident; Laurent St. Martin, MSc candidate (IMS); Sandra de Montbrun, Colorectal Surgery Fellow, MEd candidate (OISE); Priyanka Patel, MSc candidate (IMS); Jacob Gallinger, Research Assistant

Current Research

1) *Explore how surgeons experience risk in the moment of practice.*

This project focuses on surgeons' perspective on risk. Using constructivist grounded theory methodology we have set out to explore how surgeons experience risk in the moment of practice, the factors that cause a surgeon to be on either extreme of the risk-taking spectrum, and how surgeons' self-perception of risk tolerance affects their clinical practice.

2) *Examine surgeon's detection of situationally responsive moments when critical events occur.*

This research project will focus on the surgeon's detection of situationally responsive moments when critical events occur that are unanticipated pre-operatively. The project will examine the detection of these situationally responsive cues using videotapes of laparoscopic cholecystectomies, some with common duct injuries and some without, across a cohort of general surgeons. Surgeons will then be asked to 'think aloud' as they watch these videos to look for consistencies amongst their cognitive processes.

3) *Exploring the transition process from a surgical resident to attending staff.*

One of the most significant transitions in a physician's career is the transition to independent practice. Despite this, literature on this critical transition period is sparse. This project takes a constructivist grounded theory approach exploring the transition process from surgical resident to attending staff. The objective of our study is develop an understanding of the influences and factors that affect this transition process and how the transition process itself can impact a surgeon's career trajectory.

4) *Examining how social pressures implicit within the surgical culture may influence a surgeon's judgment and decision-making abilities*

This project focuses on how social pressures implicit within the surgical culture may influence a surgeon's judgment and decision-making abilities and consequently, their ability to 'slow down' when they should. To reconstruct the social dynamics of the operating theatre, this project will explore surgeons' perceptions and experiences of these sociological forces, as well as the perceptions of non-surgeon team members (surgical trainees, anaesthetists, nurses, surgical trainees) on behaviors and characteristics of the staff surgeon. To further my understanding of the surgical culture, we will observe the surgeon and operative team in their natural environment to identify and understand social factors, which may impact their judgment or patient care.

5) *Explore if similarities exist in expert thinking and whether these can be utilized as a training tool for surgical trainees.*

With a recent push in medical education for competency-based training, surgical residents and fellows are expected to possess a large set of technical competencies with minimal focus on preoperative planning skills. Using the think aloud protocol, my project focuses on the cognitions that surgeons have preoperatively when viewing a CT scan and mapping out their cases. Through an assessment of senior surgeon's thoughts during their planning stages, we are

curious if similarities in expert thinking can be found and whether these cognitions can be utilized as a training tool for surgical trainees.

Dr. Avery Nathens, Surgeon Scientist

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St. Michael's Hospital, ICES, American College of Surgeons

Main Area of Interest

Health services research related to trauma care delivery and trauma quality improvement

Students under Supervision

Sunjay Sharma, Neurosurgery Resident, MSc candidate (IMS); Charles de Mestral, General Surgery Resident, MSc candidate

Current Research

1) *Access to trauma care and trauma system development*

Using a variety of unique datasets we use mixed methods approaches to evaluate how severely injured patients can be assured prompt access to care in a trauma center. Methodologic approaches include quantitative and qualitative analyses along with GIS to provide a spatial component.

2) *Trauma Quality Improvement Program (TQIP - www.acstqip.org)*

This is a large program which I run through the American College of Surgeons that allows benchmarking of trauma center performance. These data are maturing, but will allow the identification of best practices in trauma care and other unique attributes of high performing trauma centers.

3) *Access to neurosurgical care*

This project will address the gaps in the delivery of emergency neurosurgical (primarily neurotrauma) care using large population based datasets complemented with surveys of emergency medicine providers.

4) *Population-based evaluation of acute biliary syndromes in Ontario*

In this project we will evaluate the present management of patients who present to the emergency department with acute cholecystitis throughout Ontario. Specifically, we will describe the current practice in terms of early versus delayed cholecystectomy, along with outcomes and resource utilization for both approaches. Our goal is to proceed with a cost utility analysis to determine the optimal approach for patients presenting to the ED with acute cholecystitis.

Dr. Allan Okrainec, Surgeon Scientist

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Toronto Western Hospital

Main Area of Interest

Dr. Okrainec's research interest is in the use of simulation for the teaching and assessment of laparoscopic skills. His educational research lab at the Toronto Western Hospital is primarily dedicated to the development and use of telesimulation technologies for teaching surgical skills in remote areas and resource-restricted countries. His work is supported by numerous research grants, including the Ministry of Health Innovation Fund, the Health Technology Exchange, and the Royal College of Physicians and Surgeons of Canada.

Dr. Michael Reedijk, Surgeon Scientist

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University Health Network, Ontario Cancer Institute, Campbell Family Institute for Breast Cancer Research

Main Area of Interest

Signal transduction, Notch Signaling, Breast Cancer

Students under Supervision

Pavel Goldvasser, MSc candidate (Department of Medical Biophysics); Julia Izrailit, PhD candidate (Department of Medical Biophysics)

Current Research

1) Notch Signaling in breast cancer

Currents efforts in the laboratory are directed towards elucidating the mechanism(s) by which activated Notch signaling contributes to breast cancer development. We are using genome-wide approaches including expression array analyses, chromatin immunoprecipitation and a large-scale RNA interference-based short hairpin RNA (shRNA) barcode to identify novel regulators and targets of Notch activation in breast cancer. The value of identifying Notch regulators and targets is for their ultimate exploitation as biomarkers or therapeutic targets in Notch-activated breast cancer. This work is imperative as Phase I and II breast cancer clinical trials with Notch inhibitors emerge (see 2, below).

2) Notch inhibitor clinical trials

We are involved with the Princess Margaret Hospital Phase I and II consortium and the National Cancer Institute Cancer Therapy Evaluation Program in the conduct of five Phase I/II trials to study a Notch inhibitor (Roche R04929097), in the treatment of solid malignancies, including breast cancer. The majority of the correlative science being conducted to support these trials is being carried out in our laboratory.

Dr. Sandro Rizoli, Surgeon Scientist

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Sunnybrook Health Sciences Centre

Main Area of Interest

Trauma, Coagulopathy, Resuscitation, Thromboelastography, Clinical Trials

Students under Supervision

Bartolomeu Nascimento, Clinical Fellow & MSc Candidate (IMS)

Current Research

1) Age of Blood Evaluation (ABLE Study) in the resuscitation of critically ill patients

Determine the clinical outcome (number of days on the ventilator, length of ICU stay, length of hospital stay, 28-day, and 90-day, and 6-month mortality) of patients who receive extremely fresh blood (< 7 days) vs. patients who receive standard of care (~ 22 days).

2) Early coagulopathy in trauma and thromboelastography (TEG)

Coagulation parameters are investigated using thromboelastography (TEG) and standard functional tests. Blood is analyzed for markers of activation of the coagulation and inflammation/complement.

3) *Management of occult pneumothoraces in mechanically ventilated patients (OPTICC Study)*

A study investigating the need for chest drainage in small to moderate size occult pneumothoraces on pulmonary mechanics and potential influences on the known risks of ventilator-induced lung injury inherent with mechanical ventilation. This information will tell us whether the invasive intervention of placing a chest tube is really necessary.

4) *Formula-driven vs. laboratory-guided transfusion practices in bleeding trauma patients*

Investigate whether a pre-defined ratio of FFP to PLT to RBC transfusion (1:1:1) protocol reduces the rate of death by exsanguination when compared to a laboratory driven transfusion protocol in a population of massive bleeding trauma patients.

5) *Changes in the severity of Clostridium difficile infectious colitis*

Investigating changes in *C. difficile* colitis seen in the past 2 years, specifically in those patients that required surgical intervention, and developing a program of care for these patients that may improve clinical outcomes.

Dr. Ori Rotstein, Surgeon Scientist

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St. Michael's Hospital, Li Ka Shing Knowledge Institute

Main Area of Interest

Patients who have sustained major trauma with associated hemorrhagic shock are at increased risk of developing multiple organ dysfunction in the post resuscitation phase. Our research group investigates the cellular and molecular mechanisms whereby shock/resuscitation primes the immune system for increased responsiveness to inflammatory stimuli and as a result increased injury to tissues including the lung and liver. Using a number of model ranging from in vitro cell culture to animal models, the laboratory performs translational research which endeavours to understand basic mechanism in vitro and in vivo with a view to applying this information to develop novel therapeutic interventions aimed at minimizing inflammation and hence tissue injury. The lab environment has multiple senior investigators, postdoctoral fellows and graduate students, which makes it a vibrant and productive environment. In addition to your own work, there are regular lab meetings, journal clubs, and lectures at the Li Ka Shing Knowledge Institute at St. Michael's Hospital.

Dr. Markus Selzner, Surgeon Scientist

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Toronto General Hospital, MARS

Main Area of Interest

Hepatic ischemia and reperfusion injury

Current Research

1) *Determining mechanisms of sinusoidal endothelial cell injury after hepatic ischemia and reperfusion*

In a mouse model we investigate the induction of sinusoidal endothelial cell death early after hepatic ischemia and reperfusion. We evaluate the binding of inflammatory mediators to surface receptors on endothelial cells and the subsequent induction of apoptotic cell death.

2) *Ex vivo liver perfusion for the evaluation and repair of marginal liver grafts*

We are using a pig liver model of ex vivo liver perfusion to evaluate liver graft function and injury prior to liver transplantation. Inhibition of mediators of injury and induction of survival signals are used to improve the outcome of marginal grafts.

Dr. Ranil Sonnadara, Non-Clinician Scientist (in conjunction with Dr. Helen MacRae, Surgeon Scientist)

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Mount Sinai Hospital, Wilson Centre for Research in Education, Faculty of Physical Education and Health

Main Areas of Interest

Skill evaluation; proficiency-based training; skill acquisition; motor learning

Students under Supervision

Shawn Garbedian, M.Ed. candidate (OISE); Timothy Leroux, M.Ed. candidate (OISE); Brian Seeto, Orthopaedic Surgery Resident; Justin Hodgins, Orthopaedic Surgery Resident; Jim Burkitt, PhD candidate (Kinesiology, McMaster University)

Current Research

1) New methods for evaluating technical skills

We are developing a new suite of tools to allow us to more effectively evaluate proficiency levels in surgical trainees. Prospective students would have the opportunity to work as part of a multidisciplinary team to help develop and validate new methods for evaluating skill acquisition and learning, as well as helping to establish markers of 'typical' performance.

2) Optimizing skill acquisition

We are taking recent advances in the sport sciences (specifically in the fields of motor learning and control) and applying them to inform and improve the way that residents are trained. Prospective students would be exposed to current models of motor control and would gain insight into models of learning, and how these models can be applied to surgical education.

3) Sensory-motor interactions

We study how the auditory, visual and motor systems interact with each other under varying cognitive load in an effort to better understand the processes which support the learning and execution of complex skills. Prospective students would be exposed to several models of perception and action, and would gain a strong grounding in basic scientific research.

4) Attention studies

We examine how attentional resources are allocated at various stages in the surgical training process. Prospective students would gain experience in models of attention, memory and learning, and would gain a strong understanding of research methods.

Dr. Carol Swallow, Surgeon Scientist

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Mount Sinai Hospital

Students under Supervision

Francis Zih, General Surgery Resident, MSc candidate (IMS); Karineh Kazazian, General Surgery Resident, MSc candidate (IMS)

Current Research

- 1) *Defining genes that differ between metastases and primary colorectal cancer (both in terms of expression and mutations)*
We are using banked specimens from the same patient, and comparing primary to metastasis. The goal is to understand what permits/facilitates metastases, and therefore how we might intervene at a molecular level.
- 2) *Understanding how aberrant expression of the cell cycle protein polo like kinase 4 contributes to carcinogenesis, particularly hepatoma.*
- 3) *Studying the effect of Plk4 on cell motility and invasion, new functions for this gene*

Dr. David Urbach, Surgeon Scientist

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Centre for the Evaluation of Health Services in Surgery (University Health Network), ICES

Main Area of Interest

Clinical Epidemiology, Surgical Health Services Research, Health Technology Assessment

Students under Supervision

Lakho Sandhu, General Surgery Resident, PhD candidate (HPME); Robert Tasevski, Surgical Oncology Fellow, MSc candidate (HPME); Anna Bendzsak, Thoracic Surgery Fellow, PhD candidate (IMS); Binu Jacob, PhD candidate (IMS)

Current Research

- 1) *Structures, processes and outcomes of care in cancer surgery*
Our research group is conducting a number of studies on the quality of cancer care, including analyses of structures (characteristics of hospitals where care is provided), processes (what providers actually do in the course of providing clinical care), and clinical outcomes. These projects are funded by a number of agencies, including a 5-year, \$1.2 million CIHR grant to study structures, processes and outcomes in colorectal cancer.
- 2) *Applied surgical health services research at the Institute for Clinical Evaluative Sciences (ICES)*
The student will choose a project of interest to them. Previous students have looked at questions related to esophageal surgery, gall bladder disease, lung cancer, colorectal cancer, thyroid cancer, and gynecologic cancers. Typical research questions may include epidemiology, patterns of health services, and innovative methods of evaluating treatment outcomes. We provide guidance on refinement of the research question, study design, data analysis, and data presentation. Protocols are developed through weekly research-in-progress meetings in the Centre for the Evaluation of Health Services in Surgery at the University Health Network. Students attend ICES student Research-in-Progress rounds twice a month. Past students have published their thesis projects in high-impact journals such as JAMA. Through course work and applied research, all students gain familiarity with study design, analytic methods including regression models, scientific writing, and presentation skills.

The Centre for the Evaluation of Health Services in Surgery is an inter-disciplinary research unit focusing on health services research in surgery, located at the University Health Network. This collaborative unit is currently comprised of five surgeon-scientists, two non-clinician PhD scientists (one biostatistician and one qualitative researcher), four research coordinators, an administrative coordinator, six graduate students and a varying number of medical students and summer students. We provide a comprehensive research experience for clinical trainees and non-clinical trainees at all levels of training. The Centre occupies excellent research office space, provides research trainees with computers, software, and other research supplies, has appropriate rooms for meetings and workshops, and provides trainees with immediate support for research problems. Students develop, refine and present their research at weekly 1/2 day research meetings/workshops.

Dr. Thomas K. Waddell, Surgeon Scientist

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Toronto General Hospital

Main Area of Interest

Stem Cell Biology of Lung Regeneration and Lung Cancer

Students under Supervision

Humberto Lara-Guerra, PhD candidate (IMS); Sarah Gilpin, PhD candidate (IMS); Siba Haykal, Plastic Surgery Resident, MSc candidate (IMS); Lily Guo, PhD candidate (IMS); Kota Ishizawa, PDF; Yingzhe Zhou, PDF; Paula Marcus, PDF; John Soleas, MSc candidate (IMS); Geoffrey Frost, MSc candidate (IBBME)

Current Research

1) Lung Regeneration

i) Bone marrow-derived cells

Numerous studies have suggested that bone marrow cells can contribute to recovery and repair following lung injury. We have identified specific bone marrow cells that seem to be particularly useful in this regard. We are systematically pursuing the therapeutic potential of these cells for patients with advanced lung disease using human patients, transgenic animal models, and in vitro studies.

ii) Pluripotent cells

Directed differentiation of pluripotent cells towards lung phenotype will be critical for success in developing alternatives to human lung transplantation, including cell therapy approaches. In collaboration with Drs Janet Rossant, Gordon Keller, Mick Bhatia and Martin Post, we are developing the in vivo applications of such cells to both test their function and direct the phenotype. In collaboration with Andras Nagy at Mount Sinai Hospital, we are pursuing novel means of directing pluripotent cells toward a lung epithelial phenotype.

iii) Decellularization of Airway and Lung for Scaffold

Decellularization of human tissues for use as a scaffold for reconstitution of human organs has moved surprisingly rapidly towards generation of functional tissues. The first decellularized tracheal allograft was implanted in 2008 and we are pursuing pre-clinical development of second generation approaches to overcome some of the limitations seen. Moving beyond the airway, the prospect of decellularizing an entire human lung for reconstitution with stem cell-derived progenitors is an exciting new project in the lab under active pursuit with engineering faculty from the Institute of Biomaterials and Biomedical Engineering.

2) Lung Cancer

Studies in leukemia and some other solid organs have suggested that only a subset of all tumour cells is capable of initiating tumour growth. We are attempting to isolate tumour-initiating cells in early stage lung cancer, using human specimens and xenograft models. Other cancer projects including laboratory based analysis of lung cancer biopsies before and after therapy with epidermal growth factor inhibitors

Dr. Paul Wales, Surgeon Scientist

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The Hospital for Sick Children Research Institute

Main Area of Interest

Paediatric Short bowel syndrome and Intestinal Failure. Outcomes research (HPME) and Translational neonatal porcine model.

Students under Supervision

Megan Carricato, MSc candidate (HPME, Clinical Nutrition); Carol Oliveira, MSc candidate (Surgical Resident); Megha Suri, General Surgery Resident, MSc candidate (IMS); Xu Zheng, MSc candidate (Paediatrics, University of Alberta)

Current Research

1) *Omega-3 lipids and parenteral nutrition cholestatic liver disease*

Using a neonatal porcine model of short gut, the mechanism of omega-3 lipids in liver cholestasis is investigated. Students would get excellent translational research experience.

2) *Role of GLP-2 in intestinal adaptation in a porcine model of short bowel syndrome*

3) *Transition of care to adult facilities for patients with intestinal failure*

Students would get experience in qualitative methods.

Dr. Alice Wei, Surgeon Scientist

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Centre for the Evaluation of Health Services in Surgery (University Health Network)

Main Area of Interest

Quality improvement, surgical outcomes

Current Research

1) *Exploring barriers to access to care high quality surgical care for patient with liver metastases from colorectal cancer*

This is a mixed methods project that evaluates current practice patterns and access to liver resection for metastatic colorectal cancer. The impact of a knowledge translation strategy, with the implementation of an evidence based guideline is being assessed.

2) *Improving the quality of surgery through changes in processes of care*

This is a multi-faceted research program that includes development and implementation of process improvement tools for GI surgery.

Surgical Process Improvement Tools in Cancer Surgery

This project will develop a conceptual framework and catalog of surgical process improvement tools available. This study is the initial step in a multi-faceted quality improvement project that will develop process improvement tools for use in gastrointestinal cancer surgery.

Development of evidence based clinical pathways in pancreas cancer surgery

This project works with surgeons from all the high volume HPB sites in Ontario. It focuses on quality of care and knowledge exchange of best evidence. The objective of this project is to develop a clinical pathway for patients undergoing pancreatic surgery in Ontario using a point of care instrument that will bring best practices into clinical care. This research project includes developing and implementing an evidence-based clinical pathway in Ontario.

3) *Development of surgical registries*

The Ontario HPB Clinical Database Project

- 4) *This project is a prospective provincial database of HPB surgical cases. This database has been the starting point for several surgical outcome research projects to date.*

Dr. Frances Wright, Surgeon Scientist

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Odette Cancer Centre, Sunnybrook Health Sciences Centre

Main Area of Interest

Health Services Research (Surgical Oncology), qualitative methodology

Students Under Co-Supervision (in conjunction with Nancy Baxter)

Andrea Covelli, General Surgery Resident, PhD candidate (HPME)

Previous Student Projects

Nicole Look Hong - Understanding barriers and enablers to establishing multidisciplinary cancer conferences. This work was used to inform Cancer Care Ontario's implementation strategy for multidisciplinary cancer conferences.

Current Research

- 1) *Why are more women choosing mastectomy for breast cancer?*

This exploratory study is seeking to understand why women chose mastectomy rather than breast conserving surgery when diagnosed with breast cancer. Dr. Covelli who is completing this study will learn qualitative methodology, and interview techniques.

- 2) *Qualitative study of barriers and enablers of Sentinel Lymph Node Biopsy for breast cancer*

We are completing a qualitative study using interview methods to identify the barriers to adoption of sentinel lymph node biopsy for breast cancer. We had consent from 48 general surgeons, administrators, pathologists and nuclear medicine radiologists. Grounded theory is the predominant qualitative methodology used. This study was completed with Dr. May Lynn Quan.

Dr. Kazuhiro Yasufuku, Surgeon Investigator

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Toronto General Hospital, Toronto Medical Discovery Tower

Main Area of Interest

Minimally-invasive diagnostic and therapeutic techniques in lung cancer, Translational research in thoracic image guided therapeutics, Molecular staging and therapies in thoracic oncology

Students under Supervision

Takahiro Nakajima PDF; Takashi Anayama, PDF

Current Research

- 1) *Development of new technology in early diagnosis and ultra-minimally invasive thoracic surgery*

Our laboratory focuses on the development and evaluation of advanced bronchoscopic technology (high performance bronchoscopy, endobronchial US, narrow band imaging (NBI), endocytoscopy, endoscopic RFA) as well as new thoracoscopic technology for early diagnosis and ultra-minimally invasive thoracic surgery. Using a clinically relevant disease and intervention model of central and peripheral lung tumor in animals, the newest technologies are being evaluated.

2) *Translational research in thoracic image guided therapeutics (GTx)*

As part of the Guided Therapeutic Program at UHN, we are investigating the utility of different imaging modalities in the detection and treatment of lung cancer. Currently, a pig model of small peripheral lung tumor is being developed to evaluate a new GPS-guided intraoperative localization technique of small lung nodules, in the frame of minimally-invasive approach. The feasibility and reliability of this new method and its possible application area in the lung is being investigated.

3) *Molecular profiling of advanced stage lung cancer that predict response to chemo-radiation by minimally invasive procedures*

Optimal management of locally advanced lung cancer remains undefined. Patients with mediastinal nodal disease (N2/N3) are treated with chemo-radiotherapy with or without surgery. Overall prognosis is poor for these patients. We are looking at the role of minimally invasive endoscopic techniques (EBUS, EUS) for molecular profiling of these patients. Tissue obtained by minimally invasive procedures from tumors as well as mediastinal lymph nodes are being used for various molecular assays. This will perhaps provide genetic signatures that will predict response to treatment.

SSP RESIDENTS

Andrea Covelli

SSP Year: 4 (PhD Stream)

Department: HPME

Supervisor: Dr. Frances Wright and Dr. Nancy Baxter

Projects Underway

1) *Qualitative Analysis of Surgical Decision Making in Breast Cancer*

We are currently conducting a qualitative research project interviewing women who have undergone either a mastectomy rather than lumpectomy, or elected for a contralateral prophylactic mastectomy to try to identify themes that influence surgical decision making.

Marvin Hsiao

SSP Year: 3 (PhD Stream)

Department: IMS

Supervisor: Dr. Avery Nathens and Dr. Prabhat Jha

Projects Underway

1) *Quantifying burden of surgical diseases in India*

We are using a nationally representative vital statistics database (Million Death Study – www.cghr.org) to generate improved estimates of the burden of surgical diseases in India. Results of the study will help with public health priority setting for the country's 1.2 billion people.

2) *Road traffic injury mortalities in India - Characterizing injury mechanisms and barriers to access*

Also using the Million Death Study database, road traffic injury patterns and barriers to access of health care facilities are characterized.

3) *Effect of distance to health centre on mortality due to surgical conditions in India*

A geographic information system (GIS) approach is used to study various factors affecting access to health centres.

4) *Factors affecting physician agreement on verbal autopsy of surgical conditions in India*

The internal validity of the verbal autopsy tool (used in the Million Death Study) for surgical conditions is analyzed using statistical methods.

Karineh Kazazian

SSP Year : 2 (MSc Stream)

Department : IMS

Supervisor : Dr. Carol Swallow

Projects Underway

- 1) *Identification and investigation of novel genes that drive metastatic progression in Colorectal Cancer. Identification of Polo-Like Kinase 4 (PLK4) interactors in cancer cells.*
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Debbie Li

SSP Year: 1 (MSc Stream)

Department: HPME

Supervisor: Dr. Avery Nathens

Projects Underway

- 1) *A population based analysis of the management of appendicitis.*
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Charles de Mestral

SSP Year: 3 (PhD Stream)

Department: IMS

Supervisor: Dr. Avery Nathens

Projects Underway

- 1) *Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: practice patterns, effectiveness and cost-utility.*
Using population-based data available through the Institute for Clinical Evaluative Sciences, we are comparing the effectiveness of early vs. delayed cholecystectomy as well performing an economic evaluation of both strategies and examining practice patterns in Ontario.
 - 2) *Traumatic injuries:*
Using retrospective trauma registries, we are looking at various traumatic injuries (eg. vascular trauma, mangled extremity, flail chest).
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Jennifer Muir

SSP Year: 1 (MSc Stream)

Department: HPME

Supervisor: Dr. Calvin Law

Projects Underway

- 1) *Exploring patterns of care for gastric cancer in Ontario: do urban-rural differences exist?*

Marisa Louridas

SSP Year: 1 (MSc Stream)

Department: IMS

Supervisor: Dr. Teodor Grantcharov

Projects Underway

- 1) *Coping with complicated situations. Mental practice and simulator training to enhance surgical performance in the operating room and in adverse situations.*

Lakho Sandhu

SSP Year: 5 (PhD stream)

Department: HPME

Supervisor: Dr. David Urbach

Projects Underway

- 1) *An Empirical Study of Bias in Non-randomized Studies of Surgical Interventions*

Findings from RCTs are considered less biased than those from non-randomized studies because in the former, randomization balances *unknown* confounders between both study groups. We are using Bayesian modeling techniques to determine which characteristics of non-randomized studies are most often associated with bias.

Chethan Sathya

SSP Year: 1

Department: HPME

Supervisor: Dr. Avery Nathens

Projects Underway

- 1) *Determining and analyzing predictors of quality of care within pediatric trauma centers.*

Megha Suri

SSP Year: 2 (MSc Stream)

Department: IMS

Supervisor: Dr. Paul Wales

Projects Underway

- 1) *The Effect of Exogenously Administered Glucagon-like Peptide-2 in Neonatal Piglets with Short Bowel Syndrome*

Short bowel syndrome, common in the neonatal population, results from congenital or acquired intestinal abnormalities requiring extensive surgical resection. In order to with short bowel syndrome, parenteral nutrition is typically required. Since long-term administration of parenteral nutrition is associated with significant morbidity and mortality, early adaptation and growth of the native intestine is desired.

Glucagon-like peptide-2 is a naturally occurring hormone involved in the regulation of intestinal mucosal integrity, permeability, and nutrient absorption. We are investigating the effect of exogenously administered glucagon-like peptide-2 in a short bowel neonatal piglet model of two common intestinal anatomical variants observed in the clinical setting of short bowel syndrome.

Boris Zevin

SSP Year: 3 (PhD Stream)

Department: IMS

Supervisor: Dr. Teodor Grantcharov

Projects Underway

- 1) *Design and Validation of a Surgical Skills Assessment Tool for Laparoscopic Roux-en-Y Gastric Bypass (LRYGBP).*
 - i) DELPHI methodology to attain expert consensus on the key steps and sub-steps of LRYGBP to be included in the assessment tool. ii) Validation of the tool by comparing expert and novice surgeons and demonstrating a difference in scores for two groups.

- 2) *Design and Validation of Simulation-based Technical Skills Training Curriculum for Laparoscopic Bariatric Surgery.*
 - i) Development of a cognitive, technical and non-technical components of the curriculum. ii) Prospective, single-blinded randomized trial of PGY 3-5 residents subjected to newly developed curriculum to demonstrate validity.

Nathan Zilbert

SSP Year: 1 (MEd Stream)

Department: O.I.S.E.

Supervisor: Dr. Carol-Anne Moulton

Projects Underway

- 1) *We are investigating how surgeons prepare for operations, looking at the differences between staff surgeons and trainees. Ultimately we hope to develop tools to facilitate the transition from trainee to expert.*