Chair’s Report
Department of Laboratory Medicine & Pathology
Faculty of Medicine & Dentistry
University of Alberta

Letter from the Chair

Dear Colleagues, Learners & Friends!

Welcome to the first Chair’s Report in 2022! After two years of pandemic I hope that we enter a year of less stress for our personal and professional lives. However, we can expect phases of uncertainty and change to occur with entering into the transition and implementation phase of the outcome from the Community Lab Services outsourcing. Knowing our teams and with DynaLife Medical Labs as a longstanding partner, I am confident that many new promising opportunities will arise to advance our academic mission. For example, we just recently received 3 million dollars in funding from Alberta Innovates to form a partnership between our department, Alberta Precision Laboratories, DynaLife Medical Labs, and the University of Calgary to advance research discoveries in the area of laboratory diagnostics into clinical use and commercialization. I encourage all of you to stay curious for the opportunities arising from such partnerships and to build on our strong educational, clinical, and research programs. Please do not hesitate to connect with me directly with any questions or concerns arising during the upcoming transition.

I very much enjoyed reading the Spotlight on Research for this issue of the Chair’s Report as an example of our strong clinical, translational research activities in the department. Recently we were able to recruit back Dr. Cheng-Han Lee into the endowed San Baldwin Research Chair in Ovarian Cancer at the Cancer Research Institute of Northern Alberta (CRINA). Cheng is a well-recognized translational cancer researcher with a focus on tumors of the gynecologic tract. His clinical practice as a sub-specialized gynecological and soft tissue pathologist is at the Royal Alexandra Hospital which is a leading center for Women’s Health. Please take a moment to read more about the cutting-edge and quite exciting work of Dr. Lee.

Please also join me in welcoming our new faculty members and students, and also our new Graduate Program Advisor Lennora Crilov who will support our program part-time to facilitate the ongoing success of our graduate students. I congratulate our students for their recent achievements (page 5), as well as our faculty members and colleagues for their impressive scholarly productivity over the last quarter. Just another strong academic quarter – Way to go LMP!

The planning activities for the 2022 DRIvE Days, which will be a virtual event on April 22 & 23, 2022, and Banff Pathology Course (2022 Topic: Genitourinary Pathology), which will be an in person event Sept 8 – 10, 2022, are fully underway (see last page of the report to save the dates in your calendars!)

I hope and look forward to reconnect with all of you in person throughout 2022!

Michael

Dr. Michael Mengel, MD
Professor and Chair
Department of Laboratory Medicine & Pathology, University of Alberta
North Sector Medical Director, Alberta Precision Laboratories (APL)

uab.ca/LMP

February 2022
Dr. Cheng-Han Lee is an Associate Professor and Anatomical Pathologist in the Department of Laboratory Medicine and Pathology at the University of Alberta and Royal Alexandra Hospital. He is the current endowed Sawin-Baldwin Chair in Ovarian Cancer and is part of the team of researchers at the Women and Children's Health Research Institute (WCHRI).

I am a cancer researcher with a long-standing interest on the tumors of the gynecologic tract. While my initial focus was on identifying genomic drivers that are involved in the development of gynecologic cancer, I have over the past few years shifted my focus on identifying more effective treatment options, particularly for gynecologic cancer types that are clinically aggressive and refractory to conventional standard-of-care treatment. This is best exemplified by the work we have done on dedifferentiated endometrial/ovarian cancer, which is a highly aggressive type of gynecologic tract cancer that frequently presents with advanced stage disease and is resistant to standard platinum/taxane-based chemotherapy. Histologically, dedifferentiated cancer occurs when a low-grade endometrioid-type adenocarcinoma that is associated with excellent prognosis undergo an extreme form of transformation – “dedifferentiation”, in which a well-differentiated gland/papillae-forming adenocarcinoma transform into a solid sheet-like growth of undifferentiated tumor that are primitive stem-cell like with upregulated stem cell markers and downregulated epithelial/Mullerian differentiation markers. In 2016, we identified the critical genetic switch for dedifferentiation, in that genomic inactivation resulting in loss of expression of core SWItch/Sucrose Non-Fermentable (SWI/SNF) complex proteins through one of the three mutually exclusive mechanisms – ARID1A and ARID1B co-inactivation, SMARCA4 (BRG1) inactivation or SMARCB1 (INI1) inactivation are associated with this phenomenon of dedifferentiation in endometrial/ovarian cancer. This initial discovery was subsequently confirmed by follow-up studies from us and other groups. It also led to the increasing utilization of ARID1B, SMARCA4 and SMARCB1 immunohistochemistry in the clinical setting to confirm the diagnosis of dedifferentiated cancer. Moreover, together with Dr. Lynne Postovit and Dr. Mackenzie Coatham (Ph.D. student Lynne and I co-supervised, with successful thesis defense in December 2021), and with support from Canadian Cancer Society and CIHR, we proceeded to evaluate how core SWI/SNF protein inactivation result in dedifferentiation. Mackenzie demonstrated through her thesis study using CRIPR knockout (KO) model of SMARCA4 in human endometrial cancer cell line that SMARCA4 inactivation/protein loss result in the formation of dedifferentiated cancer. However, in order for dedifferentiation to occur, the SMARCA4 KO cells need to be subjected to appropriate in vivo growth environment – serial tumor passaging as cell line-derived xenograft. This 3-dimensional in vivo xenograft environment appears to induce dramatic shift in epigenetic/methylation landscape of the tumor cells, which is required in addition to SMARCA4 inactivation to give rise to dedifferentiated tumor. In addition to the engineered model of dedifferentiated cancer, we were also successful in developing primary cell lines and patient-tumor derived xenograft (PDX) tumor lines from patient samples of dedifferentiated endometrial cancer. Guided by the biologic insights and additional multi-omics analyses including shRNA screen, we are currently evaluating the efficacy of novel therapies using these engineered and patient tumor-derived preclinical models of dedifferentiated cancer. Given the dismal prognosis of SWI/SNF-inactivated dedifferentiated cancer (medium disease-specific survival of 4 months in stage III-IV setting) and the lack of response to standard platinum/taxane-based chemotherapy, we believe our efforts will in the near future help to identify more effective treatments for this highly aggressive type of gynecologic cancer.

In addition to dedifferentiated cancer, we are also studying other aggressive gynecologic cancer types lacking effective therapeutic options. This includes uterine and ovarian carcinosarcoma. With funding support from Cancer Research Society of Canada and in collaboration with Dr. Mark Carey from Vancouver, we were able to successfully establish several patient tumor derived cell line and PDX tumor line models of carcinosarcoma. We have identified high level receptor tyrosine kinase genomic amplification (i.e. FGFR1, FGFR3, ERBB2) in a number
Spotlight on Research (cont’d)

of these carcinosarcoma models. We are currently evaluating the therapeutic efficacy of pharmacologic inhibition of the amplified kinases in these preclinical models and initial results are promising. Most recently, we have started to study homologous repair-proficient (HR-proficient) high-grade tubo-ovarian serous cancer (HGSC). HR-proficient molecular type of HGSC do not harbor BRCA1/2 mutations, and are less responsive to both conventional platinum/taxane-based chemotherapy as well as newer targeted therapy such as Poly (ADP-ribose) polymerase (PARP) inhibitors. Biallelic NF1 deletion occurs in about 20% of HR-proficient HGSC and loss of NF1 can result in increased activity of RAS such that it amplifies the signalling effect from upstream receptor tyrosine kinases (i.e. EGFR, PDGFRA, MET) and increases the activation of downstream effectors that include RAS-MEK-ERK and PIK3CA/AKT/mTOR pathways. NF1 inactivation therefore may signify potential therapeutic opportunity in this major subset of HR-proficient HGSC. Rachel Yang, who is a MSc student co-supervised by Dr. Yangxin Fu and myself, will devote her study on HR-proficient HGSC harboring biallelic NF1 deletion. She will be applying phosphokinase/phosphoprotein screen to identify potential pathway(s) to target in NF1-inactivated HGSC. As part of this research effort, we also plan to develop additional preclinical models of HR-proficient HGSC, particularly ones with NF1 inactivation, for future therapeutic evaluation.

As the ultimate research aim of our group is on identifying more effective therapies for aggressive gynecologic cancer types that lack effective treatment, we are constantly looking to innovate our approaches and techniques to optimize the comprehensiveness of our molecular analyses to better inform treatment strategies and to improve the predictiveness of the preclinical experimental models. For instance, in terms of analytics, we are working with collaborators at both the University of Calgary and Queen’s University to further characterize the tumor immune microenvironment to further inform on potential immune-modulatory treatment strategies. In terms of preclinical model development, we also plan to establish microfluidic-based system for in situ study of freshly dissected human tumor tissue, which would enable for evaluation of tumor-stromal interaction.

Currently, we have a relatively small research team in our laboratory given my recent arrival to the University of Alberta. I have introduced Dr. Mackenzie Coatham (post-doctoral research fellow working with Dr. Lynne Postovit and myself) and Rachel Yang (MSc student co-supervised by Dr. Yangxin Fu and myself). Dr. Jiahui Liu is an senior research associate in our lab who I have worked with over the past several years. We also work closely with Dr. Postovit (Queen’s University), Dr. Fu in the Department of Oncology and the team of Gynecologic oncologists at Royal Alexandra Hospital. We have active collaboration with other gynecologic cancer researchers across the country, including Dr. Martin Koebel from the University of Calgary and Dr. Mark Carey from the University of British Columbia, and are establishing additional research collaboration with researchers from the University of Saskatchewan, University of Toronto, Queen’s University and McGill University. While the pandemic has presented some challenges, we are optimistic that our ongoing collaborative research efforts will soon result in findings that can be translated into the clinical setting to improve the lives of women affected by these aggressive gynecologic cancers.

Dr. Mackenzie Coatham (Post-doctoral research fellow)
Dr. Jiahui Liu (Senior research associate)
Rachel Yang (MSc student)
New Appointments

The Department welcomes:

- Dr. Ingo von Both – Assistant Clinical Professor – Forensic Pathologist and Assistant Chief Medical Examiner, Office of the Chief Medical Examiner
- Dr. Natalia Volodko – Clinical Lecturer – Molecular Scientist, DynaLiFE
- Dr. Joseph Andrews – Clinical Lecturer – Pathologist, University of Alberta Hospital

Dr. Ross Mclean
- Member of Alberta Colorectal Cancer Screening Program (ACRCSP) Advisory Committee
- Member of Alberta Colorectal Cancer Screening Program (ACRCSP) Polyp Surveillance Committee
- Member of GI Provincial Interest Group

Grants

Dr. Michael Mengel
1. Project: Alberta Diagnostics Ecosystem Platform for Translation (ADEPT) – Stage 2
   Grant agency: Alberta Innovates, Total amount awarded: $3,000,000
   Duration: 01/2022 – 12/2024

Congratulations!!

Dr. Victoria Higgins successfully passed the Canadian Academy of Clinical Biochemistry (CACB) written certification exam, written on November 1, 2021.
Graduate Studies

Milestones

Congratulations to the following students on their successful doctoral candidacy exam:

- Nicholas Wawryk (supervisor Xing-Fang Li)
- Alexa Thompson (supervisors Carmen Charlton and Greg Tyrrell)

Congratulations to Wenhui Li (supervisor Jason Acker) on getting her PhD proposal approved by the Graduate Studies Committee.

Awards

Congratulations to these students who received awards acknowledging their research and/or supporting their graduate programs:

- Claire Feng - Alberta Graduate Excellence Scholarship
- Serena Li - Alberta Graduate Excellence Scholarship
- Teresa Kublathan - Alberta Graduate Excellence Scholarship
- Yasmine Rais - Alberta Graduate Excellence Scholarship
- Janet Zhou - Alberta Graduate Excellence Scholarship
- Tanya Podilchak - Bell McLeod Pathologist Assistant Entrance Scholarship
- Gabrielle Mendler - Bell McLeod Pathologist Assistant Entrance Scholarship

Congratulations to All!

In January we welcomed two additions to the LMP Graduate Program:

Camille Huang (supervisor, Chris Le) to our thesis-based master’s program

Lennora Crilov, Graduate Program Advisor
Lennora has a legal background with a Masters in Law (LL.M) from the Pennsylvania State University, U.S.A. and has worked in various administrative capacities with universities from the United States and Kazakhstan. Lennora will be working with the LMP Graduate Program in 0.5 FTE capacity (Mondays, Wednesdays and Fridays) and can be reached through our program email lmpgrad@ualberta.ca.
Presentations

Dr. Jason Acker

Abstracts:


Dr. Ben Adam

Invited Presentations:

2. Shaukat Khanum Memorial Cancer Hospital and Research Centre Annual Symposium, Peshawar, Pakistan (virtual due to COVID-19), November 6, 2021. "Fundamentals of Native and Transplant Kidney Pathology: A Pattern-Based Approach"

3. American Society of Nephrology Kidney Week, San Diego CA (virtual due to COVID-19), November 4, 2021. "Beyond the Biopsy: Diagnosis Rejection - More than meets the eye: long live the biopsy!"


Dr. Sumit Das

Presentations:


Dr. Victoria Higgins

Oral Presentation:
1. OSCC Annual Scientific Meeting; Virtual; 2021 November 9. Higgins V. "Harmonized Lipid Reporting Model for Clinical Laboratories based on the 2021 Canadian Lipid Guidelines".

Dr. Ross Mclean

1. "Alveolar Hydatid Disease in Canada: past and present" University of Western Ontario Jan 20, 2021

Dr. Susan Nahirniak


Recent Publications

Dr. Jason Acker


Dr. Ben Adam

Peer-reviewed Papers:


Dr. Will Chen

1. Chen ZW, Wizniak J, Shang C, Lai R. "Flow cytometric detection of the double positive (CD4+CD8+)/PD-1 bright T-cell subset is useful in diagnosing nodular lymphocyte predominant Hodgkin lymphoma". Arch Pathol Lab Med. 2021 Sep 10
Recent Publications continued...

Dr. Will Chen (continued):

Dr. Matthew Croxen
Peer-Reviewed Papers:

Dr. Sumit Das:

Drs. Janet Elliott & Locksley McGann
Peer-reviewed papers:

Dr. Victoria Higgins:

Dr. Mao-Cheng Lee:

Dr. Roger Leng:

Dr. Michael Mengel
Peer-reviewed Publications:

Dr. Susan Nahirniak
Peer-reviewed Publications:
Save the Dates 2022

DRIvE
Discovery, Research, InnoVation and Education

DRIvE 2022 will be held on Friday, April 22 and Saturday, April 23, 2022

Keynote Speakers:

Friday, April 22
Dr. John W. Macgregor Memorial Lecture
Speaker: Dr. Neeloffer Mookherjee, PhD
CIHR Sex and Gender Science Chair in Circulatory and Respiratory Health
Professor, Departments of Internal Medicine and Immunology
Manitoba Centre for Proteomics & Systems Biology
Rady Faculty of Health Sciences
University of Manitoba
Topic: Dysregulation of host defense by inhaled environmental exposures: Importance of including sex as a biological variable

Saturday, April 23
Dr. RE Bell Memorial Lecture
Speaker: Dr. Michael Houghton
Director & Professor, Li Ka Shing Applied Virology Institute
Faculty of Medicine & Dentistry
University of Alberta
Topic: Vaccine and therapeutic development programs within the Li Ka Shing Applied Virology Institute

The Banff Pathology Course
September 8-10, 2022
Urogenital Pathology