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ADVOCATE

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Medical Laboratory Professionals' Association of Ontario

MLPAO
Medical Laboratory Professionals' Association of Ontario

Advancements in Lab Science

MLPAO

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#TeamMLPAO

Correction: *In our last issue (Volume 31, Issue 2, Spring 2024) we incorrectly spelled the name of one of our contributors, Cody Clelland. We sincerely apologize for this error.*

Chair's Message

Dear Members, Stakeholders and Partners

It is with great excitement that I share my first address as your Board Chair. I have been a member of the MLPAO since I first graduated in 1999. Over the past 8 years, my passion for the profession has been reignited as I have watched the MLPAO make great strides in the profession.

As you sit in your labs and read this magazine, I am most likely working the bench doing the same work you do. Doing a job that I love, regardless of how understaffed or challenging it can be at times. I know the joys, struggles, the ups and downs the job brings. But knowing that I am an important part of the healthcare life team brings a sense of resolution to my life.

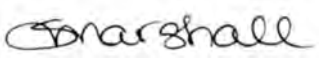
Being on the MLPAO Board of Directors has been a highlight of my career. Finally there is an association that is actually doing something for lab professionals. I have been disappointed over the past 20 years to watch other professionals grow, get recognition and prosper, while the lab always seems to be left behind or forgotten. But I know for a fact that isn't the case anymore.

The MLPAO has our backs. They are involved in many discussions at Queen's Park with all ministries making sure that lab is included in important decisions and asked for input when policies are being developed. On page 13, our CEO provides a recap of the funding we have received over the past 5 years. Did you know that MLT students going to school at Cambrian College and St. Clair College attend for free? Yes! This is just a small example of the impact the MLPAO has had.

The Board of Directors is a group of lab professionals that are ensuring that the MLPAO is getting work done for its members. We also think it's important to acknowledge the great work you do. For this reason, we have updated our awards and bursaries (page 13). If you have someone in your lab that you think should be acknowledged, I would encourage you to nominate them for an award. Our mission is to make sure that the lab voice is not only heard, but also acknowledged. You are the reason we exist.

As we approach 2025, we encourage you to tell your colleagues and friends that the lab association to join is the MLPAO. We are making progress and getting things done.

I look forward to an exciting year as your Board Chair. Things are only going to get better!



Sandra Marshall
Board Chair, MLPAO

CEO's Message

Dear Members, Stakeholders and Partners

2024 had been an incredible year and there is still so much more to do! The success with our advocacy, the increase in membership engagement, the outreach from stakeholders asking how they can help and the interest in doing lab tours, has kept us busy.

Working on Funding: After the announcement of extending the Learn and Stay Grant and furthermore adding 700 seats to the 2024 Budget, we continued to meet with our government to talk about what else is needed. We are working on the 2025 Pre-budget Submission that will look at providing relief to employers enabling them to take more students.

Another great outcome from our advocacy work is the new MLT programs that are opening up in Ontario. With current programs adding seats and new programs starting, placements will continue to be the bottleneck.

Staying Connected: We hosted a successful conference at Blue Mountain in early June. Over 250 lab professionals participated in two great days of learning and connecting. From line dancing to literally walking up the mountain, memories were made to last a lifetime. We hope you will join us in Kingston in 2025.

Med Lab Week 2024: We had another successful med lab week, with engagement with over 13,500 lab professionals. Our #wetestforthat was celebrated across the province in over 235 labs. This week is getting bigger and better every year. We are already planning for 2025!

We are working hard to ensure that our members get what they need from us. Over the past 5 years, I have been visiting labs across the province, talking to lab professionals to hear what they have to say. I will be visiting labs across the province this fall once again. If I get the opportunity to visit your lab, I hope you will drop in to say hi. It is truly a pleasure to meet the incredible members of the MLPAO. You are doing incredible work. The work we do is from the feedback you provide.

As we approach a new year, we are encouraging all our members to spread the news about the great work the MLPAO is doing, and hopefully we will see new faces in our membership. Our success so far has been because you get involved through feedback, surveys and input. Let's keep the momentum going. Let's stay connected and involved. We are your voice!

Thanks for all you do! Happy to chat anytime, you can email me at mhoad@mlpao.org.

Thanks,

Michelle Hoad, CAE
Chief Executive Officer

Advancements in Lab Science

Using TeleVU to Connect Pathology Services Over Great Geographical Distances

Jennifer Sanna-White, BSc, MLT
Manager of Laboratory Services, Red Lake Hospital

Marc is wearing the smart glasses and UHN can see exactly what he is looking at through the camera

The Kenora Rainy River Regional Laboratory Program (KRRRLP) was privileged to have two Pathologists at Lake of the Woods District Hospital (LWDH) to help serve the needs of all six hospitals within the region, however with the national shortage of pathologists, it was a challenge to recruit prior to their retirement in 2022. Without an on-site pathologist, the ability of all hospitals in the region to continue with surgical procedures was at risk. Fortunately, a partnership was developed with the University Health Network Laboratory Medicine Program to ensure the continuation of all regional laboratory services, including a new model for surgical pathology.

The new pathology structure required Medical Laboratory Technologists (MLTs) at LWDH to take on the task of grossing surgical pathology samples. This process was mostly new to the region aside from a small subset of urgent grossing previously performed at Sioux Lookout Meno Ya Win Health Centre (SLMHC) which was guided by real-time remote support with a tablet connected to a pathologist at LWDH. This process was quite cumbersome, and the imaging capabilities of the tablet were mediocre. It was clear that going forward with the new model, real-time remote access to the UHN Pathology team would be required to support the MLTs at LWDH in a similar fashion for the more complex cases presented to them. Fortunately, the SLMHC laboratory team discovered a technology in use in their wound care clinic which seemed fitting to translate to laboratory use to more effectively provide the needed virtual support. This technology is called TeleVU and was adopted by LWDH.

TeleVU is a collaboration technology that provides remote medical assistance using augmented reality, artificial intelligence and IoT devices. With the TeleVU system, users can obtain live medical guidance and support from other medical professionals from afar. The solution integrates IoT devices like smart glasses, cameras, and other smart devices. Screensharing and recording join geographically separate teams together to provide care.

With the TeleVU system, users can obtain live medical guidance and support from other medical professionals from afar.

The tablet stand allows LWDH to see what UHN is seeing and will be used for competency assessments and training.

Technologists at Lake of the Woods District Hospital were very excited about the prospect of using TeleVU smart glasses for communication with Pathology Assistants (PAs) more than 1900 km away. Although they received robust hands-on training to improve their competence and comfort in grossing, there was still a clear need for real-time, visual communication. With the generous support of the FDC Foundation, the hospital purchased the system in June 2023. Implementing the technology was a multi-department collaborative effort. Once the local IT and laboratory training occurred virtually, the LWDH IT department worked diligently on the connectivity and the technologists dove into the use of the TeleVU glasses in practice.

When a difficult case arises in the lab, the MLT will request that a UHN Pathologist Assistant sign into the system on a desktop computer, and the TeleVU glasses are donned by the LWDH MLT. An internal camera captures what the MLT is seeing with excellent clarity, and a built-in microphone allows the operator to speak to the PA or dictate their observations. The PA can simultaneously direct and guide the MLT in grossing the specimen. The two-way audio and visual can be captured in a recording for future uses such as dictation, pathologist review if future questions arise, and training and competence assessment, thus adding overall efficiency and quality to a lab experiencing HHR issues, like most others in the province.

The KRRRLP partnership with UHN LMP, and implementation of the TeleVU system has played a vital role in maintaining regional lab and surgical services, allowing patients in Northwestern Ontario to receive care close to home. It has also helped to ensure sample integrity through on-site processing of tissues, improved turn-around-times thus improving patient outcomes, and allowed for the continuation of certain surgical procedures such as limb amputations and mastectomy procedures, among others.

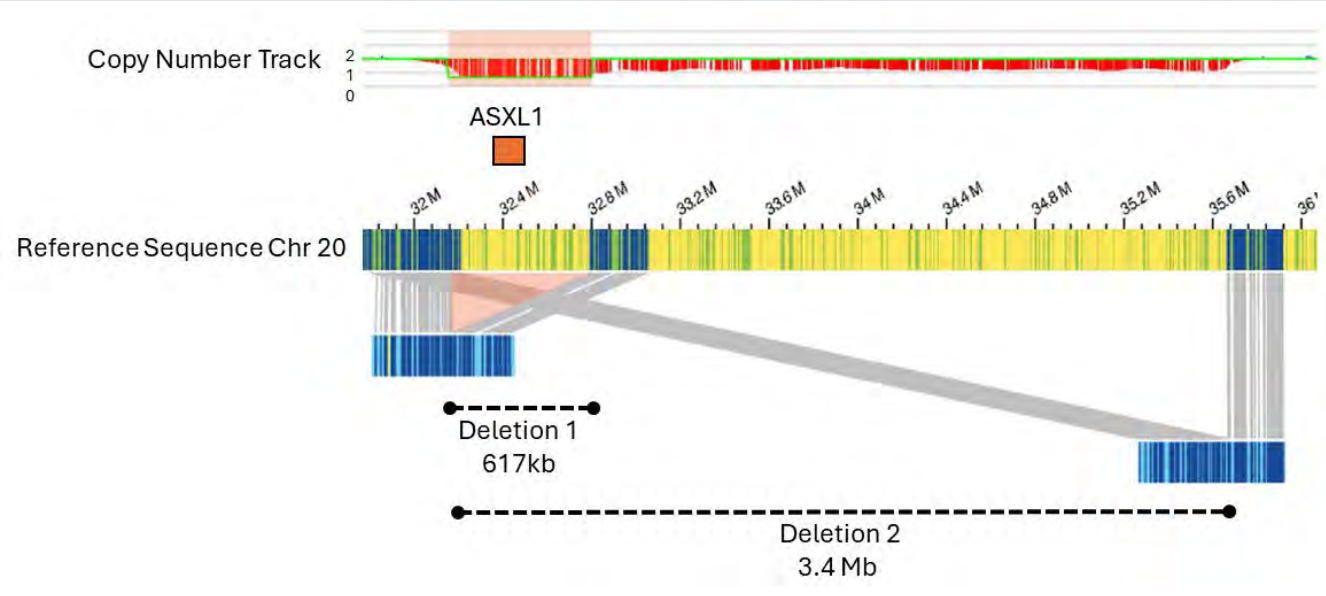
Future plans include implementing a digital pathology scanner to advance care in the Northwest region which will further support bridging the gap to care in a region facing unique challenges and remote geography. This additional advancement is expected to be implemented in October 2024.

The Structural Variation Gap: How High-Resolution Optical Genome Mapping is Changing Cytogenetics Practice

Adam C. Smith, PhD, FCCMG, FACMG, erCLG
Assistant Professor, University of Toronto
Clinical Molecular Scientist, Sunnybrook Health Sciences Centre

The detection of genomic alterations is of growing importance in many areas of medicine. Especially in hematologic malignancies, like acute myeloid leukemia, the underlying genetic changes have become synonymous with their diagnostic categories and carry important prognostic and treatment considerations. These changes have occurred over the last 30 years since the largely morphological French-American-British (FAB) classification of AML[1] has been replaced by the largely genetic classification of the World Health Organization[2] and International Consensus Classification.[3] Consequently, the amount and complexity of genetic testing performed has grown exponentially.

The most recent classification of AML (2022) divides genetic abnormalities into two main categories: cytogenetic abnormalities (structural) and sequence abnormalities (molecular).[4] The cytogenetic abnormalities have been catalogued and studied over many years using karyotyping. A growing number of sequence variants are now part of the classification thanks to the growing utilization of next generation sequencing. However, the "gap" between small sequence variants (e.g. single nucleotide substitutions, 4bp NPM1 deletions, up to 100's of base pair internal tandem duplications of FLT3) and large structural variation detected by cytogenetics (> 10 megabases) is not insignificant. Despite the profound ability of karyotyping to detect structural changes at the single cell level – with the current gap between sequencing and karyotyping, a lot can be missed. This can be because the rearrangement is cryptic (doesn't result in a visible change in banding pattern), is too small or too complex to be resolved by karyotyping or requires additional assays to confirm (e.g. FISH, RT-PCR or RNA fusion panel). We demonstrated this several years ago in a study of complex



karyotype AML patients by comparing their karyotype results to genome and transcriptome sequencing.[5] We detected the presence of cryptic rearrangements and additional rearrangement complexity that could not be seen by karyotyping. While genome sequencing has been proposed as an alternative to karyotyping in myeloid malignancies,[6] it comes with some significant challenges as well. For a deeper discussion on these topics see our editorial in the 2023 special issue on Optical Genome Mapping in Hematologic Malignancies in the Journal Cancers.[7]

Enter, optical genome mapping (OGM). OGM is a technique that has been around for several years; instead of sequencing, it is an orthogonal technique that produces a map of the genome. Initially, it was primarily used to create scaffolds to order and orient sequence contigs as part of de novo genome assembly especially in plants and animals. Over the last decade, as long read sequencing has improved, OGM has played a key synergistic role in the production of essentially all modern reference genome assemblies. With further recent improvements in throughput and cost reduction of OGM, it has now become feasible to use OGM in routine human cytogenetics to detect structural variation. The technique leverages ultra-high molecular weight DNA with the median molecule length being approximately 150kb. These long molecules are key to OGM's ability to detect and map structural variation even involving highly repetitive sequences in the genome. Once the DNA has been extracted from the sample, the DNA is labelled at a 6 base pair sequence that repeats every 5-6kb throughout the genome and the molecules are then separated and imaged in a nanochannel flow cell. This information is digitized and processed bioinformatically to generate a high-resolution genome wide analysis of structural and numerical changes in the genome down to 500 bp in size. This increase in resolution above karyotyping (100-20000x) helps to considerably close the gap between molecular and cytogenetic technologies allowing us to see structural variation more clearly.

OGM is a technique that has been around for several years; instead of sequencing, it is an orthogonal technique that produces a map of the genome.

What does this mean for genetics laboratories? Current workflows for AML require the use of multiple techniques to complete a patient analysis. These may include karyotype, FISH, MLPA, chromosomal microarray, PCR and next generation sequencing (NGS). It is important to remember that recapitulating a karyotype analysis using molecule techniques is very difficult. For example, RNA fusion panels detect translocations that generate chimeric fusion proteins, but detecting

Figure 1. *Submicroscopic Dual Deletion of Chromosome 20q. This sample illustrates several interesting concepts where our knowledge meets the limits of current guidelines. The data shows two different clonal deletions of chromosome 20q. The top track shows a copy number plot across the region of chromosome 20q showing loss of a single copy of chromosome 20q across most of the region except where the two deletions overlap and the copy number track loss of both alleles in a large percentage of the sample. The reference sequence for chromosome 20q is shown with the location of OGM labels indicated by vertical lines along the reference sequence. Labels are shown in yellow (when not aligned to a hybrid sequence) or blue (when aligned with the hybrid sequence). The two deletions are shown below the reference sequence with the grey matchlines aligning to the proximal and distal breakpoints for each deletion and no aligned matchlines within the deleted region. The deletions are 617kb and 3.4Mb, respectively. Both deletions are below the resolution of karyotype analysis. The location of the ASXL1 gene is shown. This abnormality raises several questions: 1) Is this considered a deletion 20q since it is not visible by karyotype? 2) The deletions result in complete loss of ASXL1 expression in cells with both deletions (a majority of cells based on the high proportion of both deletions). Is this therefore classified by the ELN classification as mutated ASXL1 or deletion 20q? (see reference 4 to see how ASXL1 "mutations" and deletion are classified differently) 3) Using standard analysis recommendations for OGM these deletions would be considered Tier 1 (Pathogenic) abnormalities, but would not be counted towards a complex "genome" as they are below the 5Mb threshold. This situation illustrates rather simply how increasing the resolution can challenge our analysis and classification systems and will require the continued dedicated work of laboratories around the world to help describe and study the SVs we are currently missing by conventional analyses.*

enhancer-hijacker translocations, like MECOM rearrangements, are much more challenging. Further, doing a complete genome analysis for complexity requires seeing all the copy number and structural changes at once. And while genome sequencing may be able to do this to some extent it is usually only performed at relatively low coverage (30 – 80x), as higher depth would be cost prohibitive. [7,8] Compare this to targeted myeloid NGS panels that are run at ~500x coverage to achieve an approximate ~2% variant allele frequency lower limit of detection. So even if you did a genome sequence to detect structural abnormalities – you would still need to run a panel at high depth for mutations. By comparison, OGM (300x) plus a high coverage NGS panel (500x) can provide the required sensitivity for a complete genomic evaluation with the potential for significant workflow savings.[9] In some situations, standalone assays for FLT3, NPM1 and IDH1/2 are performed – but these are performed because clinical turnaround time requirements demand these results in five days before treatment is started, often before NGS results are available.

To date, many studies have compared the concordance between conventional approaches to AML diagnosis and the use of OGM.

To date, many studies have compared the concordance between conventional approaches to AML diagnosis and the use of OGM.[10–12] While every technique has its strengths and limitations – the overall conclusion from these studies is that OGM is able to detect recurrent and novel changes that are missed by current approaches. Interestingly, the impact of high resolution structural variant analysis is also likely to change the classification in interesting ways (Figure 1). For example, many genes that have sequence variants that cause loss of function and are detected by NGS panels have also shown that they can have small structural variations that also cause loss of function (e.g. deletions). Indeed, our recent publication of the comparison of detection techniques (MLPA, NGS and OGM) shows the importance of seeing the structure of these changes and interpreting it in the proper context.[13] New technologies for structural variant detection present new challenges and new opportunities for genetics laboratories to better understand the biology of disease and improve patient care.

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Biobanking and the Canadian Longitudinal Study on Aging (CLSA)

Cynthia Balion, MSc, PhD, FCACB
Clinical Biochemist, Hamilton Regional Laboratory Medicine Program (HRLMP)
Director, Biorepository and Bioanalysis Centre, Canadian Longitudinal Study on Aging (CLSA)

Biobanking has been around for a very long time. Collection and preserving biological specimens from seeds to butterflies to human body tissue and fluids creates a repository of information to access to advance our knowledge of the field. It was not until the year 2000 with the formation of the International Society for Biological and Environmental Repositories (ISBER) that biobanking became recognized as a unique discipline. It embodies more than a registry of specimen type and identification number. It requires information associated with the biospecimen and collecting these data involves a study governance structure, ethics, consent, privacy, security, document and data management systems, as well as repository design for efficient and safe storage and retrieval of biospecimens.

In laboratory medicine, the biomarker or test result is used for patient care but biomarkers are also important in clinical and epidemiological research. Laboratory medicine has a strong structure of quality processes that are fundamental to ensuring the test result produced is the best it can be. This culture of quality is also necessary in research as the evidence informs clinical decision-making as well as public health policy. Furthermore, the quality of biological samples collected is essential for biopharmaceutical and diagnostics industries that use or develop biomarker tests and require regulatory approvals for implementation for clinical care. When and how biospecimens are collected, how they are transported, processed, stored, analyzed, along with standardized protocols, quality indicators, proficiency testing are all crucial to the generation of sound biomarker data.

The Canadian Longitudinal Study on Aging (CLSA) is the one of world's largest and most comprehensive aging studies in breadth and depth of information collected from 50,000 participants starting at age 45 to 85 years every 3-years for at least 20-years (https://www.clsa-elcv.ca). This research platform has been designed to enable state-of-the-art, interdisciplinary population-based research and evidenced-based

The Canadian Longitudinal Study on Aging (CLSA) is the one of world's largest and most comprehensive aging studies in breadth and depth of information collected from 50,000 participants starting at age 45 to 85 years every 3-years for at least 20-years…

decision-making that will lead to better health and quality of life for Canadians. Data are collected across multiple domains including physical and cognitive measurements, psychosocial, health, and lifestyle and sociodemographic information. Participants provide data through telephone interviews and in-person visits to one of 11 purpose built Data Collection Sites (DCS) across Canada. All DCSs have the identical pieces of equipment and follow the same SOPs with operational oversight including training done centrally by the National Coordinating Centre (NCC) at McMaster University. This site is also home to the Biorepository and Bioanalysis Centre (BBC) where almost three million specimens are stored in cryofreezers operating at a temperature of -180°C. This ultra-low temperature ensures biospecimens have the best chance to be of value now and in the future. The screw top 2D laser etched barcoded cryovials used to store the samples provide optimum safety with no risk to a lost or unreadable label. These tubes are in automation ready 96 position boxes. All steps in the process from labelling containers, time-stamps for each step, and temperature data are managed and stored in the LIMS. The BBC is only one of two CAP accredited biorepositories in Canada. This designation provides assurance to researchers and stakeholders that this facility operates to defined quality parameters.

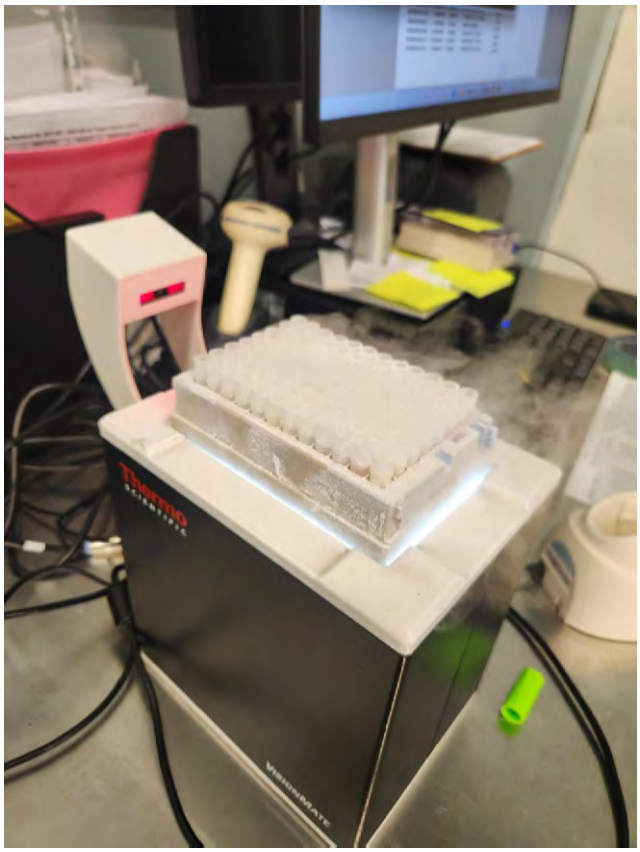
The CLSA biospecimen collection was developed to capture the widest range of specimen types to allow for the widest range of biomarker measurements to future-proof for biomarker advances. Multiple aliquots are stored in 0.5-mL volumes to eliminate freeze-thaw cycles. Well-developed protocols maximize sample integrity and minimize sample variation. All consumables are centrally ordered then distributed ensuring consistency of products and tracking of lot numbers. Serum, heparin, whole blood are collected in six different tube types with further processing for peripheral blood mononuclear cells (PBMC) and addition of cell culture media. Along with a urine specimen, there are 10 sample types and 42 aliquots per participant. Specimens are shipped from each DCS to the BBC in cryoshippers equipped with data loggers that monitor position and temperature. In addition to DCS, biospecimen collection participants have also provided at-home self-collection samples using fixed micro-sampling devices for blood in the COVID study and for stool in the Healthy Brains Health Aging study.

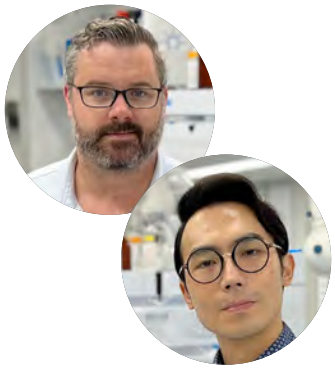
Hematology and urinalysis testing is performed within each DCS whereas chemistry, genetic, metabolomics, epigenetic and proteomic testing is conducted in various collaborating laboratories. Biomarkers selected balance cost with scientific value for maximum research potential as well as efficient use of the aliquot and high quality methods. The biomarkers chosen have relevance to age-related diseases, aging mechanisms, and have importance for repeated measures. The current measured core chemistry biomarkers include albumin, ALT, hsCRP, cholesterol, creatinine, ferritin, FT4, HbA1c, HDL, NT-proBNP, TSH, triglycerides, hsTnT, and urea. Longitudinal quality control (LQC) material is included along with participant samples to assess variation over time. These samples are regularly tested in reference laboratories for which there is a reference method.

The BBC is only one of two CAP accredited biorepositories in Canada.

Fundamentally, the goal in biobanking is to have access to good quality, well-archived, and well-annotated samples that will accelerate progress in biomarker studies with a translatable impact.

Explore the biobanking world on the ISBER website (https://www.isber.org) and at the Biobank Resource Centre (https://biobanking.org/) where you will find information for upcoming conferences, the BIO journal, webinars, courses, guidelines, tools, biobank locator, and more!





Advancing Multiple Myeloma Care: Targeted Mass Spectrometry for Measurable Residual Disease (MRD) Detection in Multiple Myeloma at London Health Sciences Centre

Dr. Matthew Nichols, PhD, FCACB; Dr. Ian H. Chin-Yee, MD, FRCP (C); Dr. Angela Rutledge, PhD, FCACB; Dr. Benjamin Chin-Yee, MD, MSc, FRCP (C); Dr. Martha L. Louzada, MD, MSc, FRCP (C); Dr. Chai W. Phua, MD, FRCP (C)

Mass spectrometry (MS) is highly sensitive and specific in identifying molecules based on mass-to-charge ratio. This technology has a plethora of successful clinical applications from toxicology to microbiology. Recently, MS has been employed in multiple myeloma (MM) to assess treatment response as it is highly sensitive in measuring myeloma proteins (M-proteins) compared to available methods such as serum immunofixation electrophoresis.

The concept of MRD, a measure of residual cancer cells or their products, has been influential for other blood cancers, such as acute lymphoblastic leukemia and chronic myeloid leukemia, where it is increasingly used as a predictive biomarker to guide treatment decisions.[1] The advent of more sensitive techniques for disease detection in MM has led to the expansion of MRD testing, founded on the premise that MRD-negativity is a clinically valid surrogate biomarker for progression-free survival and overall survival.[2] Recently, the US Food and Drug Administration's Oncologic Drug Advisory Committee voted to support using MRD as a surrogate endpoint for accelerated drug approval in MM. Myeloma Canada has also endorsed access to MRD testing to help guide the management of patients with MM.[2] Standard techniques for measuring MRD in MM include flow cytometry[3] (e.g., EuroFlow) and next-generation sequencing (NGS)[4] (e.g., ClonoSeq). Both techniques require bone marrow samples and are costly and time-consuming—the costs for flow cytometry range from $300-400 USD; NGS costs over $2000 USD and requires a baseline sample.

In 2021, the International Myeloma Working Group supported using MS in MM and highlighted its potential use for MRD assessment. One study comparing MS

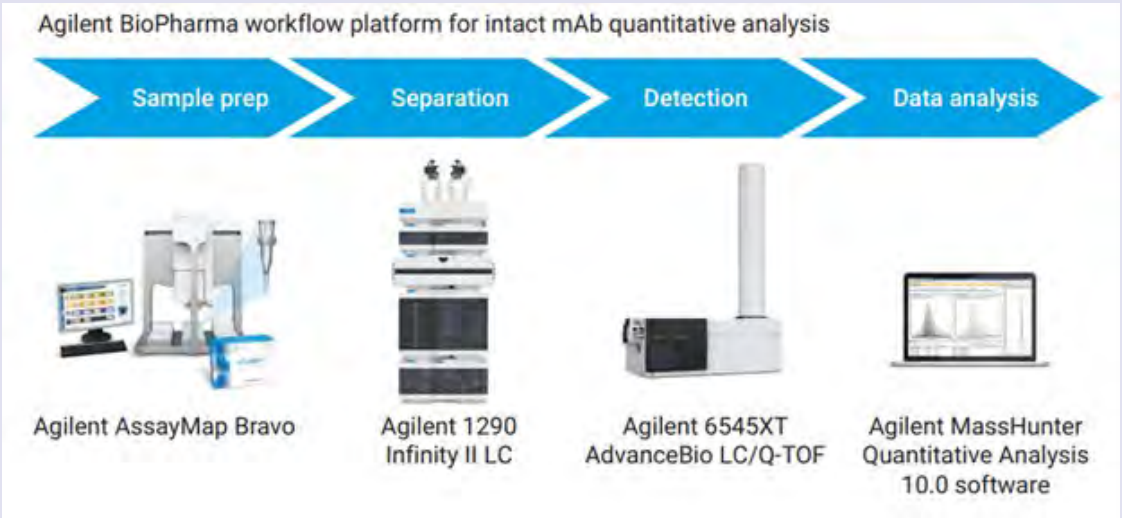
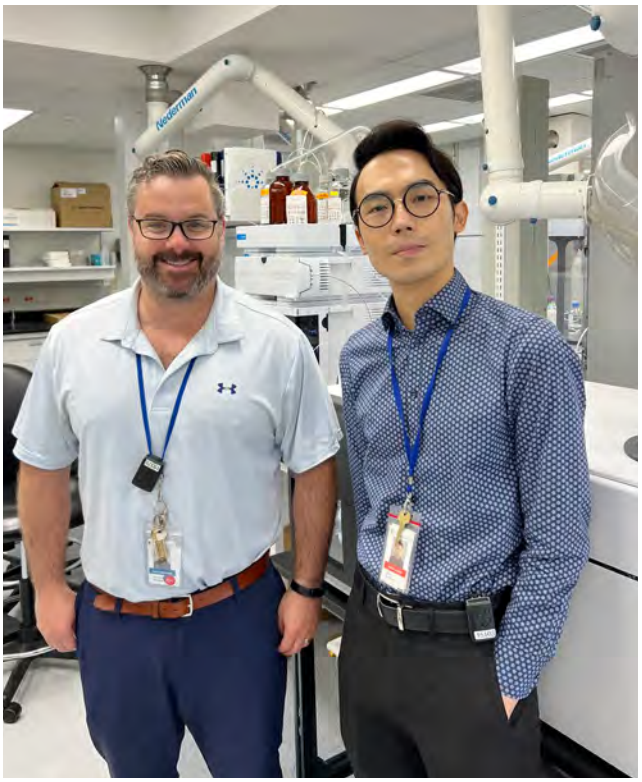
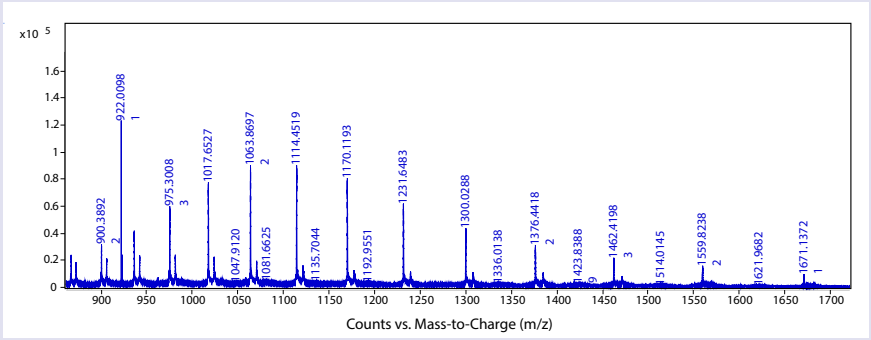


Figure 1. *Commercially-available biopharma workflow that was adapted for multiple myeloma. Samples are prepared utilizing streptavidin cartridges to which biotinyated camelids are conjugated. The camelids target the conserved regions of immunoglobulins G, A, M, kappa, and lambda. The purified extracts are eluted into 96-well plates, which are then loaded onto the autosampler, followed by separation with liquid chromatography and detection by quadrupole time-of-flight mass spectrometry. Data analysis is performed with Bioconfirm software. © Agilent Technologies, Inc. 2019. Reproduced with Permission.*

to NGS showed considerable concordance between assays ranging from 63-83%, with the best outcomes in those MS-negative alone or both MS- and NGS-negative. Discordant results have been attributed to false-negative NGS results due to spatial heterogeneity within the marrow, hemodilution of the aspirate sample, or extramedullary disease. The authors suggested that MS could be considered for MRD detection.[5] MS in MM can be divided into intact light chain and clonotypic peptide methods. Intact light chain methods employ matrix-assisted laser desorption ionization-time-of-flight (MALDI-TOF) or liquid chromatography coupled to high-resolution mass spectrometry (LC-HRMS) such as liquid chromatography-quadrupole time-of-flight (LC-Q/TOF) MS to determine the molecular mass of intact light chain-associated M-protein above the polyclonal background. Clonotypic peptide methods identify unique M-protein peptides by sequencing, which are then monitored by LC-HRMS. Intact light chain methods also offer the advantage of differentiating therapeutic antibodies from the monoclonal proteins arising from the myeloma cells. The mass accuracy of the high-resolution LC-Q/TOF system is approximately 1 Da, which provides excellent discrimination of intact light chains based on mass. Evaluating peripheral blood samples for intact light chains is a multistep analytical process involving sample preparation by affinity purification targeting the conserved regions of immunoglobulins

Myeloma Canada has also endorsed access to MRD testing to help guide the management of patients with MM.





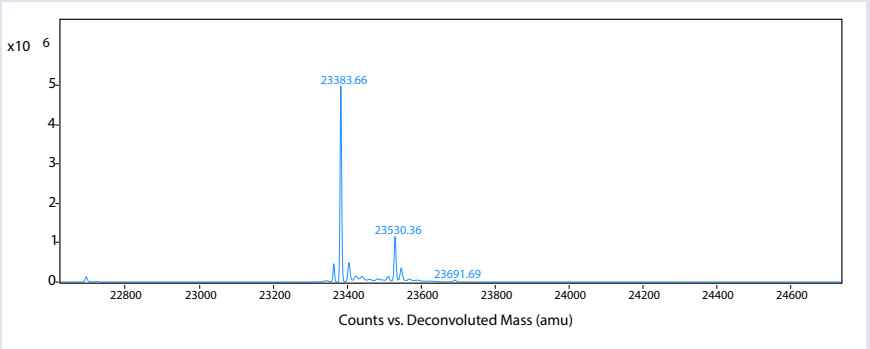


Figure 2. *LC-Q/TOF analysis of a serum sample from a patient with an IgG-kappa M-protein who is treated with daratumumab (an IgG-kappa monoclonal antibody therapy).* ***Top:*** *Charge envelope from a total IgG affinity purification, which demonstrates the presence of both a major and a minor species that are co-eluting. The spectrum is labelled with mass-to-charge (m/z) ratios on the major species and some minor species.* **Bottom:** *Spectrum demonstrating the presence of both a major species with a deconvoluted neutral mass of 23383.66 Da, consistent with daratumumab (theoretical mass 23384.2 Da), as well as the M-protein, which has an intact light chain mass of 23530.36 Da. This demonstrates the ability of the method to distinguish IgG-kappa M-proteins from IgG-kappa biological treatments.*

Intact light chain methods offer significant cost and time savings and do not require sequencing as they measure the intact mass of the light chain with a single workflow.

G, A, M, kappa, and lambda to enrich immunoglobulins and wash away unwanted serum proteins (Figure 1). Purified immunoglobulins are then separated and detected by LC-Q/TOF (Figure 2).

Access to MS testing for MM is currently limited, and commercial platforms are only just emerging. In-house developed methods have generally been restricted to select tertiary care centers and differ in cost, throughput, analytical performance, and required experience. Intact light chain methods offer significant cost and time savings and do not require sequencing as they measure the intact mass of the light chain with a single workflow. Analysis is performed on peripheral blood, allowing ease of assessment at multiple time points during the patient journey. For these reasons, intact light chain methods have generally been considered more clinically viable. MS also offers the added advantage of being able to detect post-translational modifications such as glycosylation, which have been linked to an increased risk of amyloidosis.[6]

In our laboratory, we validated an intact light chain LC-Q/TOF method. The use of this technology in our clinical laboratory represents early adoption in Canada and opens the door to evaluating this assay for MRD assessment in our patient population. Though other MRD assays, especially NGS, remain the current gold standard, MS might offer a useful sensitive screen to determine who requires this more costly and invasive testing through a comprehensive multimodal approach for MRD evaluation. For example, if MS-negative, NGS evaluation can be considered to confirm MRD-negative status, but not if MS-positive. Future studies will be required to validate the optimal approach to MRD assessment in MM.

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Halton Healthcare: A Case of Acute Promyelocytic Leukemia

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Charge Technologist, Flow Cytometry
Oakville Trafalgar Memorial Hospital

In this article, we introduce you to the Flow Cytometry (FC) service at Halton Healthcare and its collaboration with other laboratory departments. We present the workflow analysis for a case of Acute Promyelocytic Leukemia (APL) where the FC service facilitated the rapid detection of APL abnormal cells, leading to critical and timely patient care management* [Figure 1]. The laboratory department at Halton Healthcare is an ISO 15189 Plus™ accredited laboratory that offers an essential and integrated diagnostic services to a diverse patient population. ISO 15189 Plus™ certification, provided by Accreditation Canada, certifies that a laboratory has met the quality and competence standards for providing medical laboratory services in Ontario.

APL is a highly aggressive hematological malignancy, that if untreated, typically confers toward irreversible life-threatening coagulopathy.

APL is a highly aggressive hematological malignancy, that if untreated, typically confers toward irreversible life-threatening coagulopathy.[1] Diagnosis of APL relies on morphological identification of leukemic cells, followed by molecular/cytogenetic detection of PML-RARA fusion gene formation - a product of

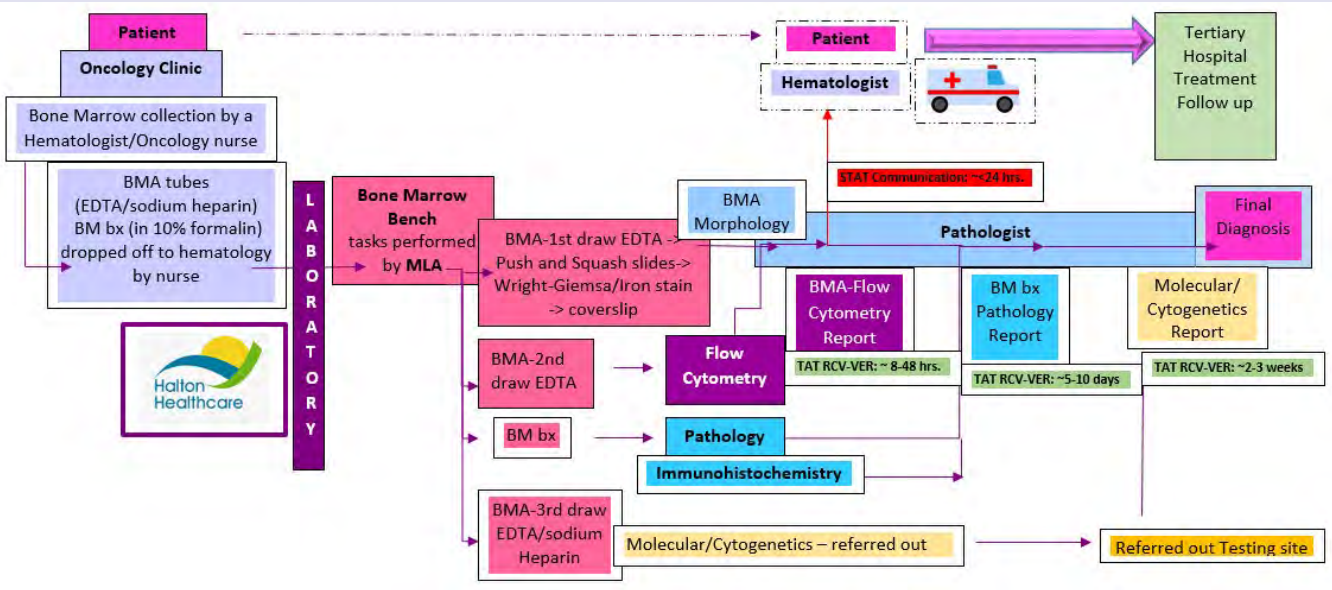

Figure 1: *Outlines the effective collaboration among various teams, both within and outside the laboratory department that ensured critical processing of this bone marrow sample and ultimately led to timely patient care management and diagnosis.* ***BMA:*** *Bone Marrow Aspirate.* ***BM bx:*** *Bone Marrow biopsy.* ***EDTA:*** *Ethylenediaminetetraacetic acid.* ***TAT RCV-VER:*** *Turnaround time for service from specimen received to specimen report verified in patient's Electronic Health Record (Meditech).*

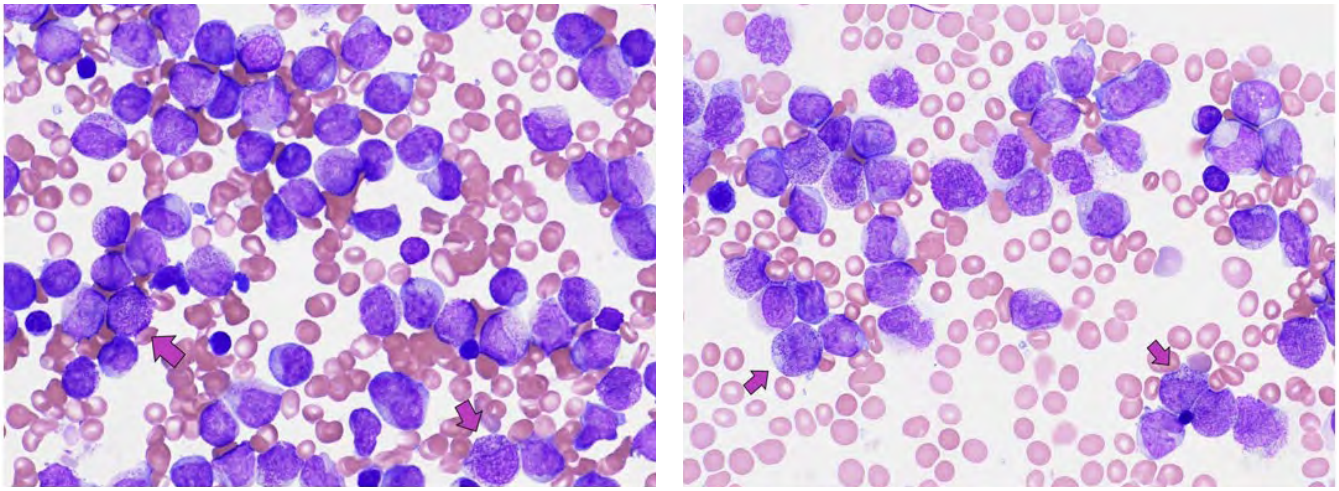

Figure 2: *Bone marrow Aspirate (BMA) in an Acute Promyelocytic Leukemia (APL) case. Wright-Giemsa stain. Purple arrow points towards some of the neoplastic promyelocytes that have the hallmark of heavily granular cytoplasm and lobulated nuclei.*

translocation between the long arm of chromosome 15, with a breakpoint at 15q24, and the long arm of chromosome 17, with a breakpoint at 17q21.[2] Since early mortality is a significant concern, initiating treatment with all-trans retinoic acid (ATRA)/ combination therapy as soon as APL is suspected, is crucial to improve overall patient survival.[3,4]

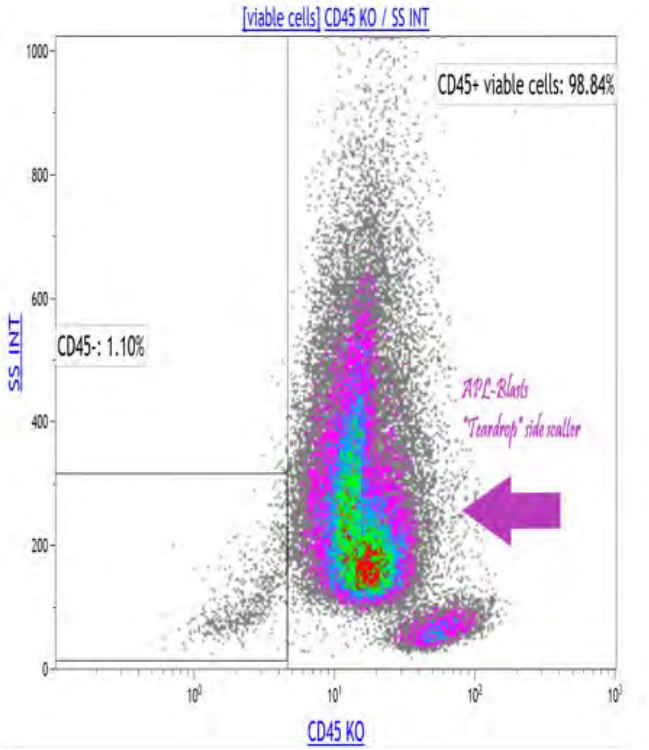

Figure 3: *APL blasts demonstrating "teardrop" shape side scatter*

One of the symptoms a patient with APL could present to the emergency department with is an acute onset of fatigue. In such a case, the physical exam would note increased bruising. A complete blood count (CBC) would most likely reveal pancytopenia with marked leukopenia, demonstrating a white blood cell (WBC) count lower than the normal reference range (RR) of 4.0-11.0 x10^9/L.

Additionally, both the hemoglobin (Hgb) and platelets (PLT) would be low, <115g/L (RR: 115-155 x10^9 g/L) and <150 x10^9 g/L (RR: 150-440 x10^9/L), respectively. The CBC morphology can show a few blasts. In coagulation studies, the fibrinogen would be lower than the normal reference range (RR: 1.9-4.7 g/L). In light of these findings, the patient would be referred to the oncology clinic at Halton Healthcare to be seen by a hematologist and have an urgent bone marrow (BM) collection.

Bone Marrow Aspirate (BMA): Morphology

The BMA can show an alarming picture of increased blasts with numerous neoplastic promyelocytes [Figure 2] and rare Auer rods. As a result, the pathologist would alarm the flow cytometry technologist to urgently process the FC sample.

BMA: Flow Cytometry

The FC analysis of the BMA usually shows 99% viable events. The population of interest (blasts) would be characterized as having dim CD45 expression with high side scatter (SS), demonstrating “teardrop” shape SS [Figure 3]. The blasts encompass both the typical blast and granulocytic regions. These blasts are

Since early mortality is a significant concern, initiating treatment with all-trans retinoic acid (ATRA)/ combination therapy as soon as APL is suspected, is crucial to improve overall patient survival.

positive for surface (s)CD117, sCD33 (bright), cytoplasmic (cy) myeloperoxidase, and negative for sCD19, sCD20, sCD22, cyCD79a, sCD3, cyCD3, sCD5, sCD4, sCD8, sCD16 and sCD14, sCD11c, cyTdT, sCD34 and sHLA-DR.

These immunophenotypic features would be highly suggestive of APL.[5] The pathologist would communicate these results to the hematologist which would lead to the patient urgently being transferred to a tertiary hospital for appropriate follow-up with APL-related treatment.[3,4]

Bone Marrow Biopsy (BM bx): Pathology and Final Diagnosis

The BM bx hematoxylin-eosin stain (H&E) stained slides would show markedly hypercellular BM for age, lack of maturation in myeloid cell line, and marked reduction in erythroid precursors and megakaryocytes. Additionally, the immunohistochemistry stains would correlate with FC findings of the blasts being positive for CD117 and negative for CD34. Finally, the molecular and cytogenetic results would confirm the presence of PML-RARA translocation, and the final diagnosis of APL.

This analysis highlights how FC at Halton Healthcare correlates with the morphologic evaluation and aligns with pathology and molecular/cytogenetic studies for accurate diagnosis of APL. Additionally, we are fortunate at Halton Healthcare that through the collaborative work of our routine and specialized services and other healthcare providers, we are able to provide our patients with a rapid diagnosis so that they can receive the timely care they need.

Acknowledgment

This article was written and reviewed in consultation with Dr. Sanjeev Deodhare, Pathologist - Laboratory Medicine, and was approved for submission to the ADVOCATE magazine by Halton Healthcare Laboratory Leadership Team and the Communication and Public Affairs department.

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About Halton Healthcare

Halton Healthcare is a healthcare organization comprised of three community hospitals - Georgetown Hospital, Milton District Hospital and Oakville Trafalgar Memorial Hospital. Together these hospitals, along with their community locations, provide healthcare services to nearly 400,000 residents in the communities of Halton Hills, Milton and Oakville. Halton Healthcare hospitals have been recognized for their best practices in several patient safety and patient care initiatives. For more information, visit www.haltonhealthcare.com.

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#TeamMLPAO

Welcome Our New MLPAO Board Members

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District 2, MLT

SANDRA MARSHALL
Chair, District 4, MLT

CAMERRA YUILL ROBAR
District 6, MLT

DEB CROTEAU
District 8, MLT

TRACY CARRIER
Director at Large, MLT

TANIA TOFFNER
Vice Chair/Treasurer, Director at Large, MLT

Please join us in welcoming our new 2024–2025 MLPAO Board Members. Please visit our website for a full listing of the MLPAO Board of Directors.

MLPAO Awards

MLPAO is happy to announce the following winners:

Tania Toffner

The **Trillium Award** is presented in recognition of a significant contribution to the advancement of the association and the medical laboratory profession in Ontario. The 2024 Trillium Award recipient is Tania Toffner. Tania is the Senior Manager of Quality, Regulatory Affairs and Customer service at Public Health Ontario (PHO). She worked for the MLPAO until the beginning of the pandemic, when she chose to join the frontlines and battle COVID-19. From 2009 – 2012, Tania was the Director of Certification and Prior Learning Assessment at the CSMLS. She also served on the CSMLS Board from 2013 – 2016 and was President in 2015. Her experience also includes MLT in Transfusion Medicine, acting Senior Technologist Flow Cytometry and Quality Assurance and Safety Officer for Hematology at Sunnybrook Health Sciences Centre. Tania's commitment to the profession, as a lab professional and ongoing commitment as a volunteer, makes her the perfect candidate for this award.

Robyn White

The **Jim Braidwood Outstanding Professional Award** is given to the MLT or MLA/T who is highly regarded by professional colleagues for improving work life and professional practice through their passion for shared learning and development. The 2024 Jim Braidwood award recipient is Robyn White. Robyn is the Education, Transportation and Safety Manager at the Hamilton Regional Lab Medicine Program (HRLMP). She has been a Genetics MLT since 2007 where she was active in lab initiatives and an informal leader. She moved into a Senior MLT position in 2018 and shortly thereafter moved into an interim manager role and began to make her mark as a formal leader. In 2021, she became a Quality Specialist and began to impact all labs in the program through her focus on the HRLMP Quality Management System. She became the go-to for many people, working with many teams on multiple projects and supporting all aspects of lab accreditation. Robyn is forward thinking, positive, and approachable.

Dr. Lei Fu

The **Richard Lafferty Excellence in Writing Award** is presented for the best feature article published in the ADVOCATE magazine during the year. Although there were many great articles published this year, there was one article that clearly stood out among the rest. The winner of the 2024 Richard Lafferty award is Dr. Lei Fu. Dr. Fu's article entitled "Pharmacogenetic Testing: A Tool for Personalized and Precision Drug Treatment" was a fascinating look into the way that pharmacogenetic testing can allow for patients to receive individualized treatment that can really make a difference in optimizing their care.

MLPAO: Exciting News About **Awards and Bursaries**

We are excited to share some fantastic news and updates with you regarding our MLPAO awards and bursaries.

Michelle Hoad Advocacy Award

The MLPAO Board of Directors is pleased to announce the new Michelle Hoad Advocacy Award in partnership with BD Canada. Over the past 6 years, Michelle has been at the forefront of our advocacy work at a time when lab professionals needed to be recognized. Her work received recognition at the local, national and international levels which ignited stakeholders in the industry to add their voice to this important message. BD Canada wanted to acknowledge this great work and encourage lab professionals to advocate.

MICHELLE HOAD

JESSIE CLELLAND

The first recipient of the **Michelle Hoad Advocacy award** is Jessie Clelland. Jessie has demonstrated exemplary advocacy efforts within the medical laboratory profession, going above and beyond to enhance our visibility and drive positive change. Jessie joined the MLPAO board 6 years ago and has completed 3 full terms. During this time, she has attended every lobby day, presented to the Standing Committee of Finance and participated in many government meetings. Jessie was the Board Chair during these past two years, where for the first time in the history of lab we have witnessed the Ontario Government invest in labs. Congratulations Jessie!

We are also thrilled to announce some changes to our existing bursaries and introduce new opportunities to support our members, effective 2025.

MLA/T and MLT Bursaries

We have increased the value of our bursaries to provide greater support to members. The MLA/T bursaries will now be $1,000 each (two awards available), and the MLT bursary will be $2,000.

Early Career Bursary

This new bursary of $1,500 is designed for new graduate MLA/Ts or MLTs who may need financial assistance as they enter their profession. Applicants will need to provide a letter describing why they need the funding and how it will help them jumpstart their career.

Champion of Joy Award

This new award honors an individual who exemplifies teamwork, consistently steps up to help, maintains a positive culture in the lab, and supports others. The winner will receive a plaque and a lunch for their lab, allowing them to share their joy with colleagues.

We believe these initiatives will not only recognize outstanding contributions but also provide vital support to our members as they advance in their careers. Stay tuned for more information about these new bursaries and awards in early 2025.

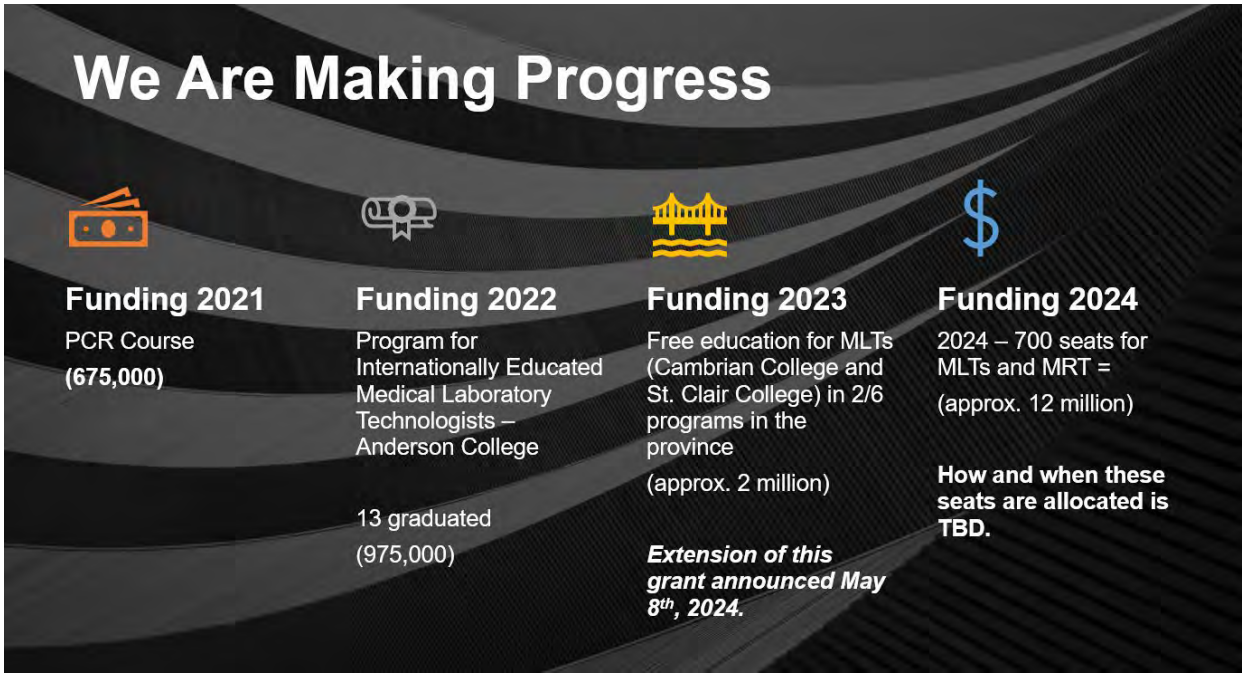
Advocacy Update

Michelle Hoad, CAE, Chief Executive Officer

Our advocacy work has continued strong through the first half of 2024. With great results!

We are excited to announce the Ontario 2024 Budget: Building a Better Ontario includes an additional 700 seats for MLTs and MRTs. The Minister of Health's Office contacted me prior to the release of the budget to share the wonderful news.

We are very happy to see that the advocacy work at the MLPAO is finally making an impact. Over the past 4 years we have seen an increase in investments for medical labs.



This announcement came right before Med Lab Week which provided us an opportunity to say thank you and reach out to all MPPs and encourage them to visit their local labs. Many MPPs had limited availability for hospital tours during this week due to competing priorities at the Legislative Assembly of Ontario. We received many responses and got confirmations from the following MPPs that toured their labs:

On Thursday April 19th, the Minister of Health Sylvia Jones visited Hamilton General Hospital where she met the new CEO of Hamilton Health Sciences (HHS) Tracey McCarthy. The tour was conducted by Tracy Carrier, an MLPAO board member, who is the Director of Lab Operations for HHS, and our CEO, Michelle Hoad, in partnership with a large leadership team at HHS.

cont'd on page 26

Advocacy Update cont'd

On Friday April 20th, Minister Vic Fedeli, Minister of Economic Development, Job Creation and Trade, visited his local lab at the North Bay Regional Hospital in North Bay. Our MLPAO board member Rachel Desjardins, our MLPAO board chair Jessie Clelland, and our CEO Michelle Hoad provided the Minister a tour of the hospital.

At the same time on Friday April 20th, MPP Todd McCarthy, toured the Bowmanville Hospital. Grant Johnson, Director Laboratory and IPAC at Lakeridge Health, Frank Cerisano, CEO Bowmanville Hospital Foundation, Kirsten Burgomaster, Health System Executive at Lakeridge Health, and our MLPAO VP Operations, Andrea Tjahja, provided Mr. McCarthy a tour and provided insight into the challenges facing lab professionals.

> **“We are grateful to the Ontario government for being included in the 2024 Budget and for these MPPs for visiting hospital labs across our province.**

We received a request from Minister David Piccini, Minister of Labour, Immigration, Training and Skills Development expressing interest to visit a local lab and a lab in Ottawa, but due to a busy schedule has requested this happen over the next few months. We are looking forward to his visit.

The investment in additional seats is historic. We are grateful to the Ontario government for being included in the 2024 Budget and for these MPPs for visiting hospital labs across our province.

The federal government tabled their 2024-25 Budget in April titled “Fairness for Every Generation” with measures aimed at addressing affordability, housing and growing the economy. The budget includes significant investments for health research and artificial intelligence as well as $1.5 billion over five years for the first phase of a universal pharmacare program in Canada.

Med Lab Week also included the announcement of new MLT and MLA/T programs at Humber College in partnership with BD Canada, to provide new opportunities for student placement and work-integrated learning with BD. This will offer Humber students practical, hands-on experience and help facilitate their transition from academic learning to professional practice. These are the type of innovative ideas that we need in Ontario to keep finding solutions.

It is also apparent that the need for MLTs in the north is dire. With the announcement of new MLT and MLA/T programs over the past 24 months, there is still work to do. Cambrian College is the sole school training students in the north and we need more programs in this part of the province to help rural, remote and northern labs with their staffing issues.

Our work doesn’t stop here. MLPAO will continue to work with the Government of Ontario and other stakeholders to continue finding solutions and to ensure these new programs have the supports required for clinical placements.

Winter is coming.
Are you prepared?

LOOK FOR THESE
SYMPTOMS

Often spiking during the winter season, COVID-19, RSV disease and the flu are contagious respiratory illnesses that share many of the same symptoms. The three illnesses could possibly seasonally surge, posing a triple threat to you and your family. Here's how symptoms overlap:

	COVID-19[1]	RSV[2]	FLU[3]
Fever	●	●	●
Runny Nose	●	●	●
Coughing	●	●	●
Fatigue	●		●
Body Aches	●		●
Sore Throat	●	●	●
Nausea	●		●
Vomiting	●		●
Chills	●		●
Headache	●	●	●
Diarrhea	●		●
Shortness of Breath	●		
Loss of Taste	●		
Loss of Smell	●		
Sneezing		●	
Loss of Appetite		●	
Wheezing		●	

ABOUT
COVID-19, RSV DISEASE & THE FLU

While impacting people of all ages, the viruses causing COVID-19, RSV disease, and the flu render the following populations especially vulnerable: children, the elderly, those who are immunocompromised, and people with underlying conditions. Coughing, sneezing, and potential contact with virus-contaminated surfaces all contribute to virus spread.

THE IMPACT OF RESPIRATORY VIRUSES*

COVID-19[4]

96 million
More than 96 million people in the U.S. have **suffered** from COVID-19.

5.4 million
More than 5.4 million have been **hospitalized**.

1 million
More than 1,058,692 have **died**.

RSV[5]

2 million
On average, more than 2 million people **suffer** from RSV disease each year.

235,000
On average, more than 235,000 are **hospitalized** each year.

14,000
On average, more than 14,000 **die** each year.

FLU[6]

35 million
More than 35 million people in the U.S. **suffered** flu-related illnesses between 2019-2020.

380,000
More than 380,000 million were **hospitalized** between 2019-2020.

20,000
More than 20,000 **died** between 2019-2020.

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