CCMG Genetic and Genomic Diagnostics Training: Update on Changes in Training of Laboratory Genetics Professionals

Clinical Genetics laboratories, which undertake genetic testing on patient samples, provide a critical service, important for diagnosis, prognosis, and treatment of a range of referral indications from both within the medical genetics community and across a range of other medical specialties including pediatrics, neurology, oncology, maternal fetal medicine, endocrinology, psychiatric medicine and others. Clinical genetics laboratories are often operated through tertiary care centers and are usually directed by laboratory geneticists. Given the increasing complexity of genetic testing, relevance to a broad range of medical disciplines and risk of harm that can occur as a result of improper genetic testing, appropriate training and certification of laboratory geneticists remains an important issue. The training for laboratory geneticists include a doctoral degree (either PhD, MD or equivalent), usually additional postdoctoral training and a specialized two-three years of laboratory genetics training offered through the Canadian College of Medical Geneticists (CCMG) or the American Board of Medical Genetics and Genomics (ABMGG).

Until recently there were three medical laboratory specialties for which the CCMG offered training. These included laboratory biochemical genetics, cytogenetics and molecular genetics. As of July 2020 the fellowship training in either cytogenetics or molecular genetics was replaced by Genetic and Genomic Diagnostics (GGD) (joint molecular genetics and cytogenetics) training.

Snapshot of this edition:
- CCMG Genetic and Genomic Diagnostics Training: Update on Changes in Training of Laboratory Genetics Professionals
- Hematology News: Dr. Menaka Pai named to The Ontario COVID-19 Science Advisory Table
- Microbiology News: What has been keeping the HRLMP Virology Team so busy this year?

IN THIS ISSUE

CCMG Genetic and Genomic Diagnostics Training: Update on Changes in Training of Laboratory Genetics Professionals

News from Administration
Education News
News from Genetics
Hematology News
Microbiology News
News from Pathology
Quality News

Editorial Board:
Chemistry: Dr C Balion
Microbiology: Dr M Smieja
Pathology: Dr C Ross
Genetics: Dr D Grafodatskaya
Hematology: K Moffat

Editorial Office:
Co-Editors: Dr C Ross; K Moffat
Communication Editor: G Kiers

THE EDITORIAL OFFICE WELCOMES YOUR FEEDBACK, SUGGESTIONS AND NEW IDEAS
Historically, separation of training into cytogenetics and molecular genetics has reflected differences in genetic testing depending on the type of alteration being measured. Generally, cytogenetics techniques have evaluated changes in chromosome structure, while molecular genetic methods identify changes in nucleic acid (DNA or RNA) sequence at the gene or locus level.

Cytogenetics involves the examination of chromosomes to identify gains and losses of portions of the genome, as well as rearrangements within and among chromosomes. Since cytogenetic testing evolved in the mid-twentieth century, Cytogenetics laboratories have relied on karyotype analysis (assessment of stained chromosomes by microscopy) as the primary tool for visualizing chromosomes and elucidating clinically relevant abnormalities. Chromosome abnormalities (gains, losses, or incorrect location of material) are visible under the microscope through karyotype analysis if the abnormality involves 5-10 megabases of DNA (5-10 million base pairs) or more and there are sufficient cells undergoing cell division. For detection of smaller chromosome abnormalities and analysis in tissues without cells in active cell division, molecular cytogenetic tools are employed. Fluorescent in situ hybridization (FISH), for example, uses fluorescently labelled DNA probes to specifically measure the number and/or location of targeted chromosome loci by hybridizing the probes directly to chromosomes in fixed cells. The resolution of FISH could be as low as 200 kilobases of DNA (200,000 base pairs), but only enables assessment of a few chromosomal loci at a time. Chromosome microarrays are also routinely used in most cytogenetic laboratories to detect even smaller gains or losses of chromosome material (as small as 10-50 kb in size). The evolution of other molecular cytogenetic techniques has provided improvements to cytogenetic evaluations by reducing the requirement for dividing cells to examine chromosome changes. Rapid aneuploidy detection by quantitative fluorescent PCR (QF-PCR), for example, allow cytogeneticists to detect extra copies of chromosomes 13, 18, 21, X or Y using DNA extracted directly from tissues. This is particularly important in the prenatal and perinatal setting when cell cultures could delay the result by several weeks or when cell culture to harvest dividing cells is not possible (for example in instances of in utero fetal demise).

Karyotype testing remains an important tool for evaluation of chromosome abnormalities in a broad range of clinical scenarios. For example, carriers of balanced chromosome rearrangements are at increased risk for transmitting unbalanced chromosomes to their offspring and may experience recurrent pregnancy losses and/or infertility. Karyotype testing of individuals with recurrent miscarriages or infertility can detect a balanced chromosome rearrangement in approximately 2-8% of patients, thus providing important information about contributing factors and reproductive risks for having a child with medical concerns related to inherited chromosome abnormalities. In acquired cancers both balanced and unbalanced chromosomal rearrangements are common, and both karyotype and FISH are used to identify these abnormalities in bone marrow specimens of patients with hematological cancers. In addition, FISH can be performed in formalin-fixed paraffin embedded solid tumor specimens to identify recurrent genomic rearrangements.

Chromosomal karyotype analysis may be used to characterize chromosome abnormalities in patients that may contribute to congenital or developmental abnormalities in both the prenatal and postnatal settings. However, due to the limited resolution of karyotype for detection of submicroscopic chromosome changes and restricted ability of FISH to examine more than 1-3 loci simultaneously, there has been an increasing shift towards molecular cytogenetic techniques (i.e., quantitative fluorescence PCR or chromosomal microarray) as a first tier test, with karyotype and FISH being reserved as a reflex method. Chromosome microarrays tests are now recommended as a first-tier test for the investigation of children with congenital anomalies and/or neurodevelopmental issues, and has an improved diagnostic yield for small chromosomal gains/losses compared to karyotype assessment.
Molecular Genetics techniques assess smaller changes in DNA at the gene level, such as point mutations and small deletions/duplications. There are a number of single analyte molecular techniques to detect known recurrent point mutations. Multiplex ligation-dependent probe amplification can detect exon level deletions or duplications in a gene of interest. Targeted methodologies like PCR, restriction enzyme digest and allele-specific tests can allow rapid testing of recurrent genetic variants that may contribute to monogenic disorders (genetic disorders associated with mutations in only one or a few genes). Similarly, direct DNA sequencing can be used to identify point mutations throughout the gene. Sanger sequencing was a gold standard for DNA sequencing for several decades, but is now increasingly replaced by next generation sequencing (NGS), which allows massive parallel sequencing of multiple genes in multiple samples.

HRLMP Genetics Laboratory performs a number of molecular genetics tests including single analyte and NGS Panels for a variety of disorders, including hemoglobinopathies, mitochondrial disorders, hereditary and acquired cancers.

In the modern genetics laboratory, the boundary between cytogenetics and molecular genetics is increasingly blurred as chromosome- and gene-based testing both increasingly become reliant on similar technologies and testing material. It is becoming increasingly apparent that clinical manifestations of chromosome abnormalities are dependent on the genes involved. Likewise, gene-level mutations are not always isolated to a single locus and can result from large chromosomal rearrangements. Emerging DNA and RNA based technologies can detect alterations at both the chromosomal and gene levels in a single assay, thus further enabling convergence of molecular genetic and cytogenetic investigations. For example, some of the NGS panels can detect chromosome gains and loss similarly to chromosomal microarray. RNA based NGS assays and reverse-transcription PCR assays can also detect instances when two genes located on different chromosomes have become fused together through chromosomal rearrangement. The promise of whole genome sequencing further brings a theoretical ability to detect clinically relevant point mutations, gene level and chromosome level gains/losses, and structural chromosome rearrangements anywhere in the genome, all in a single test. However at this time the high cost of whole genome sequencing does not allow this test to be widely used in a government subsidized healthcare system that must balance sustainability and fiscal responsibility with medical innovation.

Despite of the increasing diversity of molecular based technologies, these cannot fully replace classical cytogenetics. Both cytogenetic and molecular genetic tests remain important complementary tests for a broad range of clinical indications. Frequently a complete genetics work up of a patient could include both molecular and cytogenetics techniques. For example, routine analysis for a patient with acute myeloid leukemia through the HRLMP Genetics Laboratories includes molecular analysis for common fusion genes caused by chromosomal translocations (PML-RARA, BCR-ABL, RUNX1-RUNX1T1, CBFB-MYH11), DNA mutations in 26 different genes using single analyte and NGS techniques and karyotype analysis. These test results are considered along with clinical findings and other laboratory test result to assess prognosis and inform treatment plans for the patient. Another example is identification of a common trisomy such as trisomy 21 in a patient by QF-PCR, which is always followed by karyotype analysis to assess whether the trisomy is the result of an extra chromosome or due to a structural chromosome rearrangement, which would have different implications for follow up parental testing to determine recurrence risk. These examples highlight the importance for a laboratory geneticist to be competent in both cytogenetics and molecular genetics.

Training programs for medical laboratory technologists in genetics technology merged the cytogenetics and molecular genetics training programs more than a decade ago. Also, the American Board of Medical Genetics and Genomics training program merged cytogenetics and molecular genetics training programs into
Laboratory Genetics and Genomics Program in 2017.

Prior to July 2020, both CCMG-accredited molecular genetics and cytogenetics programs were two-year postdoctoral training programs. The training programs included specific requirements focusing on both technical and interpretative/consultative aspects with a range of case requirements to be recorded in the trainee’s logbooks. In addition, training in molecular genetics required a rotation in a cytogenetics laboratory, and vice versa, to ensure familiarity with the second closely related specialty. The outcome of the training was determined through an assessment by a credentialing committee and successful participation in the certification examination process which includes written exam in general genetics, and written and oral exams in the chosen specialty of training. There was also the possibility for individuals certified in one specialty to undertake training in a second specialty, thus CCMG certified laboratory scientists are frequently certified in both cytogenetics and molecular genetics. With increasing convergence of molecular genetic and cytogenetic testing, an increasing demand for dually trained laboratory scientists has also emerged. A transition to merged molecular genetics and cytogenetics training programs in the United States in 2017 added to pressure on Canadian training programs to also merge these programs. Such a merger ensures that trainees obtain a more holistic training and remain competitive as they establish a career in Laboratory Medicine.

Merged molecular genetics and cytogenetics training provides several academic challenges, particularly as training curriculum formerly spread over three years is now synthesized into a two year training program. In 2018, the CCMG formed an Ad Hoc Working Group to set a framework for the merged training program. This working group, including two HRLMP Scientists, Suzanne Demczuk and Elizabeth McCready, defined the core competencies that enable GGD Laboratory Scientists to practice in a safe and knowledgeable manner to best serve patients and the medical community at large. The CCMG Training Committee, chaired by Dr. Demczuk subsequently developed the GGD training guidelines which were formally launched in July 2020 (https://www.ccmg-ccgm.org/documents/Training/GGD/GGD-Training-Guidelines.pdf).

GGD specialty training has also been launched in July 2020 within McMaster CCMG training Program and we currently have two trainees in the GGD program, Dr. Nasim Vasil (full time) and Dr. Landry Nfonsam (part time). We wish the best of luck to Nasim and Landry with their training as CCMG GGD scientists!

Submitted by:
Dr. Daria Grafoodatskaya
Dr. Elizabeth McCready
Dr. Suzanne Demczuk

References:

News from Administration

Congratulations to Dr. Cheryl Main, Medical Microbiologist and Head of Service, Bacteriology, HRLMP, for being awarded the Dr. Clive Davis Award – Hamilton General Hospital.

“Nominated by Dr. Sharon Grad, Dr. Cheryl Main is celebrated for always being ready to help her
colleagues and patients in collaborative and innovative ways. She is a McMaster graduate and a dedicated postgraduate teacher, researcher and clinician. Dr. Main is never too busy to share her wisdom and to assist with patient management. She is kind and empathetic to patients who are often difficult to manage and who often have challenging personalities. She is a strong patient advocate and a valued team player.

Dr. Main has had a busy year with COVID-19 but is never too busy to respond to calls or emails, and to assist with patient management.

Congratulations, Dr. Main!”

~ HHS News, Feb 05, 2021

Education News

In December 2020, the HRLMP hosted a virtual tour of the laboratory for Grade 12 students from St. John Henry Newman High School.

We provided them with a virtual tour of the lab, an overview of the role of the lab professional, and most of all, encouraged them to consider a career as a laboratory professional!

A note of thanks is provided below:

“Thank you very much for sharing what you do in the lab. It was an amazing presentation. The students loved the tour of the lab! That was something that would not have been possible without the technology. It means so much to us that even during a pandemic you continued to share your expertise with us.

Hopefully things can get back to normal soon. We would love to learn more from you in person in the future.”

~Michael Fuchs, Teacher
St. John Henry Newman
Stoney Creek, ON

Registration is now open for the virtual version of CSMLS and BD’s annual phlebotomy event, connecting you with the latest trends and best practices in phlebotomy and beyond.

Click on the link below for further details: https://www.csmls.org/Professional-Development/Events/Beyond-Phlebotomy-Virtual-Symposium.aspx

Hold the date for CBS/ORBCoN 16th Annual Transfusion Medicine Education Symposium ...

“Game, Set, Match: Finding Blood for Difficult to Match Patients”
April 14, 2021

For further details and registration link, click on the link below: https://profedu.blood.ca/en/game-set-match-finding-blood-difficult-match-patients
Lab Connections

News from Genetics

Effective January 25, 2021 additional genes have been added to the melanoma and lung cancer panels. These genes include KIT for melanoma and ERBB2 for lung cancer.

The updated content of these panels is:

**Melanoma panel:** BRAF exons 11 &15, KRAS exons 2-4, NRAS exons 2-4, KIT exon 2, 9, 10, 11, 13, 14, 15, 17, 18

**Lung Cancer Panel:** BRAF exons 11 &15, EGFR exon 18-21, KRAS exons 2-4, ERBB2 exons 19-21

There are no changes to the specimen requirements or ordering process for these tests.

Hematology News

Dr. Menaka Pai

As most of you know, The Ontario COVID-19 Science Advisory Table is a group of scientific experts and health system leaders who evaluate and report on emerging evidence relevant to the COVID-19 pandemic, to help inform Ontario’s response.

I am very happy to share with you that Dr. Menaka Pai has recently been named as a member of the Ontario Science Table and as the Co-Chair of the new Drugs and Biologics Clinical Practice Guidelines Working Group (https://covid19-sciencetable.ca/about/#leadership).

This is, of course, an important recognition of Menaka’s hard work and her impressive reputation not only amongst hematologists and those involved in guideline development but in the larger medical community. The Science Table is fortunate to have her expertise.

Menaka is currently the only HHS voice on the Science Advisory Table; however, Professor John Lavis from Health Research Methods, Evidence, and Impact is also a member of the Table.

Other members of the HHS and McMaster University community have accepted to serve on the Guidelines Working Group - please congratulation/thank them if you should see (or Zoom) them:

- **Dr. Zainab Abdurrahman**, an Assistant Clinical Professor (adjunct) of Pediatrics at McMaster - and an expert in allergy and immunology
- **Dr. Stephanie Carlin**, a clinical pharmacist at HHS - and an expert in critical care and thrombosis pharmacy (currently on service in the COVID ICU at HGH!)
- **Dr. Kate Miller**, an Assistant Clinical Professor of Family Medicine at McMaster - and a family medicine specialist with expertise in rural care, community care, and maternal and newborn care
- **Dr. Andrew Healey**, an Associate Clinical Professor of Emergency Medicine at McMaster and an expert in emergency and critical care medicine, with a special interest in end-of-life care

Congratulations to all!

Submitted by:

Dr. Shannon Bates
Dr. Kylie Lepic on the Cancer Assist Show Podcast

Dr. Lepic talks with host Dr. Bill Evans about STEM cell transplantation and CAR-T Cell therapies.

Click on the link below to listen to the podcast:

https://cancerassist.ca/cancer-assist-show/

Microbiology News

What has been keeping the HRLMP Virology Team so busy this year?

Here’s a snapshot:

The past 12 months has seen incredible change, collaboration and innovation for all teams within HRLMP, but in particular, for the St Joseph’s Healthcare Virology team. The virology laboratory flow has been completely transformed to support the regional and provincial demands for COVID testing. A year ago, the HRLMP COVID PCR test was being developed in the research lab. Today, the current clinical daily capacity is 3,500 and we are implementing multiple changes to bring this daily capacity to 10,000 by end of June 2021.

To accomplish this was no easy task, but was due to the tremendous dedication, collaboration and support of the entire team. Endless meetings, long hours, weeks without a day off, (you get the idea), is our excuse for taking 12 months to communicate all of the COVID-centric activities to keep you, our colleagues at HRLMP, informed of work that has been completed to support COVID testing.

Over the last year, the Virology laboratory has increased staff numbers 3-4 fold and COVID samples have been tested around the clock. To date, over 441,000 COVID samples have been processed, while continuing to conduct routine Virology tests. In the initial stages of the crisis, other SJH labs redeployed some of their staff to help Virology. The original Virology staff were exceptionally resilient and trained the massive influx of new staff. Two MLTs stepped into senior roles on very short notice and they have been doing an amazing job. After developing and validating ‘routine’ COVID tests, the Molecular Technical Specialist is now busy implementing a test to detect Variants of Concern. Our LIS Specialist has provided exemplary support at each new step along the way. The professional physicians and laboratory scientists have been guiding clinical, quality and automation aspects of testing. Every facet of COVID testing has provided its own challenges. Acquiring sufficient supplies of transport media, equipment, disposables and reagents has been nearly impossible at various times (everyone in the WORLD was trying to obtain these products on an emergency basis). A great deal of time has been spent working with various SJHH/HHSC programs and external clients to ensure that COVID samples are collected, delivered, tested and reported in a way that provides rapid turn-around-time and meets their needs. The Virology team has a lot to be proud of but it has been an exhausting, roller coaster of a ride – and it isn’t over yet!

Automation and Robotics

Hamilton STAR and Vantage: The laboratory has acquired 4 new automated liquid handling platforms: three new Hamilton Microlab STARs and one Hamilton Vantage. These can be changed or upgraded throughout its life to accommodate changing workflows, while flexible programming can accomplish any task, from simple to complex. The pipetting technology achieves high accuracy, precision, and repeatability from sub-microliter to large volumes.
**Amplitude:** In December 2020, Ontario Health (OH) secured a contract with ThermoFisher to purchase 6 automated systems for the province that can each process 7,000 COVID samples per day. HRLMP was selected to implement one of the six systems. The system consists of a Module 1 and Module 2 robotics. The anticipated go live for the Amplitude to be installed is July 2021.

**Renovations:** To accommodate all of the new robotics and people, more space is required to set up the new work flows. With little space to spare, renovations are required to convert the current office space of L402 to a Class 2+ Laboratory. Initial floor plans were designed for all the Hamilton Instrumentation, EpiMotion equipment and specimen receiving and were signed off in November with an anticipated construction start of December 2020. However, once SJHH was selected by OH as a site for one of the Amplitude systems, the team was back to the drawing board to re-design the floor plan (HVAC, electrical) to accommodate an Amplitude module and the Hamilton robotics. We are happy to report that these drawings have been signed off as of February 2021, with construction to begin in March 2021.

**Inventory:** As you can imagine, all of this testing and robotics comes with a lot of stuff!

**Inventory management system**

Elizabeth O’Sullivan, formally a director at HHS with demonstrated Lean expertise, came back from retirement for six months to help the team build a COVID inventory management system. Natalie Daily, HRLMP LRC & Business Manager, developed a template to identify the inventory of initial stock, current inventory used, daily inventory, safety stock and re-order point for COVID stock. A computer inventory receivables template was developed based on previous work by the HGH microbiology team. Once the COVID inventory is complete, work will begin on virology inventory that will be computerized. These learnings can eventually be spread to other labs in HRLMP that wish to adopt this model.

**Call Centre:** COVID positive results are considered a critical test and therefore we are required to phone...
the ordering provider to inform of the positive result, as well as informing the Public Health Unit for that patient. At the end of March 2020, a COVID call centre was established and clerical support was hired to complete this work. The call centre is staffed with a 1 to 2 clerical staff (depending on volumes) from 07:00 – 23:00, 7 days a week. Important to note, is that this was implemented within 2 weeks of a request to initiate a call centre, making this the fastest hiring, onboarding and training that Deb Johnson and Amanda Hurdowar have ever participated in, in their careers!

We will continue to provide ongoing updates, not only work for COVID, but as other projects move forward so we can highlight the amazing work our teams are involved in.

Submitted by: Amanda Hurdowar and Deb Johnson on behalf of the COVID Project Team

News from Pathology

Dr. Tiffany Shao, MD, FRCPC, FCAP, joined the Department of Pathology and Molecular Medicine in January 2021 as a Renal/Anatomical Pathologist. She completed her MD (2013) and residency training in Anatomical Pathology (2013-2018) at the University of Toronto. Further specialized training followed in renal pathology at the University of Washington Medical Center in Seattle, Washington.

Dr. Shao’s clinical and research interests include kidney diseases occurring in native and transplant kidneys, in both adults and pediatric patients. Other interests include medical education and curriculum development.

Submitted by: Dr. Cathy Ross

Quality News

The IQMH Centre for Accreditation is now known as “Accreditation Canada Diagnostics”.

With this name change, there is a new logo:

To our knowledge, there have been no announcements regarding changes to the format or content of the Accreditation program. This is a name change only.

Submitted by: HRLMP Quality Team

Thank you to Stacey Nezic, MLA at the Juravinski site for always thinking of her co-workers.