HAMILTON REGIONAL LABORATORY MEDICINE PROGRAM

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LAB CONNECTIONS

IN THIS ISSUE

WHAT'S NEW

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Technological Advances in Cytogenetics

Traditionally, karyotyping has been used for detecting chromosome abnormalities but is limited to the detection of abnormalities that are larger than 3 to 10 megabasepairs (Mb) in size. Chromosome microarray(CMA) testing is a molecular cytogenetic assay used to detect gains or losses of chromosomal material (copy number variants; CNV) at a higher resolution than traditional cytogenetic approaches. Chromosome microarrays can be used to reliably detect CNVs as small as 100 kilobasepairs (kb) (Miller, et al. 2010). Modifications of the arrays to also assess single nucleotide variations in the genome (single nucleotide polymorphisms; SNPs) can further expand the testing capabilities of these chromosome microarrays allowing detection of aberrant patterns that could indirectly suggest alternate genetic mechanisms of disease (ie. uniparental disomy or isodisomy of autosomal recessive genes). The significant improvements in detection of chromosome abnormalities using CMA compared to traditional methods led to a consensus statement through the American College of Medical Geneticists recommending that CMA should be used as a first tier test for the genetic investigation of individuals with developmental delay, intellectual disability, autism spectrum disorder and/or multiple congenital anomalies (Miller, et al. 2010). This recommendation was further recapitulated in a position statement by the Canadian College of Medical Geneticists (CCMG) that was approved by the CCMG board in September 2009 (Duncan, et al. 2009).

Chromosome microarray testing is now available through the HRLMP Genetics Laboratory for the genetic investigation of individuals with developmental delay, intellectual disability, autism spectrum disorder and multiple congenital anomalies. ***Chromosome analysis by classical cytogenetic approaches is no longer available in this laboratory for these clinical indications.*** The chromosome microarray used in the Laboratory is a whole genome array with an increased density of probes in gene regions (Cytoscan HD microarray assay, Affymetrix Inc. Santa Carla, USA). This array also contains probes specific for SNP loci that enables detection of a broader range of genetic disease mechanisms.

Given that consanguineous matings can lead to atypical SNP patterns detectable by CMA, Health Care Practitioners have the opportunity to "opt-out" of SNP analysis if they do not want this information included in the final report, unless there is a family history of microscopically-visible chromosome rearrangement.

Peripheral blood samples submitted to the HRLMP for CMA testing should be collected in EDTA tubes (10 ml) and should be accompanied by an HRMLP Microarray requisition form. This is available from the HRLMP Laboratory Test Information Guide http://ltig.hrlmp.ca/AttachedFiles/RequisitionForm/HRLMPMicroarrayRequisition.PDF. The accurate interpretation and reporting of CMA genetic test results are contingent upon the laboratory's awareness of the reason for referral and clinical information provided; to provide the best possible service, health practitioners are encouraged to provide as complete clinical information on the requisition as possible.

References:

Duncan A, et al. (2009). CCMG Position Statement: Use of array genomic hybridization technology in constitutional genetic diagnosis in Canada. Epub. http://www.ccmg-ccgm.org/.

Miller, et al. (2010). Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am. J. Hum. Genet*. 86:749-764.

New Genetics protocol to Rule out Myelodysplastic Syndrome

The myelodysplastic syndromes (MDS) are hematological blood disorders that involve an ineffective production of the myeloid blood cells. These patients may develop severe anemia due to a progressive bone marrow failure and often require blood transfusions. The diagnosis, classification and prognostic assessment of MDS often relies on cytogenetic analysis that may include interphase fluorescence in situ hybridization (FISH) studies for MDS associated abnormalities. Traditionally this testing has been performed on bone marrow examinations. However, on the basis of recently published studies, the HRLMP Genetics Laboratory now offers 5q- FISH testing on peripheral blood. (Coleman et al. 2011) In some cases testing 5q- on peripheral blood may eliminate the need for performing a bone marrow in patients for whom treatable MDS is suspected. This test is performed on a 5mL peripheral blood specimen collected in sodium heparin and sent with a cytogenetics requisition available from the HRLMP Laboratory Test Information Guide that has indicating"5q FISH ONLY" is to be done.
http://ltig.hrlmp.ca/AttachedFiles/RequisitionForm/Cancer%20Genetics%20Requisition.pdf

Bone marrow examination should still be considered for those patients with a high clinical suspicion for MDS and a negative peripheral blood test and for patients in whom either AML or MDS moving to AML is a consideration.

References:

Coleman et al. (2011) Diagnostic yield of bone marrow and peripheral blood FISH panel testing in clinically suspected myelodysplastic syndromes and/or acute myeloid leukemia. . *Am. J. Clin Pathol.* 135:915-920.

Education News

The **Medical Biochemistry** Resident Training Program is preparing for their Internal Review on Tuesday April 9, 2013.

The **General Pathology** Resident Training Program is preparing for their Internal Review on Monday May 27, 2013.

Congratulations to General Pathology resident **Leena Narsinghani** who was awarded the Best Resident award at the recent St. Josephs Hospital annual staff meeting Jan 11, 2013.

Congratulations to Medical Microbiology resident **Khuloud Nuri** who has been awarded the Harry Richardson Quality Management Award for 2012.

PGY5 Anatomical Pathology resident **Etienne Mahe** was accepted to 3 highly competitive, fully funded fellowships (Mediastinal Pathology Fellowship at MD Anderson Hospital; Houston Texas, USA, CIHR fellowship in Molecular Pathology at University of Toronto and Integrated Hematopathology Fellowship at University of Calgary). He has accepted the fellowship at the University of Calgary and starts his fellowship July 1, 2013.

The Anatomical and General Pathology programs are pleased to announce that community electives will now be available at the Kitchener/Waterloo campus with regional educational leader, **Dr. Namrata Juneja,** and at the Niagara Health System campus with **Dr. Franco Denardi** as regional education leader.

For information and the latest news on our residency training programs follow the link: http://fhs.mcmaster.ca/pathres/news/index.html

Information on the postdoctoral fellowship: http://fhs.mcmaster.ca/pathology/education/postdoctoralfellowshiptraining.html

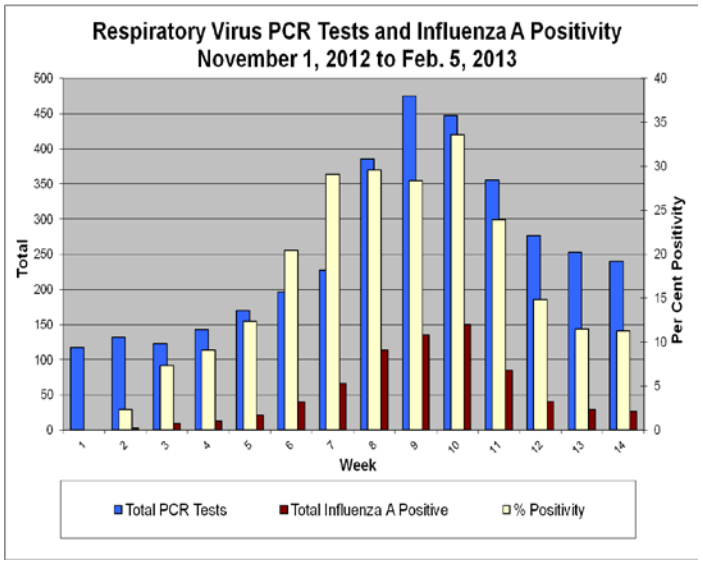
Pathology News

Head Injury Session	
Introduction	**John Provias/ Boleslaw Lach**
Pathophysiology, neuro-imaging in management of sport related acute head injury	**C.H. Tator, University of Toronto**
Radio-imaging of brain injury in children	
Update on the role of tau protein in normal brain and pathological conditions	**John Provias McMaster University**
John Groves Lectureship in Neuropathology: Chronic post-traumatic encephalopathy in professional sport	**Ann McKee Boston University**
Brain Tumour Session	
Immunotherapy of glioblastoma multiforme	**Anthony E Maida North West Biotherapeutics, Maryland**
Neurocytoma: Review of material from Hamilton Health Sciences	**B. Manaranjan, J. Provias, B. Lach McMaster University**
Myofibroblastic meningeal sarcoma – new variant of malignant meningioma	**B. Lach McMaster University**
Primary carcinoma of the brain. Case presentation and review of literature	**R. Baweja McMaster University**
Dural lymphoma “en plaque”. Case presentation and review of primary CNS lymphomas in Hamilton Health Sciences	**C. Connolly McMaster University**
Medulloblastoma stem cells: Where development and cancer cross pathways	**S. Singh McMaster University**

Microbiology News

Microbiology MLT **Leslie Roik** and her husband Chris climbed Mount Kilimanjaro January 14-20 to raise funds and awareness for the non-profit organization, Organics 4 Orphans. This organization is working to eliminate malnutrition in Africa by creating sustainable agricultural based solutions. They raised $585.00, which is enough to provide the support and instruction required to empower a village to take control of their future. For more information on this organization check out www.organics4orphans.org.

The Virology Lab at St. Joseph's Hospital has weathered another huge increase in workload which typically arrives during "Flu Season". Over the space of about two months, nasopharyngeal specimens (NPS) received in Virology increased by approximately 400% from the beginning of November to the end of December 2012 (about 1 month earlier than most flu seasons). By the first week in January 2013, the positivity rate had peaked at 33% with one out of every 3 NPS positive for influenza A. By early February, total numbers of samples, and those positive for Influenza A, were still elevated but beginning to taper off.



The Hamilton General Hospital has just launched an exciting new **Antimicrobial Stewardship** Initiative in the ICU-East. The HHS Antimicrobial Stewardship Program has implemented the provincial wide **CAHO ARCTIC program** which is being led Infectious Disease physician, **Dr. Cheryl Main** and Infectious Disease Pharmacist **Neal Irfan** along with the Intensivists who work in ICU-East. Patients are reviewed regularly by the team to ensure that the right drug is being used for the right duration for every patient. Outcome measures being examined include infection related to broad spectrum antibiotic use such as *Clostridium difficile* and fungal infections, antimicrobial resistance patterns and antimicrobial utilization. The program is off to a very promising start and we look forward to sharing our findings.

Chemistry News

Expanding Allergy testing for Clinical Service and Research through the *Hybrid Laboratory*

The concept of the Hybrid Laboratory (HL) was first proposed by Dr J Macri (Clinical Biochemist, HRLMP) in 2009 as a vehicle to address the ever present dilemma faced by hospital and research laboratories….. *providing the best and most up to date testing menu with limited budgets*. In essence, the HL serves as an interface between Health Care, Academia and the Private Sector with respect to common needs and goals. By combining resources (budgets, infrastructure, expertise), the HL facilitates completion of the projects and initiatives that would otherwise be extremely difficult for any one institute. In addition, it creates novel synergies that serve to provide sustainability through long-term partnership and also forms an identity for the HL as an institute.

With the launch of an expanded allergy test menu in the Clinical Chemistry and Immunology Department on April 1st 2013, the concept of the HL will become a reality. Working with clinician/scientists Drs Susan Waserman (Allergist), Malcolm Sears (CHILD study) and Judah Denburg (CEO AllerGen NCE), Dr Macri applied the concept of the HL to offer an expanded allergy test menu in support of hospital services, clinical research and R & D partnership in the area of allergy and immune disease. The added value associated with the HL helped to establish a strategic partnership with Somagen Diagnostics, thus enabling the implementation of their PHADIA 250 technology for allergy testing. Finally, in support of this novel concept, the McMaster Children's Foundation has provided a 100 k donation to assist with allergy research.

Based on the excellence and expertise found in Hamilton Hospitals and McMaster, the hope is the HL model will be replicated many times in the future as a mechanism to initiate, develop and sustain projects that simultaneously benefit health care and research.

HRLMP Open Staff Forum

The next HRLMP Open Staff Forum will take place on **Tuesday February 26, 2013** at the times below.

09:30-10:30 Stelco Amphitheater SJH

Videoconferencing Room 4E20 MUMC
Boardroom HGH
Auditorium JH
Kemp Auditorium CAHS

11:30-12:30 Boardroom HGH

Videoconferencing Auditorium JH
Stelco Amphitheater SJH
Room 2G61 MUMC
Kemp Auditorium CAHS