MALDI-TOF VITEK® MS – Introduction of a New Technology at HRLMP

Matrix-assisted laser desorption ionisation time-of-flight (MALDI-TOF) is a novel technology that can provide rapid identification of bacteria and yeast by analyzing proteins in intact organisms using mass spectrometry. The HRLMP microbiology laboratory introduced Vitek® MS initially for yeast identification in February 2014 and has expanded testing to include anaerobic organisms, enteric pathogens and a range of gram positive and gram negative bacteria.

Principles:
MALDI-TOF involves inoculating a target plate with a spot from a culture. A chemical matrix is applied to the spot which is then targeted by a laser. The chemical matrix protects the proteins and helps in vaporizing and ionizing them. The ionized proteins enter a flight tube under vacuum and are separated by the mass to charge ratio. A spectrum with a unique signature of peaks corresponding to proteins often ribosomal, and other housekeeping proteins is compared to a database of species-specific reference protein profiles. For the Vitek® MS, a weighting algorithm is used to generate an “Advanced Spectra Classifier”. A confidence level is provided for each identification with ≥95% considered acceptable.

Performance of MALDI-TOF:
One of the major advantages of the MALDI-TOF has been the reduction in time to identification. On average, it takes 45-90 minutes to identify 14 isolates from inoculation of the target plate to generation of a result. In contrast, routine methods for identification require from 4-18 hours using semi-automated biochemical methods for identification and may require manual reagent tests, further growth on solid media, and referral to a reference laboratory - adding days to the time to identification.
A number of studies have been published evaluating the accuracy of identification using the Vitek® MS for a wide range of organisms compared to the gold standard of molecular sequencing (1, 2, 3). Identification of yeast, both Candida and non-Candida species, are correctly identified to the species level in 98.4% and 91.6-95.2% respectively. Identification of anaerobic bacteria ranges from 91-100%. For aerobic bacteria, correct identification ranges from 85-96.2% with the lower range occurring in difficult to identify organisms such as aerobic gram positive bacilli and certain non-fermenting gram negative bacilli from cystic fibrosis patients. An internal verification performed by HRLMP Microbiology showed improved identification of anaerobes, some *Pseudomonas* species and some gram positive cocci. Identification could be performed on mono-microbial blood cultures after as little as 2-4 hours of growth.

There are some limitations to the MALDI-TOF. *Shigella* and *E. coli* cannot be differentiated and other identification tests are required. In addition, if the organism is very mucoid or dry, a result may not be obtained. Organisms such as yeast, mycobacteria and some other gram positive bacilli require an extraction step for cell wall lysis. Mycobacteria and some other less common organisms may require use of a separate research-only database. Additionally technologists must be very careful to inoculate the target plate without contaminating other spots.

**MALDI-TOF and Antibiotic Stewardship:**

One of the most promising applications of MALDI-TOF is in antimicrobial stewardship. A study performed at Hamilton Health Sciences evaluated the accuracy of MALDI-TOF identification and using plates with two to 12-hours of growth from positive blood cultures compared to routine identification. Additionally, the potential impact of earlier identification using the MALDI-TOF was assessed with respect to appropriate antibiotic prescribing. The retrospective chart review found the potential impact of the MALDI-TOF as follows:

- Earlier discontinuation of antibiotics in 10.6%
- Earlier modification of empiric treatment to narrow spectrum in 22.7%
- Improved activity for 3%
- Results were available 22.8 hours earlier (range 2-70 hours)

This is consistent with several studies (4,5) that have shown a reduction in time to appropriate therapy, reduction in antibiotic usage, decreased length of stay and decreased hospital costs. The potential impact of MALDI on stewardship is promising, and optimizing different stewardship strategies requires further study in well-designed randomized trials.

**Future impact:**

The use of MALDI-TOF for an expanded range of organisms is likely to include significant invasive moulds. Additionally, identification from positive liquid cultures such as blood cultures and positive urines, may further reduce the time to identification. MALDI-TOF is also being explored as a microbial typing method.

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**Summary of Key Points:**

- MALDI-TOF uses mass spectrometry to identify a wide range of bacteria and yeast.
- Identification is rapid and more streamlined than routine methods and integrates well into workflow in the laboratory.
- Rapid identification can have a positive impact on antibiotic stewardship, patient outcomes and costs.

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**Dr. D. Yamamura, MD FRCP, Medical Microbiologist, HRLMP**

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**References:**

News from the HRLMP

7th Annual HRLMP Rapid Fire Showcase – A Great Success!

On Saturday November 22nd, the HRLMP hosted its 7th Annual Rapid Fire Showcase. The event was a huge success, drawing the largest number of participants in its history from both the HRLMP and across our LHIN. Being part of a large laboratory program can make it difficult to stay in tune with what’s happening across the different laboratories; the Rapid Fire Showcase provides a venue for us to do just that.

The showcase consisted of 11 speakers from within the HRLMP sharing their expertise on esoteric testing, new instrumentation, new technologies, and case studies. Some of the topics included Next Generation Sequencing, testing in the Sputum and Platelet Immunology Laboratories, PKU testing, Biosafety and Ebola Preparations. Kudos to all of the speakers who did a fantastic job of sharing their experiences and expertise.

If you were not able to make it to this year’s Rapid Fire, mark it on your calendar for next year – it’s a great event!

We are very pleased to announce that Michelle Somers has accepted the interim position of Manager, Core Laboratories, St. Joe’s and MUMC sites effective December 8th, 2014.

Michelle comes to this role with an extensive management background in healthcare. Most recently, she has very successfully managed the office operations for the HRLMP. She joined us in 2011 and has demonstrated tremendous leadership. Michelle’s personality, skills, background and experience are well suited to the role of Manager in our Core Laboratories.

Please join us in welcoming Michelle into her new interim manager’s role within the HRLMP.

Education News

The Laboratory Medicine Training Programs are excited to announce the Resident Research Education Forum which will be held on February 20, 2015. This event is being organized by the new Chair of Pathology and Molecular Medicine, Dr. M. Crowther.

The Medical Microbiology Resident Training program is pleased to announce that Dr. Yang Yu is the recipient of the 2014 Harry Richardson Award for her project entitled “Organism Identification on Early Subculture Colonies by VitekMS Matrix-Assisted Laser Desorption Ionization-Time of Flight (VITEKMS) and its Impact on Antibiotic Stewardship”. Dr. Harry Richardson (1939-2007) was a pioneer in Quality Management and the annual award created in his honour recognizes the best quality management project in Medical Microbiology.

News from Hematology

Recently, new oral anticoagulants have been introduced into clinical practice. Although the published literature is limited, some new oral anticoagulants have variable effects on coagulation laboratory test results, causing potential false positive and negative results depending on the assay and anticoagulant, as outlined in the June edition of Connections http://hrlmp.ca/workfiles/HRLMP/Connections_June_2014_isue131.pdf. Routine screening tests, such as the PT/INR, APTT and thrombin time, are not sensitive enough to detect the presence of all anticoagulants.

As a result, on November 3, 2014, the HRLMP Special Coagulation Laboratory stopped performing reflex testing to determine if an abnormal result was caused by warfarin or heparin as many patients are now on other anticoagulants and these tests are not able to detect the anticoagulant effect of all possible anticoagulants. Effective November 3, 2014 Special Coagulation now performs all testing that is ordered on a sample.

The Special Coagulation laboratory staff will no longer reflex or make the decision not to run immunological testing for antithrombin, protein C and/or protein S total as that decision should be made by the physician. Also on November 3, 2014, our laboratory went live with detailed, updated interpretive comments for antithrombin, protein C, protein S and activated protein C resistance assays. Physicians are encouraged to read these comments in their entirety as we have strived to provide detailed explanations of possible interferences and the suggested next steps in the investigation of abnormal results.

If you have any questions regarding these changes, or any other coagulation laboratory issue, please contact
Karen Moffat, Technical Specialist, Coagulation at moffat@hhsc.ca or 905 521 2100 ext. 73124.

**News from Microbiology**

**Duo e-Swabs are coming in 2015**

This swab system allows for 2 body sites (nares and rectum) to be tested for MRSA surveillance in one sample to improve efficiency for nurses and lab staff. **Watch for it early in 2015!**

**In appreciation of Candy Rutherford**

Each year, SIHH has **Excellence in Professional Practice Awards** to showcase health professionals who go above and beyond to provide excellence in patient care, leadership and research.

This year, **Candy Rutherford**, Technical Specialist in Virology, was nominated for 3 awards:

- Excellence in Practice Award for Individual Innovation in Practice
- Excellence in Practice Award for Individual Research
- Excellence in Practice Award for Individual Clinical Practice

![Photo by Sylvia Medeiros and Melanie Skakle](image)

Candy's most recent achievement, the development of a rapid test for typing enterovirus EV-D68, is just one example of her continual pursuit of discovery and collaboration with our clinical partners.

Please join us in congratulating Candy on her nominations and thanking her for the tremendous work she does every day for our patients.

We are extremely fortunate to have a “molecular rock star” as part of our team!

Microbiology is sad to announce that **Michael McConnell** is leaving the HRLMP, to start a new position with Copan Diagnostic, as Senior Field Applications Specialist. Congratulations Mike!

**News from Genetics**

It is with mixed emotions that we announce that **Dr. Ron Carter** has resigned from his position from the Hamilton Regional Laboratory Medicine Program, effective December 15, 2014. Dr. Carter has accepted a position with LifeLabs.

Dr. Carter has been the Discipline Director for Genetics since 1990, during which time he has made numerous contributions to Genetic Services within both Hamilton and the LHIN Region. He has also represented the HRLMP at various Provincial Committees and is well respected for his educational and research contributions at McMaster University. He will be greatly missed and we all wish him well! Please join us for a “Farewell Tea” to recognize his contributions to the HRLMP.

Dr. John Waye has accepted the role of Interim Discipline Director for the Division of Genetics, effective **December 1, 2014**.
Dr. Ron Carter is leaving us!

After years of hard work and dedication, he is leaving the HRLMP for a position at LifeLabs

Please join us for Cake, Tea & Coffee as we offer Ron our best wishes . . .

December 11, 2014
2 to 4 PM
Location: McMaster Hospital Blue Room
(Contributions for his gift gratefully accepted – See Tammy, Room 3N12 or robertton@hhsc.ca)

News from Chemistry

In an effort to maintain high quality testing for cardiac troponin I, the HRLMP laboratories will be switching to a high-sensitivity cardiac troponin I test [Troponin I (HS)] within all Hamilton Hospitals. Concurrent with changing to the Troponin I (HS) test on November 25, 2014, the following are important items:

New assay will be reported in whole numbers rather than decimals.
Reporting unit change from ug/L to ng/L; with <1 ng/L being the lower limit of reporting

Cutoff will be 30 ng/L which remains the same as our previous >0.03 ug/L cutoff.
A positive result would be Troponin I (HS) > 30 ng/L

For evaluating patients with suspected Acute Coronary Syndrome, blood samples for the measurement of Troponin I (HS) should be drawn on first assessment and repeated 3 hours later.
Later samples may be required if further ischaemic episodes occur, or when the timing of the initial symptoms is unclear

Assay has better specificity & sensitivity
There are less analytical outliers and the Troponin I (HS) test can measure “normal” troponin

Collection of the sample tube remains the same.
Purple top – EDTA plasma tested

The following comment will be appended to the Troponin I (HS) results for further clarity
<=30 ng/L No evidence of Myocardial Injury
>30 ng/L Evidence of Myocardial Injury
*Units (ng/L) as high-sensitivity assay

For further information please contact Dr. Tony Chetty (Discipline Director Clinical Chemistry) at chetty@hhsc.ca or Dr. Peter Kavsak (Biochemist) at kavsak@hhsc.ca.

Dr. M. J. McQueen is retiring!

After a highly productive career during which he made many significant contributions to medicine and research, and provided leadership to the HRLMP, Dr. McQueen has decided to retire from the HRLMP.

His legacy includes mentorship of numerous faculty and residents, the Clinical Research and Clinical Trials Laboratory and Biobank, more than 200 publications, and over $125 million in research funding. We wish Matt all the best in his retirement and in his research career, which he will be continuing!

Happy Holidays

From the HRLMP