



News and Updates from the Public Health Laboratory Birmingham

Find out more information about the tests and services offered at the Public Health England Public Health Laboratory Birmingham please visit www.heftpathology.com

TB Genomic Service (TBGS)

All laboratories using our mycobacterial reference service are invited to take part in a project to establish an accredited whole genome sequencing (WGS) service for TB and to evaluate it against current standard-of-care TB tests and reference/specialist services.



The RCM and TBGS Team

Mycobacterium tuberculosis (TB) has been identified a priority area for implementation of whole genome sequencing (WGS) of human pathogens. WGS for TB has a great potential to provide information that will impact patient care.

The Birmingham Public Health Laboratory has been selected to lead on a Public Health England pilot project for TB-WGS. This has been endorsed by Genome England and builds on successful feasibility studies undertaken with partners at Oxford University. The new Birmingham pilot will inform wider implementation of WGS as part of the routine management of NHS patients with TB.

TBGS Objectives:

- To accelerate the introduction of WGS into the NHS TB care pathway
- To deliver improved patient care through a personalised therapeutic approach, especially for drug resistance prediction

In this issue

TB Genomic Service (TBGS)	1
New managers for laboratory and Regional Centre for Mycobacteriology	2
Evaluating the impact of direct identification of bacteria from positive blood cultures by MALDI-TOF	3
MALDI-TOF identification service	4

- To deliver improved public health control of TB through better understanding and management of transmission networks and with automated national surveillance

In the autumn of 2013 an Illumina MiSeq machine was installed at the Birmingham Laboratory with support from the Health Innovation Challenge Fund grant. Our staff members have established methods to sequence the whole genomes of TB isolates and raw genome data can now be sent electronically to an analytical pipeline hosted at Oxford. Results on the mycobacterial species identity, drug resistance predictions and typing can be returned within approximately 48 hours.



The Illumina MiSeq with TBGS Team Members: Tanya and Debbie

The TB Genome Service (TBGS) pilot will be launched in July and we will be contacting our TB users to provide more information about it and to discuss possible modifications of the process for sending cultures. Service users do not need to do anything different at present.

New managers for laboratory and Regional Centre for Mycobacteriology

We are pleased to announce that Mrs **Priti Rathod** is the new manager for the Regional Centre for Mycobacteriology. Priti has worked in the Birmingham Public Health Laboratory for several years and took on the lead role for the CL3 laboratories in February. She follows on from **Sarah Gardiner**, who is now our Laboratory Manager.



Sarah Gardiner and Priti Rathod

Evaluating the impact of direct identification of bacteria from positive blood cultures by MALDI-TOF

Why use MALDI-TOF on blood cultures?

With its speed and accuracy, the use of MALDI-TOF has revolutionised the way the clinical microbiology laboratory identifies bacterial colonies from agar plates. This technology can also be used to identify micro-organisms directly in samples before sub-culture is carried out.

Early, appropriate antibiotics have been shown to have a significant positive impact on the outcome of sepsis. However, current blood culture identification (ID) techniques rely on 24 hour agar plate subculture once the bottle has become positive. The clinical microbiology team at the Public Health Laboratory Birmingham therefore decided to evaluate the performance and impact of using MALDI-TOF to identify bacteria from blood cultures on the same day the bottles become positive.

What we evaluated

Over four weeks we analysed positive blood cultures with micro-organisms seen in the Gram stain. All bottles had conventional sub-culturing and also analysis by MALDI-TOF. One millilitre of culture from the bottle was lysed with a buffer, washed and extracted with formic acid:acetonitrile to remove red blood cells and haemoglobin that may interfere with the MALDI system.

Corresponding clinical data for the patients with positive bottles were also collected and examined. Clinical advice given on day one based on the Gram stain result alone was compared with the follow up advice given on day two based on organism ID. Any changes in clinical advice between day one and two were recorded. All culture results were then compared with the results of direct MALDI-TOF ID.

Results and clinical impact

A total of 115 cases were included in the study. For 73 cases (63.5%) the organism ID was obtained by direct MALDI-TOF on day one. Of those with a direct ID, 70 of 73 (95.9%) had a result concordant with that from plate culture. The three discordances were in polymicrobial cultures where 16S rDNA PCR and DNA sequencing agreed with the direct MALDI result.

In 28 of the 115 cases (24.3%) a direct MALDI ID on day one would have had a clear clinical impact:

- In 11 cases (9.6%) the direct ID would have indicated a different source or a different approach to investigation
- In 11 cases (9.6%) direct ID would have indicated a different antibiotic regimen on day one, resulting in five patients receiving appropriate antibiotics 24 hours earlier in their illness

- With the benefit of a MALDI ID on day one, 14 cases (12%) would not have required any microbiology input and been designated as unlikely to be clinically significant

Direct MALDI-TOF cannot achieve 100% organism ID on day one and polymicrobial positive blood culture bottles remain a challenge as direct MALDI can only detect one organism in a bottle. We have however demonstrated that where organism ID is available on day one of blood culture positivity, this can have a positive clinical impact. Faster ID by use of MALDI-TOF could assist the medical microbiologist in assessing the clinical significance of a blood culture isolate on day one. It can allow earlier appropriate empirical choice of antimicrobial agents, even in the absence of susceptibility testing and can help in narrowing down the potential source and provide a focus for investigation, more quickly than conventional techniques alone.



The MALDI-TOF Spectrometer

MALDI-TOF identification service

We are now able to offer identification of bacterial isolates by MALDI-TOF. If you would like to refer isolates for this reference service please contact Dr Abid Hussain for more details: abid.hussain@heartofengland.nhs.uk