QuantiFERON-TB Gold Plus
A New Interferon-γ Release Assay (IGRA) for the Indirect Detection of *Mycobacterium tuberculosis*
Disclosures

• None

Utilization Message

• As you view this presentation, consider the following important points regarding testing:
  • How is the testing going to be used in your practice?
  • When should the tests be used?
  • How will results impact patient management?
  • Begin planning for transition to the new QuantiFERON-Tb Gold Plus assay
Evolution of Laboratory Diagnostics for *M tuberculosis*: Slow...

- **1884**
  - "Koch’s Bacillus"

- **1907-1910**
  - Tuberculin Skin Test (TST)

- **2000**
  - Still relying on:
    - TST
    - Culture (4-6 weeks)
    - Direct smear

- **2000-2015**
  - Probe ID Sequencing
  - PCR
  - IGRAs

**HOT TOPIC / QuantiFERON-TB Gold Plus**

Commercially Available IGRAs for *M tuberculosis*

- 3 FDA-cleared IGRAs:
  - T.SPOT-TB (Oxford Immunotec)
  - QuantiFERON-TB Gold In-Tube (QFT-Gold; Qiagen)
  - **NEW**: QuantiFERON-TB Gold Plus (QFT-Plus; Qiagen)

- IGRAs are indirect tests for infection with *M. tuberculosis* (MtB)
- Concept: Detect IFN-γ produced by MtB ‘primed’ T-cells following exposure to MtB antigen

## QuantiFERON-Tb Gold Plus

- FDA-cleared June 2017
- Developed with the goal to increase sensitivity for both LTBI and active disease
- Includes peptides to stimulate CD4+ and CD8+ T-cells

**CD4 T Cell**
- Essential for MTb control
- Secrete cytokines to regulate/assist immune response
- IFN-γ for macrophage activation

**CD8 T Cell**
- Secrete cytokines, including IFN-γ
- Directly kill MTb-infected cells
- Lyse intracellular MTb

### QFT - Gold
- Antigens: PHA*, ESAT-6, CFP-10, Tb7.7
- Peptide Length/MHC-class: Long/Class II
- T Cells Stimulated: CD4+
- Mitogen Control
- Tb Antigens
- Nil Control

### QFT - Plus
- Antigens: None, ESAT-6, CFP-10
- Peptide Length/MHC-class: Long/Class II, Long + short/Class II + I
- T Cells Stimulated: CD4+, CD4+/CD8+
- Mitogen Control
- Tb 1 Antigens
- Tb 2 Antigens
QFT-Plus Specimen Collection

Transport to Laboratory

- Draw whole blood into lithium-heparin tube
- Aliquot into QFT-Plus tubes and process

- Mayo Medical Laboratories will **only** accept incubated and centrifuged QFT-Plus Tubes for testing
- Lithium-Heparin tubes will not be accepted
- For more information on specimen collection, handling and processing of Lithium-Heparin tubes please refer to manufacturer instructions or contact Mayo Medical Laboratories for more information

QFT-Plus Processing is Identical to QFT-GIT Processing

- Mix tubes (Firmly invert 10 times)
- Incubate at 37°C 16-24 hrs
- Centrifuge to collect plasma
- APC takes up Tb antigen
- Tb antigen processed by APC
- Tb antigen presented to T-cell
- T-cell produces IFN-γ
- Calculate and Report Results
### QuantiFERON-TB Gold Plus: Results and Interpretation

<table>
<thead>
<tr>
<th>Nil</th>
<th>TB1 - Nil</th>
<th>TB2 - Nil</th>
<th>Mitogen - Nil</th>
<th>Qualitative Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤8.0 IU/mL</td>
<td>≥0.35 and ≥25% of Nil</td>
<td>Any</td>
<td>Any</td>
<td>Positive</td>
<td>M. tuberculosis infection likely</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>≥0.35 IU/mL and ≥25% of Nil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.35 IU/mL</td>
<td>≥0.35 IU/mL and &lt;25% of Nil</td>
<td>≥0.5 IU/mL</td>
<td>Negative</td>
<td></td>
<td>M. tuberculosis infection NOT likely</td>
</tr>
<tr>
<td>&gt;8.0 IU/mL</td>
<td>Any</td>
<td>&lt;0.5 IU/mL</td>
<td></td>
<td>Indeterminate</td>
<td>Likelihood of M. tuberculosis infection cannot be determined</td>
</tr>
</tbody>
</table>

- Cutoff criteria identical to QFT-Gold
- QFT-Plus is considered positive if either one or both Tb Ag tubes are positive

### Summary

- The QFT-Plus assay for indirect detection of *M. tuberculosis* infection received FDA clearance in June 2017
- The assay is intended to improve sensitivity for detection of *M. tuberculosis* over the prior QFT-Gold version
  - Stimulation of both CD4+ and CD8+ T-cells
  - Data suggests non-inferior or similar performance between these two IGRAs
  - Additional studies are ongoing
Next Steps
- Mayo Medical Laboratories will be converting to the QFT-Plus assay on February 13th, 2018
  - The QFT-Gold test will not be orderable after this date
  - If not already initiated, MML clients are encouraged to begin the conversion process
    - QFT-Plus tubes will be available to order on January 13th, 2018
    - Consider whether whole blood will be collected into a single lithium-heparin tube vs. directly into the QFT-Plus 4 tubes
    - **NOTE:** MML will not accept lithium-heparin tubes or unprocessed QFT-Plus tubes
- For questions and assistance during the conversion process, please contact Mayo Medical Laboratories

References
Questions or requests…
Email to: MMLHotTopics@mayo.edu
For more information…

Visit MayoMedicalLaboratories.com
or call Mayo Laboratory Inquiry at 800-533-1710