

QuantiFERON-TB Gold Plus

A New Interferon- γ Release Assay (IGRA) for the Indirect
Detection of *Mycobacterium tuberculosis*

HOT TOPIC / 2018

HOT TOPIC / QuantiFERON-TB Gold Plus



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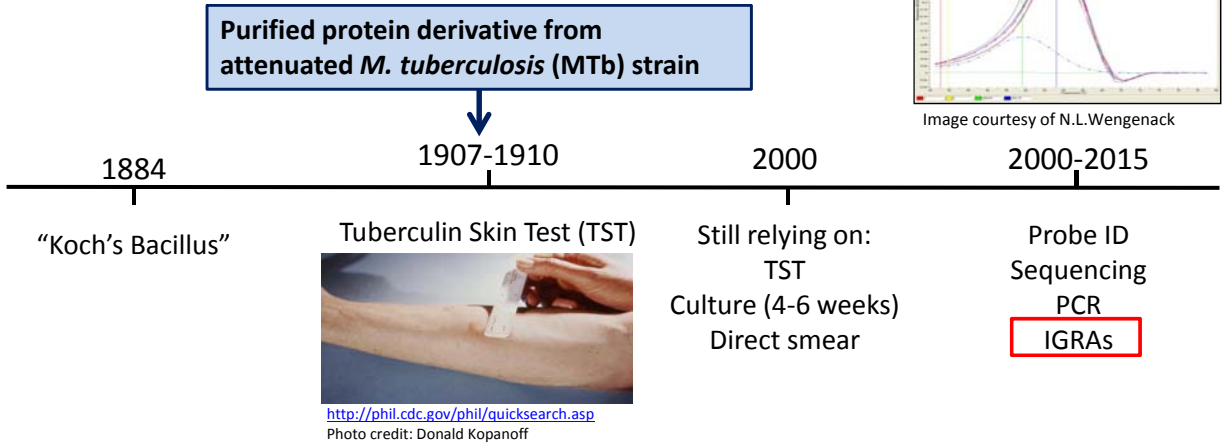
Disclosures

- None

Utilization Message

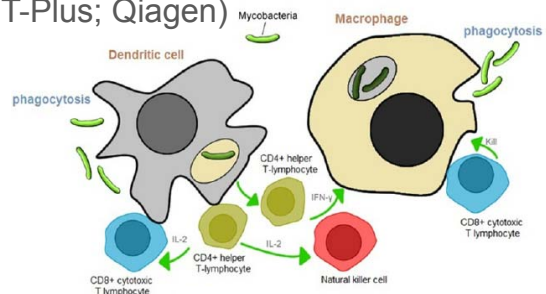
- As you view this presentation, consider the following important points regarding testing:
 - How is the testing going to be used in your practice?
 - When should the tests be used?
 - How will results impact patient management?
 - Begin planning for transition to the new QuantiFERON-Tb Gold Plus assay

Evolution of Laboratory Diagnostics for *M tuberculosis*: Slow...



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



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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



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CD4 T Cell



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

CD8 T Cell

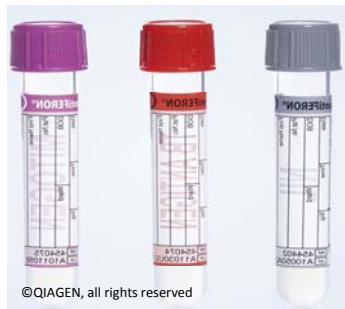


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- Secrete cytokines, including IFN-γ
- Directly kill MTb-infected cells
- Lyse intracellular MTb

QFT-Gold

Mitogen Control Tb Antigen Nil Control



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Antigens: PHA* **ESAT-6, CFP-10, Tb7.7** None

Peptide Length/MHC-class: **Long/Class II**

T Cells Stimulated: **CD4+**

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Nil Control Tb 1 Antigen Tb 2 Antigen Mitogen Control



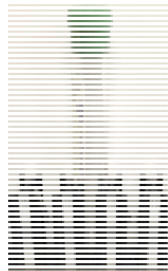
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None **ESAT-6, CFP-10** **ESAT-6, CFP-10** PHA*

Long/Class II **Long + short/ Class II + I**

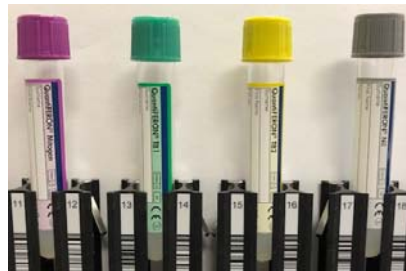
CD4+ **CD4+/CD8+**

QFT-Plus Specimen Collection



Draw whole blood into lithium-heparin tube

Transport to Laboratory



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

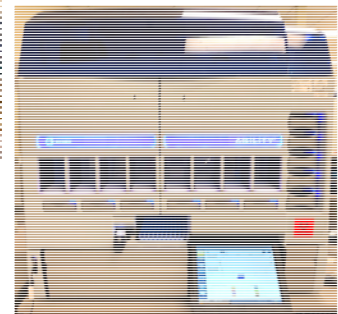


Mix tubes (Firmly invert 10 times)

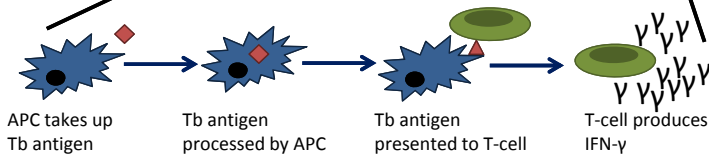
Incubate at 37C 16-24 hrs



Centrifuge to collect plasma



Calculate and Report Results



QuantiFERON-TB Gold Plus: Results and Interpretation

Nil	TB1 - Nil	TB2 - Nil	Mitogen - Nil	Qualitative Result	Interpretation
≤8.0 IU/mL	≥0.35 and ≥25% of Nil	Any	Any	Positive	<i>M. tuberculosis</i> infection likely
	Any	≥0.35 IU/mL and ≥25% of Nil			
	<0.35 IU/mL OR ≥0.35 IU/mL and <25% of Nil		≥0.5 IU/mL	Negative	<i>M. tuberculosis</i> infection NOT likely
>8.0 IU/mL	Any	<0.5 IU/mL		Indeterminate	Likelihood of <i>M. tuberculosis</i> infection cannot be determined

- 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

1. Arroyo-Ornelas MA, Arenas-Arrocena C, Estrada HV, et al. 2012. Immune Diagnosis of Tuberculosis Through Novel Technologies, Understanding Tuberculosis - Global Experiences and Innovative Approaches to the Diagnosis. InTech. Cardona PJ(Ed.). Available from: <https://www.intechopen.com/books/understanding-tuberculosis-global-experiences-and-innovative-approaches-to-the-diagnosis/immunodiagnosis-of-tuberculosis-through-novel-technologies>
2. Barcellini L, Borroni E, Grown J, et al. 2016. First evaluation of QuantiFERON-TB Gold Plus performance in contact screening. Euro Resp Soc 48(5):1411-1419
3. Moon HW, Gaur RL, Tien SS, et al. 2017. Evaluation of QuantiFERON-TB Gold-Plus in healthcare workers in a low-incidence setting. J Clin Micro 55(6):1650-1657
4. Telisinghe L, Amofa-Sekyi M, Maluzi K, et al. 2017. The sensitivity of the QuantiFERON-TB Gold Plus assay in Zambian adults with active tuberculosis. Int J Tuberc Lung Dis 21(6):690-696



Questions or requests...

Email to: MMLHotTopics@mayo.edu

For more information...

Visit MayoMedicalLaboratories.com
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