SELECTED OPPORTUNITIES IN INFECTIOUS DISEASES

Diagnosis of latent Mycobacterium Tuberculosis infection (BIO13394)

DIAGNOSIS OF LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION (BIO13394)

Product factsheet

Stage:
Pre-Analytic
Validation

- **Biomarker:**
  - Rv2626c antigen, IFNγ
- **Technology:**
  - ELISA
- **Sample:**
  - Blood
- **Information:**
  - Diagnostic

- **Scientific and Clinical Rationale:**
  - Current antigens used for diagnosing M. tuberculosis (CFP-10 and ESAT-6) do not discriminate between active and latent infection.
  - Rv2626c is a dormancy regulon-encoded antigen.
  - Previous studies suggest that Rv2626c antigen is recognized by household contact individuals or TB patients.
- **POC:**
  - Healthy Donors (HD, n=60) vs Tuberculosis patients (TB, n=56) and Latently infected TB patients (LTBI, n=56)
  - Additional cohort of Healthy (HD, n=23), Tuberculosis (TB, n=18), Close contacts (CC, n=47), or LTBI (n=8)
  - LTBI profile was assigned to any subject with a positive QuantiFERON-TB Gold In-Tube test (QFT) and no clinical or radiological evidence of active TB.
  - PBMCs from different subjects were cultured with Rv2626c or CFP-10+ESAT-6 (early secretory antigens currently used to diagnose M. tuberculosis in IFN-γ release assays) : cell-free supernatants were evaluated for IFN-γ production by ELISA.

Diagnosis of latent Mycobacterium Tuberculosis infection (BIO13394)

Product factsheet

Stage:
Pre-Analytic
Validation

Clinical State and Market Opportunity

- **Clinical State:**
  - **Epidemiology:**
    - TB in the top 10 causes of death worldwide: more than 9M incident cases[1]
    - More than 50% worldwide death in India, Indonesia, China and South Africa[1]
  - **Treatment:**
    - Multiple chemical classes of TB drugs (Rifamycins, fluoroquinolones, oxazolidinones …)[2]
- **Clinical needs:**
  - Current tests do not discriminate latent or active TB
  - One third of world population has latent TB but are not ill yet
- **Opportunity:**
  - **Market:**
    - Part of 1b$ annual market of TB diagnostics[3]
    - EME are dominated by latent TB testing[3]
  - **Current Gold Standard:**
    - TB skin tests, IGRA, T-SPOT…

Unique Selling Points

- **Priority :**
  - EP14 306 329.5 on 2014/08/29
  - PCT/EP2015/069791 on 2015/08/28
- **Product:**
  - Rv2626c antigen Peptide
- **Scientific Publication(s):**
  - EBioMedicine, 2015 May 30, *Peña D. et al.*, doi: 10.1016/j.ebiom.2015.05.026.
- **Development opportunities**
  - Ongoing clinical studies on bigger cohorts for further validation
  - Ongoing research open for partnering

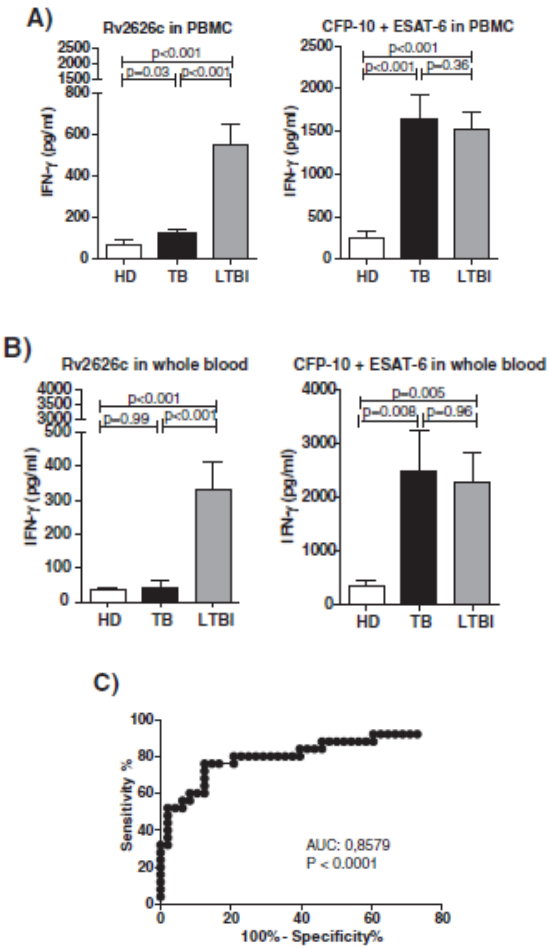
[1] The World Health Organization
[2] WHO & TDR, 2013, Priorities for tuberculosis research
[3] FIND & TDR, 2006, Diagnostics for tuberculosis

DIAGNOSIS OF LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION (BIO13394)

Proof of concept

- **<u>Pre-Analytic Validation:</u> LTBI individuals, but not TB patients, secrete IFN-γ against Rv2626c, in contrast to stimulation with CFP-10+ESAT-6 which elicit IFN-γ in both LTBI individuals and TB patients**
  - (A) Peripheral blood mononuclear cells (PBMC) from healthy donors (HD), patients with tuberculosis (TB) and latently by M. tuberculosis-infected individuals (LTBI) were cultured with Rv2626c or CFP-10+ESAT-6 for 5 days. Cell free supernatants were then recovered and IFN-γ production was evaluated by ELISA.
  - (B) Whole blood from HD, TB patients and LTBI individuals was cultured with Rv2626c or CFP-10+ESAT-6 for 24h. Plasma samples were then collected and IFN-γ production was evaluated by ELISA. Bars represent the Mean ±SEM. Mann-Whitney test was used for unpaired samples.

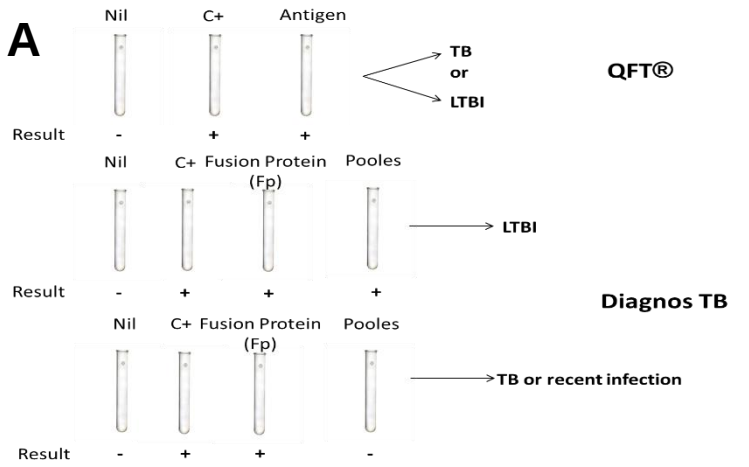
- **ROC curve analysis for IFN-γ responses to Rv2626c reinforces the potential of Rv2626c antigen for discriminating LTBI individuals from non-LTBI individuals**
  - (C) ROC curve analysis for evaluation of the predictive value of whole blood IFN-γ levels produced in response to Rv2626c for differentiating LTBI individuals from non-LTBI individuals (HD or TB). ROC, receiver operating characteristic; AUC, area under the ROC curve.

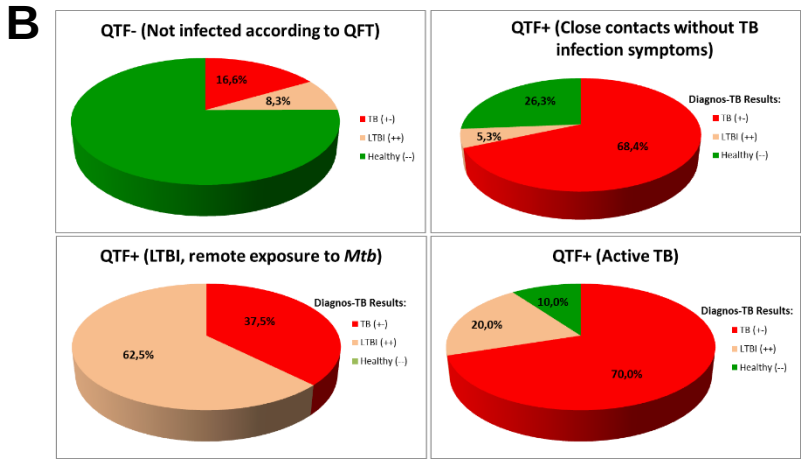


DIAGNOSIS OF LATENT MYCOBACTERIUM TUBERCULOSIS INFECTION (BIO13394)

Proof of concept

- **<u>Pre-Analytic Validation:</u> Comparison of QFT test and proposed DiagnosTB test show discrimination of LTBI vs Active TB patients when current QTF test does not enable such discrimination**
  - (A) Schematic comparison of QFT and DiagnostTB tests, and interpretation of results
  - (B) Comparison among results obtained with QFT and DiagnosTB. Colors in the graphs represent different results observed with DiagnosTB in each QFT category





InsermTransfert
Your partner in health innovation