CD4 and CD8 T cell-specific immune responsiveness of QFT®-Plus

Background

TB-specific CD8+ T cell (CD8) release of IFN-g are believed to a biomarker of intracellular TB bacilli burden. This assumption is based on immunology studies that have found TB-specific CD8 responses more frequently in those with active TB disease compared to latent infection (1, 2), associated with recent exposure to TB (3), in active TB subjects with HIV co-infection and who are young children (4, 5), and declining responses in patients on anti-tuberculosis treatment (6).

Unlike QFT-TB Gold In Tube (QFT-GIT), QuantiFERON® TB Gold Plus (QFT®-Plus) is designed to utilize both CD4+ T cell (CD4) and CD8 specific immune responses. Additionally, the isolated CD8 response can be quantified by subtracting the response of QFT-Plus' TB1 tube (TB1) from TB2 tube (TB2) to provide immunologic CD8 information that may aid in the patient's clinical assessment and management. In this report, I will introduce the recent publication on validating the CD4 and CD8 immune responses of the TB1 and TB2 tubes of QFT-Plus.

New Publication

Allen et al. studied QFT-Plus TB1 and TB2 immune responses by using CD4 and CD8 clones (7).

A CD4 clone (A. 38.1 # 1, recognizing the long-chain peptide of CFP-10) and three CD8 clones (B. D481 C10, C. D432 H12, D. D480 F6, CFP-10 recognition of short peptides) were used for their study. Each of the clones was re-suspended in 10% human serum RPMI medium with various concentrations (10^3 / mL = K / mL), and 1 mL of cell suspension was added to both TB 1 and TB 2 tubes, then mixed and incubated at 37 °C. After incubation, each tube was centrifuged, the IFN-g value (IU/mL) in supernatant was measured by QFT-Plus ELISA. The results are shown in Figure 1 and Table 1.

Immune responses of CD4 clone (A) were similar in TB1 and TB2 in dose-response manner, resulting in increased immune responsiveness (Figure 1A). The immune response of one CD8 clone (B) to TB1 was slightly elevated in response to the number of clones but the responsiveness to TB2 was overwhelmingly higher than that to TB1 (Figure 1B). Furthermore, responsiveness of CD8 clones (C) and (D) to TB1, was slight, and responsiveness to TB2 was more than 100 times responsive compared to TB1 (Table 1-C, D).

The results of this study that utilized specific CD4 and CD8 clones validate that the antigens of TB1 is CD4 specific and TB2 is specific to both CD4 and CD8, as QFT-Plus was designed.

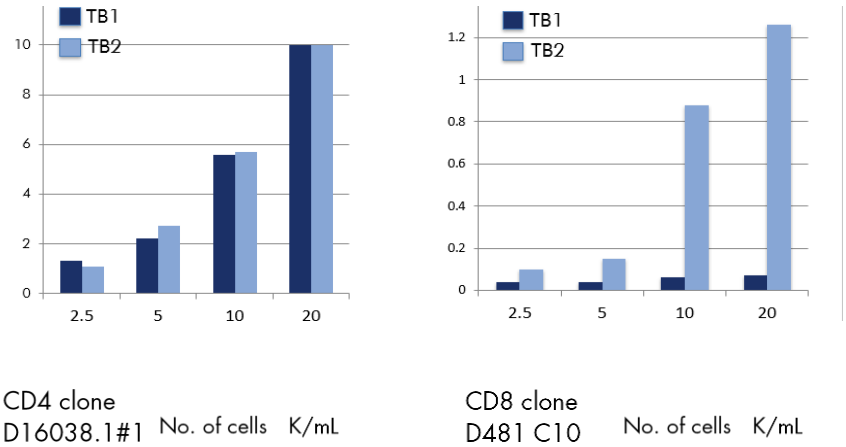

Figure 1. Immune responses of CD4 and CD8 clones to QFT-Plus TB1 and TB2 (A and B)

Table 1. Immune responses of CD8 clones to QFT-Plus TB1 and TB2 (C and D)

		IFN-γ IU/mL				
	QFT-Plus Blood Collection Tubes	No. of cells 20K	40K	60K	80K	100K
C. CD8 clone Cd432H12	TB1	0.12	0.24	0.22	0.33	0.51
	TB2	36	73	149	254	266
D. CD8 clone D480F6	TB1	N/D	N/D	N/D	0.53	0.98
	TB2	N/D	N/D	N/D	179	149

Note: If more than 10 IU/ml, the measured value was calculated by diluting in10 to 100 times.
N/D: not done, K=10^3 No. of cells.

Comment: This study provides direct evidence of the specificity of CD8 T-cell mediated response in QFT-Plus TB2 tubes. Compared with conventional existing IGRA in immunocompromised cases, QFT-Plus has been reported to be more sensitive compared to QFT-GIT due to CD8 signal in addition to CD4 (8–11)**. Further, the TB2-TB1 value is represented as the isolated immune response of CD8. The TB2-TB1 value of QFT-Plus suggests the possibility of additional clinical significance, such as a CD8 immune response associated with a higher intracellular TB condition such as active TB, developing active tuberculosis** (12)**, and recent infection in latent tuberculosis infection** (13)**. The potential clinical significance of the CD8 response of QFT-Plus shall be clarified with the accumulation of data obtained through future and ongoing studies.**

Mr. QFT

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QFT-Plus is an in vitro diagnostic aid for detection of Mycobacterium tuberculosis infection (including disease) and is intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations. QFT-Plus results alone cannot distinguish active TB disease from latent infection. QFT-Plus Package Inserts, available in multiple languages, as well as up-to-date licensing information and product-specific disclaimers can be found at www.QuantiFERON.com.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

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