

QFT-Plus: What is the evidence?

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Overview

- Variability and accuracy of IGRAs
- Sources of IGRA variability
- QFT-Plus

IGRAs entered the scene with a lot of promise

More sensitive and specific than TST

More reproducible/objective

More predictive



TB testing
has evolved –
has your TB
screening
program?

QuantIFERON®-TB Gold



www.QuantiFERON.com

T-SPOT.TB

**Oxford
Immunotec**
Harnessing the power of T cell measurement



Products & Services

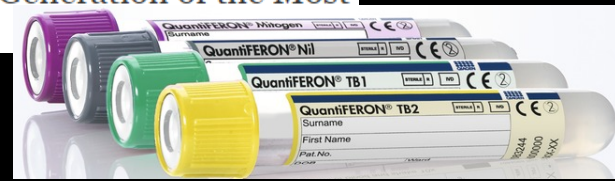
‘A 21st Century Solution for Latent TB Detection’

QuantIFERON®-TB Gold.
One blood test, One clear answer

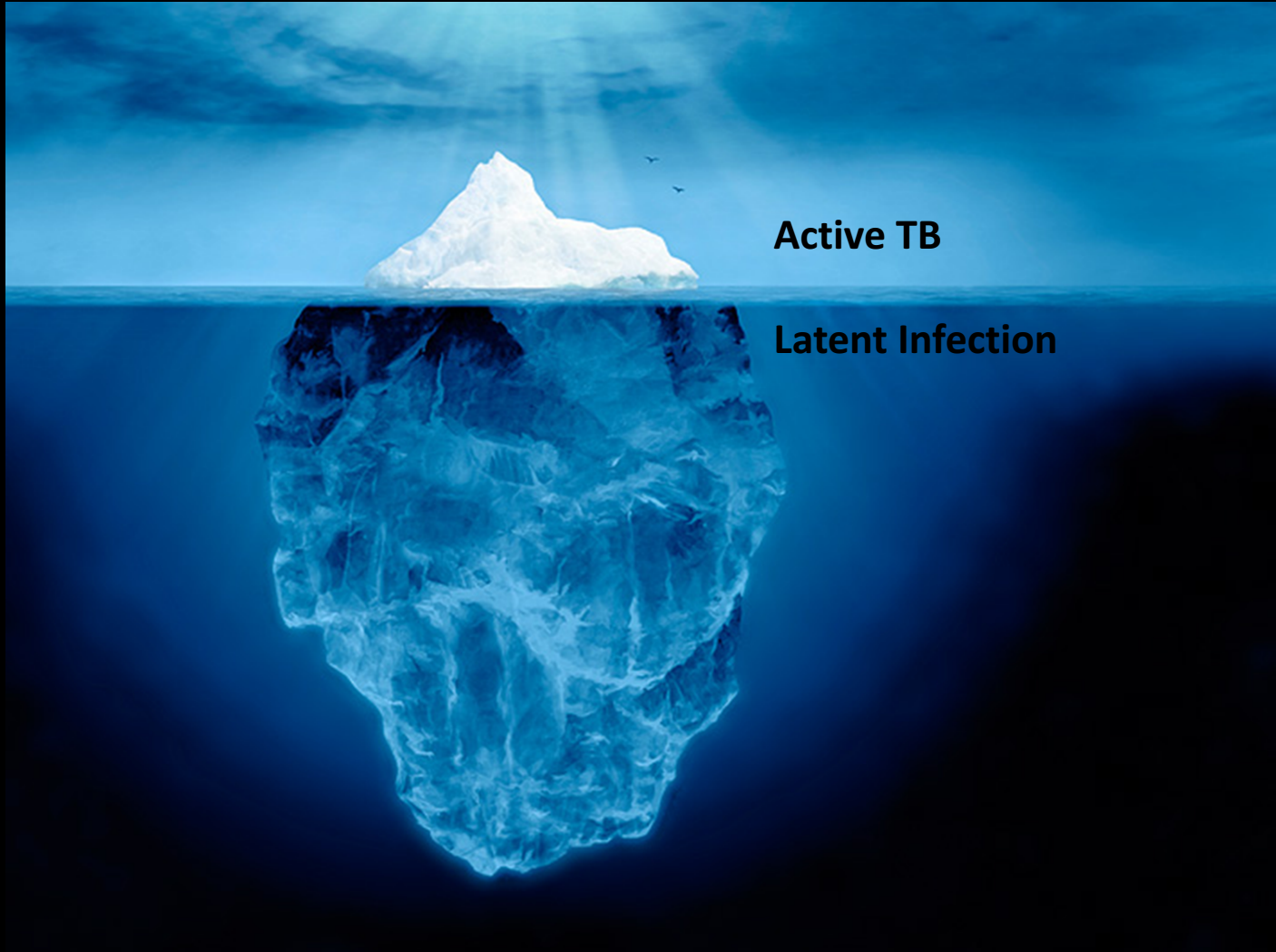


January 7, 2015 /PRNewswire/ --

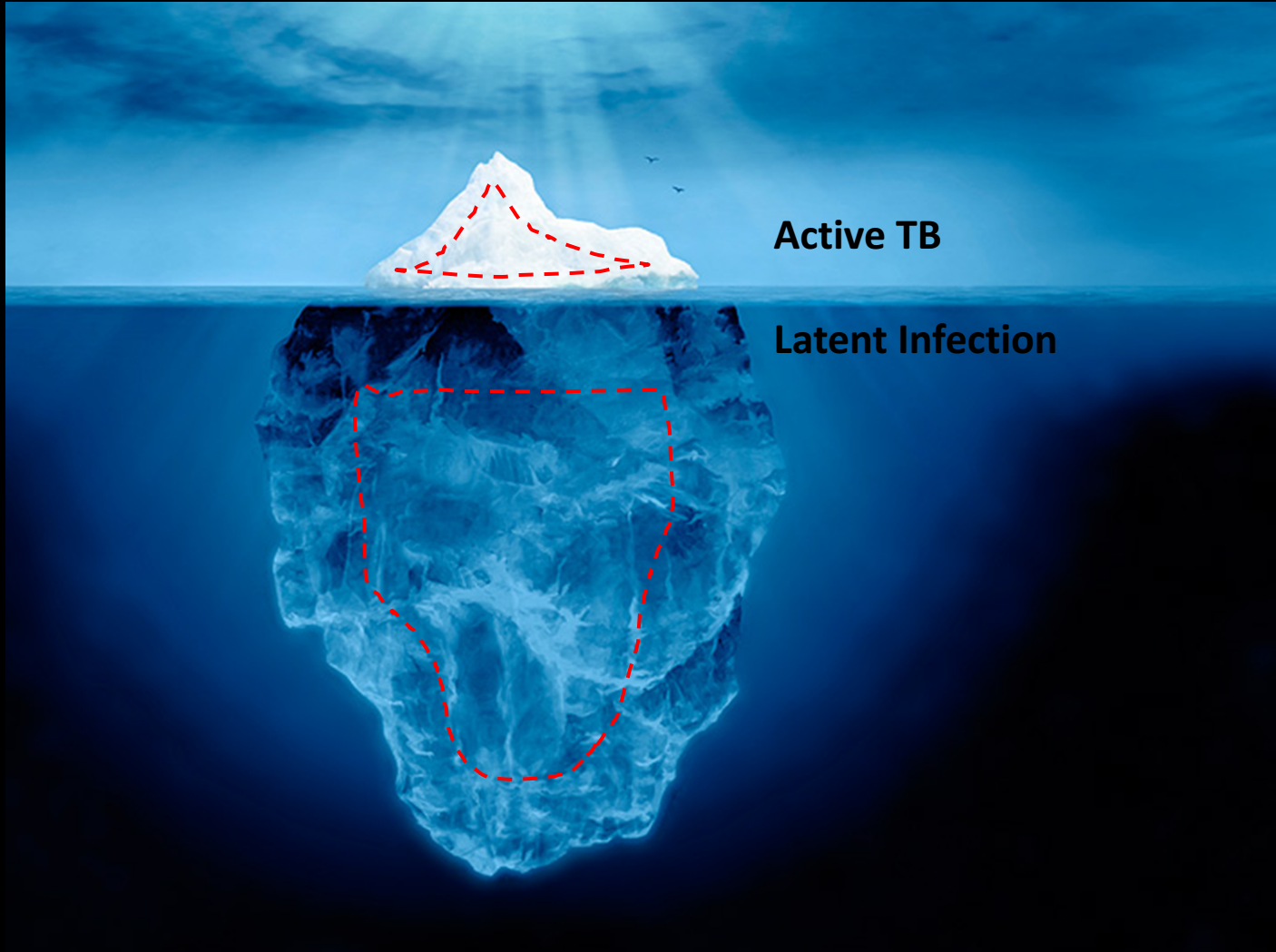
QIAGEN Launches QuantIFERON®-TB Gold Plus - A New Generation of the Most Accurate Test for Detecting Tuberculosis Infections



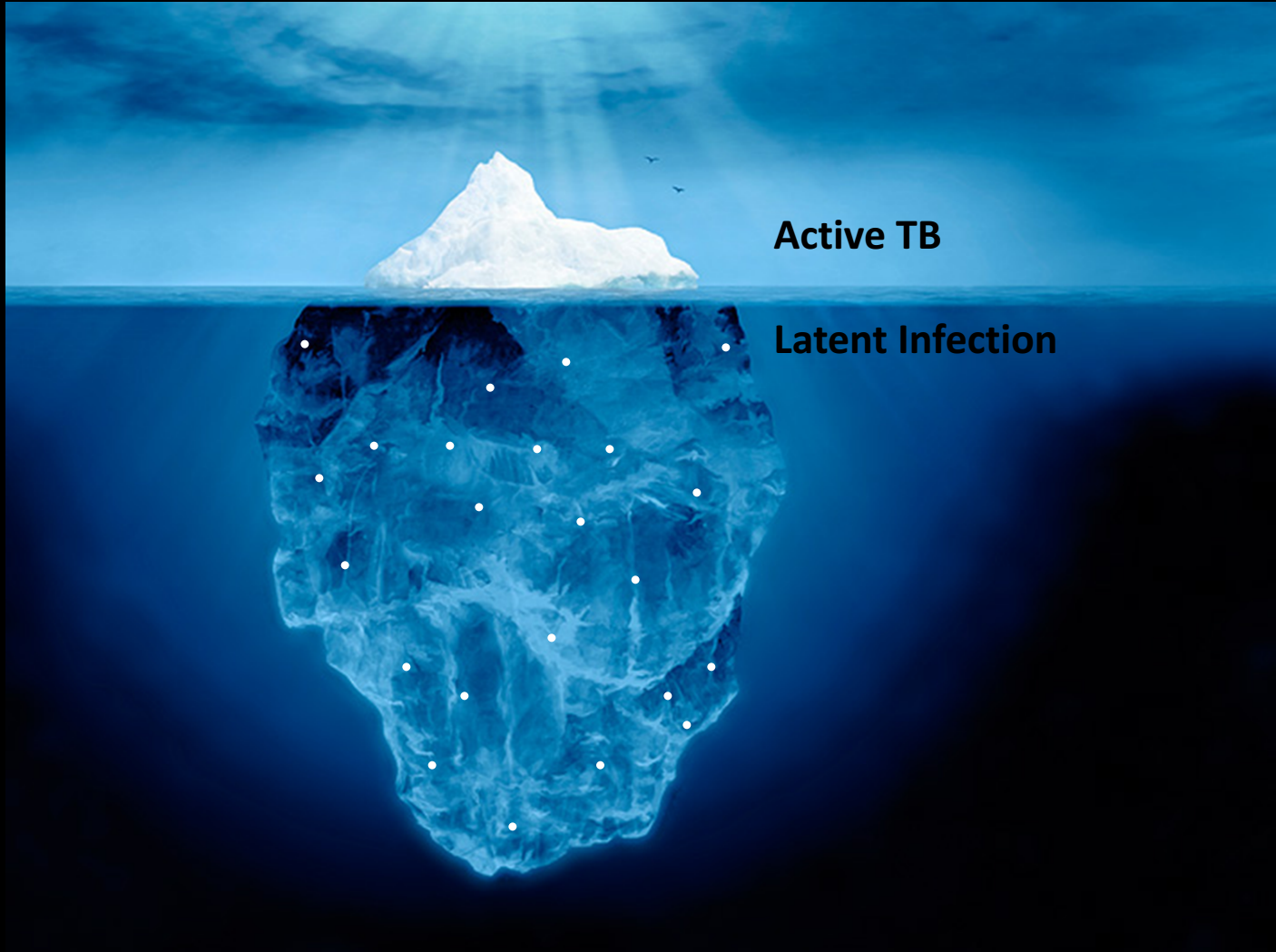
Spectrum of Infection with *M. tuberculosis*



IGRAs Have Poor Sensitivity for LTBI



IGRAs Have Poor PPV for Progression



Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States

Prepared by

Gerald H. Mazurek, MD, John Jereb, MD, Phillip LoBue, MD, Michael F. Iademarco, MD, Beverly Metchock, PhD, Andrew Vernon, MD
Division of Tuberculosis Elimination, National Center for HIV, STD, and TB Prevention

Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings, 2005

CDC guidelines in 2005 recommended use of IGRAs for HCW screening with:

- no published data on serial testing
- no independent, peer-reviewed literature on IGRA reproducibility

BOX 2. Interpretations of tuberculin skin test (TST) and QuantiFERON®-TB test (QFT) results according to the purpose of testing for *Mycobacterium tuberculosis* infection in a health-care setting

Purpose of testing	TST	QFT
1. Baseline	1. ≥ 10 mm is considered a positive result (either first- or second-step)	1. Positive (only one-step)
2. Serial testing without known exposure	2. Increase of ≥ 10 mm is considered a positive result (TST conversion)	2. Change from negative to positive (QFT conversion)
3. Known exposure (close contact)	3. ≥ 5 mm is considered a positive result in persons who have a baseline TST result of 0 mm; an increase of ≥ 10 mm is considered a positive result in persons with a negative baseline TST result or previous follow-up screening TST result of ≥ 0 mm	3. Change to positive

Simplistic neg to pos change was defined as conversion (since there were no data)

IGRA Reproducibility in Low-Risk HCWs



Largest study of >2000 HCWs (CDC Task Order 18 study Dorman et al AJRCCM 2014):

TST	= 0.9 %
QFT	= 6.1%
T-SPOT	= 8.3% conversion rates

Coversions 2% to 15%
Reversions 20% to 40%

Largest report of 9153 HCWs (Slater et al AJRCCM 2014):

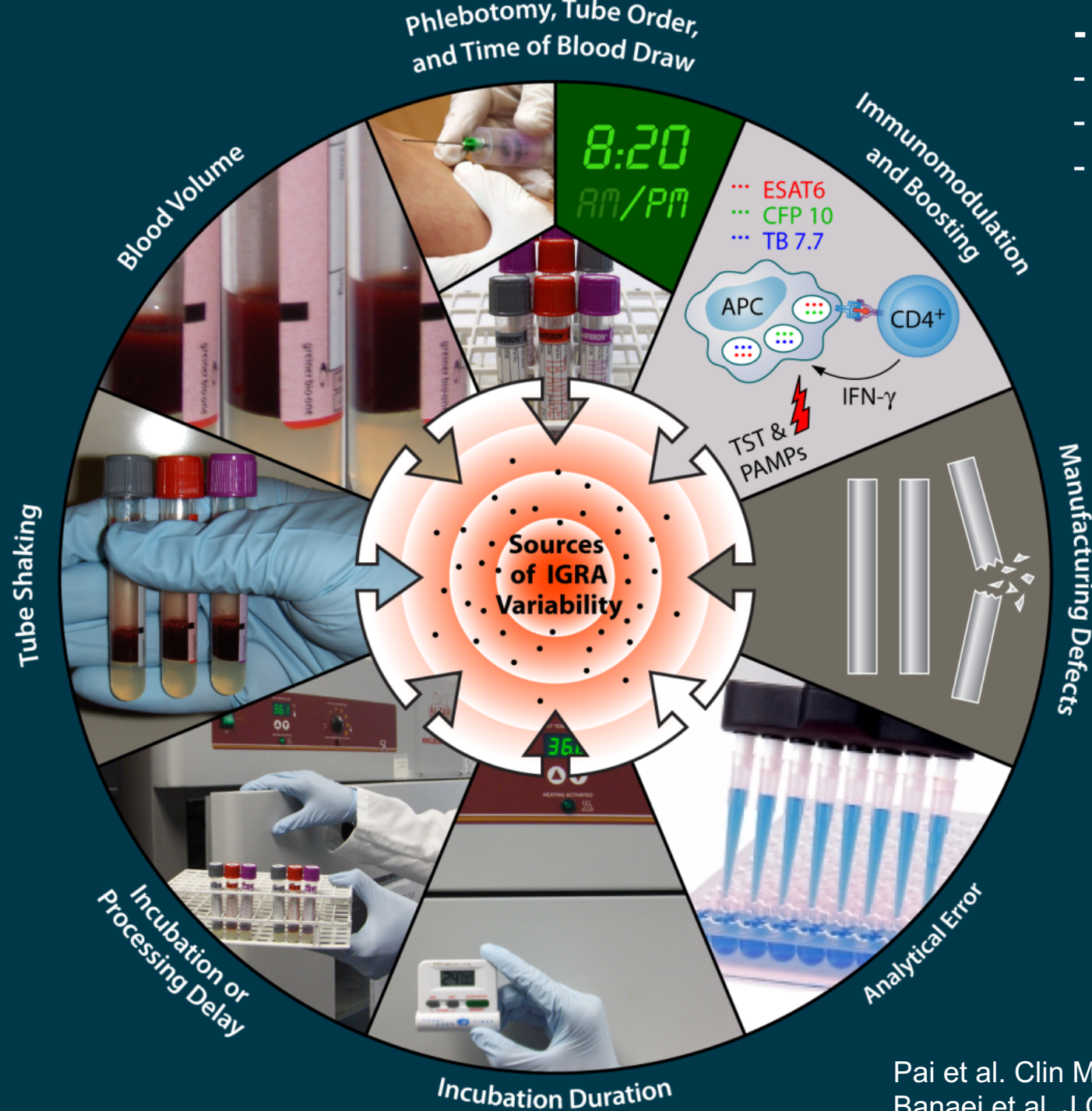
TST	= 0.4% Historical rate
QFT	= 4.4% conversion rates

Canadian study in HCWs (Zwerling et al. PLoS ONE 2013):

TST	= 0%
QFT	= 5.3% conversion rates

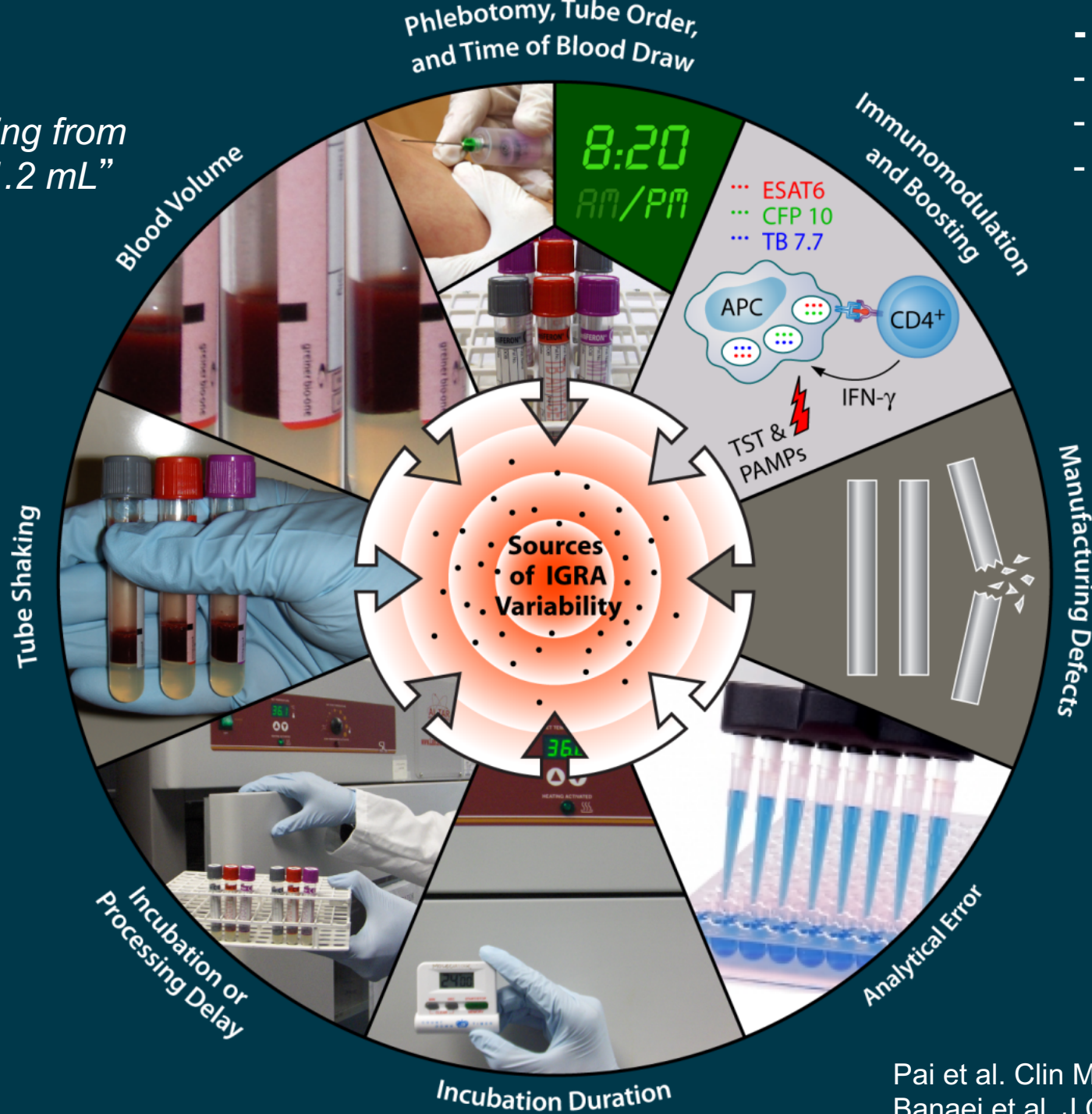
Sources of IGRA Variability

- Pre-analytical
- Analytical
- Manufacturing
- Immunological

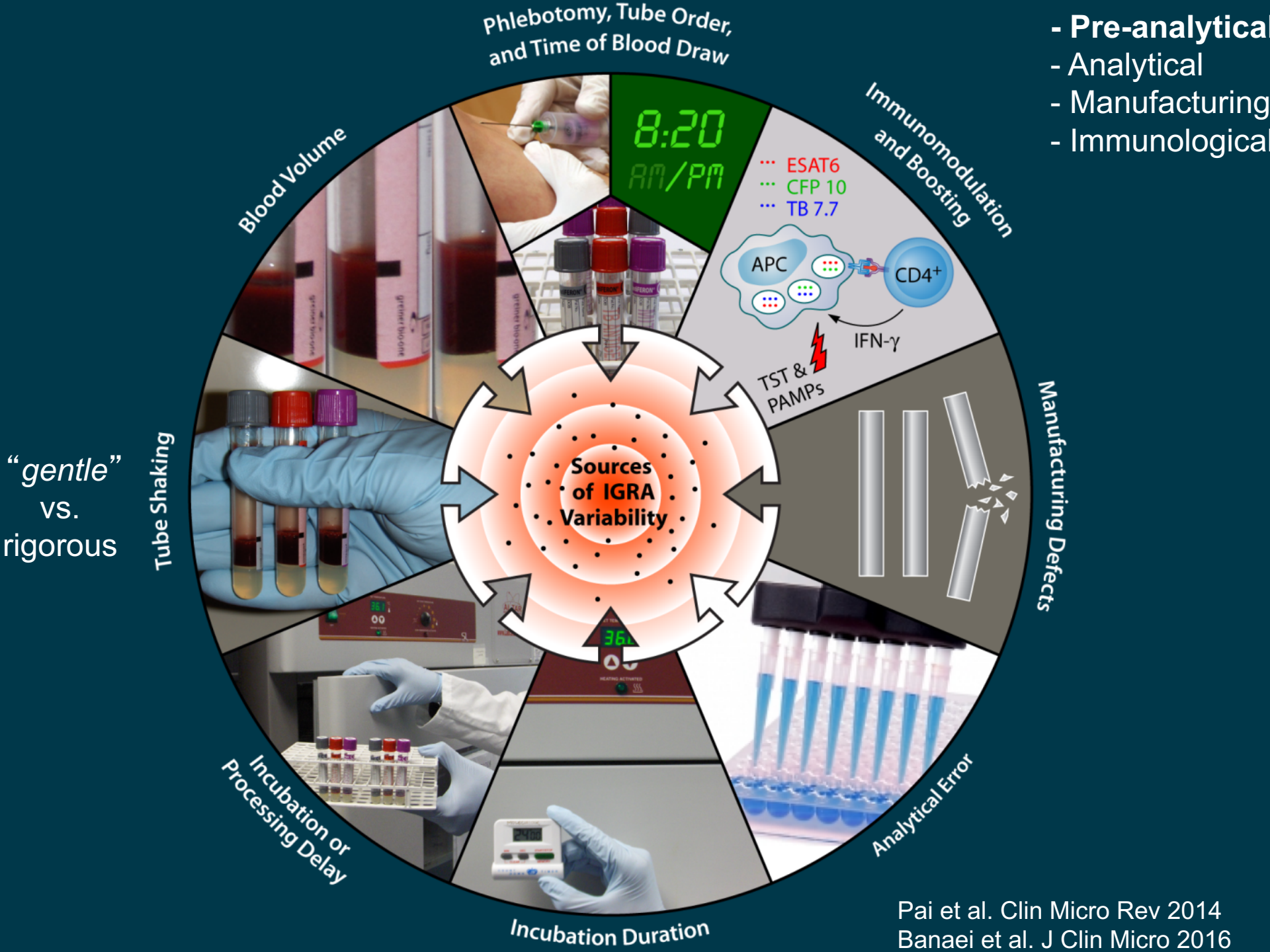


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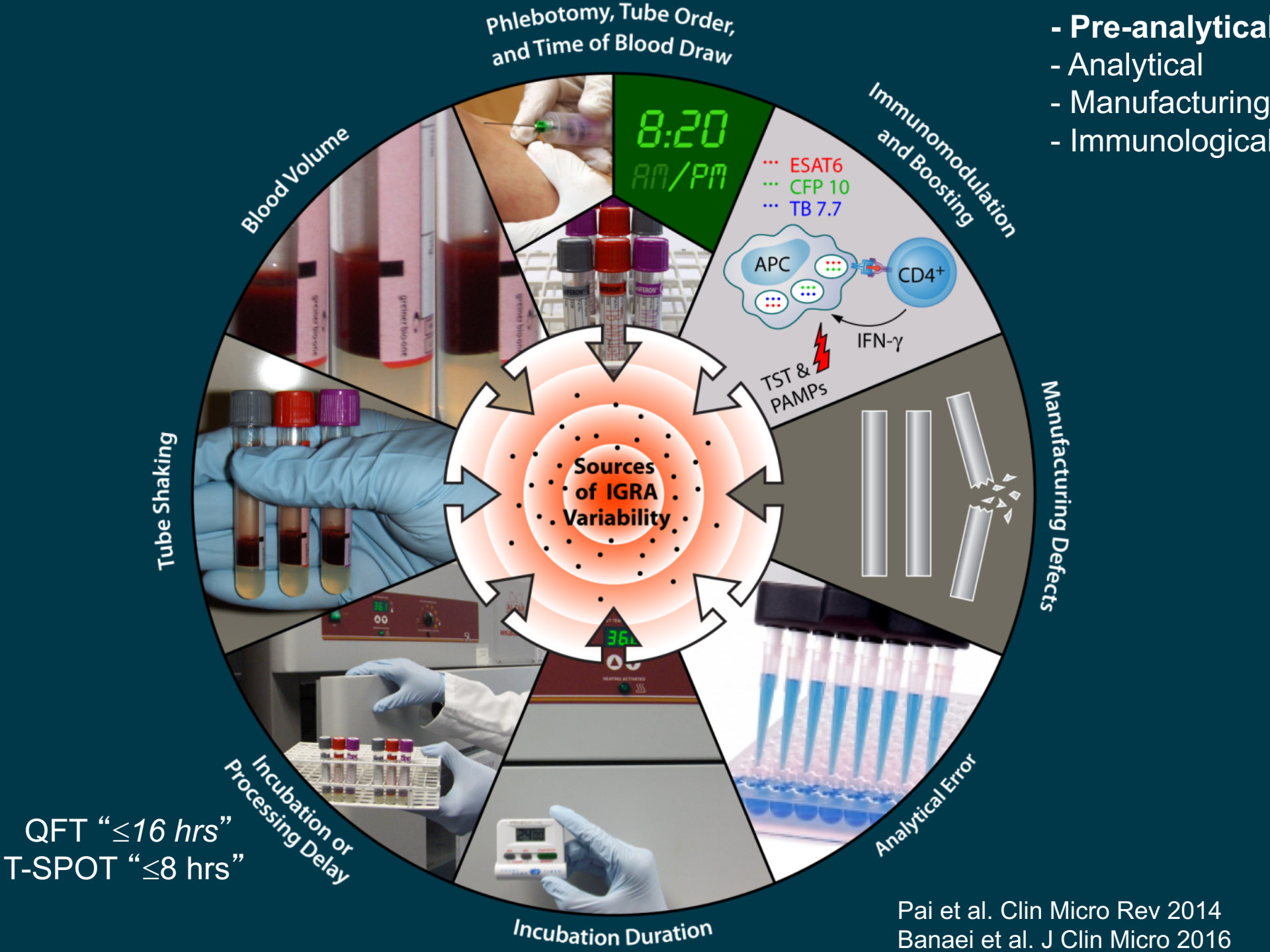
“ranging from
0.8-1.2 mL”

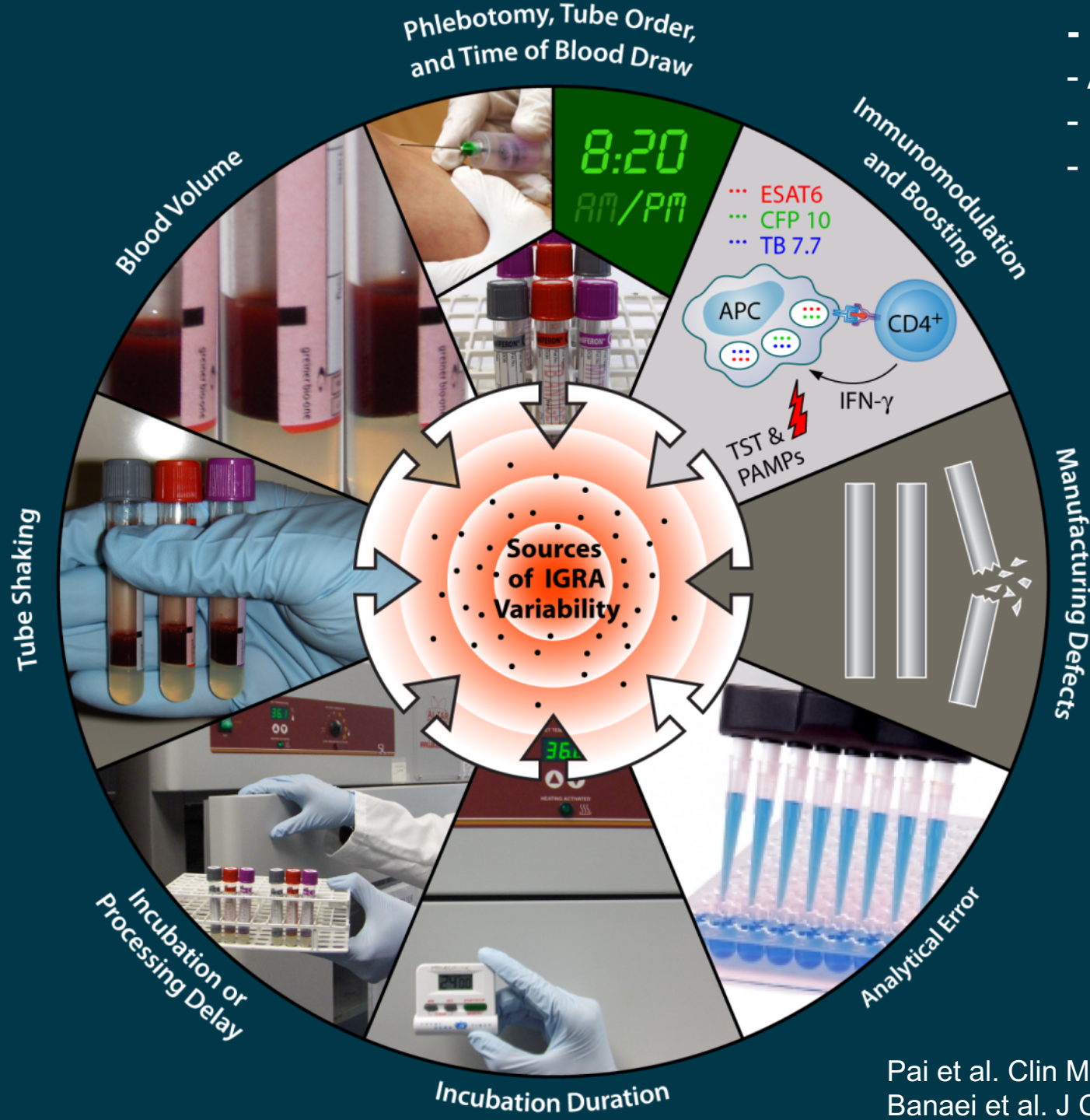


- Pre-analytical
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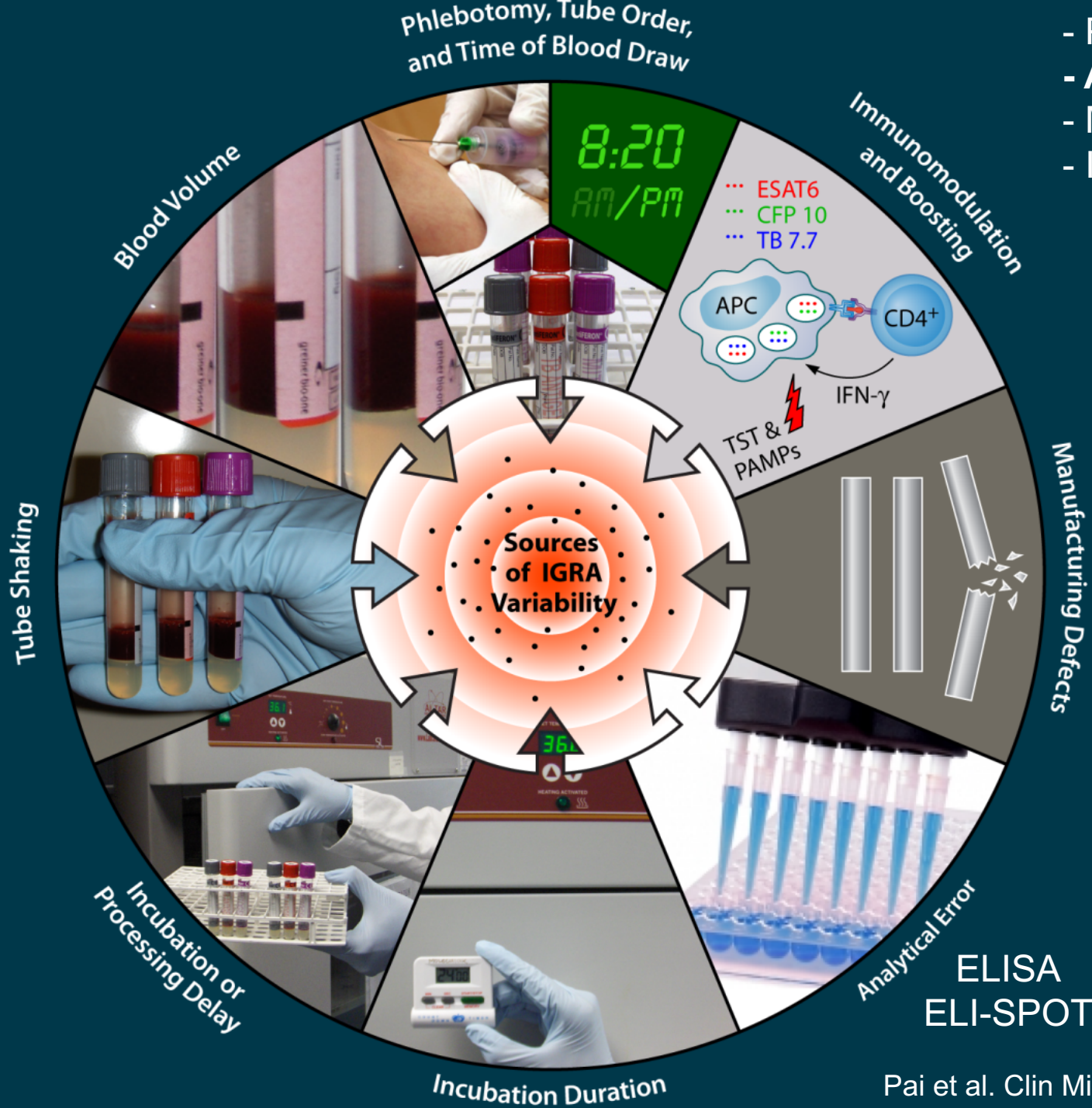


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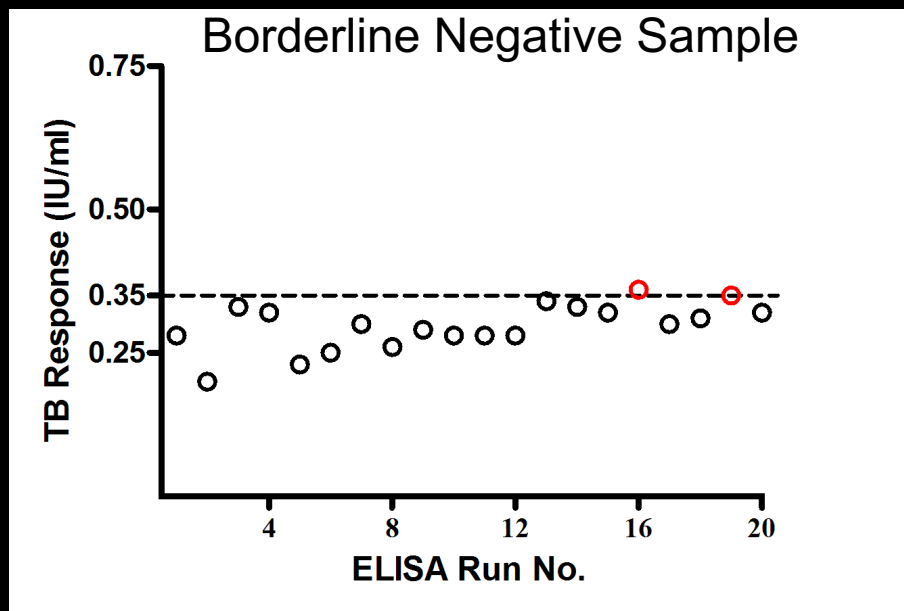


- Pre-analytical
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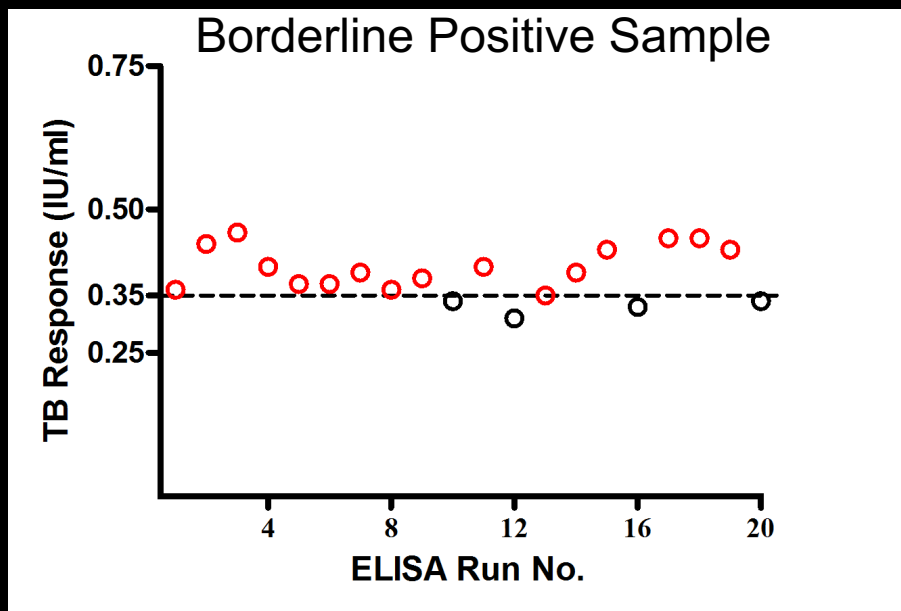


- Pre-analytical
- **Analytical**
- Manufacturing
- Immunological

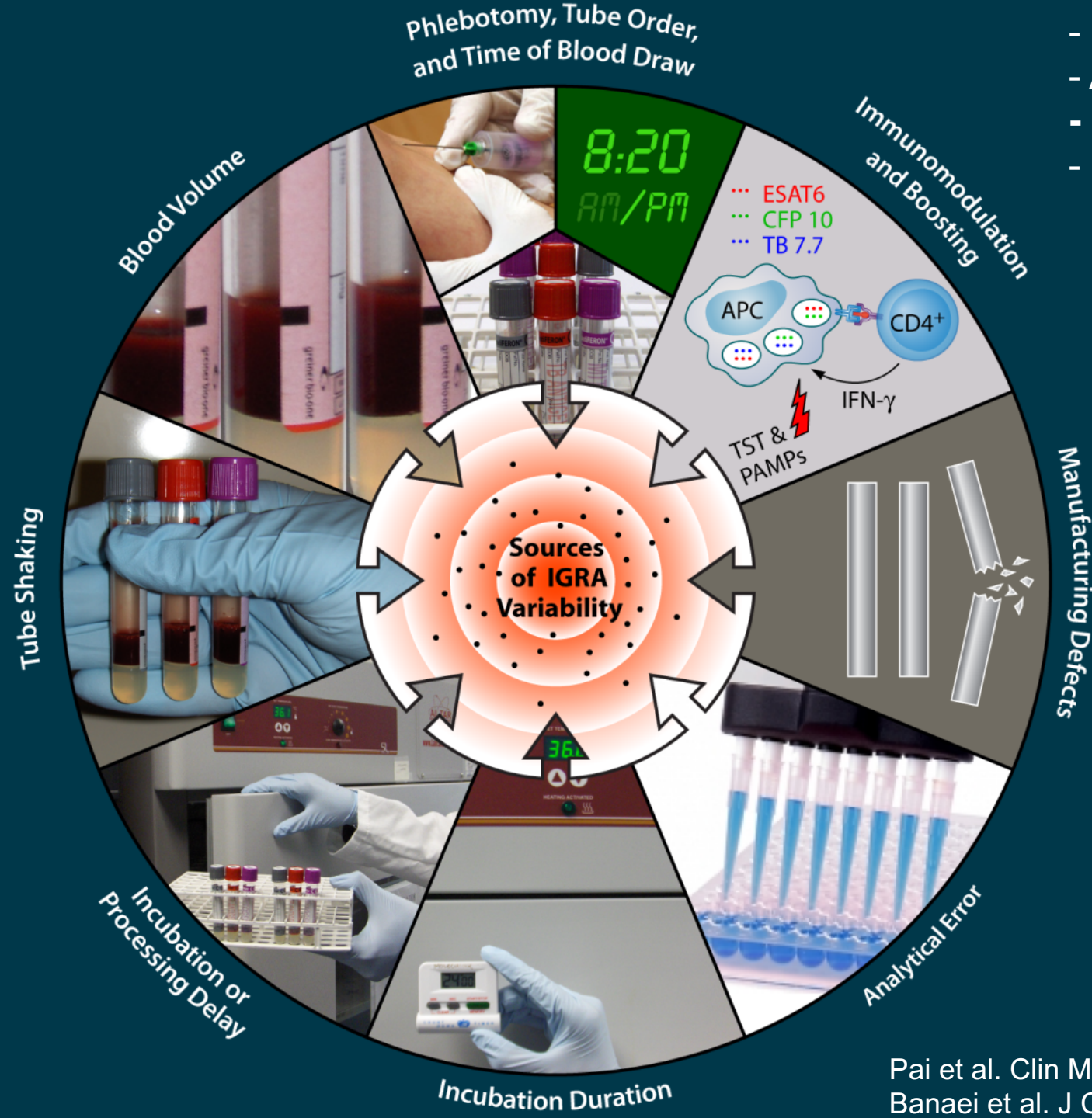
Analytical Imprecision of QFT-GIT Assay: Between-Run Variability (n=20 ELISA runs)



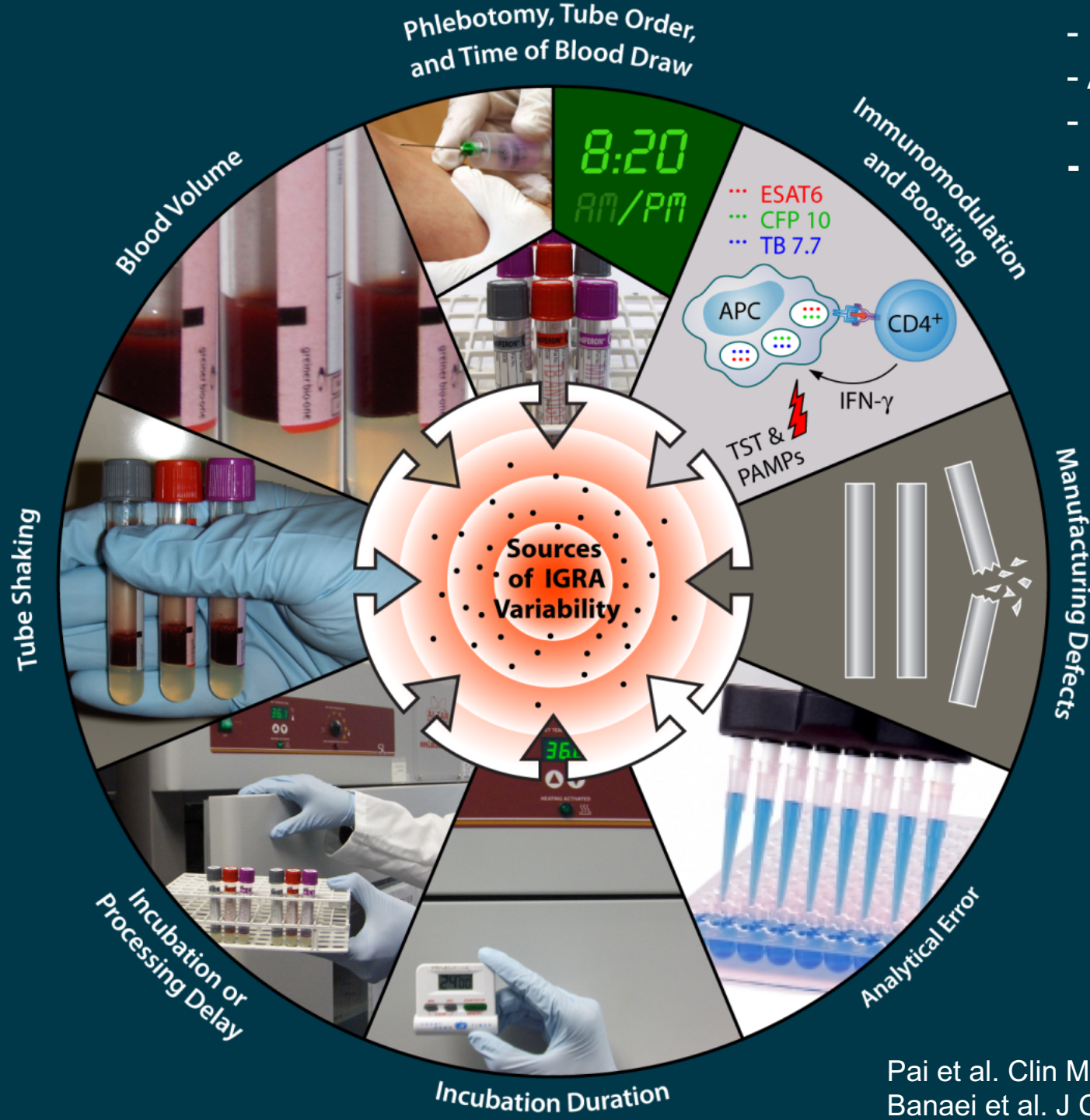
CV 14%
Conversion 10% (2/20)



CV 11%
Reversion 20% (4/20)



- Pre-analytical
- Analytical
- **Manufacturing**
- Immunological

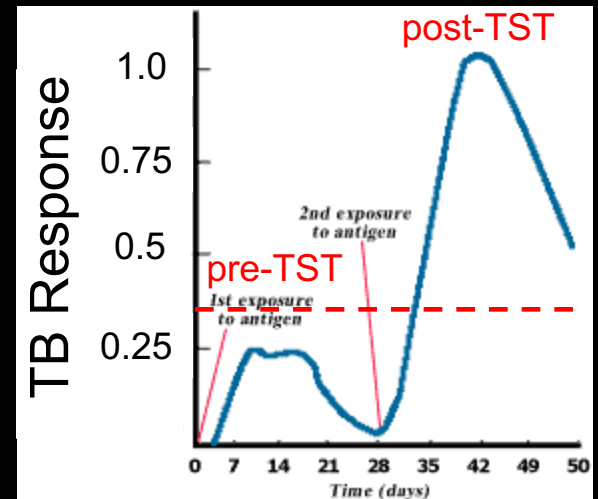
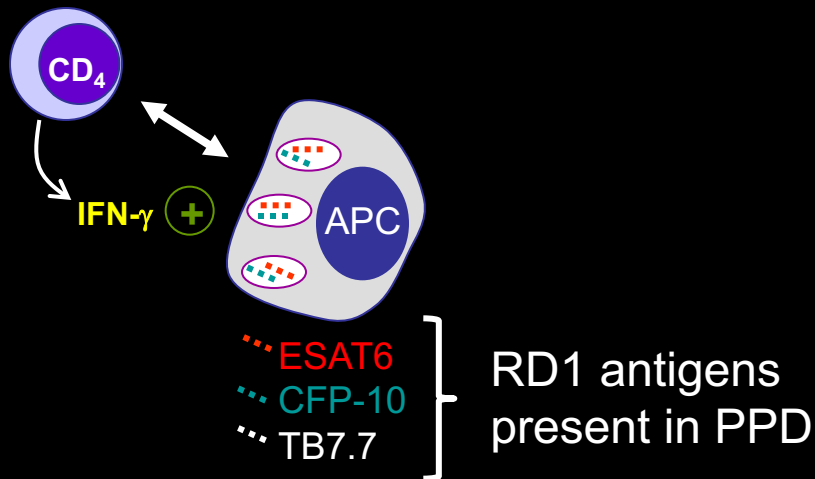


- Pre-analytical
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Amnestic Response to PPD

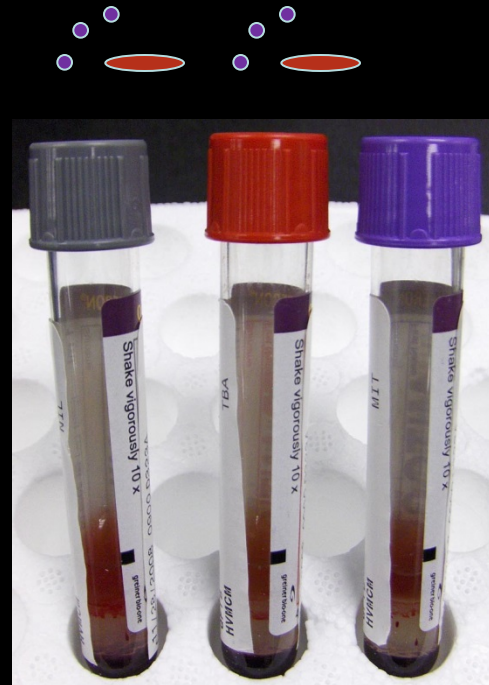
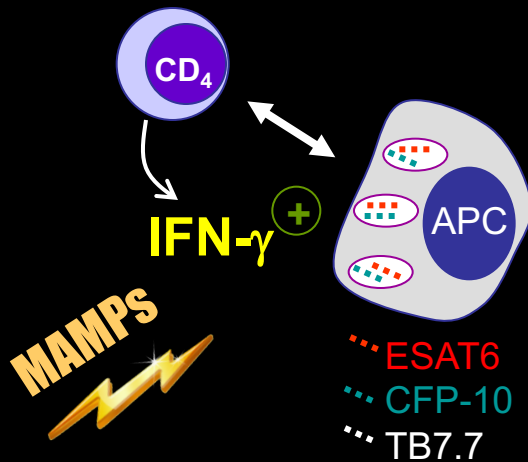
IGRA Boosting by PPD

- PPD contains RD1 antigens
- In TST+ subjects
- Observed >3 days post TST



van Zyl-Smit et al PLoS ONE 2009
Ritz et al Ritz Int J Tuberc Lung Dis 2011
Sanzullo et al Tuberculosis 2011

Effect of Microbes on IGRA Response

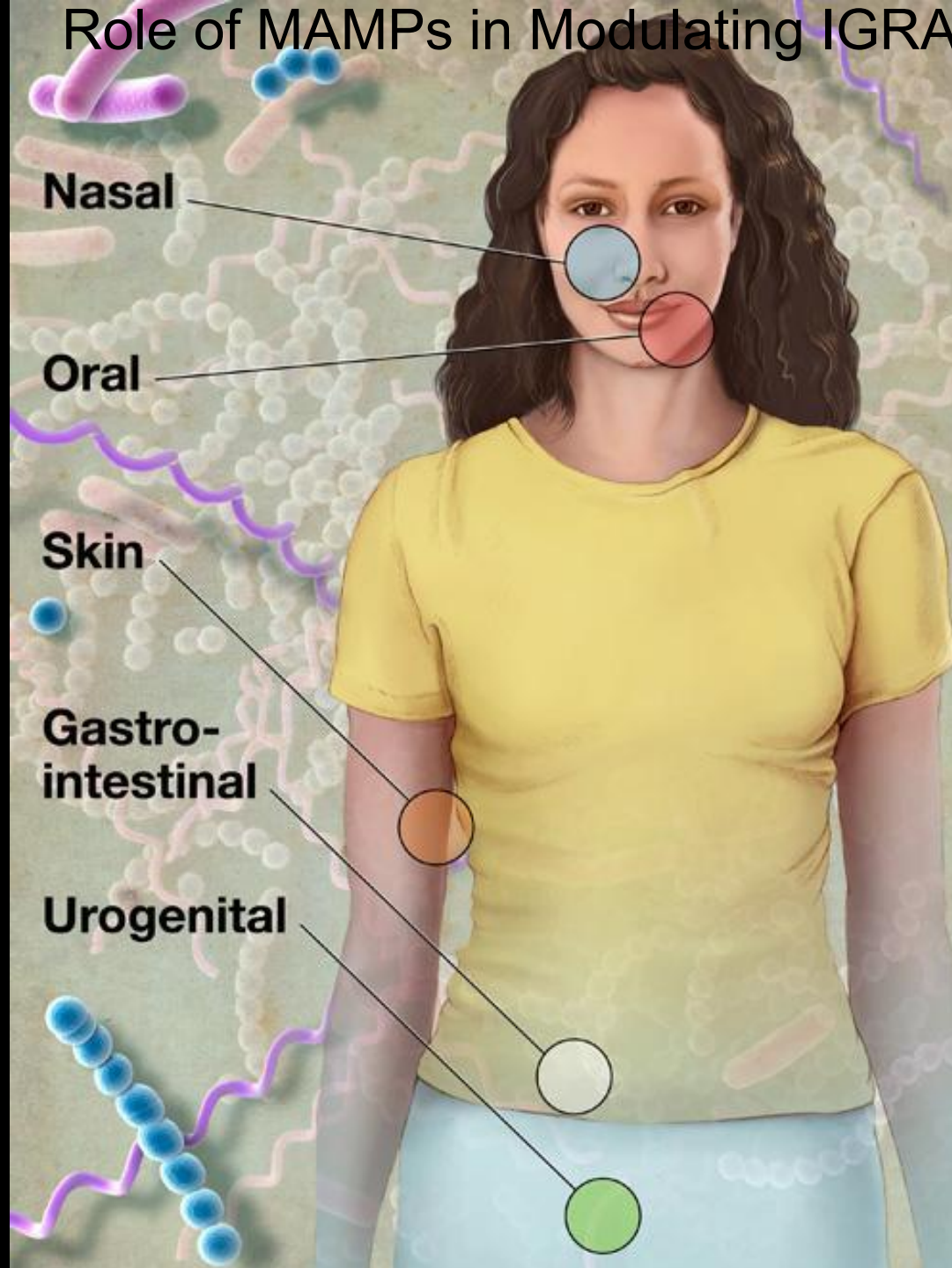


QFT

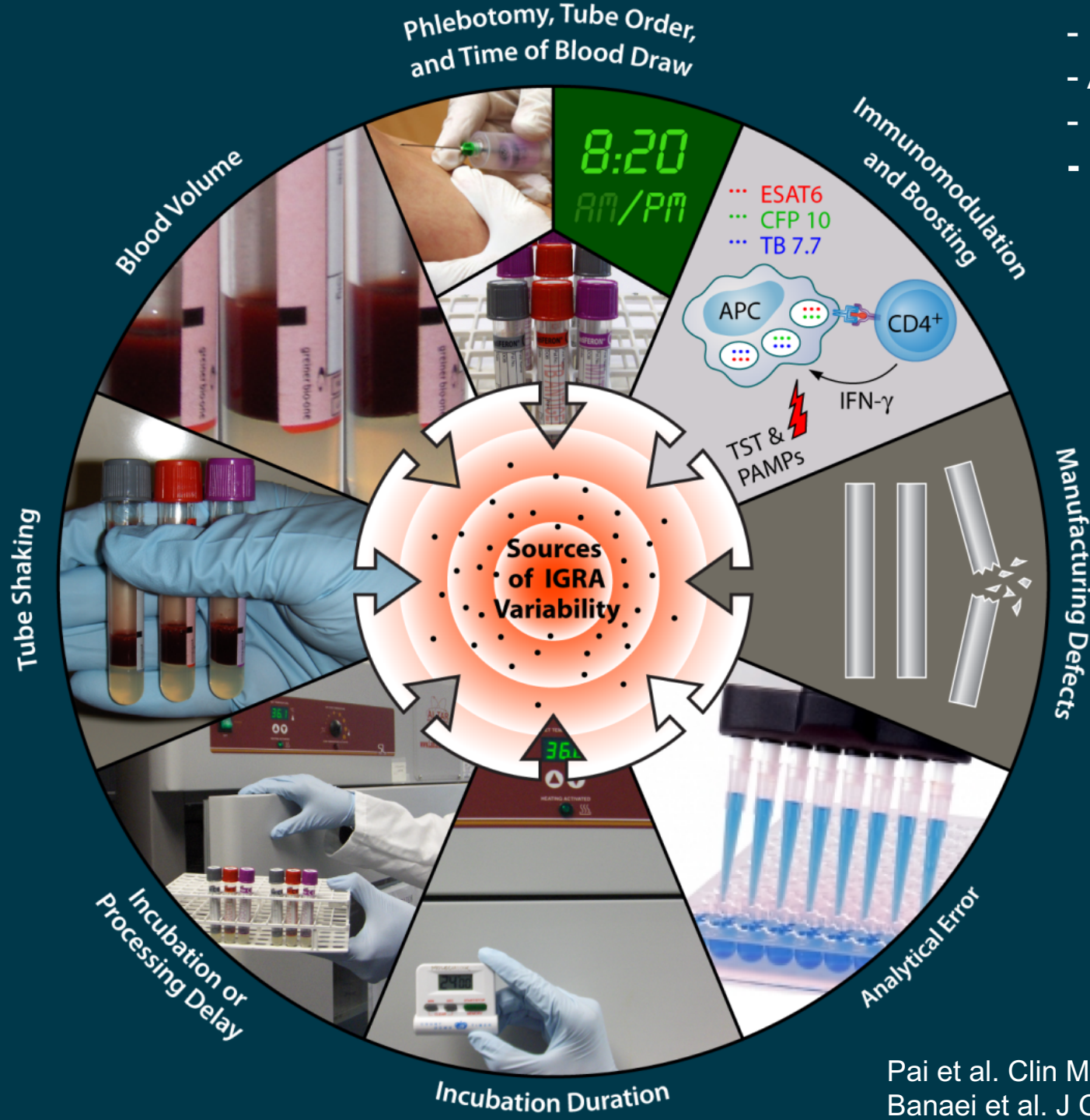


T-SPOT.TB

Role of MAMPs in Modulating IGRA

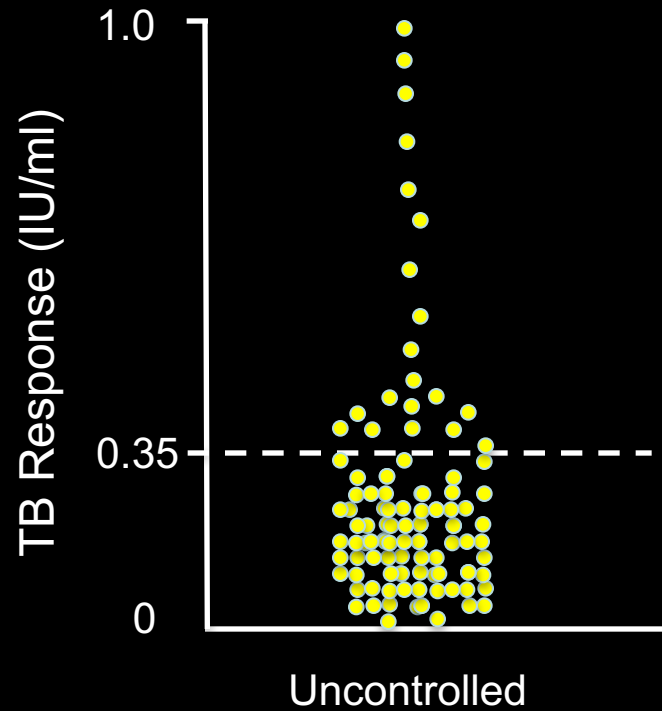


Clarke et al Nat Med 2010
Ichinohe et al PNAS 2011

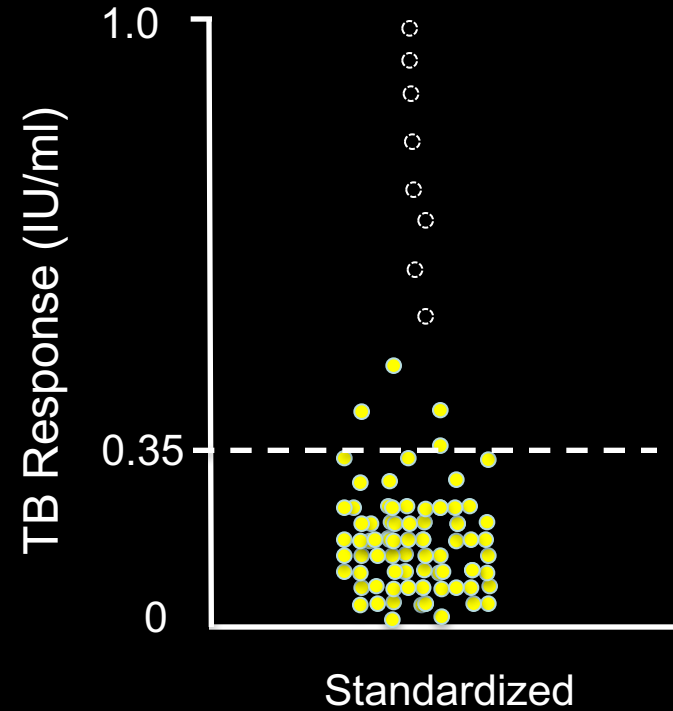
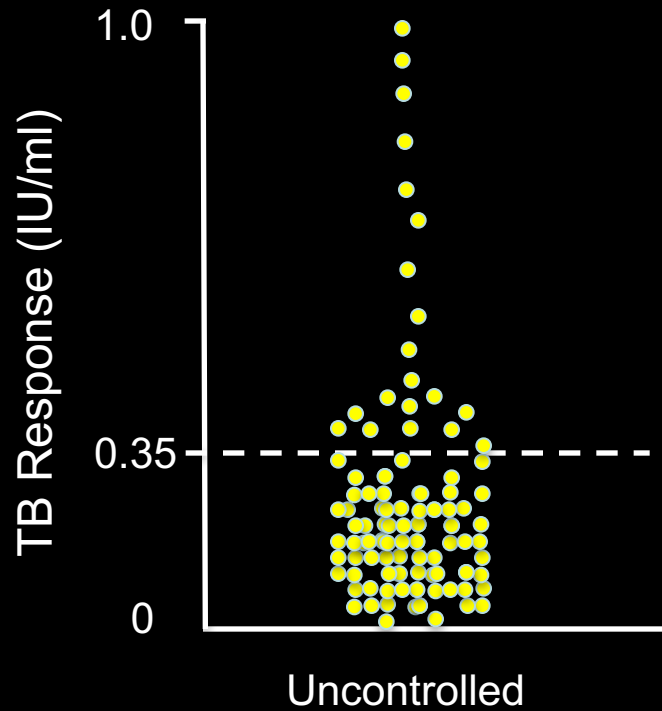


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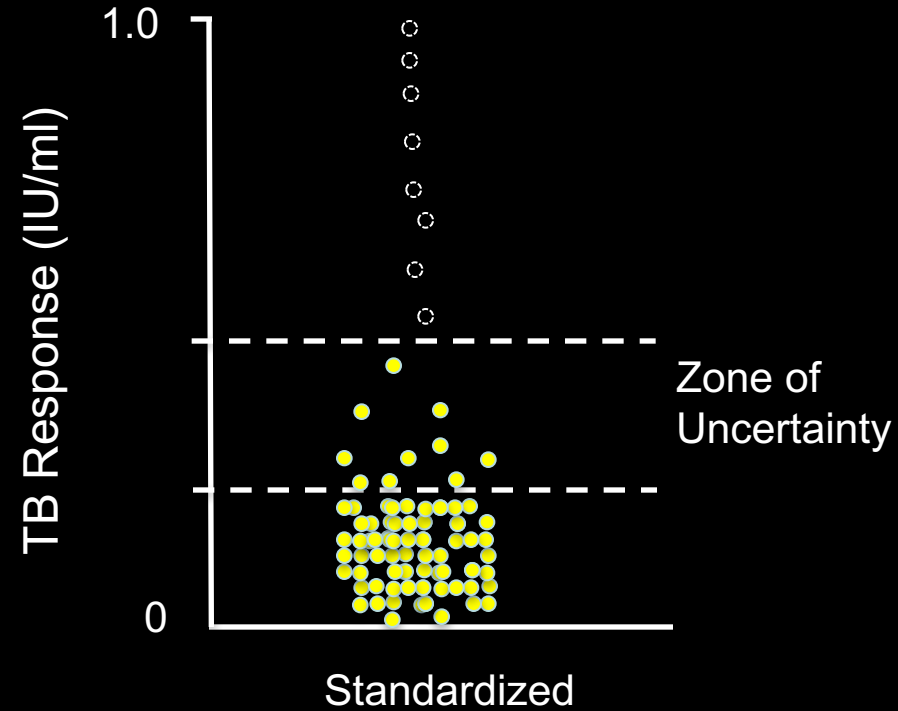
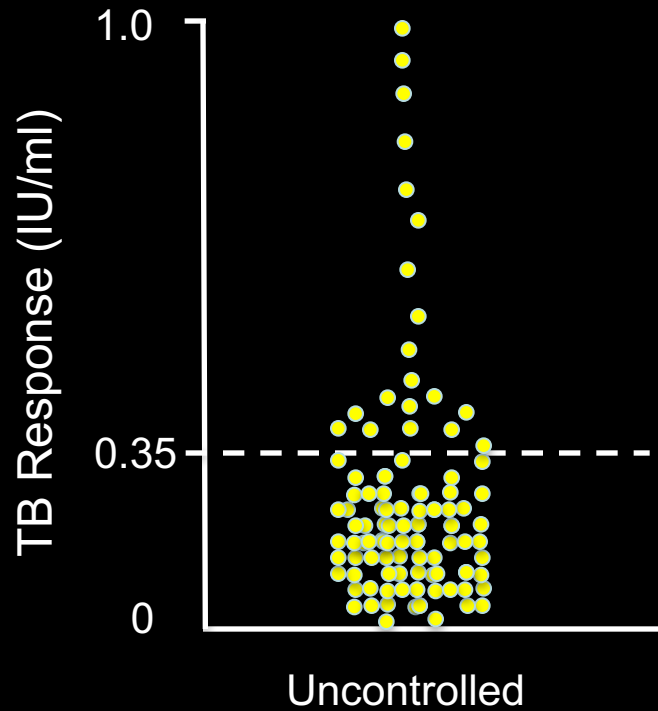
1. Can we eliminate predictable sources of variability?



1. Can we eliminate predictable sources of variability?



1. Can we eliminate predictable sources of variability?
2. Can IGRA interpretation address the net effect of random sources of variability/error?



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Press Release

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QIAGEN's QuantiFERON®-TB Gold Plus gains U.S. FDA approval

Fourth generation Latent TB blood test combines breakthrough CD4/CD8 design for comprehensive immune response detection with the most flexible blood collection workflow

Germantown, Maryland, and Hilden, Germany, June 8, 2017 – QIAGEN N.V. (NASDAQ: QGEN; Frankfurt P Standard: QIA) today announced the U.S. regulatory approval of QuantiFERON®-TB Gold Plus (QFT®-Plus) the fourth generation of the market leading blood test for detecting latent tuberculosis (TB) infection.

QuantiFERON®-TB Gold Plus



TB Ag Tube 1 (TB1): ESAT-6 and CFP-10 peptides for CD4 T Cells
TB Ag Tube 2 (TB2): ESAT-6 and CFP-10 peptides for CD4 and CD8 T Cells

Interpretation of QFT-Plus Results

- Interpretation of QFT-Plus using manufacturer's interpretation

	QFT-Plus pos			QFT-Plus neg
TB1	+	+	-	-
TB2	+	-	+	-

Why Target CD8 T Cells in QFT-Plus?

- Evidence for role of CD8+ T cells in TB immunity
- IFN- γ positive Mtb-specific CD8+ T cells
 - More frequently detected in active TB vs. latent infection
 - Mycobacterial burden-dependent
 - Associated with recent exposure to TB
 - Detectable in active TB subjects with HIV co-infection and young children
 - Decline after anti-tuberculosis treatment

First evaluation of QuantiFERON-TB Gold Plus performance in contact screening

Lucia Barcellini¹, Emanuele Borroni¹, James Brown², Enrico Brunetti³, Daniela Campisi⁴, Paola F. Castellotti⁴, Luigi R. Codecasa⁴, Federica Cugnata⁵, Clelia Di Serio⁵, Maurizio Ferrarese⁴, Delia Goletti⁶, Marc Lipman², Paola M.V. Rancoita⁵, Giulia Russo¹, Marina Tadolini⁷, Elisa Vanino⁷ and Daniela M. Cirillo¹

Study Design

QFT-Plus vs. QFT-GIT

Prospective contact screening. Retested 10-12 wks if negative

Location: Milan, Italy

Contacts: 119 adults with newly positive TST ($\geq 5\text{mm}$)

Immunocompromised included (9%)

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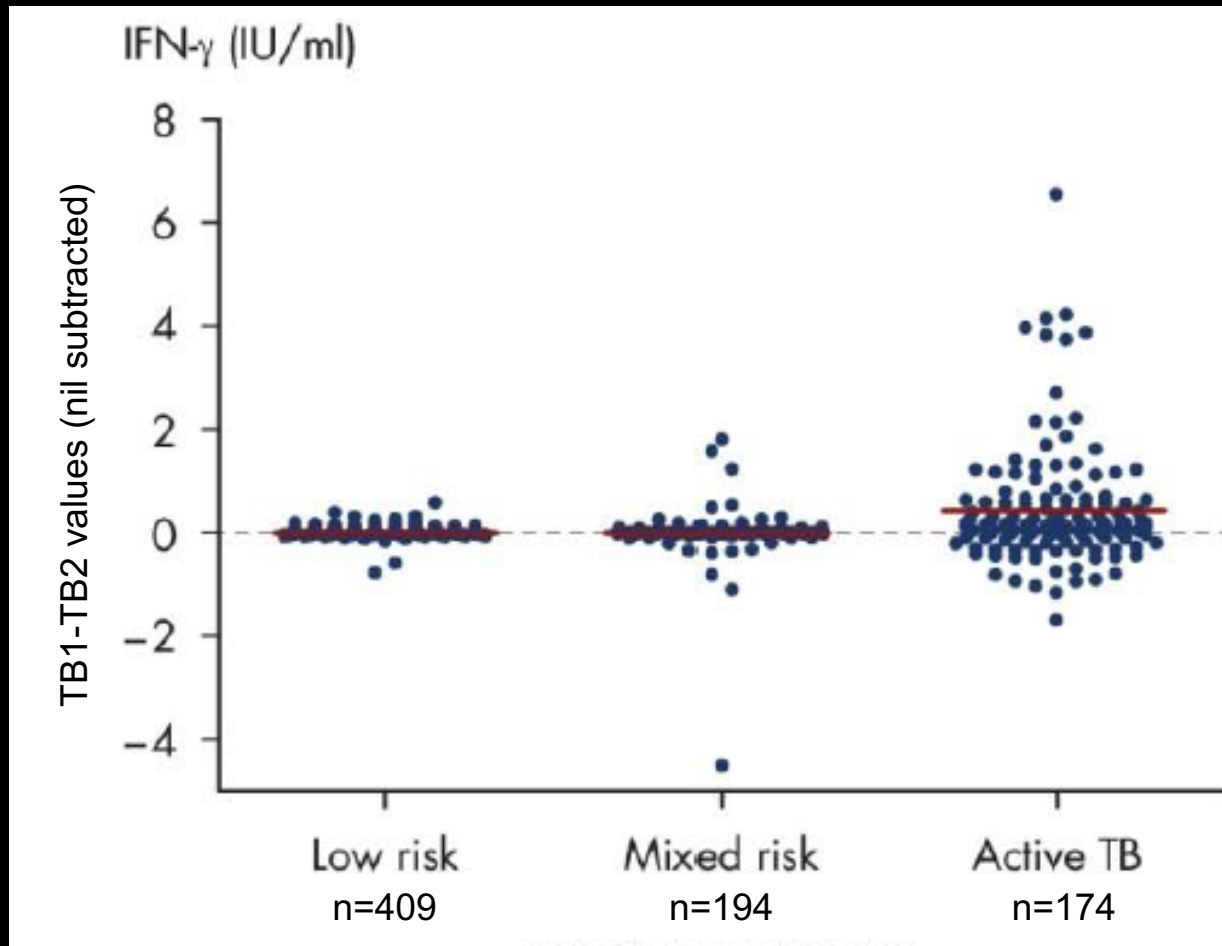
TABLE 2 Test results

QFT-GIT results	Subjects	QFT-Plus results		Positive results per tube		QTF-Plus IFN- γ concentrations IU·mL ⁻¹	
		Negative	Positive	TB1	TB2	TB1-nil	TB2-nil
Negative	63	51 [80.95]	12 [19.05]	10 [#]	1 [¶]	0.01 [-0.01-0.17]	0.04 [0-0.23]
Positive	56	0	56 [100]	56	56	10.60 [2.94-16.57]	11.00 [3.32-17.75]
Total	119	51 [42.86]	68 [57.14]	66	66	0.74 [0.01-9.65]	0.67 [0.04-8.94]

Data are presented as n, n (%) or median (interquartile range). [#]: two were positive to TB1 only; [¶]: two were positive to TB2 only. QFT-GIT: QuantiFERON-TB Gold in Tube; QFT-Plus: QuantiFERON-TB Plus; IFN: interferon.

- QFT-Plus pos: 57.1% (68/119) vs. QFT-GIT pos: 47.1% (56/119)
- 12 discordant: 11 TST ≥ 10 mm; 2 converted after retest
- If exposure >12 h/days, odds for positive 6x \uparrow for QFT and 14x \uparrow for QFT-Plus
- TB2-TB1 >0.6 IU/mL associated with exposure (sleeping in same room OR 4.34)

QFT-Plus TB2 is More Sensitive than TB1 for Active TB





First independent evaluation of QuantiFERON-TB Plus performance



@ERSpublications

QuantiFERON-TB Plus improves sensitivity for active TB and maintains high specificity among unvaccinated controls <http://ow.ly/XjYYPK>

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Study Design

Single arm (partial comparison vs. QFT-GIT)

Prospective

Location: 4 sites in Italy

Cases: 119 consecutive adult patients

NAAT or culture positive TB

<15days of anti-TB therapy

HIV+/- (63% HIV+)

Controls: 109 healthy students



CrossMark



@ERSpublications

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First independent evaluation of QuantIFERON-TB Plus performance

TABLE 1 QuantIFERON-TB Plus (QFT-Plus) performance characteristics in different study groups

	Frequency	QFT-Plus result			Positive results in each tube		IFN- γ concentration [†] IU·mL ⁻¹		TB2–TB1 IU·mL ⁻¹
		Indeterminate	Negative [#]	Positive [#]	TB1	TB2	TB1	TB2	
Low-risk controls	106	0	103 [97.17]	3 [2.83]	2	1	0.1 [0.09–0.13]	0.11 [0.09–0.13]	0 [–0.01–0.01]
Active TB	119	3	14 [12.07]	102 [87.93]	96	101	2.09 [0.83–6.52]	2.88 [1–7.89]	0.14 [–0.13–0.79]
Sex									
Male	72	1	7 [9.86]	64 [90.14]	59	64	2.08 [0.86–6.38]	2.91 [1.17–7.62]	0.23 [–0.14–0.88]
Female	47	2	7 [15.56]	38 [84.44]	37	37	2.09 [0.71–7.03]	2.85 [0.88–7.80]	0.11 [–0.11–0.50]
Smear									
Negative	65	1	12 [18.75]	52 [81.25]	51	52	2.12 [0.89–9.51]	2.69 [1.01–9.66]	0.05 [–0.17–0.55]
Positive	54	2	2 [3.85]	50 [96.15]	45	49	2 [0.67–6.04]	3.26 [0.92–6.31]	0.29 [0–1.16]
Localisation									
PTB	79	3	9 [11.84]	67 [88.16]	62	66	1.93 [0.57–6.04]	2.82 [0.75–6.22]	0.26 [–0.12–0.80]
EPTB	40	0	5 [12.5]	35 [87.5]	34	35	2.29 [1.23–10]	2.95 [1.15–10]	0.06 [–0.17–0.46]
BCG									
Negative	6	0	2 [33.33]	4 [66.67]	4	4	1.15 [0.33–1.86]	1.47 [0.4–2.75]	0.07 [0.01–0.44]
Positive	54	0	4 [7.41]	50 [92.59]	44	50	2.01 [0.9–6.57]	2.79 [1.02–8.2]	0.14 [–0.20–0.65]

QFT-Plus Sensitivity: 88% (102/116)

TB1+/TB2+: 95

TB1+/TB2–: 1

TB1–/TB2+: 6

Higher TB2 vs. TB1

2.88 IU/·mL vs 2.09 p=0.0002



First independent evaluation of QuantiFERON-TB Plus performance



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QuantiFERON-TB Plus improves sensitivity for active TB and maintains high specificity among unvaccinated controls <http://ow.ly/XjYYPK>

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Head-To-Head Comparison

QFT-Plus vs. QFT-GIT 73 TB cases

QFT+/QFT-Plus+: 68

QFT+/QFT-Plus-: 1 (QFT-Plus IDT)

QFT-/QFT-Plus+: 4

TB1+/TB1: 1

TB1-/TB2+: 3

Sensitivity:

QFT 95% (69/73) vs. QFT-Plus 100% (72/72) P = 0.12

Original article

Equal sensitivity of the new generation QuantiFERON-TB Gold *plus* in direct comparison with the previous test version QuantiFERON-TB Gold IT

H. Hoffmann^{1,2},  , K. Avsar³, R. Göres³, S.-C. Mavi³, S. Hofmann-Thiel^{1,2}

Study Design

Head-to-head QFT-Plus vs. QFT-GIT

Prospective

Location: Pulmonary hospital in Germany

Patients:

Active TB, bacteriologically confirmed	24
Active TB without bacteriological confirmation	33
No TB, but post-specific changes in chest X-ray	10
No TB, patient with other diagnosis	19
No TB, HCW Healthy, low risk	77

} 98% immunocompetent

Original article

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Table 1
Results of the two test generations QFTG-IT and QFTGplus for different study groups (absolute numbers, %)

Diagnosis	Positive ^a		Negative ^b		Invalid		Total
	QFTG-IT	QFTGplus	QFTG IT	QFTGplus	QFTG IT	QFTGplus	
Active TB, bacteriologically confirmed	23 95.8%	23 95.8%	1 4.2%	1 4.2%	0 0.0%	0 0.0%	24 14.7%
Active TB without bacteriological confirmation	28 84.8%	28 84.8%	5 15.2%	5 15.2%	0 0.0%	0 0.0%	33 20.2%
No TB, but post-specific changes in chest X-ray	5 50.0%	6 60.0%	5 50.0%	4 40.0%	0 0.0%	0 0.0%	10 6.1%
No TB, patient with other diagnosis	3 15.8%	3 15.8%	14 73.7%	16 84.2%	2 10.5%	0 0.0%	19 11.7%
No TB, HCW	8 10.4%	10 13.0%	69 89.6%	67 87.0%	0 0.0%	0 0.0%	77 47.2%
Total	67 41.1%	70 42.9%	94 57.7%	93 57.1%	2 1.2%	0 0.0%	163 100.0%

Original article

Equal sensitivity of the new generation QuantiFERON-TB Gold *plus* in direct comparison with the previous test version QuantiFERON-TB Gold IT

H. Hoffmann^{1,2}, K. Avsar³, R. Göres³, S.-C. Mavi³, S. Hofmann-Thiel^{1,2}

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Diagnosis	Positive ^a		Negative ^b		QFTG plus		
	QFTG-IT	QFTGplus	QFTG IT	QFTGplus	QFTG-IT	TB1	TB2
Active TB, bacteriologically confirmed	23 95.8%	23 95.8%	1 4.2%	1 4.2%	0.07 1.23	0.16 0.18	0.62 0.20
Active TB without bacteriological confirmation	28 84.8%	28 84.8%	5 15.2%	5 15.2%	0.34 0.62	0.39 0.06	0.53 0.06
No TB, but post-specific changes in chest X-ray	5 50.0%	6 60.0%	5 50.0%	4 40.0%	0 0.0%	0 0.0%	10 6.1%
No TB, patient with other diagnosis	3 15.8%	3 15.8%	14 73.7%	16 84.2%	2 10.5%	0 0.0%	19 11.7%
No TB, HCW	8 10.4%	10 13.0%	69 89.6%	67 87.0%	0 0.0%	0 0.0%	77 47.2%
Total	67 41.1%	70 42.9%	94 57.7%	93 57.1%	2 1.2%	0 0.0%	163 100.0%

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H. Hoffmann^{1,2},  , K. Avsar³, R. Göres³, S.-C. Mavi³, S. Hofmann-Thiel^{1,2}

Average concentrations of IFN-g were higher in the QFTG-IT than in the QFT-plus test tubes

QFTG-IT	4.67 ± 3.25 U/mL
TB1	3.1 ± 3.2 U/mL; p 0.007
TB2	3.7 ± 3.4 mL; p >0.09

The sensitivity of the QuantiFERON®-TB Gold Plus assay in Zambian adults with active tuberculosis

L. Telisinghe,* M. Amofa-Sekyi,[†] K. Maluzi,[†] D. Kaluba-Milimo,[†] M. Cheeba-Lengwe,[†] K. Chiwele,[†]
B. Kosloff,^{†‡} S. Floyd,[§] S-L. Bailey,^{†‡} H. Ayles^{†‡}

Study Design

Single arm

Prospective

Location: Zambia

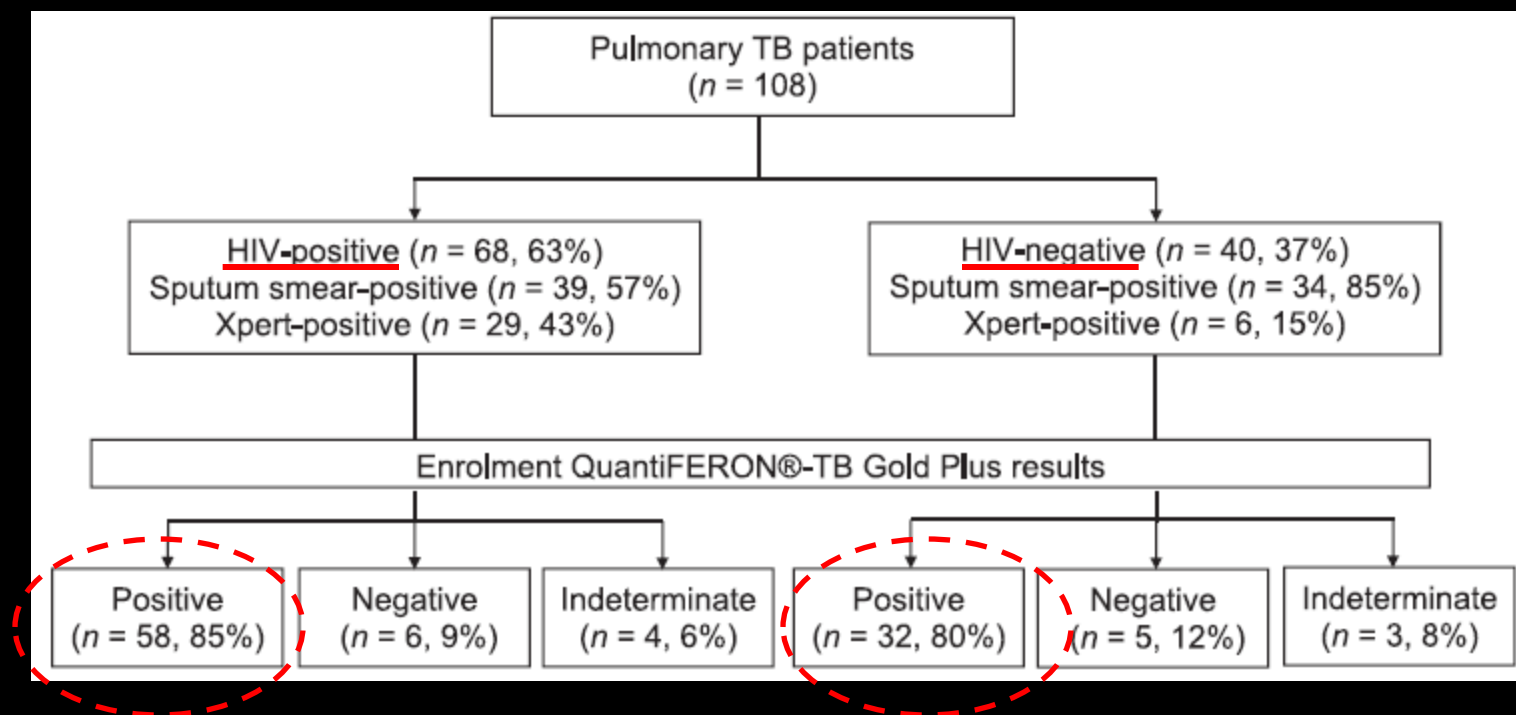
Patients: Smear+ or Xpert+

HIV+/-

<3 days of anti-TB therapy

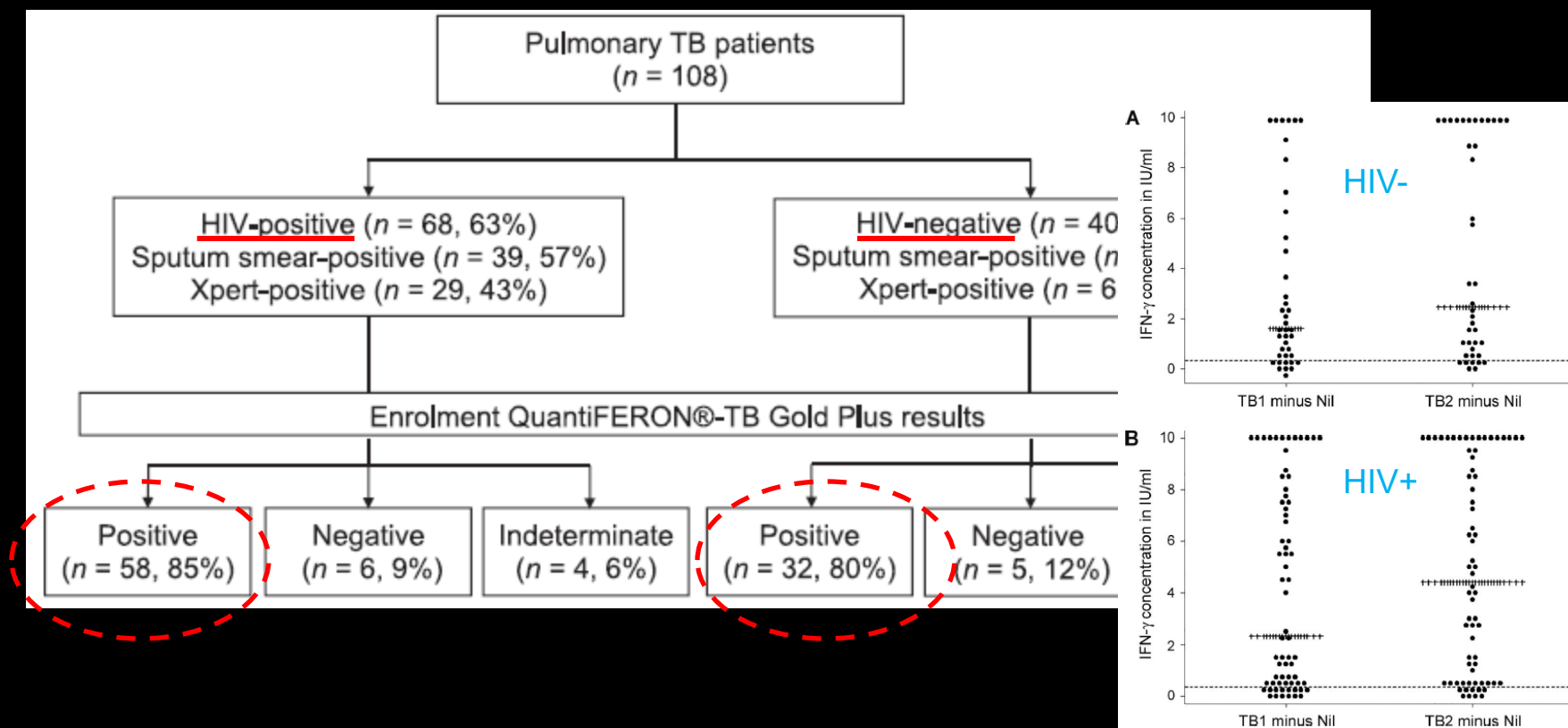
The sensitivity of the QuantiFERON®-TB Gold Plus assay in Zambian adults with active tuberculosis

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Table 3 Distribution of QuantiFERON®-TB Gold Plus results by patient characteristics and univariate logistic regression analysis of factors associated with positive QFT-Plus results in pulmonary TB patients (*n* = 108)

Characteristic	Distribution of QFT-Plus results*			<i>P</i> value [†]	Characteristics associated with QFT-Plus results [‡]	
	Indeterminate <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)		Univariate analysis ^{§¶} OR (95% CI)	<i>P</i> value [#]
HIV status						
Positive	4 (5.9)	6 (8.8)	58 (85.3)	0.59	1	0.31
Negative	3 (7.5)	5 (12.5)	32 (80.0)		0.57 (0.20–1.66)	
CD4 cell count category (<i>n</i> = 52/68)^{††}						
≥100 cells/μl	2 (4.6)	3 (6.8)	39 (88.6)	0.02	1	0.05
<100 cells/μl	2 (25.0)	2 (25.0)	4 (50.0)		0.15 (0.02–0.96)	
On antiretroviral therapy (<i>n</i> = 64/68)^{††}						
No	1 (2.8)	4 (11.1)	31 (86.1)	1.00	1	1.00
Yes	2 (7.1)	2 (7.1)	24 (85.7)		1.00 (0.23–4.26)	
Body mass index, kg/m² (<i>n</i> = 104)						
≥18.5	2 (4.1)	2 (4.1)	45 (91.8)	0.04	1	0.02
<18.5	4 (7.3)	9 (16.4)	42 (76.4)		0.27 (0.08–0.91)	

Table 4 Comparing the performance of QGIT assay, the TST and QFT-Plus among adult (age ≥ 18 years) pulmonary TB patients

Study features	Raby et al. ¹¹		<u>QFT-Plus</u> (n = 108)
	<u>QGIT</u> (n = 112)	TST (n = 92)	
Case definition	Smear +ve; within 1 month of treatment		Smear or Xpert +ve within 2 days of treatment
TB-HIV co-infection, %	61		63
Median CD4 cell count among PLHIV, cells/ μ l	212		246
	% (95%CI)	% (95%CI)	% (95%CI)
Overall			
<u>Sensitivity</u>	<u>74 (66–82)</u>	67 (58–77)	<u>83 (75–90)</u>
Quantiferon-negative	12 (6–19)	NA	10 (5–17)
Quantiferon-indeterminate	14 (8–22)	NA	6 (3–13)
Sensitivity by			
<u>HIV-positive</u>	<u>63 (50–74)</u>	55 (40–70)	<u>85 (75–93)</u>
HIV-negative	<u>84 (71–96)</u>	81 (62–92)	80 (64–91)
CD4 cell count, cells/ μ l			
<u><100</u>	<u>23 (5–54)</u>	—	<u>50 (16–84)</u>
100–199	70 (46–88)	—	91 (59–99)
200–349	74 (52–90)	—	85 (62–97)
≥ 350	88 (75–95)	—	92 (64–99)

Summary of QFT-Plus Studies

- No evidence for increased sensitivity of QFT-Plus over QFT-GIT in active TB cases and recently exposed contacts
- No evidence for higher TB2 vs. TB1 response in active TB and recently exposed in HIV-

IGRA Non-Reproducibility in Low-Risk HCWs



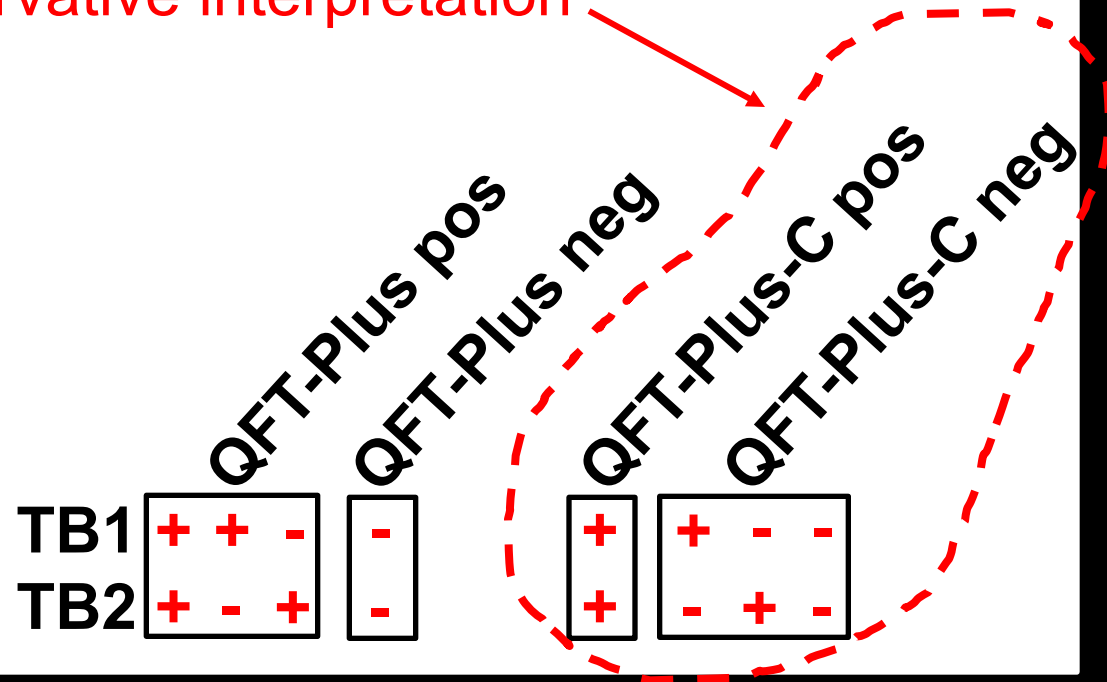
Interpretation of QFT-Plus Results

- Interpretation of QFT-Plus using manufacturer's interpretation

	QFT-Plus pos			QFT-Plus neg
TB1	+	+	-	-
TB2	+	-	+	-

Interpretation of QFT-Plus in Low-Risk HCWs

- Interpretation of QFT-Plus using a conservative interpretation



Performance of QFT-Plus in Low-Risk HCWs



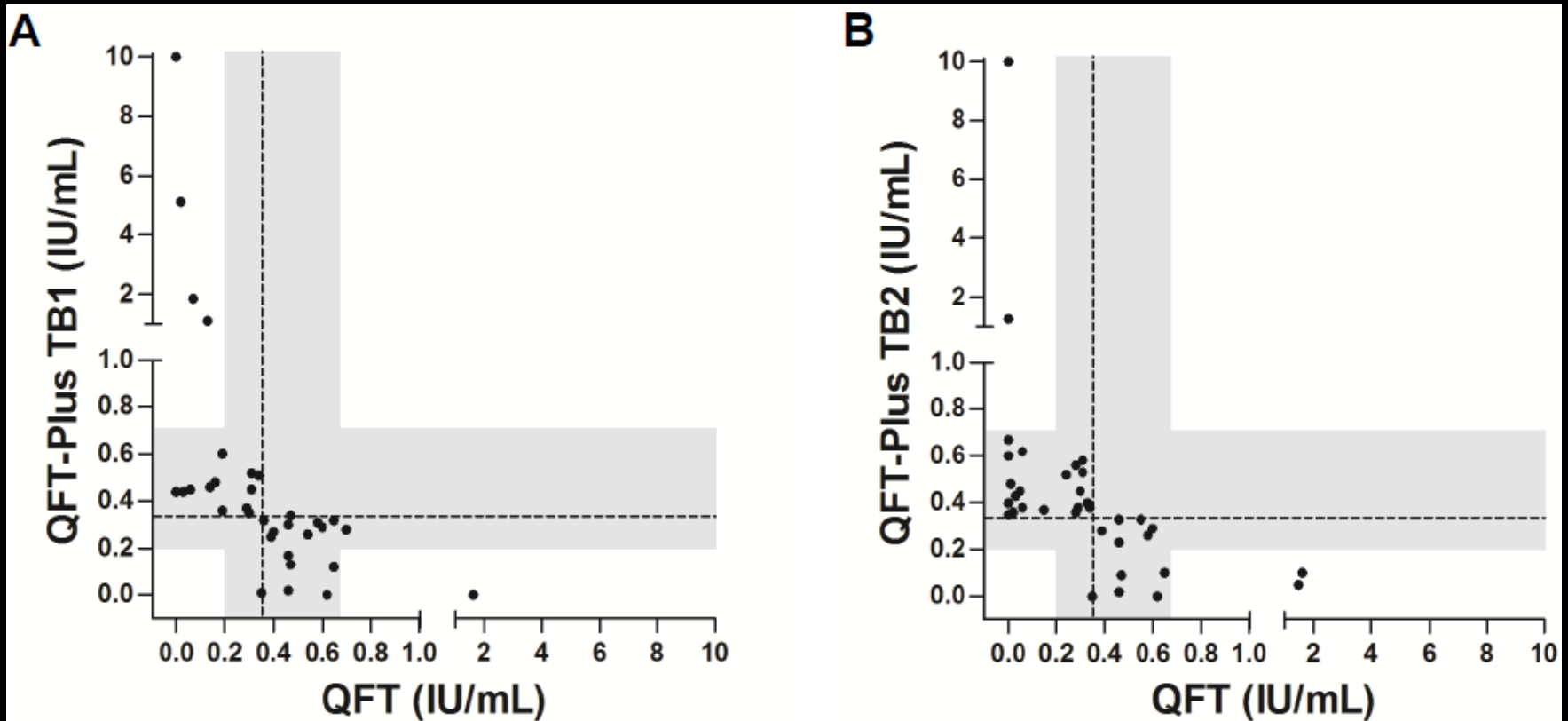
Study Design

- Single center at Stanford Health Care
- Prospective Aug 2015 to Nov 2015
- QFT vs QFT-Plus performed in 989 HCWs during annual or new employee screening
- Risk assessment
- Compared agreement of QFT with QFT-Plus using manufacturer's and a conservative interpretation

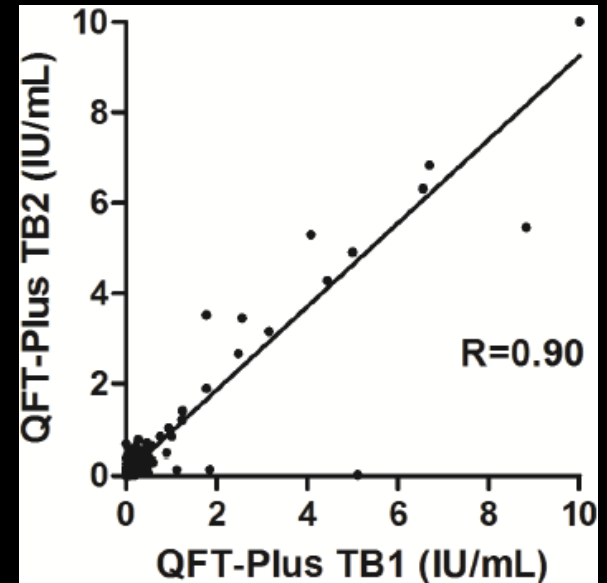
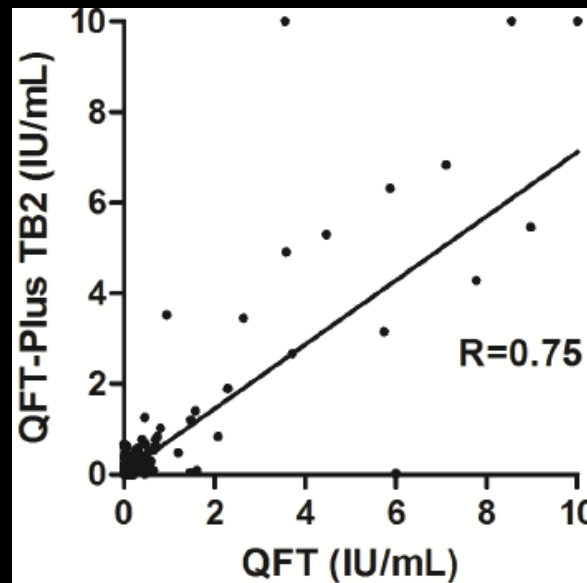
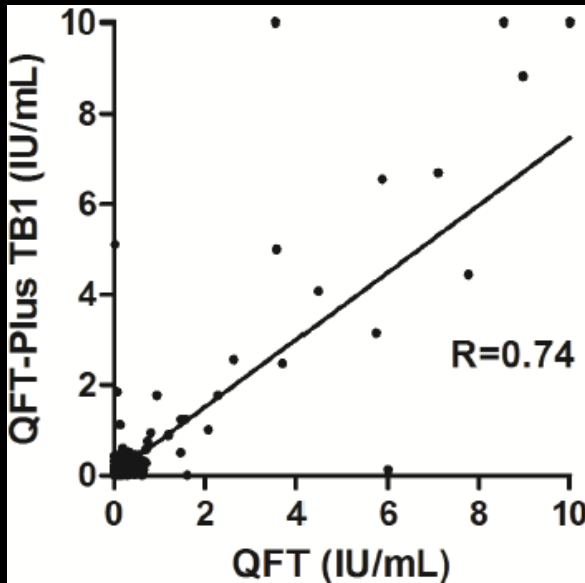
Qualitative Agreement Between QFT and QFT-Plus

Comparison	Agreement (%; 95% CI)	Kappa (95% CI)
QFT vs QFT-Plus	944/987 (95.6, 94.3-96.9)	0.57 (0.44-0.70)
QFT vs QFT-Plus TB1	954/987 (96.7, 95.6-97.8)	0.59 (0.45-0.72)
QFT vs QFT-Plus TB2	952/987 (96.5, 95.4-97.7)	0.61 (0.48-0.73)
QFT vs QFT-Plus-C	962/987 (97.4, 96.4-98.4)	0.64 (0.50-0.78)
QFT-Plus TB1 vs QFT-Plus TB2	953/987 (96.6, 95.5-97.7)	0.61 (0.49-0.74)

Discordant QFT and QFT-Plus Results Fell Within Borderline Range of 0.2-0.7 IU/mL



Quantitative Correlation Between QFT and QFT-Plus TB1 and TB2



Positivity Rate in 626 HCWs with no Risk Factors

Assay	No. of positives	Positivity rate (95% CI)	<i>P</i> *
QFT	13	2.1% (1.0-3.2)	-
QFT-Plus	19	3.0% (1.7-4.3)	0.24
QFT-Plus TB1	10	1.6% (0.6-2.6)	0.58
QFT-Plus TB2	15	2.4% (1.2-3.6)	0.80
QFT-Plus-C [†]	6	1.0% (0.2-1.7)	0.07

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QFT	13	2.1% (1.0-3.2)	-
QFT-Plus	19	3.0% (1.7-4.3)	0.24
QFT-Plus TB1	10	1.6% (0.6-2.6)	0.58
QFT-Plus TB2	15	2.4% (1.2-3.6)	0.80
QFT-Plus-C [†]	6	1.0% (0.2-1.7)	0.07

Among 310 HCWs with a documented history of negative QFT and no risk factors

QFT	2.6% (CI, 0.8-4.4)	-
QFT-Plus	2.6% (CI, 0.8-4.4)	<i>P</i> = 0.03
QFT-Plus-C	0.6% (CI, 0-1.5)	<i>P</i> = 0.03

Follow-up for 13 HCWs With discordant QFT-Plus

Study No.	Age (yr)	Sex (M/F)	Enrollment Result				Follow-up Result						
			QFT		QFT-Plus		QFT		QFT-Plus		Since last screen		
			Initial screen	Short-term retest	TB1	TB2	Annual screen	Short-term retest	TB1	TB2	Interval (mo)	TB exposure	Active TB
6937	53	M	0.4	0.44	0.27	0.77	1.01	ND	0.91	1.12	13	No	No
823	30	M	0.47	0.16	0.34	0.36	0.16	ND	ND	ND	12	No	No
907	28	F	1.47	0.02	0.5	0.05	0.03	ND	ND	ND	13	No	No
1716	38	F	0.06	ND	0.45	0.25	0.16	ND	0.21	0.25	12	No	No
3958	28	F	0.07	ND	1.85	0.14	0	ND	0.03	0.01	13	No	No
6258	28	F	0.02	ND	5.11	0.02	0	ND	ND	ND	10	No	No
3720	26	F	0	ND	0	1.26	0	ND	0.13	0.15	13	No	No
4749	58	F	0	ND	0	0.67	0	ND	0.00	0.34	12	No	No
885	34	F	0.06	ND	0.23	0.62	0.03	ND	0.01	0.17	9	No	No
6156	23	F	0	ND	0.04	0.60	ND	ND	ND	ND	NA	NA	NA
2262	51	M	0.01	ND	0.06	0.48	0.01	ND	0.01	0.03	11	No	No
1588	55	M	0.28	ND	0.23	0.36	0.6	0.15	ND	ND	12	No	No
4698	43	F	0	ND	0.01	0.35	ND	ND	ND	ND	NA	NA	NA

Summary of Stanford HCW QFT-Plus Study

- A conservative interpretation of QFT-Plus results yielded a positivity rate of 0.6% in low-risk HCWs.
- A conservative interpretation of QFT-Plus results may be a useful strategy for minimizing false positive results in low-risk populations if confirmed by other studies.

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