EVALUATI IMA RELEASE ASSAY USI *osis* ANTIGENS FOR DIAGNC BERCULOSIS IN BCG VACC F KELANTAN, MALAYSIA

by

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ANOVA	One-Way Analysis Of Variance
ATB	Active TB
AUC	Area under Curve
BAL	Bronchoalveolar Lavage
BCG	Bacillus Calmette–Guerin/ Bacille de Calmette et Guérin
CMI	Cell-Mediated Immunity
CR3	Complement Receptor 3
CSF	Cerebrospinal Spinal Fluid
CT	Computed Tomography
DOTS	Directly Observed Therapy Strategy
ECL	Enhanced luminol-based Chemiluminescent
ELISA	Enzyme Linked Immunosorbent Assay
ESAT-6	6-kDa Early Secreted Antigenic Target
HC	Healthy Contact
HCW	Health Care Workers
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HRP	Horseradish Peroxidase
ICT	Immunochromatographic Test
IFN-γ	Interferon-gamma
IGRA	Interferon Gamma Release Assay
LJ	Lowenstein Jensen

LTB	Latent TB
MDR	Multi-Drug Resistant
MHC	Major Histocompatibility Complex
MTB	*Mycobacterium tuberculosis*
NAAT	Nucleic Acid Amplification Techniques
NTM	Non Tuberculous Mycobacteria
NF-κβ	nuclear factor-kappa beta
PBMC	Peripheral Blood Mononuclear Cell
PHA	Phytohemaglutinin
PPD	Purified Protein Derivative
QFT-G	QuantiFERON®-TB Gold
QFT-GIT	QuantiFERON®-TB Gold In Tube
RD	Region of Difference
ROC	Receiver Operating Characteristics
SDS-PAGE	Sodium Dedocyl Sulphate-Polyacrylamide Gel Electrophoresis
TB	Tuberculosis
TBIS	TB Information System
tblastn	Translated Basic Local Alignment Sequence Tool
TST	Tuberculin Skin Test
USFDA	US Food and Drug Administration
WB	Western Blot
WHO	World Health Organization

PENILAIAN KE ATAS ASAI PELEPASAN GAMA INTERFERON (IGRA) YANG MENGGUNAKAN ANTIGEN-ANTIGEN *Mycobacterium tuberculosis* UNTUK DIAGNOSIS TUBERKOLOSIS PULMONARI DI KALANGAN POPULASI YANG DIBERI VAKSIN BCG DI KELANTAN, MALAYSIA

ABSTRAK

Walaupun Malaysia merupakan antara negara yang mempunyai beban kes tuberkulosis (TB) yang sederhana, namun sejak kebelakangan ini jumlah kes baru telah meningkat. Pencegahan TB berpaksi pada kebolehan mengenal pasti jangkitan ini pada peringkat awal dan pemberian rawatan yang efisien. Asai yang menggunakan QuantiFERON®-TB Gold In-Tube (QFT-GIT) telah menunjukkan hasil kepekaan dan kekhususan yang meragukan dalam diagnosis jangkitan TB paru-paru aktif dan TB pendam. Untuk kajian ini, dua antigen yang berasal daripada *Mycobacterium tuberculosis* (MTB) iaitu VacIII dan Ubi-VacIII juga turut diuji bagi mengenal pasti kesan tindak balas antigen tersebut terhadap sel T dalam populasi yang menerima suntikan vaksin BCG. Seramai tiga puluh enam pesakit yang menghidapi TB pulmonari dan 38 individu sihat telah dipilih sebagai kumpulan kawalan dari sebuah hospital di Kelantan untuk diuji melalui kaedah piawai standard dan IGRA. Di dalam populasi yang sudah menerima vaksin BCG, kepekaan dan kekhususan adalah seperti berikut; QFT-GIT (30.4% dan 88.9%), VacIII (47.8% dan 55.6%), dan Ubi-VacIII (30.4% dan 18.5%). Secara keseluruhannya perbandingan antara kaedah piawai standard dan IGRA menunjukkan hubungan yang lemah (nilai κ=0.320), namun, tindak balas sel-T terhadap antigen-antigen menunjukkan perbezaan statistik yang signifikan (P<0.001). Kajian ini telah membuktikan setiap antigen menunjukkan kepekaan dan kekhususan yang rendah, maka dapat disimpulkan bahawa ketiga-tiga antigen ini tidak mampu membezakan pesakit yang menghidap TB, dan populasi yang sihat. Sungguhpun begitu, QFT-GIT masih menunjukkan kekhususan yang lebih baik berbanding VacIII dan Ubi-VacIII, walaupun kepekaannya tetap rendah disebabkan antigen TB7.7 yang tiada dalam variasi MTB klinikal di Asia Tenggara.

EVALUATION OF INTERFERON GAMMA RELEASE ASSAY (IGRA) USING *Mycobacterium tuberculosis* ANTIGENS FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN BCG VACCINATED POPULATION OF KELANTAN, MALAYSIA

ABSTRACT

Although Malaysia is an intermediate tuberculosis (TB) burden country, the absolute number of new cases has been increasing recently. Improvement in early diagnosis followed by efficient chemotherapy is the major control strategy for TB. Currently, T-cell based interferon-gamma release assays using *Mycobacterium tuberculosis* (MTB) antigens from QuantiFERON®-TB Gold In-Tube (QFT-GIT) assays have shown unclear values in terms of sensitivity and specificity in the diagnoses of active pulmonary and latent TB infections. For this study, two MTB antigens known as VacIII and Ubi-VacIII were evaluated for their diagnostic potential based on dynamic T-cell responses among BCG-vaccinated populations were investigated. Thirty-six patients with active pulmonary TB and 38 healthy controls (HC) from a selected hospital in Kelantan, Malaysia were recruited and tested by using gold standard assays and IGRA. The sensitivity and specificity of QFT-GIT, VacIII and Ubi-VacIII antigens among BCG vaccinated population were 30.4% and 88.9%, 47.8% and 55.6%, and 30.4% and 18.5%, respectively. Even though the overall agreement between IGRA and the gold standards assays showed fairly poor correlation (κ-values=0.320), the T-cell responses against the antigens were considered statistically significant ($P<0.001$). In conclusion, all the 3 antigens were unable to discriminate between TB and HC due to high variability of the sensitivities and specificities they demonstrated. As compared to VacIII and Ubi-VacIII, QFT-GIT showed better specificity however its low sensitivity was expected due to the fact that the TB7.7 antigen is absent in clinical MTB strains of South East Asia.