UNIVERSITI SAINS MALAYSIA
GERAN PENYELIDIKAN UNIVERSITI PENYELIDIKAN
LAPORAN AKHIR

TYPING OF BURKHOLDERIA PSEUDOMALLEI AND ASSOCIATION OF ITS GENOTYPES WITH CLINICAL PRESENTATIONS AND VIRULENCE

PENYELIDIK

DR. AZIAN HARUN

PENYELIDIK BERSAMA

DR. ZAIDAH ABDUL RAHMAN
ABDEL RAHMAN MOHAMMAD ZUETER

2015

BORANG ERGS – P3(R) ✓

Kod Projek : ERGS/1/2011/SKK/USM/03/11

KEMENTERIAN PENDIDIKAN MALAYSIA

FINAL REPORT
EXPLORATORY RESEARCH GRANT SCHEME (ERGS)

Laporan Akhir Skim Geran Penyelidikan Eksploratori (ERGS) IPT
2014

A

PHASE : 1/2011
Fasa

RESEARCH TITLE : **Typing of *Burkholderia pseudomallei* and association of its genotypes with clinical presentations and virulence**
Tajuk Penyelidikan

PROJECT LEADER : **DR AZIAN HARUN**
Ketua Projek

PROJECT MEMBERS (including GRA) : 1. DR ZAIDAH ABDUL RAHMAN
2. ABDEL RAHMAN MOHAMMAD ZUETER
Ahli Projek

PROJECT ACHIEVEMENT *(Please Tick)*

B

ACHIEVEMENT PERCENTAGE			
Project progress according to milestones achieved up to this period	**0 - 50%**	**51 - 75%**	**76 - 100%**
Percentage			√

RESEARCH OUTPUT

Number of articles/ manuscripts/ books *(Please attach the First Page of Publication)*	**Refereed Journal**	***Non-Refereed Publication***
	FIVE (5) publications in progress (3 original articles & 2 case reports) *(refer Appendix 1)*	
Conference Proceeding *(Please attach the First Page of Publication)*	**International**	***National***
	TWO (2) *(refer Appendix 1)*	
Intellectual Property *(Including Paten,Copyright, Industrial Design,layout Design of Integrated Circuit & Trademarks)*		

HUMAN CAPITAL DEVELOPMENT

Human Capital	**Number**				**Others** (please specify)
	On-going		**Graduated**		
Citizen	Malaysian	Non Malaysian	Malaysian	Non Malaysian	
PhD Student		1			
Master Student					
Undergraduate Student					
Total		1			

EXPENDITURE *(Perbelanjaan)*

C

Budget Approved *(Peruntukan diluluskan)* :
Amount Spent *(Jumlah Perbelanjaan)* :

Balance *(Baki)* :
Percentage of Amount Spent :
(Peratusan Belanja)

ADDITIONAL RESEARCH ACTIVITIES THAT CONTRIBUTE TOWARDS DEVELOPING SOFT AND HARD SKILLS
(Aktiviti Penyelidikan Sampingan yang menyumbang kepada pembangunan kemahiran insaniah)

D

International		
Activity	Date (Month, Year)	Organizer
(e.g : Course/ Seminar/ Symposium/ Conference/ Workshop/ Site Visit) *(refer Appendix 1)*	1. ICMSM 12-15 December 2013 2. ICMHS 22-24 May 2014	Malaysian Society for Microbiology School of Medical Sciences, Universiti Sains Malaysia
National		
Activity	Date (Month, Year)	Organizer
(e.g : Course/ Seminar/ Symposium/ Conference/ Workshop/ Site Visit)		

PROBLEMS / CONSTRAINTS IF ANY *(Masalah / Kekangan sekiranya ada)*

E

No major technical problem encountered throughout the study period.
The high cost of DNA sequencing limited the number of isolates included in the genotyping study.
As all 581 new sequences generated in this project must be correctly annotated, approved and assigned unique accession numbers by GenBank prior to inclusion in manuscripts, delay in manuscript submission was expected.
In addition, the researchers expect highly of the quality of this research work and aim to publish in high impact factor journals. Time needed to bring the manuscripts' quality to their best, which may include re-analysis of data using newer, sophisticated population genetics softwares.

RECOMMENDATION *(Cadangan Penambahbaikan)*

F

RESEARCH ABSTRACT – Not More Than 200 Words (*Abstrak Penyelidikan – Tidak Melebihi 200 patah perkataan*)

G *Burkholderia pseudomallei* is a soil dwelling Gram-negative bacteria found mainly in the Southeast Asia region and northern Australia. Bacterial isolates from recent cases of melioidosis were collected and the genotypic diversity among these was explored using multi-locus sequence typing (MLST). Massive genotypic heterogeneity was observed among the 85 strains in which 23 different sequence profiles were observed. Sequence type 54 (ST54) was noted to predominate and two novel sequence types were discovered. Most of sequence types in this study were genetically related to each other and were clustered in a same group with those from Southeast Asian region and derived from the same ancestor which was ST48. Analysis of association between the genotypes and clinical presentations explored the association of genotypes with predisposing factors, type of manifestation, severity of sepsis and mortality due to melioidosis. With regard to virulence association with genotypes, survival study and tissue burden analysis have been explored.

Date : 11 Jan 2015
Tarikh

Project Leader's Signature:
Tandatangan Ketua Projek

COMMENTS, IF ANY/ ENDORSEMENT BY RESEARCH MANAGEMENT CENTER (RMC)
(Komen, sekiranya ada/ Pengesahan oleh Pusat Pengurusan Penyelidikan)

H .....

.....

.....

Name:
Nama:

PROF. DR LEE KEAT TEONG
Pengarah
Pejabat Pengurusan & Kreativiti Penyelidikan
Universiti Sains Malaysia
11800 USM, Pulau Pinang.

Signature:
Tandatangan:

Date:
Tarikh:

18/1/15

Appendix 2

UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN FUNDAMENTAL
PENYATA PERBELANJAAN SEHINGGA 30 JUN 2014

Jumlah Geran

Peruntukan 2011 (Tahun 1)

Peruntukan 2012 (Tahun 2)

Peruntukan 2013 (Tahun 3)

Ketua Projek: DR AZIAN HARUN

Tajuk Projek: TYPING OF BURKHOLDERIA PSEUDOMALLEI AND ASSOCIATION OF ITS GENOTYPES WITH CLINICAL PRESENTATIONS AND VIRULENCE

Tempoh: 30 BULAN (15 OGOS 2011-13 FEBRUARI 2014)

Kwgan	Akaun	PTJ	Projek	Peruntukan Projek	Perbelanjaan Terkumpul sehingga Tahun lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
203	11000	PPSP	6730024	-	12,677.41	(12,677.41)	-	1,500.00	1,500.00	(14,177.41)
203	14000	PPSP	6730024		-	-	-		-	-
203	15000	PPSP	6730024	-	-	-	-		-	-
203	21000	PPSP	6730024	11,000.00	-	11,000.00	-		-	11,000.00
203	22000	PPSP	6730024	-	-	-			-	-
203	23000	PPSP	6730024		-	-	-		-	-
203	24000	PPSP	6730024		-	-	-		-	-
203	25000	PPSP	6730024		-	-	-		-	-
203	27000	PPSP	6730024	74,250.00	60,262.80	13,987.20		16,970.00	16,970.00	(2,982.80)
203	28000	PPSP	6730024		-	-			-	-
203	29000	PPSP	6730024	28,800.00	21,850.00	6,950.00			-	6,950.00
203	35000	PPSP	6730024	31,500.00	31,220.00	280.00			-	280.00
203	52000	PPSP	6730024		-	-			-	-
203	A11102	PPSP	6730024	-	-	-		-	-	-
				145,550.00	126,010.21	19,539.79	-	18,470.00	18,470.00	1,069.79

RESEARCH TITLE **Typing of *Burkholderia pseudomallei* and association of its genotypes with clinical presentations and virulence**

PROJECT LEADER **DR AZIAN HARUN**

PROJECT MEMBERS **1. DR ZAIDAH ABDUL RAHMAN**
2. ABDEL RAHMAN MOHAMMAD ZUETER

OUTPUT

1. Publications

Original articles

Title: Genotyping of *Burkholderia pseudomallei* revealed high genetic variability among isolates from a single population group.
Authors: AbdelRahman Zueter, Zaidah Abdul Rahman, Chan Yean Yean, Azian Harun
Manuscript under review at the American Journal of Tropical Medicine and Hygiena (IF 2.7)

Title: Multi-locus sequence typing (MLST) of Malaysian *Burkholderia pseudomallei* strains showed significant genetic variability with clinical correlation.
Authors: Zueter A, Zaidah AR, Chan YY, Price E, Harun A
Manuscript in writing for submission to PLOS Neglected Trop Dis (IF 4.48)

Title: Comparison of virulence among different genotypes of *Burkholderia pseudomallei* using *in vivo* murine model
Authors: AbdelRahman Zueter, Azian Harun
Manuscript in writing for submission to Microbial Pathogenesis (IF 2.0)

Case reports

Title: Pediatric melioidosis showing variability of clinical manifestations and genotypic association.
Authors: Zueter AR, Zaidah AR, Wahab MSA, Van Rostenberghe H, Harun A
Manuscript in writing for submission to Journal of Clinical Microbiology (IF 4.23)

Title: Accidental finding of soft tissue infection caused by an emerging *Burkholderia thailandensis.*
Authors: Zueter A, Harun A
Manuscript in writing for submission to Tropical Biomedicine (IF 0.82)

2. Conference presentations

AbdelRahman Zueter, Azian Harun. Genetic diversity of clinical *Burkholderia pseudomallei* isolates from Kelantan, Malaysia. Presented at the International Congress of Malaysia Society for Microbiology (ICMSM) at Langkawi, Kedah, Malaysia, 12-15 December 2013

AbdelRahman M. Zueter, Azian Harun. Genotyping of clinical *Burkholderia pseudomallei* isolates – a preliminary report. Presented at the Intenational Conference of Medical and Health Sciences (ICMHS), Kota Bharu, Kelantan Malaysia, 22-24 May 2013.

3. Human capital development

PhD candidate: AbdelRahman Mohammad Abdallah Zueter
Matric no. P-UD0002/13(R)
Expected thesis submission: January 2016

4. **Others**

Publication of 11 novel sequence types (ST1317 - ST1327) of *Burkholderia pseudomallei* at the publically accessible website www.bpseudomalle.mlst.net
GenBank submission of 581 partial sequences of *ace, gltB, gmhD, lepA, lipA, narK, ndh* genes of *Burkholderia pseudomallei.*

Genotyping of *Burkholderia pseudomallei* revealed high genetic variability among isolates from a single population group

AbdelRahman Zueter*, Zaidah Abdul Rahman, Chan Yean Yean, Azian Harun

Department of Medical Microbiology and Parasitology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

Abstract

Burkholderia pseudomallei is a soil dwelling Gram-negative bacteria predominates in Southeast Asia zone and the tropical part of Australia. Genetic diversity has been explored among various populations and environments worldwide. In this report, thirteen culture positive *B. pseudomallei* cases from a single population of Terengganu state in the eastern Peninsular Malaysia, were analyzed. The genotypic diversity among bacterial isolates was explored using multi-locus sequence typing (MLST). Massive genotypic heterogeneity was observed (8 different sequence types) with predominance of sequence type 54 (ST 54) and discovery of two novel sequence types. Some of sequence types in this study were genetically related to each other and were clustered in a same group with those from Southeast Asian region and derived from the same ancestor which was ST 48.

Keywords: *Burkholderia pseudomallei, melioidosis, multi-locus sequence typing, sequence type, MLST.*