

**UNIVERSITI SAINS MALAYSIA  
GERAN PENYELIDIKAN UNIVERSITI PENYELIDIKAN  
LAPORAN AKHIR**

**THE CLINICAL EPIDEMIOLOGY STUDY OF OROFACIAL  
CLEFTS AND GENOME-WIDE LINKAGE ANALYSIS  
AMONG LARGE EXTENDED FAMILIES WITH  
NONSYNDROMIC OROFACIAL CLEFT**

**PENYELIDIK**

**DR. WAN AZMAN WAN SULAIMAN**

**PENYELIDIK BERSAMA**

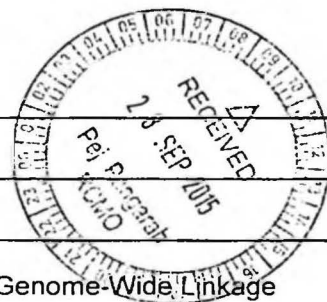
**PROF. DR. AHMAD SUKARI ABDUL HALIM  
PROF. DR. ZILFALIL ALWI  
PROF. MADYA MOHAMED RUSLI ABDULLAH  
DR. MOHD FAIZAL ALI  
DR. SAHWALTUL AKMAL ZAINUL RASHID  
DR. NAJIHAH SHARIDA ZAKARIA**

**2016**

**UNIVERSITI SAINS MALAYSIA**



UNIVERSITY RESEARCH GRANT  
FINAL REPORT  
Geran Penyelidikan Universiti  
Laporan Akhir



Please email a copy of this report to [rcmo@usm.my](mailto:rcmo@usm.my)  
 dan emel salinan laporan ini ke [rcmo@usm.my](mailto:rcmo@usm.my)

**PARTICULARS OF RESEARCH / MAKLUMAT PENYELIDIKAN:**

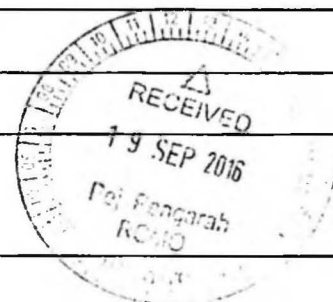
**Title of Research:**  
*Tajuk Penyelidikan:* The Clinical Epidemiology Study Of Orofacial Clefts And Genome-Wide Linkage Analysis Among Large Extended Families With Nonsyndromic Orofacial Cleft.

**Account Number:** 1001/PPSP/812083  
*Nombor Akaun:*

**PERSONAL PARTICULARS OF RESEARCHER / MAKLUMAT PENYELIDIK:**

**Name of Research Leader:**  
*Nama Ketua Penyelidik:* Dr Wan Azman Wan Sulaiman

**Name of Co-Researcher:**  
*Nama Penyelidik Bersama:* Prof Dr Ahmad Sukari Abdul Halim  
 Prof Dr Zilfalil Alwi  
 Dr Sarina Sulong  
 Prof Madya Mohamed Rusli Abdullah  
 Dr Mohd Faizal Ali  
 Dr Sahwaltul Akmal Zainul Rashid  
 Dr Najihah Sharida Zakaria



**RUJUKAN**

**School/Institute/Centre/Unit:**  
*Pusat Pengajian /Institut/Pusat/Unit:* Reconstructive Sciences Unit, School of Medical Sciences, Universiti Sains Malaysia.

**Duration of this research:**  
*Tempoh masa penyelidikan ini:*

**\*Duration :** 3 YEARS  
*Tempoh :*

<b>From</b>	: 1st January 2011	<b>To</b>	: 31st december 2013
<b>Extended Date 1</b>	: 1st January 2014	<b>To</b>	: 30th June 2014
<b>Extended Date 2</b>	: 1st July 2014	<b>To</b>	: 31st December 2014
<b>Extended Date 3</b>	: 1st January 2015	<b>To</b>	: 31st March 2015

a) Results/Benefits of this research

*Hasil Penyelidikan*

No. Bil:	Category/Number: Kategori/ Bilangan:	Promised	Achieved
1.	<b>Research Publications (Specify target journals)</b> <i>Penerbitan Penyelidikan (Nyatakan sasaran jurnal)</i>	2	1)International : 2 (Attachment 4) 2)Submitted (Under review): 3 3) Draft: 1
2.	<b>Human Capital Development</b>		
	a. Ph. D Students	1	2
	b. Masters Students	2	0
	c. Undergraduates (Final Year Project)	-	-
	d. Research Officers	-	-
	e. Research Assistants	2	2
	f. Other: Please specify	-	-
3.	<b>Patents</b> <i>Paten</i>	-	-
4.	<b>Specific / Potential Applications</b> <i>Spesifik/Potensi aplikasin</i>	-	-
5.	<b>Networking &amp; Linkages</b> <i>Jaringan &amp; Jalinan</i>	3	
6.	<b>Possible External Research Grants to be Acquired</b> <i>Jangkaan Geran Penyelidikan Luar Diperoleh</i>	1	

- Kindly provide copies/evidence for Category 1 to 6.

b) Equipment used for this research.

*Peralatan yang telah digunakan dalam penyelidikan ini.*

Items Perkara	Approved Equipment	Approved Requested Equipment	Location
<b>Specialized Equipment</b> Peralatan khusus	Affymetrix Microarray System, PCR Machine, Hybridization Oven, Affymetrix Chip Scanner.		Universiti Sains Malaysia
<b>Facility Kemudahan</b>	Affymetrix 250K Chip and Reagents for Microarray.		Affymetrix Company
<b>Infrastructure</b> Infrastruktur			

- Please attach appendix if necessary.

**E. ABSTRACT OF RESEARCH**

(Please Refer Attachment 1)

*Abstrak Penyelidikan*

(Sila Rujuk Lampiran 1)

**F. SUMMARY OF RESEARCH FINDINGS**

(Please Refer Attachment 2)

*Ringkasan dapatan Projek Penyelidikan*

(Sila Rujuk Lampiran 2)

**G. COMPREHENSIVE TECHNICAL REPORT**

(Please Refer Attachment 3)

*Laporan Teknikal Lengkap*

Applicants are required to prepare a comprehensive technical report explaining the project.

(This report must be attached separately)

(Sila Rujuk Lampiran 3)

Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.

[Laporan ini mesti dikepilkan]

**List the key words that reflect our research:**

*Senaraikan kata kunci yang mencerminkan penyelidikan anda:*

English	Bahasa Malaysia
Non-syndromic Cleft Lip and/or Palate	Sumbing bibir dan lelangit
Demographic data	Data pemetaan
Malay Population	Populasi Melayu
Oral Cleft	Sumbing mulut

a) Results/Benefits of this research

*Hasil Penyelidikan*

No. Bil:	Category/Number: Kategori/ Bilangan:	Promised	Achieved
1.	<b>Research Publications (Specify target journals)</b> <i>Penerbitan Penyelidikan (Nyatakan sasaran jurnal)</i>	2	1)International : 2 (Attachment 4) 2)Submitted (Under review): 3 3) Draft: 1
2.	<b>Human Capital Development</b>		
	a. Ph. D Students	1	2
	b. Masters Students	2	0
	c. Undergraduates (Final Year Project)	-	-
	d. Research Officers	-	-
	e. Research Assisstants	2	2
	f. Other: Please specify	-	-
3.	<b>Patents</b> <i>Paten</i>	-	-
4.	<b>Specific / Potential Applications</b> <i>Spesifik/Potensi aplikasin</i>	-	-
5.	<b>Networking &amp; Linkages</b> <i>Jaringan &amp; Jalinan</i>	3	
6.	<b>Possible External Research Grants to be Acquired</b> <i>Jangkaan Geran Penyelidikan Luar Diperoleh</i>	1	

- Kindly provide copies/evidence for Category 1 to 6.

b) Equipment used for this research.

*Peralatan yang telah digunakan dalam penyelidikan ini.*

Items Perkara	Approved Equipment	Approved Requested Equipment	Location
<b>Specialized Equipment</b> Peralatan khusus	Affymetrix Microarray System, PCR Machine, Hybridization Oven, Affymetrix Chip Scanner.		Universiti Sains Malaysia
<b>Facility</b> Kemudahan	Affymetrix 250K Chip and Reagents for Microarray.		Affymetrix Company
<b>Infrastructure</b> Infrastruktur			

- Please attach appendix if necessary.

I. **BUDGET / BAJET**

**Total Approved Budget** : RM 223724.00  
**Total Additional Budget** : RM 0.00  
**Grand Total of Approved Budget** : RM 223724.00

**Yearly Budget Distributed**


Year 1 : RM 79984.00  
Year 2 : RM 111940.00  
Year 3 : RM 31800.00

**Additional Budget Approved**

Year 1 : RM  
Year 2 : RM  
Year 3 : RM

**Total Expenditure** : RM 223148.22  
**Balance** : RM 575.78

- **Please attach final account statement from Treasury**

  
\_\_\_\_\_  
**Signature of Researcher**  
Tandatangan Penyelidik

15/9/15  
\_\_\_\_\_  
**Date**  
Tarikh

**COMMENTS OF PTJ'S RESEARCH COMMITTEE**  
**KOMEN JAWATANKUASA PENYELIDIKAN PERINGKAT PTJ**

**General Comments:**

*Ulasan Umum:*

Excellent output  
Fully endorse for grant closure.

**PROFESOR (DR) ROSLINE HASSAN**  
Chairman Of Research committee  
School Of Health Sciences  
Health Campus  
Universiti Sains Malaysia  
16150 Kubang Kerian, Kelantan.



**Signature and Stamp of Chairperson of PTJ's Evaluation Committee**  
*Tandatangan dan Cop Pengerusi Jawatankuasa Penilaian PTJ*

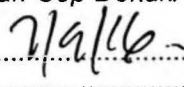
Date : .....  
Tarikh : .....



**Signature and Stamp of Dean/ Director of PTJ**  
*Tandatangan dan Cop Dekan/ Pengerusi PTJ*

Date : .....  
Tarikh : .....

**PROFESOR (DR) AHMAD SUKARI HALIM**  
Dekan  
Pusat Pengajian Sains Perubatan  
Kampus Kesihatan  
Universiti Sains Malaysia  
16150 Kubang Kerian, Kelantan.



## ATTACHMENT 1

### ABSTRACT OF RESEARCH

Non-syndromic oral clefts is one of the most common birth defect in the world. Approximately 70% of cleft lip and/or palate (CL/P) cases are non-syndromic and it varies among races and geographic region. In a first phase, a descriptive epidemiological study was carried out in all CL/P cases registered in Hospital Universiti Sains Malaysia (HUSM) from year 1997-2013. Large extended family with more affected family members was identified through database for the second phase experimental work. In second phase, genome-wide linkage analysis was carried out to the 8 selected large extended families using microarray platform and validated by copy number variation (CNV) analysis. The demography data analysis has been done for a cleft lip and/or palate in Kelantan and certain regions in Malaysia including Selangor, Johor, Terengganu and Pahang. The total of this cleft patient is up to 550 patients with 274 cases for male and 276 cases of female. The study found that 454 total cases in Kelantan, 74 cases in Terengganu, 16 cases in Pahang, Johor and Kedah with 2 and 1 cases only. A preliminary study has detected *IRF6* mutations. Seven variants, including five known (c.-75-4A>G, c.-73T>C, c.459G>T, c.820G>A, and c.1060+37C>T) and two novel (c.-75-23G>C and c.1380G>T), were found. A significant nonparametric linkage (NPL) score and suggestive NPL and logarithm of the odds (LOD) scores were attained from family 50, 58, 99 and 100 under autosomal recessive mode. Several linkage intervals were attained. The study of the demography data using a statistical data analysis, divided cleft into several types. There are Unilateral cleft lip and palate (UCLP), Unilateral cleft lip (UCL), Bilateral cleft lip and palate (BCLP), Bilateral cleft lip (BCL) and Cleft palate (CP). From the result, the total of the cleft study in the HUSM, report with 550 of cleft cases with total of UCLP cases is 227, UCL with 68 cases, BCLP with 116 cases, only 3 cases for BCL and CP with 136 cases. A comprehensive investigation of the candidate genes in orofacial clefts is warranted. *IRF6* variants could, at best, contribute to clefting as part of a complex inheritance pattern, with both additional genes and environmental factors having a role. The findings of *LPHN2* at 1p31, *PVRL3* at 3q13.3, *SATB2* at 2q31.1 q35 would shed more light on the disease mechanism that has been discovered through genome-wide linkage analysis.