ANALYSES OF DNA VARIANTS IN MALAYS WITH HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC)

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LAPORAN AKHIR GERAN PENYELIDIKAN UNIVERSITI (RU)

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(JAB. SURGERI)

TAJUK: "ANALYSES OF DNA VARIANTS IN MALAYS WITH HEREDITARY NONPOLYSIS COLORECTAL CANCER"

(NO AKAUN: 1001/PPSP/812112)

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Please use this checklist to self-assess your report before submitting to RCMO.
Checklist should accompany the report.

NO.	ITEM	PLEASE CHECK (✓)		
		PI	JKPTJ	RCMO
1	Completed Final Report Form	✓		✓
2	Project Financial Account Statement (e-Statement)	✓		✓
3	Asset/Inventory Return Form *(Borang Penyerahan Aset/Inventori)*	✓		✓ (Tidak ada aset tidak)
4	A copy of the publications/proceedings listed in Section D(ii) (Research Output)	✓		✓
5	Comprehensive Technical Report	✓		✓
6	Other supporting documents, if any			
7	Project Leader's Signature	✓		✓
8	Endorsement of PTJ's Evaluation Committee			✓
9	Endorsement of Dean/ Director of PTJ's			✓

Igram, ok, reload output, TK

5/5/2017

Project Code :
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FINAL REPORT FORM

Please email a softcopy of this report to rcmo@usm.my

A	**PROJECT DETAILS**
i	**Title of Research:** Analyses of DNA Variants in Malays with Hereditary Nonpolyposis Colorectal Cancer
ii	**Account Number:** 1001/PPSP/812112
iii	**Name of Research Leader:** Assoc. Prof. Dr Andee Dzulkarnaen Zakaria
iv	**Name of Co-Researcher:** 1. Prof. Dr. Zilfalil bin Alwi 2. Prof Dr Xu Shuhua 3. Dato' Dr Rosemi Salleh 4. Datuk Dr Muhammad Radzi Abu Hassan 5. Assoc. Prof. Dr Andee Dzulkarnaen Zakaria 6. Dr Khairul Bariah Ahmad Amin Noordin 7. Dr Wan Faiziah Wan Abdul Rahman 8. Dr Ahmad Shanwani Mohamed Sidek
v	**Duration of this research:** **a) Start Date** : 15 March 2013 **b) Completion Date** : 14 March 2016 **c) Duration** : 3 years **d) Revised Date** (*if any*) : 14 September 2016
B	**ABSTRACT OF RESEARCH**
	(An abstract of between 100 and 200 words must be prepared in Bahasa Malaysia and in English. This abstract will be included in the Report of the Research and Innovation Section at a later date as a means of presenting the project findings of the researcher/s to the University and the community at large)

Hereditary nonpolyposis colorectal cancer (HNPCC) is caused by germline mutations in any of the mismatch repair (MMR) genes; MLH1, MSH2, MSH6 and PMS2 including EPCAM gene which is located upstream the MSH2 gene. This study aimed to investigate the underlying genetic variants in Malay HNPCC and other possible genes contributing to the risk of HNPCC. Thirty-two Malay HNPCC patients' samples were analyzed by using immunohistochemistry and direct DNA sequencing of MLH1 and MSH2 genes. Seven patients with intact protein expression were selected for further whole genome sequencing. Seven possible missense mutations and seven single nucleotide polymorphisms (SNPs) were discovered. By the whole genome sequencing data, a number of insertions and deletions (indels) and SNPs were identified. Nine rare variants from seven genes were also discovered in this study. Of the seven genes, two genes; CDK11B was known to play a role in cell cycle progression and MUC6 was associated with the outcome of colorectal cancer. A more comprehensive study and analysis in larger population is required to determine more conclusively the pathogenic nature of the genetic variants predicted in silico in the current study.

Kanser kolorektal bukan poliposis yang diwarisi (hereditary nonpolyposis colorectal cancer, HNPCC) berpunca daripada mutasi dalam gen pembaikan ketidakpadanan (Mismatch Repair gene, MMR gen) MLH1, MSH2, MSH6 and PMS2 termasuk gen EPCAM yang berada pada kedudukan atas gen MSH2. Kajian ini bertujuan untuk mengkaji variasi genetik asas pada pesakit Melayu yang menghidap kanser kolorektal bukan poliposis yang diwarisi dan gen yang berpotensi menyumbang ke arah risiko HNPCC. Sampel daripada 32 orang pesakit Melayu telah dianalisis menggunakan immunohistokimia dan penjujukan DNA gen MLH1 dan MSH2. Tujuh pesakit dengan yang menunjukkan ekspresi protein telah dipilih untuk penjujukan DNA yang menyeluruh. Dengan penjujukan DNA yang menyeluruh, terdapat penyisipan dan pemotongan dalam jujukan DNA serta polimorfisma nukleotida tunggal telah dikenal pasti. Sembilan varian yang jarang dijumpai dari tujuh gen juga telah dikenal pasti dalam kajian ini. Daripada tujuh gen tersebut, 2 gen, CDK11 diketahui berperanan dalam perkembangan kitaran sel dan MUC6 mempunyai perkaitan dengan kanser usus. Kajian dan analisis yang lebih komprehensif dalam populasi yang besar diperlukan untuk penetuan yang lebih konklusif tentang sifat variasi genetik yang dijangkan melalui siliko dalam kajian ini.

C BUDGET & EXPENDITURE

i

Total Approved Budget :

Total Expenditure :

Balance :

Percentage of Amount Spent (%) :

 # Please attach final account statement (eStatement) to indicate the project expenditure

ii **Equipment Purchased Under Vot 35000**

No.	Name of Equipment	Amount (RM)	Location	Status
-	-	-	-	-