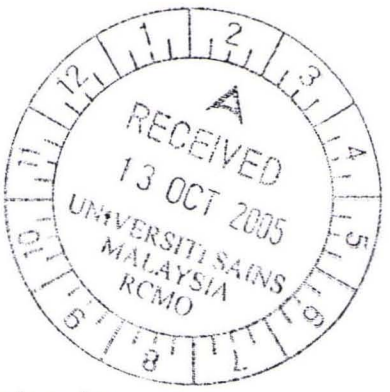
USM J/P – 06

BAHAGIAN PENYELIDIKAN & PEMBANGUNAN
CANSELORI
UNIVERSITI SAINS MALAYSIA



Laporan Akhir Projek Penyelidikan Jangka Pendek

1) Nama Penyelidik: Dr Narazah Mohd Yusoff

Nama Penyelidik- Penyelidik Lain (Jika berkaitan) : Prof Madya Dr Hans van Rosterberghe

2) Pusat Pengajian/Pusat/Unit: Institut Perubatan dan Pergigian Termaju

3) Tajuk Projek: Study of Bil-Uridine Diphosphate Glucuronyl Transferase (**BIL-UDGPT- 1**) Mutation in Neonatal Hyperbilirubinaemia with Glucose-6-Phosphate Dehydrogenase Deficiency. Nombor Geran: 304/PPSP/6131289

4) (a) Penemuan Projek/Abstrak

(Perlu disediakan makluman di antara 100-200 perkataan di dalam Bahasa Malaysia dan Bahasa Inggeris. Ini kemudiannya akan dimuatkan ke dalam laporan Tahunan Bahagian Penyelidikan & Pembangunan sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti).

Background: Gilbert syndrome is caused by defects in the uridine diphosphate– glucuronosyl-transferase 1A1 (*UGT1A1*) gene. These mutations differ among different populations and many of them have been found to be genetic risk factors for the development of neonatal jaundice.
Objectives: The objective was to determine the frequencies of the following mutations in the *UGT1A1* gene: $A(TA)_7TAA$ (the most common cause of Gilbert syndrome in Caucasians), G71R (more common in the Japanese and Taiwanese population) and G493R (described in a homozygous Malay woman with Crigler-Najjar syndrome type 2) in a group of Malaysian babies with hyperbilirubinaemia and a group of normal controls.
Methods: The GeneScan fragment analysis was used to detect the $A(TA)_7TAA$ variant. Mutation screening of both G71R and G493R was performed using denaturing high performance liquid chromatography (dHPLC).
Results: Fourteen out of 55 neonates with hyperbilirubinaemia (25%) carried the $A(TA)_7TAA$ mutation (10 heterozygous, 4 homozygous). Seven out of 50 controls (14%) carried the mutation (6 heterozygous, 1 homozygous). The allelic frequencies for hyperbilirubinaemia and control patients were 16% and 8% respectively ($p = 0.20$). Heterozygosity for the G71R mutation was almost equal among both groups (5.5% for hyperbilirubinaemia patients and 6.0% for controls; $p = 0.61$). One subject (1.8%) in the hyperbilirubinaemia group and none of the controls were heterozygous for the G493R mutation ($p = 0.476$).
Conclusions: The $A(TA)_7TAA$ seems more common than the G71R and G493R mutations in the Malaysian population.

Sindrom Gilbert berpunca daripada keabnormalan pada gen uridine diphosphate-glucuronosyl-transferase 1A1 (*UGT1A1*). Mutasi-mutasi ini berbeza bagi setiap populasi dan kebanyakannya didapati menjadi faktor genetik bagi jaundis di kalangan neonat. Objektif kajian ini adalah untuk mengira frekuensi mutasi-mutasi berikut pada gen *UGT1A1*: $A(TA)_7TAA$ (penyebab yang lazim bagi sindrom Gilbert di kalangan orang-orang Kaukasia), G71R (penyebab utama pada populasi Jepun dan Taiwan) dan G493R (dijumpai pada wanita Melayu yang membawa mutasi homozigus bagi sindrom Crigler-Najjar jenis ke-2) di dalam sekumpulan bayi Melayu yang mengalami hiperbilirubinemia dan sekumpulan bayi normal sebagai kawalan serta mengaitkan positiviti mutasi-mutasi ini dengan hiperbilirubinemia pada neonat. Analisis serpihan penyaringan gen (GeneScan) telah digunakan untuk mengesan varian $A(TA)_7TAA$. Penyaringan mutasi kedua-dua G71R dan G493R telah dijalankan dengan menggunakan kromatografi cecair denaturasi berprestasi tinggi [Denaturing high performance liquid chromatography (DHPLC)]. Seramai 14 daripada 55 orang neonat dengan hiperbilirubinemia (25%) membawa mutasi $A(TA)_7TAA$ (10 heterozigus, 14 homozigus). Seramai 7 daripada 50 kawalan (14%) membawa mutasi ini (6 heterozigus, 1 homozigus). Frekuensi-frekuensi alel bagi bayi hiperbilirubinemia dan kawalan adalah masing-masing 16% dan 8% ($p = 0.20$). Heterozigositi mutasi G71R adalah lebih kurang sama bagi kedua-dua kumpulan (5.5% bagi bayi hiperbilirubinemia dan 6% bagi kawalan; $p = 0.61$). Seorang neonat (1.8%) dari kumpulan hiperbilirubinemia dan tiada neonat dari kumpulan kawalan mengalami mutasi heterozigus bagi G493R ($p = 0.476$). Kesimpulannya, $A(TA)_7TAA$ lebih ketara daripada mutasi G71R dan G493R di dalam populasi Melayu.

(b) Senaraikan kata kunci ysng digunakan di dalam abstrak:

Bahasa Malaysia	**Bahasa Inggeris**
Neonatal jaundice	jaundis neonat
uridine diphosphate–glucuronosyltransferase 1A1	sama
mutations	mutasi
UGT1A1 gene	*UGT1A1* gene
Gilbert syndrome	sindrom Gilbert
denaturing high performance liquid chromatography	sama
GeneScan	GeneScan
Malaysia	Malaysia

5) Output Dan Faedah Projek

(a) Penerbitan (termasuk laporan/kertas seminar)
(Sila nyatakan jenis, tajuk, pengarang, tahun terbitan dan di mana telah diterbit/dibentangkan)

Bil	Jenis	Tajuk	Pengarang	Tahun	Tempat Terbit/Bentang
1	Abstrak	Analysis of A211 (G71R) Mutation of the UGT1A1 Gene in Neonatal Hyperbilirubinaemia in Malays	Surini Y, van Rosterberghe, Norlelawati AT, Abdul Aziz I, Noraida R, Nishio H, Matsuo M, Narazah MY	22-23 Mei 2004	*Supplement in The Malaysian Journal of Medical Sciences*. 11 (2). 96. 2004
2	Abstrak	Identification of UGT1A1 Gene Mutation in Babies with Early Onset of Neonatal Jaundice	Norlelawati AT, van Rosterberghe, Sutomo R, Selamah G, Nishio H, Matsuo M, Narazah MY	22-23 Mei 2004	*Supplement in The Malaysian Journal of Medical Sciences*. 11 (2). 96. 2004
3	Abstrak	Frequency of G->C1477 & G->A211 Mutations of the UGT1A1 Gene in the Malay ulation	Surini Y, van Rosterberghe, Narazah MY, Norlelawati AT, Nishio H, Matsuo M	16-21 Nov 2004	Biopolis, Singapore, 5th HUGO Pacific meeting & 6th Asia-Pacific Conference on Human Genetics
4	Penerbitan	Screening for G71R mutation of the UGT1A1 gene in the Javanese-Indonesian and Malay-Malaysian populations.	Sutomo R, Talib NA, Yusoff NM, Van Rostenberghe H, Sadewa AH, Sunarti, Sofro AS, Yokoyama N, Lee MJ, Matsuo M, Nishio H.	Volume 46 Issue 5 Page 565 - October 2004 doi:10.1111/j.1442-200x.2004.01959.x	*Pediatrics International*
5	Penerbitan	Frequencies of $A(TA)_7TAA$, G71R and G493R Mutations of the *UGT1A1* Gene in the Malaysian Population	Surini Yusoff, Hans Van Rostenberghe, Narazah M Yusoff,Norlelawati A. Talib, Noraida Ramli,N.Zainal A.N.Ismail W.Pauzi W.Ismail, Masafumi Matsuo, Hisahide Nishio	89(3):171-176 [Epub ahead of print] PMID: 16210851 [PubMed - as supplied by publisher]	*Journal of Biology of the Neonate. Biol Neonate*. 2005 Oct 6
6	Penerbitan	Association of multiple risk factors for neonatal jaundice.	Van Rostenberghe, H., Yusoff, S., Ramli, N., Yusoff, N.M., Ismail, W.P., Matsuo, M. and Nishio, H.	2005	Submitted for publication in *The Journal of Paediatrics and Child Health* on July 2005.
7.	Penerbitan	Lessons from the molecular biology of neonatal hyperbilirubinemia	Van Rostenberghe, Yusoff, N.M., R Noraida, Nishio, H., Matsuo, M., WI Wan Fauzi	2004	*Proceedings from 13th Congress of Federation of Asia & Oceania Perinatal Societies,* KL Malaysia April 14-18, 2004

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US dout MAJAL 29838

8.	Abstrak	Two Non-related babies with ABO incompatibility, negative direct Coombs test and a double mutation in the *UGT1A1* gene.	Ramli, N., Yusoff, S., Rahim, W., Yusoff, N.M., Nishio, H., Matsuo, M. and Van Rostenberghe, H	2005	*Supplement in The Malaysian Journal of Medical Sciences*. 12 (1). 43. (2005)
9.	Abstrak	A(TA)7TAA variant of the *UGT1A1* gene in Malaysian neonates with neonatal jaundice.	Yusoff, S., Van Rostenberghe, H., Yusoff, N.M., Sidek, M.R., Ramli, N., Wan Pauzi, W.I., Matsuo, M. and Nishio, H.	2005	*Supplement in The Malaysian Journal of Medical Sciences*. 12 (1). 42. 2005

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(b) Faedah- Faedah Lain Saperti Perkembangan Produk, Prospek Komersialisasi Dan Pendaftaran Paten.
(Jika ada dan jika perlu, sial gunakan kertas berasingan)

TIADA

(b) Latihan Gunatenaga Manusia

i) Pelajar Siswazah: 1 orang pelajar RKLA Surini bt Yusoff
1 orang pelajar M Med Haematology –
Dr Norlelawati Abu Talib

ii) Pelajar Prasiswazah: TIADA

iii) Lain-lain: TIADA

6. Peralatan Yang Telah Dibeli:

TIADA

UNTUK KEGUNAAN JAWATANKUASA PENYELIDIKAN UNIVERSITI

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