UNIVERSITI TEKNOLOGI MARA

REPROGRAMMING FORESKIN FIBROBLAST CELLS FROM HAEMOPHILIA TYPE-A PATIENTS INTO INDUCED PLURIPOTENT STEM CELLS

NOOR SABIRAH BINTI HUSIN

MSc

November 2017

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Noor Sabirah binti Husin
Student I.D. No	:	2013689752
Programme	:	Master of Science (Biochemistry) – MD751
Faculty	:	Medicine
Thesis Title	:	Reprogramming Foreskin Fibroblast Cells from Haemophilia Type-A Patients into Induced Pluripotent Stem Cells
Signature of Student	:	……
Date	:	November 2017

ABSTRACT

Induced Pluripotent Stem Cells (iPS cells) has an enormous potential in clinical application for example in the modelling of haemophilia. Studies on human pluripotent stem cells give hope to formulate potential cellular therapies for disease modelling. This study was designed to reprogram fibroblast cells from haemophilia type-A patients into iPS cells using four different techniques. Enzyme dissociation and explant culture technique were used to isolate primary cell fibroblast from haemophilia type-A patient. The enzymatic dissociation technique required three days to develop into fibroblast cells compared to explant culture which required 10 days in culture. Properties of the iPS cells depended on the reprogramming method. Morphological characteristics of iPS cells were observed only in Stemgent mRNA and Neon ® Reprogramming techniques. Expressions of pluripotency were verified using pluripotency markers. Downregulated and upregulated gene expression were analysed using qRT-PCR. This study provides new information on the development of haemophilia modelling, based on patient-specific iPS cells using integration-free methods.

ACKNOWLEDGEMENT

"Allah will raise up, to (suitable) ranks and (degrees), those of you who believe and who have been granted knowledge. And Allah is well-acquainted with all you do"
(Quran, Chapter Al – Mujadilah, verse 11)

In the name of Allah, the Most Gracious and the Most Merciful,

With a humble heart, I begin my expression with a verse of Quran which encourages me to seek knowledge. Highest gratitude to Almighty Allah, who guides and gives me hope along with my research journey. Not to forget, our greatest role model, Prophet Muhammad (peace be upon him), who guided us with his Sunnah and revelation to gain as much knowledge as we can together with noble moral values.

Bounty of thankfulness to my respected supervisor, Colonel Dr Amir Muhriz Abdul Latiff who has always been a kind and supportive lecturer. Full of wisdom and commitment, he has guided me throughout this challenging yet memorable journey. For the rest of my co-supervisor, Dr Siti Hamimah Sheikh Abdul Kadir, Assoc. Prof. Dr Syahrilnizam Abdullah from Universiti Putra Malaysia and Dato' Dr Faraizah from National Blood Centre, Kuala Lumpur, many thanks to all of you for your encouragement. Special appreciation to our collaborators from Epigenetics and Cell Fates Laboratory, Institute of Molecular and Cell Biology, A*Star Institute, Biopolis, Singapore, Dr Loh Yuin Han Jonathan who encouraged me a lot and gave me full of support in my research. Not to forget, his officer, Hong Yu Chen who has the perseverance to teach me and Yang Bin Xia a postdoctoral student who gave me continuous moral support.

My special and heartily thanks to our Deputy Dean of Postgraduate Studies and Professional Training, Faculty of Medicine, Prof. Dr. Azian Abd Latiff who is endlessly supports me. She also trusted me in handling the *"Postgraduate Colloquium on Medical Sciences (PCOMS 2015)"*. PCOMS 2015 was a memorable experience during my postgraduate study, which polished my leadership skills, broaden my ideas in the field of medical research and social networking. Not forgetting also her staff, Puan Nurhidayah Abdul Rahim and Encik Mohd Ahid Naupal on unwavering assistance in helping me throughout my postgraduate process.

Generous appreciation especially to my beloved husband Mohd Fandi Ahmad, my special friends, Nurul Atiqah Mohd Mokhsin, Mastura Abd Malek, Farah Amalina Mohd Affandi, Siti Munirah Md Noh, Nur Hidayah Reshidan, Dr. Azlindarita @ Aisyah Mohd Abdullah, Dr Roihan Awg Isa, Nur Hafizah Md Shaari, Khairul Fidaa' Khairul Bazli, Marlini Mahadzar, Nurul Ain Noorjamal, Ismanurain Ibrahim and Izyan Hazwani Baharuddin for their endless moral support. Not forgetting all staff of Institute of Medical Molecular Biotechnology (IMMB) especially to Puan Norita Salim, Encik Mohd Akmal Kamarudin and Datin Zuraini Dollah who assisted me during this study. Last but not the least, I would like to thank my mother Puan Sakinah Saari, my late father, Almarhum Husin Hanapi, my siblings, Mohd Amran, Mohd Ellyas, Noor Fazira and Muhammad Yasin for their understanding and prayers. Jazakumullahu kheyran kathiran.

TABLE OF CONTENTS