UNIVERSITI PUTRA MALAYSIA

ANALYSIS OF HSP27, APC AND β-CATENIN EXPRESSIONS IN GASTRIC CANCER, CHRONIC ATROPHIC GASTRITIS AND HELICOBACTER PYLORI-ASSOCIATED CHRONIC GASTRITIS

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By

TAY TAN CHOW

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

January 2013

DEDICATIONS

Specially dedicated to

My parents, sisters, brother and

Whom I love

For their invaluable love, endless support, understanding, encouragement and patience

Without them

I doubt this thesis should ever have been completed

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Science

ANALYSIS OF HSP27, APC AND β-CATENIN EXPRESSIONS IN GASTRIC CANCER, CHRONIC ATROPHIC GASTRITIS AND *HELICOBACTER PYLORI*-ASSOCIATED CHRONIC GASTRITIS

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Chair: Professor Dr. Hairuszah Ithnin, MD, MPath

Faculty: Institute of Bioscience

Gastric cancer has been noted to cause high mortality since decades ago. It is the seventh most common cancer in Malaysia. It has been said that it is a potentially curable disease if there is an efficient diagnosis of early gastric cancer. Therefore, there have been many studies to identify the biomarkers of gastric cancer but unfortunately until today, none has been found to be reliable. This preliminary study was carried out to investigate the role of Hsp27, APC and β-catenin as a possible biomarker of gastric cancer. Besides, the protein expression levels of Hsp27, APC and β-catenin in the precursor lesions were investigate. A total of 48 gastric cancer, 56 chronic atrophic gastritis and 55 *Helicobacter pylori*-associated chronic gastritis were analyzed by immunohistochemistry. In addition, 30 each from gastric cancer, chronic atrophic gastritis, *Helicobacter pylori*-associated chronic gastritis and including normal samples

were extracted and analyzed with Western blot. Our study demonstrated significant increased of Hsp27 in 97.9% (47/48) gastric cancer, 96.4% (54/56) chronic atrophic gastritis and 96.4% (53/55) *Helicobacter pylori*-associated chronic gastritis. These expressions were closely correlated with intestinal type gastric cancer (P= 0.001, correlation coefficient= 0.460) as well as moderately and well differentiated gastric cancer (P= 0.024, correlation coefficient= 0.326). For APC, there were significant increased in 83.3% (40/48) gastric cancer, 89.3% (50/56) chronic atrophic gastritis and 83.6% (46/55) *H. pylori*-associated chronic gastritis. For β-catenin, there were significant increased in 56.3% (27/48) gastric cancer, 25.0% (14/56) chronic atrophic gastritis and 18.2% (10/55) *H. pylori*-associated chronic gastritis which showed positive immunoreactivity. There was significant correlation between β-catenin expression and age in chronic atrophic gastritis (P= 0.038, correlation coefficient= 0.278). By using Western Blot, the results showed that the Hsp27 expressions were shown to be significant increased in gastric cancer and chronic atrophic gastritis when compared to normal tissues. However, decreased Hsp27 expression was found in *H. pylori*-associated chronic gastritis. In conclusion, our findings suggests that Hsp27, APC and β-catenin may play a role as possible biomarkers in gastric cancer and precursor lesions since significant increased in protein expression was observed. The results also suggested that deregulated Hsp27, APC and β-catenin occurred as early as in precursor lesions prior to gastric cancer development. Further studies should be performed to further elucidate the role of Hsp27, APC and β-catenin as biomarkers in gastric cancer.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

ANALISIS PENZAHIRAN HSP27, APC DAN β-CATENIN DALAM KANSER PERUT, GASTRITIS KRONIK ATROPIK DAN GASTRITIS KRONIK-*HELICOBACTER PYLORI*

Oleh

TAY TAN CHOW

Januari 2013

Pengerusi: Professor Dr. Hairuszah Ithnin, MD, MPath

Fakulti: Institut Biosains

Kanser perut menyebabkan kadar kematian yang tinggi sejak beberapa dekad dulu. Ia merupakan kanser yang ketujuh paling lazim di Malaysia. Ia dikatakan sebagai penyakit yang berpotensi boleh pulih sepenuhnya jika terdapat diagnosis yang cekap pada peringkat awal kanser perut. Oleh itu, terdapat banyak kajian untuk mengenalpasti biopenanda kanser perut tetapi malangnya sehingga ke hari ini, tiada satu pun yang didapati boleh dipercayai. Kajian awal ini dijalankan untuk mengaji peranan Hsp27, APC dan β-catenin sebagai biopenanda kanser perut. Selain itu, tahap penzahiran protein Hsp27, APC dan β-catenin dalam lesi precursor juga dikajikan. Sebanyak 48 kanser perut, 56 gastritis kronik atropik dan 55 gastritis kronik-*Helicobacter pylori* telah dianalisiskan dengan teknik imunohistokimia. Di samping itu, 30 sampel dari setiap kanser perut, gastritis kronik atropik, gastritis kronik-*Helicobacter pylori* dan termasuk

tisu normal perut telah dianalisiskan dengan pemblotan Western. Kajian kita menunjukkan peningkatan penzahiran Hsp27 yang signifikan dalam 97.9% (47/48) kanser perut, 96.4% (54/56) gastritis kronik atropik dan 96.4% (53/55) gastritis kronik-*Helicobacter pylori*. Penzahiran protein Hsp27 berkait rapat dengan kanser perut jenis intestinal (P= 0.001, pekali kolerasi= 0.460) dan kanser perut jenis pembezaan sederhana dan sempurna (P= 0.024, pekali kolerasi= 0.326). Untuk APC, terdapat peningkatan penzahiran yang signifikan dalam 83.3% (40/48) kanser perut, 89.3% (50/56) gastritis kronik atropik dan 83.6% (46/55) gastritis kronik-*H. pylori*. Untuk β-catenin, terdapat juga peningkatan penzahiran yang signifikan dalam 56.3% (27/48) kanser perut, 25.0% (14/56) gastritis kronik atropik dan 18.2% (10/55) gastritis kronik-*H. pylori* yang menunjukkan imunoreaktif yang positif. Terdapat hubungan yang signifikan di antara penzahiran β-catenin dan umur dalam gastritis kronik atropik (P= 0.038, pekali kolerasi= 0.278). Dengan menggunakan pemblotan Western, keputusan menunjukkan bahawa penzahiran protein Hsp27 ditunjukkan ada peningkatan yang signifikan dalam kanser perut dan gastritis kronik atropik apabila dibandingkan dengan tisu normal perut. Walau bagaimanapun, penurunan penzahiran protein Hsp27 didapati dalam gastritis kronik-*H. pylori* apabila dibandingkan dengan tisu perut yang normal. Sebagai kesimpulan, penemuan kita mencadangkan bahawa Hsp27, APC dan β-catenin menpunyai kemungkinan boleh memainkan peranan sebagai biopenanda kanser perut dan lesi precursor. Keputusan juga mencadangkan bahawa nyahkawal selia Hsp27, APC dan β-catenin berlaku seawal dalam lesi prekursor sebelum pembentukkan kanser perut. Kajian pelanjutan harus dijalankan untuk menjelaskan peranan Hsp27, APC dan β-catenin sebagai biopenanda kanser perut.

ACKNOWLEDGEMENTS

First and foremost, I would like to acknowledge my deepest gratitude and appreciation to my project supervisor, Professor Dr. Hairuszah Ithnin for her invaluable guidance, endless support and unfailing patience throughout the whole study. Without her support, nothing would have been accomplished.

In addition, I would like to express my gratitude to my co-supervisor, Dr. Norhafizah Mohtarrudin for her constructive advice and priceless comments throughout the entire course of this research. I also would like to express my gratitude to Dr. Razana Mohd Ali for her suggestions and guidance throughout the whole project.

My sincere gratitude is also accorded to Dr. Arni Talib for her generosity in sharing the tissue samples and patients clinical information to make this study possible. Not forgetting all the staff of the Department of Pathology, Kuala Lumpur Hospital for their kind assistance and tolerance during the samples collection at the department.

I would also like to acknowledge and thank all laboratory assistants of Department of Pathology, Faculty of Medicine and Health Sciences especially Mr. Anthonysamy a/l Arokiasamy, Mrs. Juita Chupri, Mrs. Normah Ibrahim and Ms Zamzarina Ahmad Bajari whom had helped and assisted me to get access to the equipment and facilities required to complete this project.

Moreover, I would like to thank all the postgraduate students of Laboratory of Histopathology and Laboratory of Hematology especially Ms Nurulhafizah Samsudin, Mr. Edwin Shiaw, Mr. Ahmad Zharif Ismail, Ms. Teh Lai Kuan, Ms. Lim Wai Feng and Mr. Lee Tze Yan for all their priceless comments, suggestions, guidance and assistance.

I also would like to extend my heartfelt gratitude to friends, Mr. Ch'ng Wei Choong and Mr. Lim Jin Yew, who have never rejected my request for assistance and support throughout my whole project especially in the teaching of laboratory techniques and skills. I am deeply indebted. Last but not least, words cannot describe my gratitude to my family and my girlfriend for their tolerance and moral support, without whom nothing would have been possible. Thanks a million.

I certify that a Thesis Examination Committee has met on 23rd January 2013 to conduct the final examination of Tay Tan Chow on his thesis entitled "**Analysis of Hsp27, APC and β-catenin Expressions in Gastric Cancer, Chronic Atrophic Gastritis and *Helicobacter pylori*-Associated Chronic Gastritis**" in accordance with the Universities and university Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P. U. (A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science in Medical Biotechnology.

Members of the Thesis Examination Committee were as follows:

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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Date:

DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other instituition.

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TAY TAN CHOW

Date: 23rd January 2013

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