UNIVERSITI TEKNOLOGI MARA

EPITHELIAL TO MESENCHYMAL TRANSITION IN MDA-MB-231 AND MCF-7 BREAST CANCER CELL LINES

AMIRUL IQHWAN BIN AZLAN NIZAM

BACHELOR OF PHARMACY

Dissertation submitted in partial fulfillment of the requirements for the Bachelor of Pharmacy (Hons.)

Faculty of Pharmacy

June 2014

ACKNOWLEDGEMENT

All the praise to the Creator for blessed me time, good health, strength and patience in completing this study successfully. First of all, I would like to express my deepest sense of gratitude to my supervisor, Dr.Aisyah Hasyila for her advice to the changes, ideas, and amendments to be made to this study, as well as for her interest shown. Without her help, the study might have not possible to be accomplished.

My thanks and appreciation also goes to my friend, Mohamad Huzaidi bin Rabbi who helped me finishing my work. Not forgotten to postgraduate students in tissue culture lab of Faculty Pharmacy which help me in doing lab work, handling equipment and share their knowledge with me.

Special thanks is also given to cell imaging centre coordinator Dr.Zolkapli bin Ishak and lab assistant Puan Norhayati for allow me to use the equipment there and help me to use the equipment and share some important information about the life cell imaging protocol.

Last but not least, greatest thanks to my family members for their tolerance of my absences, physically, and emotionally. I am blessed by their unconditional love which had indeed given me moral support and motivation to stay focused until this project was completely done.

TABLE OF CONTENT

ABSTRACT

Breast cancer is the most regular type of cancer which is diagnosed among women in the world. Breast cancer progression leads to increase in mortality rate. It can be easily spread to all part of the body due to metastasis. Metastasis can be induced via a process called epithelial to mesenchymal transition (EMT). During this process, the cell line initially with an epithelial characteristic will undergo transition to acquire mesenchymal properties which lead to increase in invasiveness, migratory capacity, resistance towards apoptosis, and the production of extracellular matrix in the cells. This transition can be induced by certain agents such as epidermal growth factor (EGF), hypoxia, and tumour necrosis factor (TNF). EMT can be indicated by morphological changes of the cell lines as well as the changes in biomarkers activity like twist, snail, and vimentin. Breast cancer cell lines consist of four general morphological characteristics which are round, mass, grape-like, and stellate type. Each type of morphology has their own characteristics and these will influence their metastatic ability. Breast cancer cell lines also have different gene cluster and receptor which indicate the characteristics of the cell lines and the prognosis outcome of the treatment. This study will focus on the morphology of MCF-7 breast cancer line in comparison with morphology of MDA-MB-231 and the characteristics that lead them to undergo metastasis through epithelial to mesenchymal transition process. The results suggested that both of these cells have the morphology and characteristics to undergo EMT.

CHAPTER 1

INTRODUCTION

1.1 Metastasis and breast cancer

Metastasis process involves dissemination of a primary tumour to other parts of the body. A series of steps is needed for the cancer cell to successfully colonise a distant area .Metastasis has been linked with poor prognosis. Normally, patients who have localised tumours have a higher chance of survival compare to those patients with metastatic tumours (Hunter et al., 2008). By the time of diagnosis, evidence has shown that about 60% to 70% of cancer patients have begun the metastatic process(Hunter, Crawford, & Alsarraj, 2008). Furthermore although the patients have no evidence of spreading of tumour during diagnosis, they are also at risk for metastatic disease(Hunter et al., 2008). Breast cancer is one of the cancers which are prone to metastasise.

According to the American Cancer Society 2013, about 1 in 8 person of the U.S. women may have invasive breast cancer (Desantis et al., 2013). In 2013, about 232,340 new cases of invasive breast cancer will be expected to be diagnosed in women in the U.S and 2,240 in men (Desantis, Ma, Bryan, & Jemal, 2013). Besides that, there are about 64,640 new cases of non-invasive breast cancer (Desantis et al., 2013). Furthermore, about 40,030 deaths are expected in 2013 which is the second highest mortality rate of cancer next to lung cancer (Desantis et al., 2013).