

CHAPTER I

INTRODUCTION

1. Rationale and background

Cervical cancer is one of important public health problems in Thailand, which is a second most common cancer with an age standardized incidence rate at 16.7 per 100,000 women in the year 2008 (Khuhaprema et al., 2013). The statistics from National Cancer Institute Thailand in 2012 has been shown that the numbers of new cervical cancer patients was 340 cases or about 14.39% of total cancer cases (National Cancer Institute, 2014). Moreover, cervical cancer is a major cause of death among Thai women and mortality rate are increasing every year (Public Health statistics, 2013). The finding for women at high risk and diagnosis in early stage of cervical cancer is a key strategy for prevention and control the cancer (National Cancer Institute, 2014). The major cause of cervical cancer is human papilloma virus (HPV) infection (Rathfisch et al., 2015). However, cervical cancer has been found to be associated with other environmental factors and host susceptibility such as receiving carcinogen and/or radiation as well as genetic background (Calhoun et al., 2002; Nunobiki et al., 2011). Therefore, genetic polymorphism of each individual may contribute to development of cervical cancer.

Multidrug resistance 1 gene (MDR1) is located on chromosomal region 7q21 of human. The human *MDR1* encodes an ATP-dependent efflux transporter with molecular weight 170 kilo Dalton (kDa), P-glycoprotein (P-gp) (Fung and Gottesman, 2009). P-gp is located on plasma membrane with function as a biological barrier by remove various substances from inside to outside the cells. This protein pump is expressed in both normal cells and cancer cells such as breast, colon, kidney and cervix (Marzolini et al., 2004). In cancer cells, P-gp pumps many chemotherapeutic agents, substrates of P-gp out of the cancer cells result in chemotherapy resistance in patients who are receiving chemotherapy (Johnatty et al., 2013). However, in normal cells, P-gp plays an physiological role in excretory function of human cells, which

protects and reduces intracellular accumulation of xenobiotic and potentially toxic substances (Wang et al., 2013).

MDR1 is a highly polymorphic gene with at least 50 single nucleotide polymorphisms (SNPs). The most three common SNPs that have been studied in several types of cancer and various populations are C1236T, G2677T/A and C3435T SNPs in exon 12, 21 and 26, respectively (Wang et al., 2013). Polymorphisms of *MDR1* were reported to be associated with developing of cancer due to the alteration of P-gp expression and activity (Penna et al., 2011). The reduction of P-gp activity may lead to increased accumulation of carcinogens in the normal cells and consequently resulting in increased risk for cancer development whereas elevation of P-gp activity may associated with reduction of cancer risk (Fung and Gottesman, 2009).

The *MDR1* polymorphism has been studied in several populations worldwide and various cancer conditions, but few reports exist regarding an association between *MDR1* polymorphism and cervical cancer in Thai women. Thus, the investigation of relationship of *MDR1* polymorphism with cervical cancer risk in Thai women is of interested.

2. Aim of this study

The present study aimed to determine the association between *MDR1* polymorphisms and the risk for cervical cancer in the Northeastern women of Thailand.

3. Scope and limitation of this study

3.1 Subjects of this study were recruited from Srinagarind Hospital, Khon Kaen University and Khon Kaen Hospital, Khon Kaen, Thailand.

3.2 Subjects were divided into two groups.

3.2.1 Cervical cancer group: women with invasive squamous cell carcinoma of cervix (SCCA).

3.2.2 Control group: healthy women without cervical cancer and/or pre-invasive lesion of the cervix.

3.3 The analysis of *MDR1* polymorphism was performed by real-time polymerase chain reaction (real-time PCR) assay.

3.4 After informative counseling, questionnaire and informed consent were obtained from subjects.

4. Hypothesis of this study

MDR1 polymorphism was associated with the risk for cervical cancer in Thai women in the Northeast of Thailand.

5. Anticipated outcomes

5.1 The genotype frequency of *MDR1* polymorphism in Thai women in the Northeast of Thailand was clarified.

5.2 The association between *MDR1* polymorphism and cervical cancer risk was beneficial to a clinical use with respect to prevention and treatment of cervical cancer.