

CHAPTER 1

INTRODUCTION

In the northern part of Thailand, especially in Chiang Mai, lung cancer is the most common malignancy and also the first cause of cancer death in both males and females. In 1993, the Cancer Committees of Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, reported that during 1988-1991 the annual average age-standardized incidence rates were 49.8 and 37.4 per 100,000 in males and females respectively (Vatanasapt *et al.*, 1993). This incidence in females was high in comparison with other countries. Furthermore, the incidence of lung cancer in Chiang Mai has been rising annually, the number of new cases observed in 1995 was twice of that observed in 1983. Several researchers carried out the etiology of the disease in this area. The reports showed that the incidence of the disease in males has been strongly related to inhalation of carcinogenic agents from cigarette smoking but the etiology factors in females has not been clarified (Vatanasapt *et al.*, 1995).

A collaboration between Faculty of Medicine, Chiang Mai University and Saitama Cancer Research Institute, Japan was founded to clarify the etiology of lung cancer in women residing in Chiang Mai in many aspects. The highest and lowest of the incidences of the disease were found in Saraphi and Chom Thong districts respectively (40.9 and 8.5 per 100,000) in spite of their cultural and occupational closenesses. The published results showed that there were no differences on rice and meat consumptions observed between the populations (Sone *et al.*, 1998). However,

females from Saraphi remarkably consumed less in both quality and variety of green or yellow fruits and confectionary than those from Chom Thong. Moreover, the epidemiological study including lifestyles, biochemical and molecular approaches were performed. Nakachi *et al.* (1999) suggested that chronic benign respiratory disease might be likely to be involved in the etiology of the disease in females from Saraphi.

It has been suggested that one of the causes of the respiratory disease is due to air pollution. The burning activities around the houses in these two areas, especially longan's leaves, and in the fields after harvesting of some other agricultural crops might be one of the major environmental risk factors. The smoke obviously yielded polycyclic aromatic hydrocarbons (PAHs) and particulate matter, which are the major groups of chemicals likely penetrating into the lung and associated with the adverse health effect, including lung cancer (Vinitketkumnuen *et al.*, 2002). However, the geographical locations of these two districts are rather different. Saraphi is an urban district situated in Chiang Mai-Lamphun Valley near the Northern Region Industrial Estate while Chom Thong is a hilly rural area. Therefore, the Saraphi population has the disadvantage of having all-year-round less air circulation than those in Chom Thong. Moreover, the accumulation of air pollutants from burning activities from engine fuel combustion and some other mutagens such as pesticides might be associated with the increasing risk of lung cancer in Saraphi population.

Biomonitoring and health risk assessment study has been available for investigation mortality incidence and potential regarding to exposure to hazardous environmental agents. The occurrence of these genotoxicants in the environment becomes a major concern of public health. A variety of approaches has been

employed by genetic toxicologists to detect both direct and inferred alterations of chromosome and/or DNA levels. The specific types of damage of chromosome and/or DNA structures can be used as valuable endpoints for investigation the effect of exposure to the genotoxic agents in human. As indicators of exposure, the changing in DNA and chromosome levels can be quite powerful tools that, in combination with independently derived genotoxic effect level, can play an important part in the risk assessment process (Salama *et al.*, 1999).

Recently, genotoxicity tests have been developed for screening and detecting clastogenic, mutagenic and/or carcinogenic activities. At the same time the tests have also been applied for the assessment of environmental exposure relating to human health risk. Classical cytogenetic methods such as chromosomal aberration and micronucleus test have been commonly used for clastogenic detection. Nevertheless, alkaline single cell gel electrophoresis (comet assay) has been developed and becoming routinely used for DNA damage detection due to its high reliability and sensitivity.

It is, therefore, necessary to start the surveillance of individuals who have not yet developed lung cancer but known to be at risk of having DNA damage from the genotoxins in their living environment in these 2 districts, in order to provide the information on exposure and health risk assessment for further effective prevention of health problems. For this purpose a variety of biomonitoring approaches have been available. We propose to use the short-term assays with such genetic endpoints as chromosomal aberration assay, micronucleus test and comet assay from peripheral blood lymphocytes of healthy subjects who have not developed lung cancer and are residing in the areas with difference in the incidences of lung cancer, Saraphi and

Chom Thong districts, in both genders concurrently. The information on genotoxic exposure and genetic damage measured by the endpoints from the tests should be used as the information for further assessment for prevention of adverse health outcomes.

The main objectives of the study are:

1. To determine whether genetic endpoints, namely chromosome aberration (CA), micronucleus (MN) tests and single cell gel electrophoresis (comet assay), could monitor the effect on genetic damage of healthy individuals who have not yet developed lung cancer, and residing in areas with different incidences of lung cancer, Saraphi and Chom Thong districts.
2. To evaluate whether the confounding factors influence the basal levels of the endpoints.
3. To assess the potential relationship between the genetic endpoints and environmental exposure in each population that should be used as an early warning signal for further prevention of adverse health outcomes.