

CHAPTER I

INTRODUCTION

1.1 RATIONALE

Hypohidrotic ectodermal dysplasia (HED) is a hereditary disease including anomalies derived from ectoderm. HED is characterized by reduced sweating (hypohidrosis), sparse hair (hypotrichosis) and multiple missing teeth (hypodontia). Several different genes in the EDA-NF- κ B signaling pathway have been found to be associated with HED. X-linked hypohidrotic ectodermal dysplasia (XLHED, OMIM 305100) is caused by mutations in the *EDA* gene, which encodes ectodysplasin. However, mutations in both the ectodysplasin receptor (*EDAR*) and the Ectodysplasin receptor-associated death domain (*EDARADD*) genes are associated with autosomal-recessive and -dominant HED.

Hypodontia, a common craniofacial anomaly, is frequently associated with other abnormalities or syndromes, such as ectodermal dysplasia and orofacial clefts.

Hypodontia is also a symbolic manifestation in HED patients. However, hypodontia can occur as an isolated condition known as non-syndromic hypodontia (OMIM 300606). To date, the *PAX9*, *MSX1*, *AXIN2*, *WNT10A*, and *EDA* mutations have been identified as the etiologies of selective tooth agenesis. Among these genes, only the *EDA* gene is associated with the X-linked mode of inheritance when mutated.

Molecular genetic analysis in patients with each disorder has been carried out in several populations, including American, Danish, Chinese, Korean, Pakistani and Japanese, but not in the Thai population. Therefore, I hypothesize that XLHED and

non-syndromic hypodontia in the Thai population may result from mutations in the *EDA* gene as well. Identification of these mutations should contribute to a better understanding of the molecular pathogenesis of these disorders.

1.2 OBJECTIVES

1.2.1 To identify *EDA* mutations in Thai patients affected with XLHED

1.2.2 To identify *EDA* mutations in Thai patients affected with non-syndromic hypodontia

1.3 HYPOTHESIS

H₀: *EDA* mutations are not detected in Thai patients affected with XLHED.

H₁: *EDA* mutations are detected in Thai patients affected with XLHED.

H₀: *EDA* mutations are not detected in Thai patients affected with non-syndromic hypodontia.

H₁: *EDA* mutations are detected in Thai patients affected with non-syndromic hypodontia.