CHAPTER I
INTRODUCTION

1.1 RATIONALE

Orofacial clefts are common congenital anomalies. The etiology of clefts is complex and involves both genetic and environmental factors (Ardinger et al., 1989; Shaw et al., 1996). It has been reported that several genes are responsible for syndromic cleft lip and cleft palate and some genes are correlated with non-syndromic forms (Stanier and Moore, 2004; Cobourne, 2004; Carinci et al., 2007). Those genes include homeobox gene MSX1 (Lidral et al., 1997), interferon regulatory factor 6 IRF6 (Hecht et al., 1992; Kondo et al., 2002), poliovirus receptor-like 1 PVRL1 (Sozen et al., 2001), p63 (Ianakiev et al., 2000; McGrath et al., 2001; Leoyklang et al., 2006), transforming growth factor beta-3 TGFβ3 (Lidral et al., 1998), and T-box transcription factor TBX22 (Braybrook et al., 2001; Braybrook et al., 2002; Marcano et al., 2004; Chaabouni et al., 2005; Suphapeetiporn et al., 2007).

TBX22 plays an important role in craniofacial development. Expression of TBX22 occurs during stages of palatogenesis. Expression of this gene involves the mesenchyme of the face, the base of the brain, the nasal, palatal, and mandibular processes, the base of the tongue, the odontogenic mesenchyme, and developing tooth buds. Recent studies have demonstrated that cleft palate and ankyloglossia in families with X-linked cleft palate are caused by mutations in TBX22 (Braybrook et al., 2001; 2002; Marcano et al., 2004; Chaabouni et al., 2005). Since cleft palate and
ankyloglossia have been observed in families with X-linked cleft palate, mutations in TBX22 may be associated with non-syndromic cleft palate and nonsyndromic ankyloglossia. Recent studies have shown that TBX22 mutations are a common cause of non-syndromic cleft palate (Marcano et al., 2004; Suphapeetiporn et al., 2007). However, the gene responsible for non-syndromic ankyloglossia has not been reported. The objectives of this study are to find relationships between TBX22 mutations and orofacial clefts and non-syndromic ankyloglossia. As TBX22 is expressed in odontogenic mesenchyme (Braybrook et al., 2002), I would like to clarify whether mutations in TBX22 are responsible for non-syndromic hypodontia. It is hoped that the findings will shed more light on the understanding of the roles of TBX22 in craniofacial development.

1.2 OBJECTIVES

1.2.1 To study if mutations in TBX22 are associated with non-syndromic and syndromic orofacial clefts.

1.2.2 To study if mutations in TBX22 are associated with non-syndromic ankyloglossia.

1.2.3 To study if mutations in TBX22 are associated with non-syndromic hypodontia.

1.3 HYPOTHESIS

H0: TBX22 mutations are not detected in patients with orofacial clefts, isolated ankyloglossia and isolated hypodontia.

H1: TBX22 mutations are detected in patients with orofacial clefts, isolated
ankyloglossia and isolated hypodontia.