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.