

TABLE OF CONTENTS

	PAGE
ACKNOWLEDGEMENTS	iii
ABSTRACT (THAI)	v
ABSTRACT (ENGLISH)	vii
LIST OF TABLES	xi
LIST OF FIGURES	xii
CHAPTER I INTRODUCTION	1
1.1 Rationale	1
1.2 Objective	2
1.3 Hypothesis	2
CHAPTER II REVIEW OF THE LITERATURE	4
2.1 Cleft lip with or without cleft palate	5
2.2 Ankyloglossia	18
2.3 Hypodontia	23
2.4 <i>TBX22</i> gene	30
CHAPTER III MATERIALS AND METHODS	38
3.1 Materials	38
3.1.1 Patients	38

	PAGE
3.1.2 PCR materials	39
3.2 Methods	40
2.2.1 DNA extraction	40
2.2.2 Polymerase chain reaction (PCR)	42
2.2.3 Gel electrophoresis	44
2.2.4 DNA sequencing	45
2.2.5 DNA sequence analysis	46
2.2.6 Protein sequence comparison	46
2.2.7 PolyPhen	47
CHAPTER IV RESULTS	48
CHAPTER V DISCUSSION	54
CHAPTER VI CONCLUSIONS	60
BIBLIOGRAPHY	61
APPENDICES	81
Appendix A List of patients in this study	82
Appendix B Coding sequence of <i>TBX22</i> (Exon1-8)	85
Appendix C <i>TBX22</i> amino acid sequence	90
CURRICULUM VITAE	93

LIST OF TABLES

TABLE	PAGE
3.1 The list of phenotype of patients in this study	39
3.2 Oligonucleotides and PCR conditions for <i>TBX22</i> analysis	40
4.1 Characteristic of patients and genetic variants in this study	49
A.1 Craniofacial genetics laboratory (CGL) DNA number and phenotype of all patients in this study	82

LIST OF FIGURES

FIGURE	PAGE
2.1 Scheme of symbolic representation for cleft lip and palate	6
2.2 Frontal view of facial development during the 4 th week	7
2.3 Frontal view of facial development during the 5 th and 6 th week	8
2.4 Hard palate formation during the 6 th week of embryonic life	8
2.5 Mandible formation	9
2.6 Frontal view of facial development during the 7 th week and 8 th week	9
2.7 Hard palate formation during the 7 th week of embryonic life	10
2.8 Hard palate formation during the 8 th week of embryonic life	10
2.9 Hard palate formation at the end of the 8 th week of embryonic life	11
2.10 Diagrams summarizing the possible fates of cells forming the Palatal midline seam	15
2.11 Various appearances of ankyloglossia	18
2.12 Frontal view of internal wall of primitive pharyngeal cavity during embryonic tongue development	20
2.13 Early stage of tooth formation	25
2.14 Middle stage of tooth formation	26

2.15	Pattern of gene expression in the developing tooth at embryonic day (E)10.5	27
2.16	Late stage of tooth formation	28
2.17	Genomic structure of <i>TBX22</i>	30
2.18	Sequence of the <i>TBX22</i> cDNA	31
2.19	<i>TBX22</i> expression	33
2.20	<i>TBX22</i> is expressed in the developing nasal septum but not in the fused palatal shelves.	34
2.21	<i>Tbx22</i> expression in developing lung epithelium and in developing whiskers of a developing mouse	35
2.22	Whole-mount, <i>in situ</i> , hybridization analysis of <i>Tbx22</i> expression during chick development	35
2.23	Pathologic variants of <i>TBX22</i> from previously reports	37
3.1	Diagram of DNA extraction from blood samples	42
3.2	Schematic drawing of the PCR cycle	43
3.3	Gel electrophoresis of exon 1-8 of <i>TBX22</i>	45
4.1	Characteristic of patient with <i>TBX22</i> mutation	50
4.2	Mutation analysis	51
4.3	<i>TBX22</i> protein sequence comparison between species	52
4.4	<i>TBX22</i> single nucleotide polymorphism (SNPs) in non-coding regions	53