TABLE OF CONTENS

	Page
ACNKOWLEDGEMENT	iii
ABSTRACT	iv
TABLE OF CONTENTS	viii
LIST OF TABLES	xi
LIST OF FIGURES	xiii
ABBREVIATIONS AND SYMBOLS	xiv
CHAPTER I: INTRODUCTION	
I. INTRODUCTION	1
II. LITERATURE REVIEW	10
2.1.Incidences of lung cancer in Thailand	10
2.2. The relationship between polymorphisms of xenobiotic metabolizing enzymes and susceptibility to lung cancer	12
2.3. The relationship between polymorphisms of DNA repairing enzyme [(human Oxoguanine Glycosylase-1(hOGG-1)] and susceptibility to lung cancer	21
2.4. The relationship between polymorphisms of p53 tumor suppressor gene and susceptibility to lung cancer	22
2.5. The relationship between polymorphisms of Matrix Metaloproteinase-1 (MMP-1) and susceptibility to lung cancer	24

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

2.6. Combination of susceptibility genotypes and the risk of lung cancer 25

2.7. Ethnic-dependent distribution of polymorphic genes 26

III. OBJECTIVES 28

CHAPTER II: MATERIALS AND METHODS 29

2.1. Study subjects 29

2.2. Extraction of DNA 31

2.3. Genotyping 33

2.3.1. PCR-RFLP (Polymerase Chain Reaction-Restriction Fragment Length Polymorphism) 34

(1) Detection of CYP1A1(Il462Val) polymorphism 35

(2) Detection of CYP1A1(MspI) polymorphism 35

(3) Detection of CYP2E1(DraI) and CYP2E1(PstI) Polymorphism 36

(4) Detection of MPO (AciI) polymorphism 37

(5) Detection of MMP1 (AluI) polymorphism 37

2.3.2. Multiplex PCR 39

2.3.3 Di-allele-specific amplification with artificially modified primers (diASA-AMP) 40

(1) Detection of p53 (Arg72Pro) polymorphism 41

(2) Detection of hOGG1 (Ser326Cys) polymorphism 42

2.4. Agarose gel electrophoresis 42

2.5. Statistical analysis 43

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

CHAPTER III: RESULTS 44

CHAPTER IV: DISCUSSION 66

REFERENCES 74

APPENDIX 85

CURRICULUM VITAE 87

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

LIST OF TABLES

Table	Page
2.1 Characteristic of lung cancer patients and control subjects	30
2.2 Lists of primer used in this study	32
2.3 Summary of genotyping methods used to detect each Polymorphisms	34
2.4 Conditions of PCR used to amplify DNA in order to detect polymorphism by PCR-RFLP	38
2.5 Lists of restriction enzymes and digestion conditions utilized in this study	38
2.6 Sizes of PCR products and RFLP pattern after restriction enzyme Digestion	39
2.7 The condition of multiplex PCR used to determine GSTM1 and GSTT1 genotypes	40
3.1 Distribution of genetic polymorphism between lung cancer cases and controls	50
3.2 Distribution of genetic polymorphism and lung cancer risk	53
3.3 Interaction of genetic polymorphism and gender on lung cancer risk	55
3.4 Effect of combined genetic polymorphisms on lung cancer risk	58
3.5 Interaction between combined genetic polymorphisms and gender on lung cancer risk	61
3.6 Interaction between combined genetic polymorphisms and gender and smoking status on lung cancer risk	63

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

3.7 Effect of muti-loci polymorphisms on lung cancer risk 65

4.1 Frequencies of gene polymorphisms in different ethnic group 69

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

LIST OF FIGURES

Figure	Page
1.1 Activation and inactivation of BaP	4
1.2. Cancer Registries in Thailand	11
1.3. Leading Cancers among Northern Thai Population by Registry in Northern Thailand.	12
1.4. Human CYP involved in xenobiotic metabolism	13
1.5 The GSTM1 gene	17
1.6 The GSTT1 gene	18
1.7 Diagram showing the role of hOGG1 in base-excision repairing system remove 8-OH-G in mammalian cells	21
2.1. Logic of SNP typing method by di-allele-specific-amplification with artificially modified primers	41
3.1. Representative agarose gel analysis of CYP1A1(MspI)	45
3.2. Representative agarose gel analysis of CYP1A1(Ilu462Val)	45
3.3. Representative agarose gel analysis of CYP2E1(PstI)	46
3.4. Representative agarose gel analysis of (CYP2E1(DraI)	46
3.5. Representative agarose gel analysis of MPO(AciI)	47
3.6. Representative agarose gel analysis of MMP-1(AluI)	47
3.7. Representative agarose gel analysis of GSTM1 and GSTT1	48
3.8. Representative agarose gel of hOGG1 polymorphism dentified by di-allele-specific amplification with artificially modified primers (diASA-AMP)	48
3.9. Representative agarose gel of p53 polymorphism identified by di-allele-specific amplification with artificially modified primers (diASA-AMP)	49

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

ABBREVIATIONS AND SYMBOLS

AMS	Associated Medical Sciences
µl	microliter
ml	milliliter
RE	restriction enzyme
ds	double strand
USA	United States of America
dNTP	deoxyribonucleotides triphosphate
bp	base pair
ng	nanogram
°C	degree celcius
µM	micromolar
mM	millimolar
s	second
pmol	picomole
Mg^{2+}	magnesium ion
$MgCl_2$	magnesium chloride
%	percentage
diASA-AMP	Di-allele-specific amplification with artificially modified primers (diASA-AMP)
PCR-RFLP	Polymerase Chain Reaction based Restriction Fragment Length Polymorphism
OR	Odds Ratio

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved

CI	Confidence Interval
g	gram
KOH	potassium hydroxide
M	molar
DNA	deoxyribonucleic acid
EDTA	ethylene diamine tetraacetic acid
TBE	tris-borate-EDTA
PAH	polycyclic aromatic hydrocarbon
BPDE	benzo (a) pyrene 7,8-diol-9,10 epoxide

ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่
Copyright© by Chiang Mai University
All rights reserved