CONTENTS

	Page
Acknowledgments	c
Abstract in Thai	d
Abstract in English	f
List of Tables	j
List of Figures	k
List of Abbreviations	1
Chapter 1 Introduction	1
1.1 Historical Background	1
1.2 Objectives	2
Chapter 2 Literature Review	3
2.1 Oral squamous cell carcinoma	3
2.1.1 Significance of Oral squamous cell carcinoma	3
2.1.2 Etiology of oral squamous cell carcinoma	3
2.1.3 Molecular pathogenesis of oral squamous cell carcinoma	4
2.1.4 Histologic features of oral squamous cell carcinoma	6
2.2 A disintegrin and metalloproteinase 9 (ADAM9)	7
2.2.1 ADAMs synthesis and structure	7
2.2.2 ADAM9 expression and function	8
2.2.3 ADAMs and cancer biology	10
2.2.4 ADAM9 and various types of cancer	11
2.2.5 ADAM9 and oral squamous cell carcinoma	13
Chapter 3 Materials and Methods	14
3.1 Immunohistochemical study	14
3.1.1 Sample selection	14
3.1.2 Data collection	15

	Page
3.1.3 Determination of ADAM9 expression in OSCC by	
Immunohistochemistry	15
3.2 In vitro studies	17
3.2.1 Cell lines and culture condition	17
3.2.2 Indirect immunofluorescence staining and flow cytometry	18
3.2.2 Isolation of total protein and Western blot hybridization	18
3.3 Statistical analysis	19
Chapter 4 Results	20
Chapter 4 Results 4.1 Immunohistochemical study	20
4.1.1 Demographic and clinicopathologic characteristics of OSCC cases	20
4.1.2 ADAM9 expression in OSCC specimens	
4.2 In vitro studies	26
4.2.1 Expression of membrane ADAM9 in some oral cancer cell lines	26
4.2.2 A significant increase in the expression of active ADAM9	
in oral cancer cell lines	27
4.2.3 Enhanced ADAM9 expression in differentiated HOKs	28
Chapter 5 Discussion	30
References	36
Appendix a an Suprange and a supra	43
Appendix A Certificate of ethical clearance	44
Appendix B Immunohistochemical score for ADAM9 expression	45
Curriculum Vitae	47

LIST OF TABLES

		U
Table 4.1	Clinicopathologic characteristics of OSCC cases	20
Table 4.2	A semi-quantitative analysis of the intensity score for ADAM9	
	expression in different histologic grading of OSCC	25

Page



ลิขสิทธิ์มหาวิทยาลัยเชียงใหม่ Copyright[©] by Chiang Mai University All rights reserved

LIST OF FIGURES

Figure 2.1	Structure of ADAM proteins	8
Figure 2.2	Ectodomain shedding by ADAM9	9
Figure 2.3	An overview of ADAMs in cancer biology	11
Figure 3.1	Four intensity scores	17
Figure 4.1	Overexpression of ADAM9 in OSCC	21
Figure 4.2	ADAM9 expression pattern in OSCC and normal tissues	22
Figure 4.3	A significant ADAM9 overexpression in OSCC tissues	22
Figure 4.4	A significant overexpression of ADAM9 in poorly-, moderately-,	
	and well-differentiated OSCC	23
Figure 4.5	Increased ADAM9 expression in relation to cancer cell differentiation	24
Figure 4.6	A positive correlation between ADAM9 expression and cell	
	differentiation in OSCC	25
Figure 4.7	Expression of membrane ADAM9 in oral cancer cell lines	26
Figure 4.8	Varying degree of ADAM9 expression in each cancer cell line	27
Figure 4.9	A significant increase in ADAM9 expression in some cancer cell lines	28
Figure 4.10	Enhanced ADAM9 expression in differentiated HOKs	29
Figure 5.1	ADAM9 expression pattern in normal skin and oral epithelium	32
Figure 5.2	Enhanced ADAM9 protein expression in a HaCaT cell line under	
ด	a high calcium concentration.	32
Figure 5.3 🔘	Varying ADAM9 mRNA expression in OSCC cell lines from	
A	a previous study g h t s reserved	33
Figure 5.4	The ADAM9/EGFR/Akt pathway	34
Figure 5.5	Increased expression of phosphorylated Akt (p-Akt) expression in	
	the same OSCC cell lines.	34

LIST OF ABBREVIATIONS

7-AAD	7-aminoactinomycin D
ADAM9	A disintegrin and metalloproteinase 9
ADAMs	A disintegrin and metalloproteinases
Akt	Protein kinase B
CCD	Charge-coupled device
CIN	Cervical intraepithelial neoplasia
DAB	3, 3'-diaminobenzidine solution
DNA	Deoxyribonucleic acid
ECM	Extracellular matrix
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
FGF	Fibroblast growth factor
HB-EFG	Heparin-binding epidermal growth factor
HOKs	Human oral keratinocytes
HPV	Human papillomavirus
hTERT	Telomerase reverse transcriptase
IHC	Immunohistochemistry
JAK	Janus kinase
kDa	Kilodalton
IL-1α	Interleukin-1 alpha
IL-1βCopyri	Interleukin-1 beta
IL8	Interleukin 8 reserved
МАРК	Mitogen-activated protein kinase
MDC-9	Metalloproteinase disintegrin cysteine-rich protein 9
MMP	Matrix metalloproteinase
MMP1	Collagenases
MMP3	Stromelysins
MMP10	Stromelysins
MMP11	Stromelysins

MMP13	Collagenases
MT1-MMP	Membrane-type 1 MMPs
mRNA	Messenger RNA
mTOR	Mammalian target of rapamycin
OSCC	Oral squamous cell carcinoma
p-Akt	Phosphorylates Akt
PBS	Phosphate-buffered saline
PE	Phycoerythrin
PI3K	Phosphatidylinositol-3-kinase
РКС	Protein kinase C
Rb	Retinoblastoma
RIPA	Radio-immunoprecipitation assay
SDS-PAGE	Sodium dodecyl sulfate-polyacrylamide gel
STAT	Signal transducer and activator of transcription
TBS	Tris-bauffered saline
TGF-α	Transforming growth factor alpha
TGF-β	Transforming growth factor beta
TNF	Tumor necrosis factor
TPA	Tetradecanoyl phorbol acetate
VCAM	Vascular cell adhesion molecule
VEGF	Vascular endothelial growth factor
ลิขสำ	าธิมหาวิทยาลัยเชียงไหม
Convri	ght [©] by Chiang Mai University

Copyright[©] by Chiang Mai University All rights reserved