Contents

Abstı	ract	Page i
Ackn	Acknowledgements	
Contents		
	f Figures	vii
List of Tables		ix
	f Symbols f Abbreviations	x xi-xii
LISCO	J ADDI EVIULIONS	Al-Alli
Chap	oter 1: INTRODUCTION	
1.1	Purpose of the Study	1
1.2	Brief Results, Scope And Future Prospects Of The Work	2
	1.2.1 Investigation of cellular and molecular pathways of innate immunity in response to amorphous nanosilica particles on different cell types	2
	1.2.2 Investigation of cellular and molecular pathways of innate immunity in the context of	2
	glioma pathophysiology	-
Chap	oter 2: Review of Literature	
2.1	Abstract	3
2.2	NLRs	3-4
2.3	NLRP3	5 6
	2.3.1 NLRP3 and Multiple sclerosis 2.3.2 NLRP3 and Alzheimer's disease	6-7
	2.3.3 NLRP3 and Prion disease	8
	2.3.4 NLRP3 and Amyotrophic lateral sclerosis	8-9
	2.3.5 NLRP3 and Depression	9-11
	2.3.6 NLRP3 and chronic alcoholism	11
	2.3.7 NLRP3 and bacterial infection	11-12
	2.3.8 NLRP3 and aging	12
2.4	NLRP1	14-16
2.5	NLRP2	16-17
2.6	NLRP6	17-18
2.7 2.8	NLRP12 NLRs and associated proteins	18-19 10-20
2.9	Currently available NLR-targeting therapeutics	19-20 20-22
2.10	Uncharted territory: Role of NLRs in glioma	24
2.11	Concluding remarks	24-25
Chap	oter 3: Investigation of cellular and molecular pathways of innate immunity in	
resp	onse to amorphous nanosilica particles on different cell types	
3.1	Abstract	27
3.2	Introduction	28
3.3	Materials and methods 3.3.1 Characterization of amorphous silica nanoparticles	29-30
	3.3.2 Cell culture	29 29
	3.3.3 MTT assay	29 29
	3.3.4 Annexin V/PI staining of cells	29
	3.3.5 Bradford assay for protein estimation	-) 29
	3.3.6 Confocal Microscopy	30
	3.3.7 Scanning electron microscopy	30
	3.3.8 Transmission electron microscopy of the cells	30
	3.3.9 Caspase-1 activity assay	30
3.4	Results and discussion	
	3.4.1 12nm and 22nm nanosilica are different in surface morphology	30-31

3.5	3.4.2 12nm and 22nm silica nanoparticles elicit differential cell death response 3.4.3 Larger silica nanoparticles shows a phagocytosis dependent cytotoxicity 3.4.4 Nanosilica induces ASC expression in epithelial and endothelial cells 3.4.5 Nanosilica induces nuclear localization of ASC protein 3.4.6 12nm and 22nm silica nanoparticles induced distinct cell death pathways 3.4.7 Nanosilica induces caspase-1 independent cell death in microglial cells Concluding remarks	32-33 33-34 34-36 37-38 39-40 40-41 42
Chapt	er 4: Investigation of Cellular and Molecular Pathways of Innate Immunity in	
-	xt of Glioma Pathophysiology	
4.1	Abstract	43
4.2	Introduction	44-45
43	Materials and methods	45-47
	4.3.1Human glioma tissue samples	45
	4.3.2 Immunohistochemistry	46
	4.3.3 Histochemical staining	46
	4.3.4 Bradford assay for protein estimation	46
	4.3.5 Western blotting	46-47
	4.3.6 Cytokine microarray	47
4.4	Results and discussion	
	4.4.1 Histopathological features of grade IV glioblastoma	47-48
	4.4.2 NLRP3 expression in normal brain and glioma tissue	48-49
	4.4.3 ASC expression in normal brain and glioma tissue	50-51
	4.4.4 AIM2 expression in normal brain and glioma tissue	51-52
	4.4.5 NLRC4 expression in normal brain and glioma tissue	53-54
	4.4.6 NLRP12 expression in normal brain and glioma tissue	54-55
	4.4.7 Caspase-3 expression in normal brain and glioma tissue	55-56
	4.4.8 Increased expression of ASC and NLRp3 in low grade and high grade glioma patients	56-57
	4.4.9 Differential expression of angiogenesis and proliferation promoting factors in glioma	57-62
	4.4.10 Differential expression of inflammatory cytokines in glioma	62-66
4.5	Concluding remarks	67
	er 5: Summary and Conclusion	-
5.1	Summary and future prospects	69-70
Annex	, ,	,
A.1	Materials	71
	A.1.1 List of Antibodies Used in the Study	, 71
	A.1.2 List of cell lines used in the study	72
	A.1.3 Glioma patients: clinical synopsis of the glioma specimens obtained for the study	72
	A.1.4 Details of the chemokines and cytokines used in multiplex microarray for glioma study	73
References		75-96