## Declaration

I, hereby declare that the work presented in this Thesis titled "*Investigation of Cellular and Molecular Pathways of Innate Immunity in Context of Glioma Pathophysiology and Cellular Inflammation*" submitted to the Indian Institute of Technology Jodhpur in partial fulfilment of the requirements for the award of the degree of Doctor of Philosophy, is a bonafide record of the research work carried out under the supervision of Dr. Sushmita Jha. The contents of this thesis in full or in parts, have not been submitted to, and will not be submitted by me to, any other Institute or University in India or abroad for the award of any degree or diploma.

*Shalini Singh*
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## Certificate

This is to certify that the thesis titled *Investigation of Cellular and Molecular Pathways of Innate Immunity in Context of Glioma Pathophysiology and Cellular Inflammation,* submitted by *Shalini Singh* (PG201384013) to the Indian Institute of Technology Jodhpur for the award of the degree of *Doctor of Philosophy*, is a bonafide record of the research work done by her under my supervision. To the best of my knowledge, the contents of this report, in full or in parts, have not been submitted to any other Institute or University for the award of any degree or diploma.

*Dr. Sushmita Jha*
Ph.D. Thesis Supervisor

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*Shalini Singh*
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# List of Symbols

| Symbol | Description |
|---|---|
| α | Alpha |
| β | Beta |
| γ | Gamma |
| g | Gram |
| µ | Micro |
| ° | Degree |
| % | Percentage |
| C | Celsius |
| h | Hour |
| l | Litre |
| m | Milli |
| m | Meter |
| M | Molar |
| N | Nano |
| pH | Hydrogen Ion Concentration |

# List of Abbreviations

| *Abbreviation* | *Full form* |
|---|---|
| AIM2 | *Absent in melanoma 2* |
| ALS | Amyotrophic lateral sclerosis |
| AMP | Adenosine monophosphate |
| ANPs | Amplifying progenitors cells |
| AOM | azoxymethane |
| APP | *Amyloid precursor protein* |
| ASC | Apoptosis associated speck like protein containing CARD domain |
| BBB | Blood Brain Barrier |
| BHB | Beta-hydroxybutyrate |
| BHT | Butylated hydroxyl toluene |
| BMMs | *Bone marrow derived macrophages* |
| CAPs | Cryopyrin associated periodic syndrome |
| CARD | Caspase recruitment domain |
| CINCA | Chronic infantile neurologic ,cutaneous and articular syndrome |
| CJD | Creutzfeldt- Jakob disease |
| CLRs | C-type lectin receptors |
| CNS | Central Nervous System |
| COP1 | Caspase-1 dominant negative inhibitor |
| COX-2 | Cyclooxygenase-2 |
| CRH | Corticotropin releasing hormone |
| CRID | Cytokine release inhibitory drugs |
| CSF | Cerebrospinal fluid |
| CUMS | *Chronic unpredictable mild stress* |
| Cyto-D | *Cytochalasin-D* |
| DAMPs | Danger associated molecular patterns |
| DED | *Death effector domain* |
| DNA | Deoxyribonucleic Acid |
| DSS | Dextran sodium sulphate |
| EAE | Experimental autoimmune encephalomyelitis |
| EGFR | Epidermal Growth Factor Receptor |
| FUS | Fused in sarcoma |
| GBM | Glioblastoma multiforme |
| G-CSF | Granulocyte colony stimulating factor |
| GM-CSF | Granulocyte macrophage colony stimulating factor |
| HIF-1α | Hypoxia Inducible Factor 1 Alpha |
| HIV | *Human immunodeficiency virus* |
| HMGB1 | High Mobility group box 1 |
| HO-1 | *Hemeoxygenase 1* |
| HPA axis | Hypothalamic-pituitary-adrenal axis |
| HUVEC | Human Umbilical Vein Endothelial |
| ICAM-1 | Intercellular adhesion molecule-1 |
| IDE | Insulin degrading enzyme |
| IDO | Indoleamine 2,3 dioxygenase |
| IFNβ | Interferon beta |
| IFN-γ | Interferon-gamma |
| Ig | Immunoglobulin |
| IKKγ | *Inhibitor of nuclear factor kappa-B kinase subunit gamma* |
| IL-17 | Interleukin-17 |
| IL-18 | Interleukin-18 |
| IL-1Ra | Interleukin-1 receptor antagonist |

| | |
|---|---|
| IL-1β | Interleukin-1 beta |
| IL-6 | Interleukin-6 |
| IL-8 | Interleukin-8 |
| iPSC | *Induced pluripotent stem cell* |
| IRAF-1 | Interleukin -1 receptor associated kinase-1 |
| IRAK-1 | Interleukin-1 receptor-associated kinase 1 |
| IV | Intravenous |
| LPC | Lysophosphatidycholine |
| LPS | Lipopolysaccharide |
| LRR | Leucine rich repeats |
| MAP1LC3B-II | Microtubule associated protein chain 3B-II |
| MAPK | Mitogen associated protein kinase |
| MCP-1 | Monocyte chemoattractant protein-1 |
| miRNA | *Micro RNA* |
| MNS | 3,4-methylenedioxy-nitrostyrene |
| MOG | Myelin oligodendrocyte glycoprotein |
| MSU | Monosodium urate crystals |
| MTT | *3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide* |
| MWS | Muckle well syndrome |
| MyD88 | Myeloid differentiation primary response 88 |
| NF1 | Neurofibromin 1 |
| NF-κβ | Nuclear factor- kappa beta |
| NIK | Nuclear Factor κB-inducing Kinase |
| NLRs | Nucleotide binding domain leucine rich repeats containing protein |
| NOD | Nucleotide oligomerization domain |
| NOMID | Neonatal onset multisystem inflammatory disease |
| NRTIs | *Nucleoside reverse transcriptase inhibitors* |
| NSC | Neural stem-like cells |
| P2X7 | purinergic receptor P2X |
| PAMPs | Pathogen associated molecular patterns |
| PDGF-BB | Platelet derived growth factor BB |
| PI | *Propidium Iodide* |
| PLY | Pneumolysin |
| $PrP^{c}$ | Prion protein cytoplasmic |
| $PrP^{sc}$ | Prion protein scrapieform |
| PRRs | Pattern Recognition Receptors |
| PS1 | *Presenlin-1* |
| PTEN | Phosphatase and tensin homolog |
| RAC-1 | Ras related C3 botulinum toxin substrate 1 |
| RAGE | Receptor of advanced glycation end product |
| RANTES | Regulated on Activation, Normal T Cell Expressed and Secreted |
| RLRs | Retinoic acid inducible gene-I- like receptors |
| ROS | Reactive oxygen species |
| $SiO_2$ | *Silicon dioxide* |
| SOCS1 | Suppression of cytokine signaling-1 |
| SOD-1 | Superoxide dismutase |
| STAT | Signal transducer and activator of transcription |
| TBI | *Traumatic brain injury* |
| TCGA | The Cancer Genome Atlas |
| TDO | Tryptophan dioxygenase |
| TDP-43 | Trans active response DNA binding protein |
| Th-17 | T helper cells-17 |
| TLR-4 | Toll-Like Receptor 4 |
| TMS1 | *Target of methylation mediated signaling* |
| TNF-α | Tumor necrosis factor-alpha |
| TNF-α | Tumor necrosis factor -alpha |

| | |
|---|---|
| TRAF6 | TNF receptor associated factor 6 |
| TSST | Trier social stress test |
| VCAM-1 | Vascular cell adhesion molecule-1 |
| VEGF | Vascular endothelial growth factor |
| WAS | Water avoidance stress |
| WHO | World Health Organization |
| XIAP | *X-linked inhibitor of apoptosis* |
| ICC | *Immunocytochemistry* |
| IHC | *Immunohistochemistry* |
| MS | *Multiple sclerosis* |
| AD | *Alzheimer's disease* |
| BIR | Baculovirus Inhibitory Repeat |
| AD | Acidic Domain |
| LRR | Leucine Rich Repeats |
| NBD | Nucleotide Binding Domain |
| PYD | Pyrin Domain |