

Declaration

I hereby declare that the work presented in this Thesis titled *Rejuvenation of Proteostasis Defects Based on Proteasomal Functions Regulates Improper Cellular Proliferation and Induces Misfolded Proteins Clearance* 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 bona fide record of the research work carried out under the supervision of Professor Amit Mishra. 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.

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Certificate

This is to certify that the thesis titled *Rejuvenation of Proteostasis Defects Based on Proteasomal Functions Regulates Improper Cellular Proliferation and Induces Misfolded Proteins Clearance*, submitted by *Sumit Kinger* (MP19BB003) to the Indian Institute of Technology Jodhpur for the award of the degree of *Doctor of Philosophy*, is a bona fide record of the research work done by him 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.



Professor Amit Mishra
Ph.D. Thesis Supervisor

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List of Symbols

<i>Symbol</i>	<i>Description</i>
α	Alpha
β	Beta
γ	Gamma
κ	Kappa
Δ	Delta
C	Celsius
°	Degree
<i>MDa</i>	MegaDalton
<i>kDa</i>	kiloDalton
®	Registered trademark
™	Trademark
μ	Micro
<i>m</i>	Milli
<i>M</i>	Molar
<i>min</i>	Minute(s)
<i>h</i>	Hour(s)
%	Percentage

List of Abbreviations

Abbreviation	Full form
AD	Alzheimer's disease
ANOVA	Analysis of variance
ALS	Amyotrophic Lateral Sclerosis
ATG	Autophagy-related
BAG	B cell lymphoma 2 (Bcl-2)-associated athanogene
Bak	Bcl-2 homologues antagonist/killer
Bax	Bcl-2-associated X protein
C9orf72	Chromosome 9 open reading frame 72
CAT	Chloramphenicol acetyl transferase
CCT	Chaperonin containing TCP-1
Cdc48	Cell division cycle 48
CFTR	Cystic fibrosis transmembrane conductance regulator
CHIP	Carboxy-terminus of Hsc70 interacting protein
CMA	Chaperone-mediated autophagy
CRL	Cullin RING ligase
d1EGFP	Destabilized enhanced green fluorescent protein with half-life 1 hour
DAPI	4',6-diamidino-2-phenylindole
DMEM	Dulbecco's modified Eagle's medium
DMSO	Dimethylsulfoxide
DPR	Dipeptide repeats
DSF Cu	Disulfiram copper
DUB	Deubiquitinase
EEVD	Glutamic acid Glutamic acid Valine Aspartic acid
EGCG	Epigallocatechin-3-gallate
EGFP	Enhanced green fluorescent protein
ER	Endoplasmic reticulum
ERAD	Endoplasmic reticulum-associated degradation
FACS	Fluorescence-activated cell sorting
FBS	Fetal bovine serum
FDA	Food and Drug Administration
FITC	Fluorescein isothiocyanate
FUS	Fused in sarcoma
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase
GFP	Green fluorescent protein
HDAC	Histone deacetylase
HD	Huntington disease
HECT	Homologous to the E6-AP carboxyl terminus
Hip	Hsc70-interacting protein
HMG-CoA	β -Hydroxy β -methylglutaryl-coenzyme A
Hop	Hsp70-Hsp90 organizing protein
Hrd1	Hydroxymethylglutaryl-coenzyme A reductase degradation protein 1
HRP	Horseradish peroxidase
HS	Heat shock
HSF1	Heat shock factor 1
Hsp	Heat shock protein
HTT	Huntingtin
IB	Immunoblotting
IgG	Immunoglobulin G

I κ B α	NF-kappa-B inhibitor alpha
JC-1	5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazol-carbocyanine iodide
KFERQ	Lysine, Phenylalanine, Glutamic acid, Arginine, Glutamine
KLHDC10	Kelch domain containing 10
LAMP-2a	Lysosomal associated membrane protein-2
LC3	Microtubule-associated protein 1A/1B-light chain 3
Ltn1	Listerin
MAPT	Microtubule associated protein tau
MTOC	Microtubule-organizing center
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NAC	Nascent polypeptide-associated complex
NEF	Nucleotide exchange factor
NEMF	Nuclear export mediator factor
NF- κ B	Nuclear factor kappa B
NIH	National Institutes of Health
NMR	Nuclear magnetic resonance
PBS	Phosphate-buffered saline
PEST	Proline, Glutamic acid, Serine, Threonine
PD	Parkinson's disease
PDB	Protein Data Bank
PFA	Paraformaldehyde
PGPH	Post-glutamyl peptide hydrolase
PI	Propidium iodide
Pirh2	p53-induced protein with a RING-H2 domain
PolyQ	Polyglutamine
PQC	Protein quality control
QC	Quality control
RAC	Ribosome associated chaperone complex
RBR	RING-in-between-RING
RING	Really interesting new gene
ROS	Reactive oxygen species
RQC	Ribosome-associated quality control
RT	Room temperature
SD	Standard deviation
SNC	Substantia nigra pars compacta
SOD1	Superoxide dismutase 1
SQSTM1	Sequestosome 1
STAT	Signal transducer and activator of transcription
TARDBP	TAR DNA binding protein
TBST	Tris-buffered saline Tween 20
TDP-43	TAR DNA-binding protein 43
TR	Texas Red
TRiC	T-complex protein ring complex
TUNEL	Terminal deoxynucleotidyl transferase dUTP nick end labeling
Ub	Ubiquitin
Ubc8	Ubiquitin-conjugating enzyme E2 8
ULK1	Unc-51-like kinase 1
UPR	Unfolded protein response
UPS	Ubiquitin-proteasome system
VCP	Valosin-containing protein
VPA	Valproate
VPS34	Phosphatidylinositol 3-kinase
WT	Wild-type

