



Gene Editing in Multiple Myeloma: A Promising Therapeutic Approach

A Thesis



Submitted for Partial Fulfillment of
M.D. Degree in Medical Biochemistry and Molecular Biology

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2019

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَفَاكِ
رَبِّ زِدْنِي عِلْمًا

صَدَقَ اللَّهُ الْعَظِيمُ

سورة طه ————— الآية : ١١٤

Acknowledgment

*First of all, and above all great thanks to **ALLAH**.*

*I would like to express my sincere appreciation and deepest thanks to **Prof. Dr. Maha Imam Ahmed**, Professor of Medical Biochemistry and Molecular Biology for her keen supervision, generous guidance and precious assistance.*

*I would like to express my appreciation and great thanks to **Ass. Prof Dr. Amr Sayed Mahmoud Moustafa**, Assistant Professor of Medical Biochemistry and Molecular Biology, for his overwhelming support to make this work possible.*

*I would also like to express my great thanks to **Dr. Nashwa Nagy El Khazragy**, Consultant of Clinical & Chemical Pathology, Faculty of Medicine, Ain Shams University, for her close observation and generous guidance.*

*Also **Dr. Marwa Ali Abd El-Khalek**, Lecturers of Medical Biochemistry and Molecular Biology for the great efforts she has done in this work.*

*I would like to thank **Prof. Dr. Eman Mahmoud El-Salahy**, Professor of Medical Biochemistry and Molecular Biology for her effort in initiation that topic of research and her encouragement.*

*Finally, I wish to express my thanks and gratefulness to all my family members especially **my mother, my father and my sisters (Marwa, Maha and Maram)** for their support and tolerance.*

Mai Khaled Abd El-Monem

Dedication

To the person who
made it possible

*(my father: Dr. Khaled
Abd El Monem)*

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List of Abbreviations

<i>Abbreviation</i>	<i>Full term</i>
A	Adenine
ACTB	Beta actin
Ag	Antigen
ALL	Acute lymphoblastic leukemia
ASCT	Autologous stem cell transplantation
ATP	Adenosine triphosphate
B-ALL	B-cell acute lymphoblastic leukemia
BCMA	B-cell maturation antigen
BCR	B-cell receptor
BM	Bone marrow
CA	Chromosomal abnormalities
CARs	Chimeric antigen receptors
Cas	CRISPR associated protein
Cat no	Catalogue number
CD	Cluster of differentiation
cDNA	Complementary DNA
CHμ	Constant region of heavy chain μ gene segment

CLL	Chronic lymphocytic leukemia
<i>Abbreviation</i>	<i>Full term</i>
CO₂	Carbon dioxide
CRAB	Hypercalcemia, renal impairment, anemia, and bone disease
CRISPR	Cluster of regularly interspaced palindromic repeats
CRISPRa	CRISPR activation
CRISPRi	CRISPR interference
crRNA	CRISPR RNA
CRS	Cytokine release syndrome
CT	Computerized tomography
C_t	Cycle threshold
DAPI	4',6-Diamidino-2-phenylindole
dCas9	Dead cas9
Del(17p)	Chromosome 17 short arm deletion
DEPC	Diethyl pyrocarbonate
DJ	Diverse and joining gene
dL	Deciliter
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid

ds	Double strands
<i>Abbreviation</i>	<i>Full term</i>
DSBs	Double strands DNA breaks
dT	Deoxy thymine
DTT	Dithiothreitol
E. coli	<i>Escherichia coli</i>
EB buffer	Elution buffer
EDTA	Ethylenediaminetetraacetic acid
FACS	Fluorescence-activated cell sorting
FBS	Fetal bovine serum
FDA	Food and Drug Administration
FDC	Follicular dendritic cells
FLC	Free light chain
FokI	<i>Flavobacterium okeanoikoites</i> 1 endonuclease
g	Gram
GC	Germinal center
gRNA	Guide RNA
HBG	Hemoglobin gamma gene
HC	Heavy chain
HCL	Hydrochloric acid

HDR	Homology directed repair
<i>Abbreviation</i>	<i>Full term</i>
HDT	High-dose therapy
HLA	Human leukocyte antigen
HO	Homothallic switching endonuclease
HPFH	Hereditary persistence of fetal hemoglobin
HR	Homologous recombination
hr	Hour
hs	Homosapien
Ig	Immunoglobulin
IMWG	International myeloma working group
indels	Insertion or deletion mutations
ISS	International staging system
KCl	Potassium chloride
KEGG	Kyoto Encyclopedia of Genes and Genomes
L	Liter
LB	Lysogeny broth
LC	Light chain
LDH	Lactate dehydrogenase

mAbs	Monoclonal antibodies
<i>Abbreviation</i>	<i>Full term</i>
MACS	Magnetic cell separation
MD	Maryland
MFs	Molecular functions
mg	Milligram
MgCl₂	Magnesium chloride
MGUS	Monoclonal gammopathy of undetermined significance
min	Minute
mL	Milliliter
MM	Multiple myeloma
mM	Millimolar
mmol	Millimole
MRI	Magnetic resonance imaging
mRNA	Messenger RNA
MTS	3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium salt
ng	Nanogram
NHEJ	Non-homologous end joining
NHLs	Non-Hodgkin lymphomas

NIH	National institute of health
<i>Abbreviation</i>	<i>Full term</i>
nM	Nanomolar
nm	Nanometer
NY	New York
OFP	Orange fluorescence protein
Oligo	oligonucleotide
PAM	Protospacer adjacent motif
PB	Phosphate buffer
PBS	Phosphate buffer solution
PCR	Polymerase chain reaction
PE	Phycoerythrin
PEG	Polyethylene glycol
PES	Phenazine ethosulfate
PET-CT	Positron emission tomography – computed tomography
pGCS vector	Plasmid of Genomic Cleavage Selection kit
pmol/μL	Picomole per microliter
Poly A	Poly adenine
pre-B	Precursor B

pro-B	Progenitor B cells
<i>Abbreviation</i>	<i>Full term</i>
pUC19	"p" prefix (plasmid) and the abbreviation for the University of California
qPCR	Quantitative polymerase chain reaction
R-ISS	Revised International Staging System
RNA	Ribonucleic acid
RPMI	Roswell Park Memorial Institute
RQ	Relative quantification
RR	Relapsed/refractory
RT	Reverse transcription
S.	Seconds
S.O.C	Super Optimal broth with Catabolite repression
SaCas9	<i>Staphylococcus aureus</i> Cas9
SEER	The Surveillance, Epidemiology and End Results Program
sgRNA	Single guide RNA/ synthetic guide RNA
SLAMF7	Signaling lymphocytic activation molecule F7

SLC	Surrogate light chain
<i>Abbreviation</i>	<i>Full term</i>
SMM	Smoldering multiple myeloma
SpCas9	<i>Streptococcus pyogenes</i> Cas9
SPSS	Statistical Package for the Social Science
ssDNA	Single-stranded DNA
T (14;16)	Translocation between chromosome 14 and chromosome 16
T4 DNA Ligase	DNA ligase from bacteriophage T4
TALENs	Transcription-activator-like effector nucleases
TCR	T-cell receptor
TE buffer	Tris and EDTA buffer
tracrRNA	Trans-activating CRISPR RNA
U/mL	Units per milliliter
USA	United states of America
V(D)J	Variable, diverse and joining gene segments
V/V	Volume per volume
V_HD_HJ_H	Heavy chain variable, diverse and joining regions of gene segments
VpreB	V-set pre-b cell surrogate light chain

W/V	Weight per volume
<i>Abbreviation</i>	<i>Full term</i>
3'	Three prime- end
5'	Five prime -end
22q11.22	Long arm chromosome 22, location 11, sub-locus 22
Δ absorbance	Delta absorbance
ΔC_t	Delta c _t
ΔΔC_t	Delta delta c _t
λ5	Lambda5
μ	Mu
μg	Microgram
μmol	Micrmole
μl	Microliter
%	Percent
+ve	Positive
-/-	Double-gene knockouts

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