



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرو فيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY

Significance of Aberrant CD 82 Expression in Pediatric Acute Lymphoblastic Leukemia

Thesis

Submitted for partial fulfillment of MSc.Degree
in Clinical Pathology

By

Mohamed Tarek Aly Ahmed Hassan
(M.B., B.Ch.) (Misr University for Science and Technology)

Prof.Dr. Tahany Aly Helmy El Kerdany
Professor of Clinical Pathology,
Faculty of Medicine, Ain Shams University

Dr. Yasmine Nabil El-Sakhawy
Assistant professor of Clinical pathology
Faculty of Medicine, Ain Shams University

Dr. Sara Mostafa Makkeyah
Lecturer at Pediatrics Department
Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University**

2021

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgment

First of all, I would like to thank **God** who allowed and helped me to accomplish this work and only by his will everything can be achieved.

I wish to express my deepest gratitude and appreciation **Prof. Dr. Tahany Aly Helmy El Kerdany**, Professor of Medical Clinical pathology, Faculty of Medicine, Ain-Shams University for her scientific insight, continuous encouragement and valuable advice.

I would like to express my deepest thanks and everlasting gratitude to **Dr. Yasmine Nabil El-Sakhawy**, Assistant Professor of Clinical Pathology Department, Faculty of Medicine, Ain-Shams University. I am truly obliged for her kindness, maternal compassion, constant support and guidance.

I would like to convey my profound gratitude and everlasting appreciation to **Dr. Sara Mostafa Makkeyah** Lecturer at Pediatrics department, Faculty of Medicine, Ain Shams University for guiding me through each step, eminent supervision, valuable advice and endless encouragement throughout this work.

Finally, I would like to extend my thanks to all the staff members and colleagues of Clinical pathology Department in Ain-Shams University their appreciated help and support during the present work.



Mohamed Tarek

Dedication

***To** those who touched my life, provided
the support and guidance whenever
needed*

***To** my father, Prof. Dr. Tarek Aly Hassan*

***To** my mother Prof. Dr. Eman Mohamed
Kandeel*

***To** my elder sister Dr. Tasneem Tarek Aly ,
my little brother Aly Tarek Aly and
my nephew Malek Mostafa*

***To** my fiancée Dr. Salma Khaled*

***To** my cousin Dr. Hagar Fathy*

***To** my professors.*

Thank you all

LIST OF CONTENTS

Title	Page No.
ABSTRACT	
AIM OF THE WORK	
INTRODUCTION.....	1
Chapter I.....	4
Acute Lymphoblastic Leukemia	4
I- Epidemiology:	4
II- Etiology of Acute Lymphoblastic Leukemia (ALL)	5
III-Diagnosis of ALL	9
IV- Classification of ALL	20
V-Treatment	24
Chapter (2).....	31
SUBJECTS AND METHODS	68
RESULTS.....	72
DISCUSSION.....	96
SUMMARY	103
CONCLUSION.....	104
RECOMMENDATION	105
REFERENCES.....	106
ARABIC SUMMARY	1

LIST OF TABLES

Title	Page No.
Table (1): Immunophenotypic types of B-ALL and their associated features.....	16
Table (2): Immunophenotyping of ALL.....	17
Table (3): The FAB classification of ALL.....	21
Table 4: WHO classification of ALL	23
Table 5. Demographic characteristics of cases and controls.....	72
Table 6. Pattern of clinical presentations in cases and controls	73
Table 7. Results of hematological work up in cases and controls.....	74
Table 8. Results of bone marrow examination in cases and controls	74
Table 9. CD82 expression in cases and controls	75
Table 10. Proportion of patients with CD82 dim or CD light in cases and controls	76
Table 11. Risk analysis for relation between CD82 dim or CD light and ALL	79
Table 12. Correlation between CD82 expression and relevant quantitative variables in cases.....	80
Table 13. Relation between CD82 expression and clinical presentation in cases.....	81
Table 14. Relation between CD82 expression and main outcome measures in cases	82
Table 15. Relation between CD82 dim or light and clinical presentation in cases.....	87
Table 16. Relation between CD82 dim or light and clinical presentation in cases.....	88

LIST OF Figures

Title	Page No.
Fig. (1): Peripheral blood smear of a child with ALL.....	13
Fig. (2): ALL bone marrow smear	14
Fig. (3): Schematic of tetraspanin molecular structure	33
Figure (4) CD82 structure and motifs	34
Fig. (5): CD82 enriched microdomains with signaling molecules.....	38
Fig. (6): Reverse transcription.....	53
Fig. (7): Schematic diagram of the basic components of a flow cytometer.....	56
Fig. (8): Work Plan.....	58
Fig.(9): Coulter Epics XL™ and XL-MCL™ Flow Cytometer.....	64
Fig (10): Preparing the permeabilization buffer.....	66
Fig (11) Adding the buffer to the sample	67
Fig (12) Sample after centrifugation	67
Fig (13) CD 82 MCAB.....	69
Fig (14): Analyzing the data on the flow cytometer	69
Fig. (15). CD82 expression in cases and controls	77
Fig. (16). Interactive dot diagram showing CD82 expression in cases of ALL and controls	78
Fig. (17). Proportion of patients with light or dim CD82 in cases and controls.	79
Fig. (18). CD82 expression in responders and non-responders to treatment	83
Fig. (19). CD82 expression in cases who relapsed and those who did not suffer relapse.....	84

Title	Page No.
Fig. (20). CD82 expression in survivors and non-survivors to treatment.	85
Fig. (21). Relation between CD82 dim or light and response to treatment.	86
Fig. (22). Relation between CD82 dim or light and relapse.	89
Fig. (23). Relation between CD82 dim or light and survival.	90
Fig. (24). Kaplan-Meier curves for time to developing response in cases with CD82 dim or CD82 light	91
Fig. (25). Kaplan-Meier curves for time to relapse in cases with CD82 dim or CD82 light	92
Fig. (26). Kaplan-Meier survival curves in cases with CD82 dim or CD82 light	93
Fig.(27). Kaplan-Meier survival curves in cases with CD82 dim or CD82 light. Difference between both curves is not statistically significant (Log rank test chi-squared (df 1) = 3.375, P-value = 0.066). Light/Dim incidence hazard ratio (HR) could not be estimated.	94
Fig.(28). Kaplan-Meier curves for time to developing response in cases with CD82 dim or CD82 light. Difference between both curves is statistically significant (Log rank test chi-squared (df 1) = 10.242, P-value = 0.001). Light/Dim incidence rate ratio (IRR) = 0.11 (95% CI = 0.03 to 0.42).	

LIST OF Abbreviations

Abbreviation	Means
ADAMs	The A Disintegrin and Metaloproteases
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
B-ALL	B cell Acute Lymphoblastic leukemia
BCP	B cell precursor
BM	Bone marrow
CBC	Complete Blood Count
CD	Cluster of differentiation
CML	Chronic myeloid leukemia
CNS	Central nervous system
CR	Completer Remission
CSF	Cerbro Spinal fluid
DFS	Disease-free survival
EBV	Epstein Barr Virus
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
ELISA	Enzyme-linked immunosorbent assay
ER	Endoplasmic reticulum
FAB	French American British haematologists

Abbreviation	Means
FAK	Focal adhesion Kinase
G-CSF	Granulocyte colony stimulating factor
GM-CSF	Granulocyte macrophage colony stimulating factor
HGF	Hepatocyte growth factor
HR	High risk
HSPC	Hamato poietic stem precursor cells
IHC	Immuno histochemistry
IPT	Immunopheno typing
IR	Intermediate risk
LSCs	Leukemia stem cells
LT-HSCs	Long term haematopoietic stell
MDR	Minimal Residual Disease
MPAL	Mixed Phenotype Acute Leukemia
NK	Natural killer
PAX5	Paired box protein 5
PB	Peripheral blood
PH+	Philadilphia chromosome positive
RB	Retinoblastoma protien
RT-qPCR	Reverse transcription-quantitative polymerase chain reaction
SR	Standard risk
TCP	T cell precursor

Abbreviation	Means
TEM	Tetraspanin-enriched microdomains
TLC	Total leucocytic count
TM4SF	Tetraspanin superfamily
WBCs	White blood cells
WHO	World Health Organization

Aim of the work

The present study was designed to assess CD82 expression in patients with pediatric ALL and to evaluate its association with the clinical data throughout the following plan of work.