## KARYOTYPING AS A PROGNOSTIC CRITERION IN PEDIATRIC SOLID TUMORS

#### **THESIS**

Presented By

Ashraf Mohamed Hosni Ibrahim Aboul Ennin

M.B. B.Ch.

Faculty of Medicine, Ain Shams University

For Partial Fulfilment of M.Sc. in Pediatrics

Under Supervision of

Prof. Dr. GALILA MOHAMED MOKHTAR

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

Dr. AMAL MAHMOUD MOHAMED

Assist. Prof. of Human Genetics

Human Genetics Department, National Research Centre

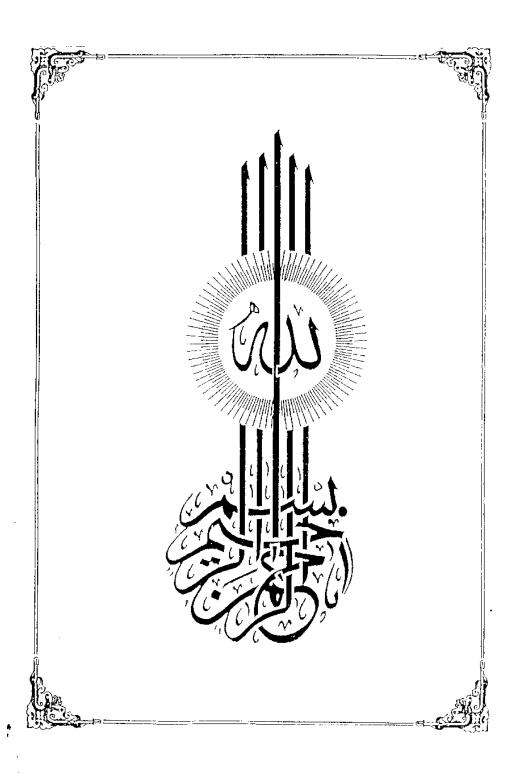
Dr. NANCY AHMED KASHEF

Lecturer of Pediatrics
Faculty of Medicine, Ain Shams University

6(8,92994 A. M

 $H \cdot M$ 

Faculty of Medicine Ain Shams University 1996 54004 1. Harbell

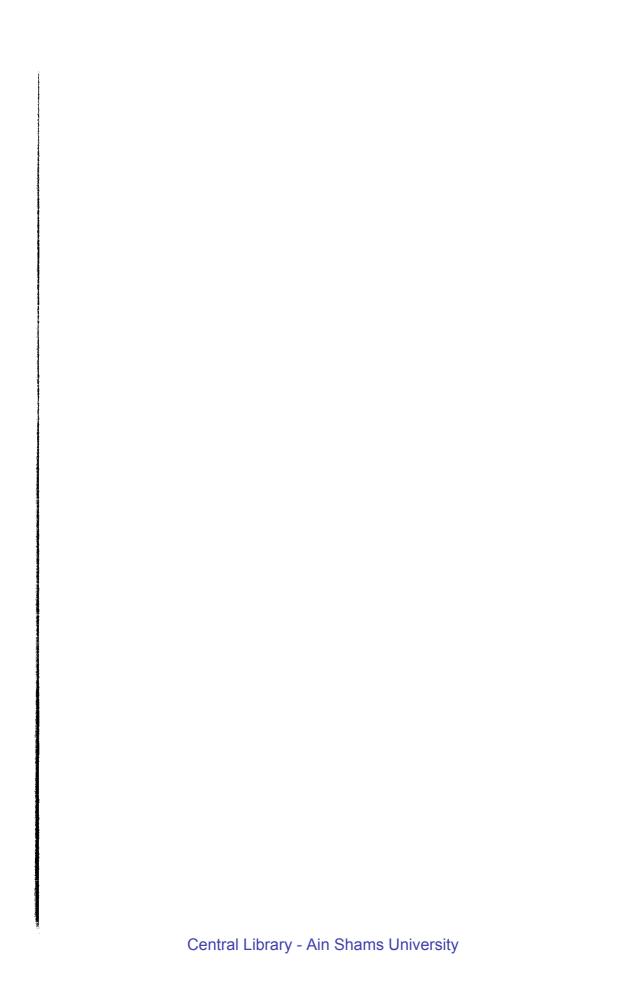




قَالُوَا شَبُحَانُكَ لَأَحِلُمُ لِنَا إِلاَمَا عَلَيْهِ الْخَالِثَ الْحَلِمُ الْحَكِمُ . فَلَمْنَا إِلاَمَا الْحَلَمُ الْحَكِمُ . وَكُونُ الْخَلِمُ الْحَلَمُ الْحَكِمُ . وَكُونُ الْخَلِمُ الْحَلَمُ الْحَلْمُ الْحَلَمُ الْحَلَمُ الْحَلْمُ الْحَلْمُ الْحَلْمُ الْحَلَمُ الْحَلْمُ الْحَلْمُ الْحَلْمُ الْحَلْمُ الْحَلْمُ الْحَلَمُ الْحَلْمُ الْحَلْم

# Dedication

To my beloved parents "Everything I do, I do it for you"



#### **ACKNOWLEDGMENTS**

First and foremost, all thanks are to "GOD" The Most Beneficent and Merciful.

I would like to express my sincere gratitude to **PROFESSOR DR. GALILA MOHAMED MOKHTAR**, Professor of Pediatrics, Ain Shams University, for giving me the honour to be one of her candidates, for her encouraging and optimistic attitude, and for many valuable lessons in scientific practice, sound advice and guidance throughout the study.

I wish to express my deepest appreciation and respect to DR. AMAL MAHMOUD MOHAMED, Assistant Professor of Human Genetics, National Research Center, for the opportunity she has given me to perform this study, for her guidance, support and beneficial comments, and her interest.

I am also grateful to DR. NANCY AHMED KASHEF, Lecturer of Pediatrics, Ain Shams University, for her care, encouraging, guidance, and valuable help.

My special appreciation and deepest thanks to DR. ALAA KHALIL KAMEL, Lecturer of Human Genetics, National Research Center, for her continued support, encouragement, innovative attitude, and for her vital role and many useful lessons in this work.

Finally, my greatest gratitude goes to everyone who made it possible, especially to my patients and their families, and the staff member of the Human Genetic Department in National Research Center.

Ashraf Hosni



## **CONTENTS**

	Page
Symbols and Abbreviations	i
List of Tables	iii
List of Figures	v
Introduction	1
Aim of The Study	3
Review of Literature	3
Genetic Basis of Childhood Cancer	5
Lymphomas	13
Non-Hodgkin's Lymphoma	13
Hodgkin's Disease	26
Neuroblastoma	33
Wilms' Tumor	48
Rhabdomyosarcoma	57
Retinoblastoma	67
Subjects and Methods	77
Results	81
Discussion	143
Summary	159
Conclusion	163
Recommendations	165
References	167
Arabic Summary	

#### SYMBOLS AND ABREMATIONS

Arrow  $(\rightarrow)$  From  $\rightarrow$  to Break

Cen Centromere

Colon, single (:) Break

Colon, double (::) Break and reunion

cs Chromosome

del Deletion

der Derivative chromosome

d mins Double minute dup Duplication

EBV Epstein-Barr virus
ESD Esterase D enzyme

HD Hodgkin's disease

HSRs Homogeneously staining regions

HVA Homovanillic acid
i Isochromosome

inv Inversion

LD Lymphocyte depletion

LP Lymphocyte predominance

LOH . Loss of heterozygosity

MC Mixed cellularity

minus (–) Loss

NHL Non Hodgkin's lymphoma

NS Nodular sclerosis

NSE Neuro-specific enolase

p Short arm of chromosome

## ii Symbols and Abbreviation

plus (+)	Gain
q	Long arn
rcp	Reciproc
RB	Retinobla
RMS	Rhabdon
S	Satellite
semicolon (;)	Separates regions i
t	Transloc
ter	Terminal
VIP	Vasoacti
VMA	Vanillylı
WT1	Wilms' t

#### LIST OF TABLES

		Page
Table (1):	Working Formulation of Non-Hodgkin's Lymphomas for Clinical Use and Related Terms in the Rappaport Classification.	17
Table (2):	St. Jude Children's Research Hospital Staging Scheme for Non-Hodgkin's Lymphoma.	24
Table (3):	Rye histopathological classification of Hodgkin's disease and their relative frequencies.	29
Table (4):	Ann Arbor Staging Classification of Hodgkin's Disease.	31
Table (5):	Histopathological grading of neuroblastoma.	38
Table (6):	International Neuroblastoma Staging System (INSS).	43
Table (7):	Clinical Genetic Subtypes of Neuroblastoma.	47
Table (8):	Clinicopathologic Staging of Wilms' tumor.	54
Table (9):	Chromosomal abnormalities in rhabdomyosarcoma.	61
Table (10):	Primary site and patterns of spread of rhabdomyosarcoma.	62
Table (11):	Intergroup Rhabdomyosarcoma Study Clinical Grouping System.	65
Table (12):	Features of hereditary and nonhereditary types of retinoblastoma.	69
Table (13):	Reese-Ellsworth Staging Classification of Retinoblastoma.	75

		Page
Table (14):	Clinical data of patients with retinoblastoma.	82
Table (15):	Ophthalmoscopic, ultrasonographic and cytogenetic data of patients with retinoblastoma.	83
Table (16):	Clinical data of patients with Non-Hodgkin's lymphoma.	107
Table (17):	Laboratory data of patients with Non-Hodgkin's lymphoma.	108
Table (18):	Roentgenographic, histopathologic and cytogenetic data of patients with Non-Hodgkin's lymphoma.	109
Table (19):	Clinical data of patients with Wilms' tumor, Neuroblastoma and Rhabdomyosarcoma.	125
Table (20):	Laboratory data of patients with Wilms' tumor, Neuroblastoma and Rhabdomyosarcoma.	126
Table (21):	cytogenetic data of patients with Wilms' tumor, Neuroblastoma and	127
m 11 (22)	Rhabdomyosarcoma.	127
Table (22):	History of malignancies and associated anomalies in the families of studied cases.	137