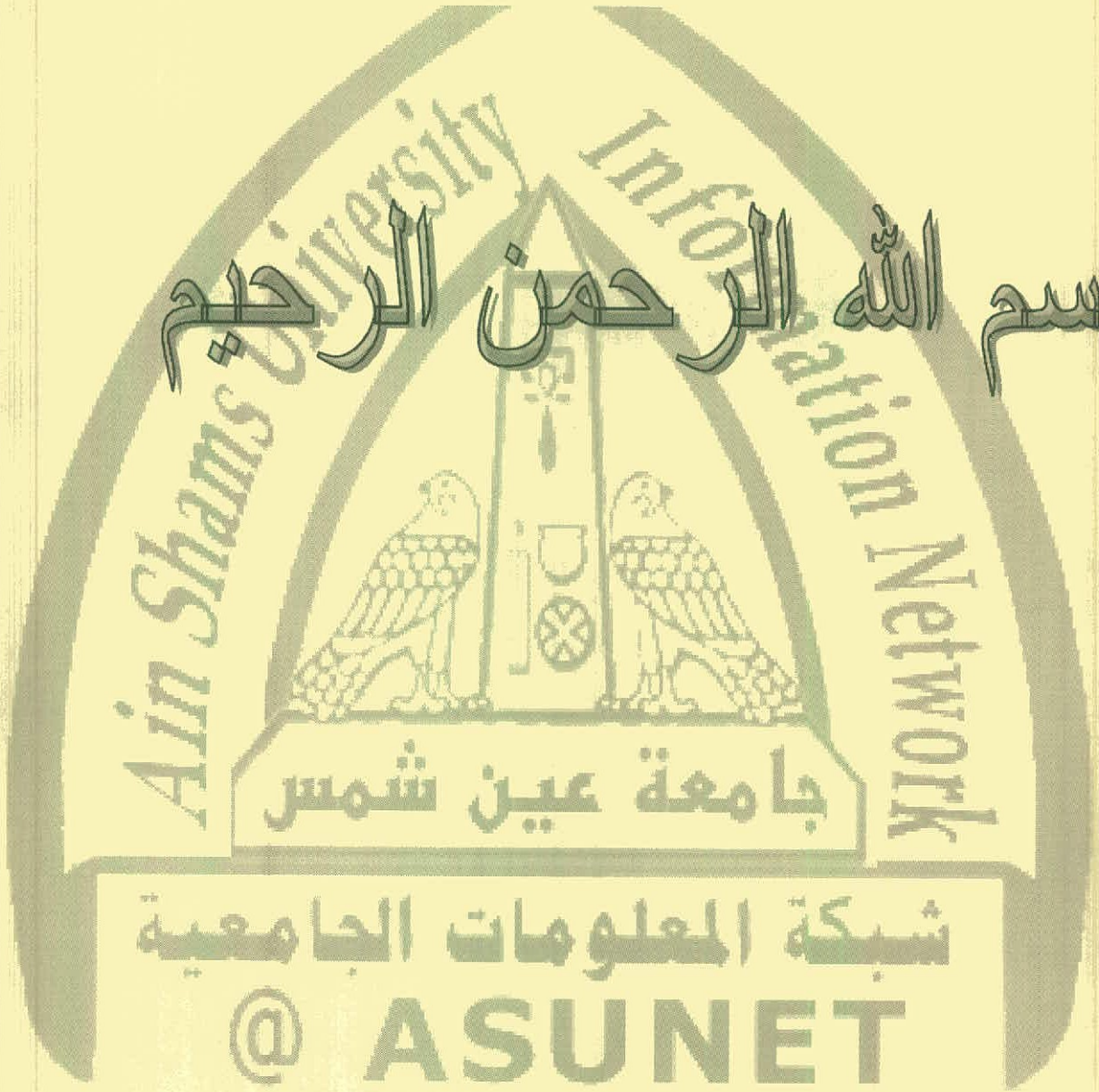
شبكة المعلومات الجامعية



بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

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

يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%

بعض الوثائـــــــق الاصليـــــة تالفـــة

بالرسالة صفحات لم ترد بالاصل

Wilms' Tumor (WT1) Gene Expression and Acute Childhood Leukemia

Thesis

Submitted for Partial Fulfillment of M.D. Degree in

Clinical and Chemical Pathology

Presented by

Nihal Saad El-Kimawy

(M.B., B.Ch.;
M.Sc. Clinical and Chemical Pathology)

Under Supervision of

Prof.

Sawsan Abd-El Moety Fayaad
Prof. of Clinical Pathology
Faculty of Medicine
Ain Shams University

Ahmad Samy Khalifa
Prof. Of Pediatrics
Faculty of Medicine
Ain Shams University

Tahany Ali Helmy El-Kerdany
Assist. Prof. Of Clinical & Chemical Pathology
Faculty of Medicine
Ain Shams University

Afaf Abdel Aziz Abdel Ghaffar
Assist. Prof. Of Clinical & Chemical Pathology
Faculty of Medicine
Ain Shams University

Dr. Azza El-Sayed Hashim
Assist. Prof. Of Clinical & Chemical Pathology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2000

﴿ قالوا سبحانك لا علم
لنا الا ما علمتنا إنك أنت
العليم الحكيم﴾

صدق الله العظيم

سورة البقرة\ آية (٣٢)

ACKNOWLEDGMENT

Thanks for God for giving the power and strength to carry out this work..

I wish to express my deep gratitude to Prof. Sawsan Fayad , for her valuable suggestion, instructive guidance and continuous encouragement throughout the whole work.

My sincere gratitude and thanks to Prof. Ahmed Samy Khalifa, for giving me the privilege of working under his supervision. His constant encouragement, close supervision and constructive guidance were the paramount axis in the initiation and the progression of this work.

My sincere thanks are to Prof. Tahany Al- Kordany, for her valuable assistance, great help and constant support.

My hearty thanks to Dr. Afaf Abdel Aziz, for her remarkable effort, considerable help and continuous guidance.

My hearty thanks to Dr. Afaf Abdel Aziz, for her remarkable effort, considerable help and continuous guidance.

My deep gratitude goes to Dr. Azza Hashim, for her faithful supervision, great cooperation and her meticulous revision of this work..

My particular and deepest thanks are expressed to Prof. Salwa Abou El-Hana, who thought me how to approach a scientific research, provides me a great deal of her valuable time, continuous advise, directions and effort to fulfill this work.

My sincere appreciation to Prof. Adel El-Missiry, Director of Medical Research Center, and to all members of MRC for there great deal of help.

Finally, I would like to record my greatest thanks and gratitude to my family for their actual help and support received in many ways.

Nihal Saad El Kinawy

2000

ABSTRACT

Wilms' tumor gene (WT1) plays an important role in leukemogenesis and has an oncogenic function rather than a tumor suppressing function in hematopoietic progenitor cells ***(Inoue et al., 1998).*** In this study, WT1 expression was detected in children with acute leukemia; to evaluate its prognostic value and its relevance as a genetic marker for detection of minimal residual blast cells. RT-PCR was used to examine relative levels of WT1 transcripts from the peripheral blood of 58 children diagnosed with acute leukemia: 33 were newly diagnosed (10 ANLL, 19 ALL & 4 ABL), 8 relapsing patients (2 ANLL, 4 ALL, 2 ABL) and 17 patients were in remission (6 ANLL & 11 ALL). Ten children were studied for controls (7 normal and 3 with leukomoid blood picture). WT1 mRNA were not expressed at detectable levels in normal individuals nor in those with leukomoid reaction but the gene transcripts were expressed in most patients in various stages of leukemia. The highest levels of WT1 transcripts were detected in relapsing AL children, while lower levels were expressed in newly diagnosed patients. On the other hand, patients in remission showed the least levels and was even undetected in 5 patients. The levels of gene expression were higher in ANLL than ALL & ABL. Furthermore, following up of 10 WT1-positive patients in remission showed a decrease in WT1 expression to low levels while the values were increased during relapse. Moreover, all patients with high risk prognostic factors express high levels of WT1>1 $x10^{-2}$, while those of low risk group the WT1 transcripts were

$<0.6 \times 10^{-2}$ showing high overall survival (OAS) probability and disease free survival (DFS). Interestingly, WT1 gene expression proved to be a prognostic criterion upon comparing it with the fate of the patients.

Due to its high frequency at diagnosis and the ability to detect significant changes in WT1 transcript number when clinical CR is achieved, WT1 transcripts may prove to be a significant tumor marker, possibly as an MRD monitor in evaluating remission status and early relapse, and may also prove to be useful in predicting outcomes in acute leukemia in children.