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شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم



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شبكة المعلومات الجامعية



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



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شبكة المعلومات الجامعية

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



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بالرسالة صفحات لم ترد بالأصل



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محت لثا فكت وقديت الر
بندر مكار

**CLINICAL SIGNIFICANCE OF DETECTION OF
TUMOUR SUPPRESSOR GENE DELETION AT
13Q14 BY FISH TECHNIQUE IN CHRONIC
LYMPHOCYTIC LEUKAEMIA**

Thesis

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By

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

سَنُرَايَهُمْ إِذْ يَقُولُ بَيْنَنَا وَبَيْنَكَ لَافِتًا وَهَاجًا وَإِذْ يَنْفُصُهُمُ الْجَحِيمُ يُدَبِّسُ لَهُمْ

أَنَّهُمُ الْخَوْدَةُ ، أَوَلَمْ يَكُنْ لَهُمْ بَرَاءةً أَنَّهُ

أَعْلَى كُلِّ نَفْسٍ فَهْلَهُ أَبَدًا

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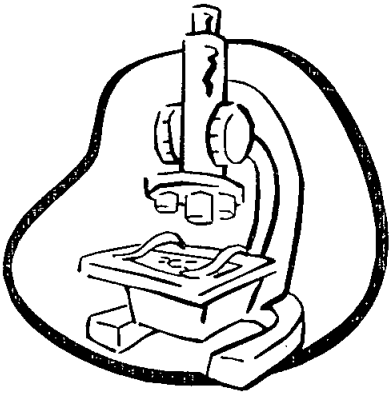
AIHA	:	Auto-immune haemolytic anemia.
CMV	:	Cytomegalo virus
ECOG	:	Eastern cooperative oncology group.
FACS	:	Activated cell sorter.
Fas I	:	Exogenous human fas ligand
FISH	:	Fluorescence in situ hybridization
LCDt	:	Lymphocyte count doubling time
LPDs	:	Lympho-proliferative disorders
PCD	:	Programmed cell death
PLL	:	Pro lymphocytes. Leukemia
RBI	:	Retino blastoma gene.
RT	:	Richter transformation
SIg	:	Surface immunoglobulin
UCB	:	umbilical cord blood
WCPP	:	Whole chromosome painting probe.

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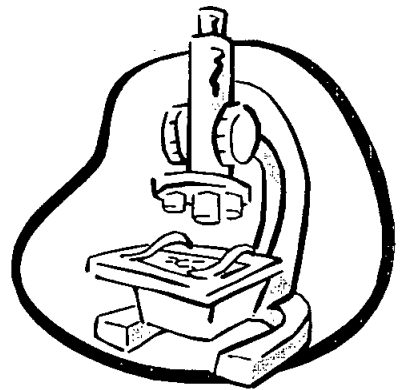
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INTRODUCTION



INTRODUCTION

INTRODUCTION

Chronic lymphocytic leukaemia (CLL) accounts for about 25% of all leukaemias, In adults over the age of 50 ys. It is the most common form, particularly in the west. In the Far East Its incidence is low. It is also the most common of the lympho-proliferative disorders accounting for 60% of CLL cases affects twice as many males as females, with a peak incidence between 60 and 80 ys. It is rarely diagnosed below the age of 40 years, even more rare below 30 years. CLL has the highest familial incidence which can be documented in 2% of patients. Pioneering work by [Dame , 1967] and [Galton, 1966], introduced the concept of CLL as a progressive accumulation of lymphocytes, starting in lymph node and or the bone marrow and gradually expanding to most of the haemopoietic organs. This concept of low progression was the basis of the clinical staging system proposed by [Raie et al., 1975].

Advanced involvement will bring about abnormalities in the normal function of the immune system and result in hypogamaglobulinaemia and less frequently autoimmune complications. The symptoms are a consequence of bone marrow Failure i.e anaemia, infection and bleeding. A proportion of patients remains asymptomatic and never need any treatment, dying of unrelated cause, in the remainder, the disease can usually be kept under control for 9 to 10 years, infection being the predominant cause of death [P. Kumar., 1994].

The diagnosis of CLL pre supposes that there is a persistent lymphocytosis of at least 10×10^9 and lymphocytic infiltration in the bone marrow of at least 40%.

Morphologically, the lymphocytes in blood films are small showing scanty cytoplasm and a characteristic pattern of nuclear chromatin clumping, the

nucleolus is inconspicuous and zurophil granules are absent. The presence of smear cells, which correlate with the level of WBC is diagnostic value. If the proportion of prolymphocytes is greater than 10% it presents avariant designated CLL/PL. The bone marrow aspirate is useful to confirm morphological features, particularly in patients with low WBC counts, and to assess haemopoiesis. The trephine biopsy shows great variability according to the extent of the disease. Early on the pattern of infiltration is interstitial or nodular and diffuse pattern in advanced CLL.

Cytogenetic analysis has shown recurring abnormalities of which the most common are trisomy 12 (10-14%), deletion at 11q 23 (20% of cases) and structural abnormalities of long arm of chromosome 13 at band q14 (15-20% of cases). It has been shown that trisomy 12 is often associated with abnormal morphology e.g. (CLL/PL) and that it is a secondary event in pathogenesis [Que et al., 1993]. These features could be translated into a worse prognosis for this abnormality as suggested by a large international study [Juliasson et al., 1990].

Deletions or translocations of chromosome 13q14 are found in approximately 20% of cases and are often the sole abnormality 20% of cases suggesting that the region contains one or more genes of importance in the pathogenesis of B-cell (75% of samples) of which the most common are 13q 12-14 and 13q14-22. The search for a candidate tumour, suppressor gene on 13q14 has been recently restricted to a region containing the band 13q14, [Matutes et al., 1996].

The previous abnormalities can now be detected by FISH in interphase cells, thus not requiring metaphase spreads, many studies have shown a greater sensitivity of FISH, as this method can detect cases without analyzable metaphases and also some of those with a normal karyotype.