Cell proliferation , PCNA, Ki-67 and P53 In acute leukemia

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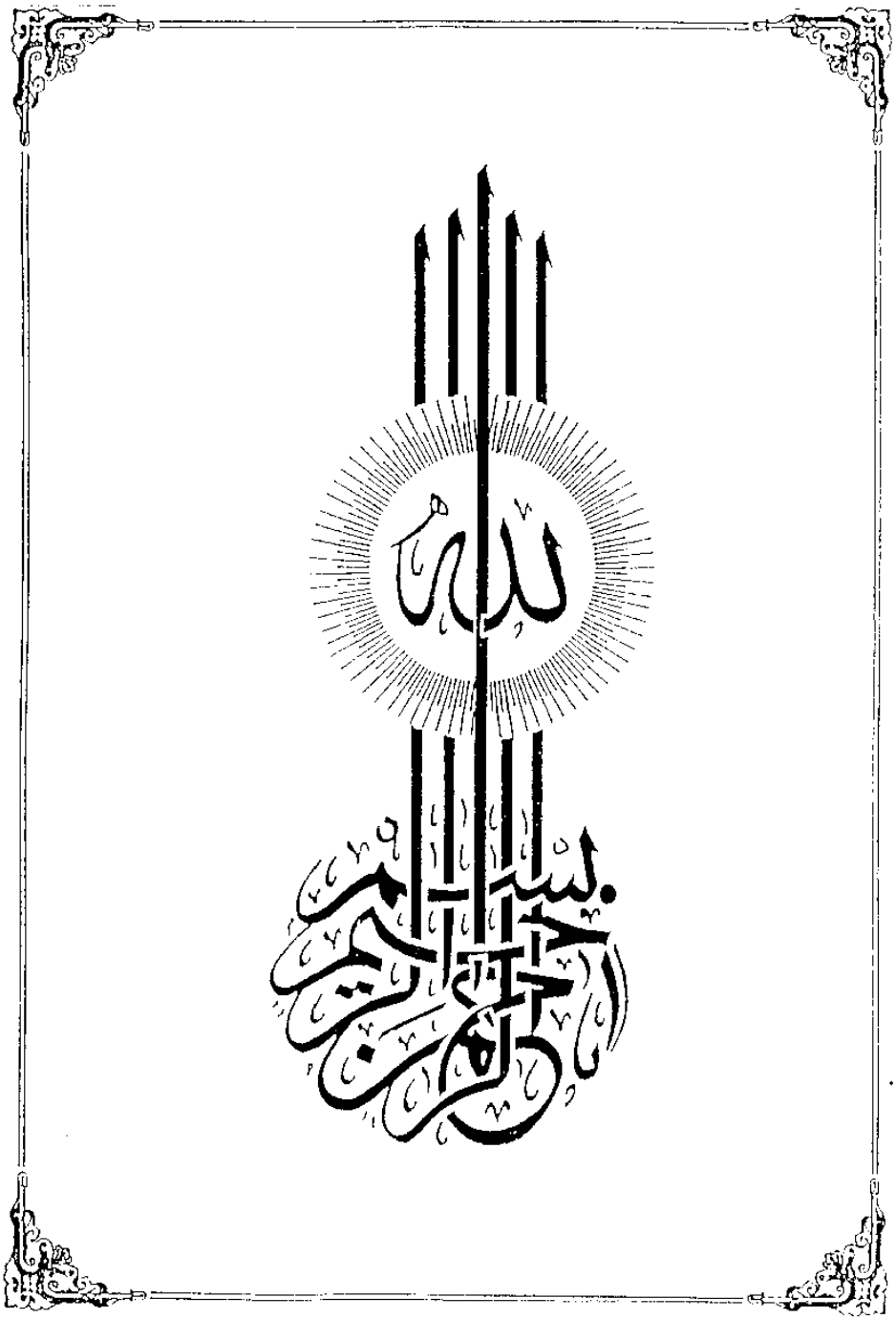

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List of abbreviations

- (AML) acute myelogenous leukemia
- (APAAP) the alkaline phosphatase-antialkaline phosphatase complex
- (APC) The anaphase-promoting complex
- (ATL) adult T-cell leukemia
- (AUL) acute undifferentiated leukemia
- (BM) bone marrow
- (B-PLL) B-cell prolymphocytic leukemia
- (BrdU) bromodeoxyuridine
- (CDKs) Cyclin-dependent kinases
- (CKIs) cyclin-dependent kinase inhibitors
- (CLL) Chronic Lymphocytic Leukemia
- (CML) chronic myeloid leukemia
- (ER) endoplasmic reticulum
- (FAB) French American British
- (FCM) flow cytometry
- (FFA-1) Foci forming activity 1 protein
- (IdUrd) iododeoxyuridine
- (LDT) lymphocyte doubling time
- (LI) labeling index
- (MAb) monoclonal antibody
- (MDSs) myelodysplastic syndromes
- (ML) malignant lymphoma
- (NHL) non-Hodgkin's lymphoma
- (PBMC) peripheral blood mononuclear cells
- (PBS) Phosphate Buffer Saline
- (PCNA) proliferating cell nuclear antigen
- (PCNA-S) S-phase specific PCNA
- (PE) phycoerythrin
- (PI) propidium iodide
- (pol) polymerase

- (pRB) The retinoblastoma tumor suppressor protein
- (RF-C) replication factor C
- (RFC) replication factor C
- (RPA) replication protein A
- (SDS-PAGE) sodium dodecyl sulfate polyacrylamide gel electrophoresis
- (SPF) S-phase fraction
- (SV 40) simian virus 40
- (T-ag) tumor antigen
- (Tpot) potential tumour doubling time
- (TSGs) tumor suppressor genes
- (wtp53) wild type p53
- (ALL) acute lymphoblastic leukemia
- (ANLL) acute nonlymphoblastic leukemia
- (cip 1) cycling interacting protein 1
- (ERCC3) excision repair protein
- (G1) (gap 1) phase
- (G2) (gap 2) phase
- (GADD45) growth arrest and DNA damage 45
- (kb) kilobases
- (KD) kilodalton
- (MPF) the M-phase promoting factor
- (RF-A) replication factor A
- (S) (synthetic) phase
- (UV) ultraviolet

INTRODUCTION

Introduction:

Actively dividing cells produce a number of unique proteins that may serve as useful antigenic markers in immunologic studies of cellular proliferation. The Ki-67 monoclonal antibody, recognizes one subprotein that is present only in the nucleus of cycling cycle but is absent in resting cells ***(Gerdes et al , 1984).*** Ki-67 is used as a tool in evaluating growth fractions and prognostic significance in haematological malignancies such as non Hodgkin's lymphoma ***(Gerdes et al , 1987)*** and acute leukemia ***(Falini et al , 1988)*** .

Antibodies to proliferating cell nuclear antigen (PCNA) were detected in some patients with systemic lupus erythematosis, they reacted with a nuclear antigen expressed predominantly by proliferating cells such as cultured cells and mitogen-transformed cells ***(Miyachi et al , 1978)***.

The function of proliferating cell nuclear antigen (PCNA) in DNA replication and repair is to form a sliding clamp with replication factor C (RF-C) tethering DNA polymerase δ or φ to DNA. In addition, PCNA has been found to interact directly with various proteins involved in cell cycle regulation ***(Schurtenberger et al., 1998).***

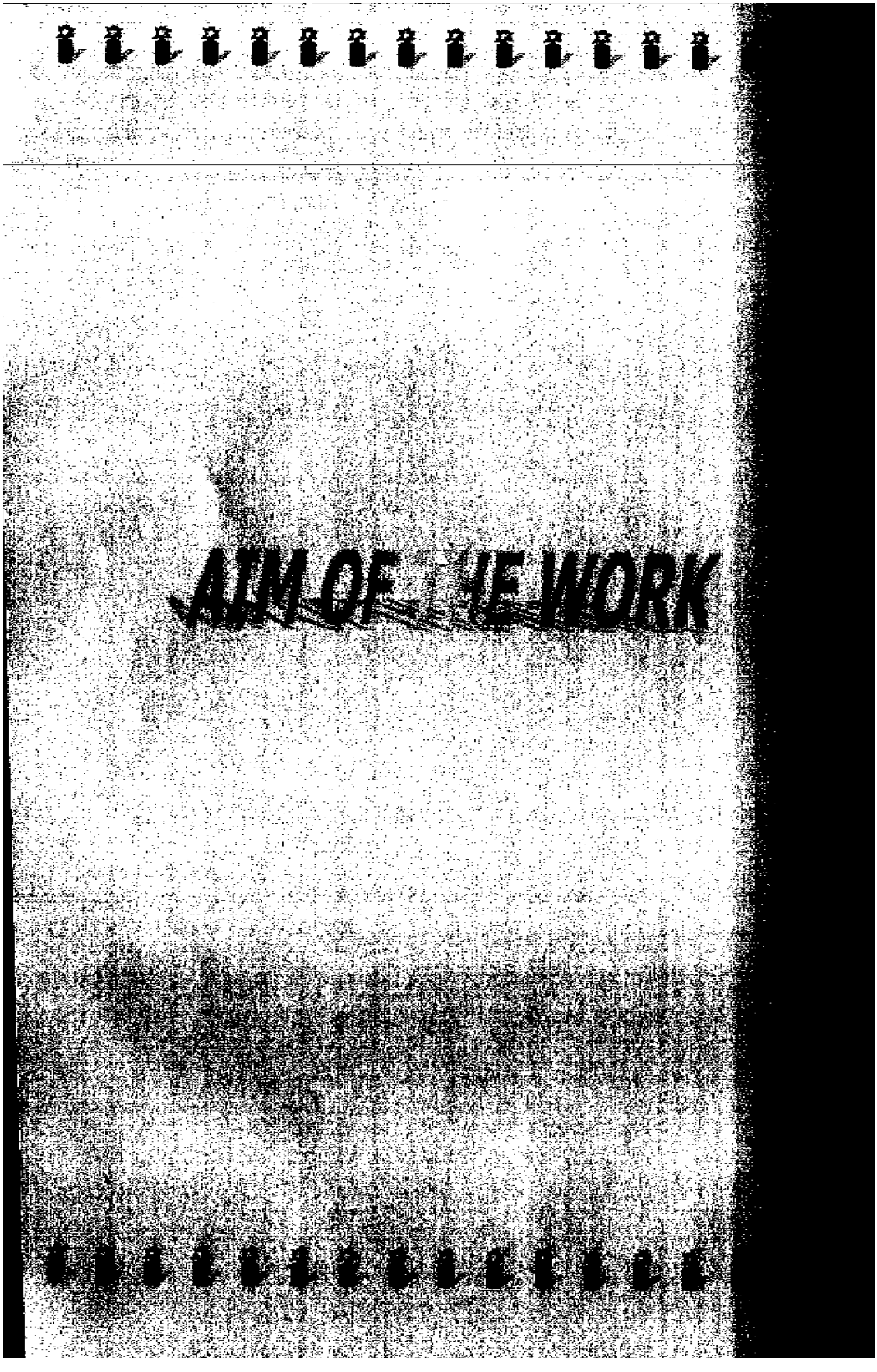
PCNA has been found in all phases of the cell cycle in actively proliferating cells. Thus it has been found to be a useful marker for detecting proliferating cells in solid tumours and identifying blast transformed cells in patients with leukemia ***(Takasaki et al , 1984).***

P53 is a nuclear phosphoprotein encoded by a gene mapped on the short arm of chromosome 17 ***(Isobe et al, 1986)***. It is usually expressed at low levels and has a short half-life (only 6 minutes in the spleen) ***(Gerdes et al, 1984).***

Mutant p53 expressed in many types of carcinoma lacks an inhibitory function on cell growth, but its role has been unclear ***(Kurose et al., 1995).***

The p53 tumour suppressor protein is a potent transcription factor. p53 is latent in cells and can be activated in response to signals arising from a range of stresses including DNA damage, hypoxia, nucleotide depletion, viral infection and cytokines. Activation of p53 leads either to cellular growth arrest at the G1/S or G2/M transitions of the cell cycle or to programmed cell death (apoptosis) ***(Meek, 1997).***

Although the investigations of Ki-67 and PCNA have suggested that both nuclear antigens are simple and fast markers of the proliferating compartment of human tumours, very little is known about the relationship between Ki-67 and PCNA expression of any given human cell subset ***(Landberg et al, 1990).***


AIM OF THE WORK