INTRODUCTION

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The polypeptide growth factors that bind to the cell surface receptors and oncogenes are intimately involved in the control of the mammalian cell cycle during the G1 phase until the restriction point which occurs 2hours prior to the onset of DNA synthesis *(Basarga 1985)*. After the restriction point, growth factors are no longer required for cells to continue their progression into the S-phase *(Dariuesz et al., 1988)*.

Concomitant with the onset of DNA synthesis the activities of several enzymes-notably thymidine kinase (TK), thymidyate synthtase and dihydro folate reductase increase dramatically.

TK exhibits periodic increase at G_1 /S boundary of the cell cycle and remains high through out s-phase to meet the demand for thymidin tri-phosphate (TTP) and declines following s-phase *(kenneth et al., 1989)*. TK, activity exists in profilerating cells but not in resting or terminally differentiated cells.

TTP is required for DNA synthesis TK catalyses the conversion of deoxy thymidine to deoxy thymidine monophosphate (dTMP) in the presence of ATP. dTMP is progressively converted to triphosphate form (TTP) and subseguently incorporated into DNA, restoring thymidine to the pool of DNA precursors. For this reason, thymidine kinase has been considered a salvage pathway for DNA synthesis but the presence of two forms of thymidine kinase, a cytoplasmic form (TK1 - TK-F) coded by a gene on chromosome 17 of the human nucleus and mitochondrial (TK2) form coded by a gene on chromosome 16 caupled with elevated thymidine kinase activity (Particularly cytoplasmic activity) in fetal tissues, many tumors and rapidly replicating tissues suggests that the enzyme plays a much more important role that of merely returning thymidine to the pool of DNA precursors *(Tayleor et al., 1981)*

The regulation of the amount of thymidine kinase is complex and occurs at transcriptional, post-transcriptonal and translation levels. Recent reports indicate that a major regulatory element in the s-phase is TK-gene promotoer *(Kenneth et al., 1989)*.

By DNA sequence analysis there are at least three types of TK transcription (TATA, GC, CCAAT) found near the transcription initiated site of the gene. Accessory proteins would bind the CCAAT binding protein causing repression until another round of DNA synthesis was stimulated.

James and Thomas 1988 identified two post-transcriptional mechanisms that largely account for the change in the rate of accumalation of thymidine kinase protein during cell cycle progression. One is due to increase in the efficiency of transilation of TK mRNA and TK activity has shown to correlate with proliferative activity of tumor cells, Additionally, certains viruses are able to induce cellular TK production and activity. Clinical studies have reported elevated serum TK levels in a variety of newplasias. The majorty of these studies concerned hematologic malignancies such as ALL, AML, CML, CLL and in non-Hodgkm's lymphoma *(Hallek et al., 1992)*. Elevated S-TK levels were found in patients with lung cancer of the small cell type, prostate cancer and breast cancer. TK seems to be a useful markers in leukemia where it correlates with clinical status of the disease and provides significant prognostic information and effect of therapy. second is due to stable of the newly synthesized enzyme.

The present study was designated to investigate how the pre-treatment level of S-TK correlates to various types of leukemias, the remission rate, maintenance and relapse trying to find out their possible role in diagnosis and to be useful for longitudinal follow up studies and monitoring the course of the disease status and assesing the prognostic relevance of S-TK

in relation to effect of therapy. And trying also to find the relation between leukemias and thymidine kinase gene regulation during the cell cycle.