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Document Title : *MUTATIONAL ANALYSIS OF T3 ONCOGNE IN ACUTE MYELOID LEUKMIN PATIENTS*

دراسة الطفرات الجينية في جين FL T3 في مرض سرطان الدم

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Abstract : Leukemia is a malignant neoplasm of hematopoietic tissue originating in and infiltrating the bone marrow. Acute myloid leukemia is a type of leukemia that is characterized by proliferation of immature myloid cells of blasts, and its classified using FAB classification based on standard morphology cytochemical stain of bone marrow. Receptor type tyrosine kinase(RTKs) constitute a family of proteins involved in growth and developmental process. Class 3 RTKs are characterized by an extracellular region composed of five immunoglobulin - like domains and by a split tyrosine kinase domain. Some of the class 3 play an important role in the hematopioesis. One of these is FLT3 receptors expressed by immature hematopoietic cells and is important for the normal development of stem cells and the immune system. Mutation of FLT3 have been detected in about 30% of Patients with acute myelogenous leukemia and a small number of patients With acute lymphocytic leukemia or myelodysplastic syndrome . patients with FLT3 mutation tend to have a poor prognosis . The mutation most often involve small tandem duplication of amino acids within the juxtamembrane domain of the receptor (25%) of AML and point mutation in the activation loop of FLT3 kinase domain (7%) result in constitutive tyrosine kinase activity. Expression of a Mutant FLT3 receptor in murine marrow cells results in a lethal myeloproliferative Syndrome. Preliminary studies, however, suggest that mutant FLT3 cooperates with other leukemia oncogenes to confer a more aggressive phenotype. In the current work 63, archival unstained bone marrow slides were studied as an AML cases, using PCR amplification for DNA and screened for mutation using Conformation Sensitive Gel- Electrophoresis (CSGE) for FLT3 exon 20 mutations, direct automated sequencing and digestion by ECORV restriction enzyme was also employed to the samples gave positive results on the CSGE. Mutation were deleted in 12/63 (19%) and was in codon835. this frequency is, however, higher than what have been reported by other workers. Taken together, the results of these two different techniques suggest that FLT3 in an attractive therapeutic target for kinase inhibitors or other approaches for patients with mutation of this gene.

Supervisor : د. سهره بنت أحمد لاري .د. فاتن بنت محمد سايس

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