عنوان مقاله:

Curing Chronic Myeloid Leukemia: Emerging and Novel Targeting Opportunities

محل انتشار:

اولین سمپوزیوم بین المللی سرطان نسترن (سال: 1394)

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خلاصه مقاله:

Many patients with chronic myeloid leukemia (CML) have a characteristic and specificchromosomal abnormality known as Philadelphia (Ph) chromosome that might be linked tothe uncontrolled clonal expansion of transformed myeloid progenitor cells in them.Reciprocal translocation between the abl gene on chromosome 9 and the bcr gene onchromosome 22 accounts for the expression of a fusion oncogene in more than 95% of CMLpatients. The resultant chimeric protein, p210bcr-abl, is a constitutively active tyrosine kinasewhich is involved in growth factor independent, resistance to apoptosis and altered adhesionof CML cells. CML starts with an indolent chronic phase (CML-CP) that is defined asenhanced proliferation of functionally and differentially normal myeloid lineage cells. Withouteffective treatment, CML progresses to blastic phase that is associated with the accumulationof undifferentiated CML cells in bone marrow and peripheral blood. Among CML therapies,molecularly targeted therapy against bcr-abl protein by small molecule tyrosine kinaseinhibitors (TKIs) has substantially improved CML prognosis. Imatinib as an undisputedinhibitor of bcr-abl protein is the current first-line therapy for CML. Despite promising results,the incidence of resistance to the imatinib motivates massive efforts for optimizing TKIsdosing and developing two and third-generation of TKIs that comprehensively cover bcr-ablmutants. However, minimal residual disease (MRD) and the presence of active diseasereveal that clinical resistance occurs despite TKI-induced inhibition of bcr-abl kinase activityin some patients. Hence, it seems that the identification of crucial targets in addition to bcr-ablprotein is an .inevitable strategy for the elimination of CML cells

کلمات کلیدی:

CML, Bcr-abl Protein, Tyrosine Kinase Inhibitors, Imatinib, Resistance