عنوان مقاله:

Evaluation Of Biological Activity And Specificity Of Mesenchymal Epithelial Transition (MET) Proto-Oncogene In KYSE-30 Cell Line

محل انتشار:

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خلاصه مقاله:

Esophageal squamous cell carcinoma (ESCC) is the sixth and ninth most common cancer betweenmen and women worldwide, respectively. ESCC is a frequently recurrent deadly cancer for which noefficient targeted drug exists. Uncontrolled cell survival, growth, angiogenesis and metastasis areessential signs of cancer. Genetic and biochemical experiments have demonstrated that hepatocytegrowth factor/scatter factor (HGF/SF) and its receptor, the tyrosine kinase MET, have an importantrole in all of these processes, thus providing a strong rationale for targeting these molecules incancer. Small Molecules Inhibitors (SMIs) of the kinases are considered as one of the mostpromising molecular strategies to combat with such aggressive cancers. Heterocyclic compoundscomposed of a common core structure and different substituents used in this study. KYSE-30 cellline was used for cellular examinations. Cytotoxicity evaluation tests at different concentrations ofcompounds were performed using Resauzurin reagent for this cell line. Graphpad Prism softwarewas used for analysis of the cell survival data and calculation of IC50 values for each compound.Another cellular and molecular experiments such as migration assay and western blot performed toidentify the specificity of compounds for MET receptor. Regarding the cytotoxic assessments, theIC50 concentration had a rising trend in D7, 1 and 5, respectively. All of them significantly inhibitedthe cell growth and proliferation ($p<0.05$). Moreover, it was observed that all of the compound, hada significant role on cell migration arrest ($p<0.05$). The western blot also approved that, these drugshave inhibited MET auto phosphorylation. Western blot analysis have shown that the D1, 5 and 7canbe introduced as specific drugs to target the MET receptors. D1 and 7have shown properly aninhibitory influence on cell growth and migration. Although, 5 was enough specific to target theMET, they require a structural optimization to have a better inhibitory function. In conclusion,regarding the importance of MET inhibition in drug selection, our drugs should be optimizedstructurally to have more specificity against the MET receptor.

کلمات کلیدی: