MET

see Methionine.

Cancer is a complex disease with profound genomic alterations and extensive heterogeneity. Recent studies on a large-scale genomics have shed lights on the impact of core oncogenic pathways which are frequently dysregulated in a wide spectrum of cancer types. Aberrant activation of hepatocyte growth factor (HGF) signaling axis has been associated with promoting various oncogenic programs during tumor initiation, progression, and treatment resistance. As a result, HGF-targeted therapy has emerged as an attractive therapeutic approach. However, recent clinical trials involving HGF-targeted therapies have demonstrated rather disappointing results. Thus, an alternative, in-depth assessment of new patient stratification is necessary to shift the current clinical course.

METHODS: To address such challenges, we have evaluated therapeutic efficacy of YYB-101, a HGF neutralizing antibody, in a series of primary glioblastoma stem cells (GSCs) both in vitro and in vivo. Furthermore, we performed genome and transcriptome analysis to determine genetic and molecular traits that exhibit vulnerability to HGF-mediated therapy.

We have identified differentially expressed genes, including MET, KDR, and SOX3 which are associated with tumor invasiveness, malignancy, and unfavorable prognosis in glioblastoma patients. We also demonstrated HGF-MET signaling axis as a key molecular determinant in GSC invasion and also discovered that a significant association in HGF expression existed between mesenchymal phenotype and immune cell recruitment.

Up-regulation of MET and mesenchymal cellular state are essential in generating HGF-mediated therapeutic responses. Our results provide an important framework for evaluating HGF-targeted therapy in future clinical settings [1].

1)
Sa JK, Kim SH, Lee JK, Cho HJ, Shin YJ, Shin H, Koo H, Kim D, Lee M, Kang W, Hong SH, Kim JY, Park YW, Song SW, Lee SJ, Joo KM, Nam DH. Identification of Genomic and Molecular Traits that Present Therapeutic Vulnerability to HGF-targeted therapy in Glioblastoma. Neuro Oncol. 2018 Jun 23. doi: 10.1093/neuonc/noy105. [Epub ahead of print] PubMed PMID: 29939324.