Targeting the epithelial to mesenchymal transition in glioblastoma: the emerging role of MET signaling.

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Abstract
Glioblastoma multiforme (GBM) is the most common human primary brain malignancy and has a dismal prognosis. Aggressive treatments using maximal surgical resection, radiotherapy, and temozolomide result in median survival of only 14.6 months in patients with GBM. Numerous clinical approaches using small molecule inhibitors have shown disappointing results because of the genetic heterogeneity of GBM. The epithelial to mesenchymal transition (EMT) is a crucial biological process occurring in the early development stages of many species. However, cancer cells often obtain the ability to invade and metastasize through the EMT, which triggers the scattering of cells. The hepatocyte growth factor (HGF)/MET signaling pathway is indicative of the EMT during both embryogenesis and the invasive growth of tumors, because HGF potently induces mesenchymal transition in epithelial-driven cells. Activation of MET signaling or co-overexpression of HGF and MET frequently represents aggressive growth and poor prognosis of various cancers, including GBM. Thus, efforts to treat cancers by inhibiting MET signaling using neutralizing antibodies or small molecule inhibitors have progressed during the last decade. In this review, we discuss HGF/MET signaling in the development of diseases, including cancers, as well as updates on MET inhibition therapy.

KEYWORDS: MET signaling; epithelial to mesenchymal transition; glioblastoma multiforme