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Hepatocyte growth factor, its receptor, and their potential value in cancer therapies

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Abbreviations: Abl, Abelson murine leukemia viral oncogene; AGTR, angiotensin II receptor; Arf, Archaeal Rieske-type ferredoxin; Arp, actin-related protein; BCL2, B-cell CLL/lymphoma 2; BID, BH3 interacting domain death agonist; cMET, receptor for hepatocyte growth factor; CDK, cyclin-dependent kinase; CMT, Chemically modified tetracycline; COX-2, cyclooxygenase-2; Creb, cAMP responsive element binding protein; Crk, Avian sarcoma virus CT10 oncogene; Crkl, CRK like protein; CTGF, connective tissue growth factor; ECM, extracellular matrix; Edg, endothelial differentiation gene; EGFR, epidermal growth factor receptor; EMT, epithelial–mesenchymal transition; EPA, eicosapentaenoic acid; ERM, ezrin/radixon/moesin family protein; Fadd, Fas (TNFRSF6)-associated via death domain; FAK, focal adhesion kinase; FGF, fibroblast growth factor; Flk, protein tyrosine kinase acting as VEGF receptor; GAB, GRB2-associated binding protein (GAB); GDI, guanine nucleotide dissociation inhibitor; GLA, gamma linolenic acid; GRB, growth factor receptor-bound protein (SH2/SH3 domain adapter protein); GSK3ß, glycogen synthase kinase 3 beta; HA, hyaluronic acid; HAI, Hepatocyte growth factor activator inhibitor; HCC, hepatocellular carcinoma; HGF, hepatocyte growth factor; HGFA, hepatocyte growth factor activator; HIF, hypoxia-inducible factor; HS, Heparan sulphate; Hsp, heat shock protein; HUVEC, human umbilical vein endothelial cells; ICAM, intercellular adhesion molecule; IGFR, insulin-like growth factor receptor; LIMK, LIM kinases that have over 40 members; MAPK, mitogen activated protein kinase; MEK, MAP kinase kinase; MIMP, Met-induced mitochondrial protein; MMP, metalloproteinase; NK4, N-termus and four kringle domain of HGF; OPN, osteopontin; PAK, p21(CDKN1A)-activated kinase; PAR, protease activated receptor; PG, prostaglandin; PI3K, phosphatidylinositol 3-kinase; PLC, phospholipase C; PPAR, peroxisome proliferative activated receptor; RA, retinoic acid; raf-1, leukemia viral oncogene 1; Ras, rat sarcoma virus oncogene; RCC, renal cell carcinoma; Rb-1, retinoblastoma 1; Rho, ras homolog gene family; Rock, Rho-associated; coiled-coil containing protein kinase; RyR, ryanodine receptor; Shc1, src homology 2 domain-containing transforming protein C1; SF, scatter factor; Src, v-src sarcoma (Schmidt–Ruppin A-2) viral oncogene homolog; SRE, serum response element; STAT, signal transducer and activator of transcription; TCF-1, transcription factor-1; TEM, specific tumour endothelial marker; TGF, transforming growth factor; TIMP, tissue inhibitor of metalloproteinase; Trk, potassium uptake system protein; TSP1, thrombospondin 1; uPA, urokinase plasminogen activator; VEGF, vascular endothelial growth factor; VHL, von Hippel–Lindau protein; WASP, Wiskott–Aldrich syndrome protein; WAVE, WAS protein family member; Wnt, wingless-type MMTV integration site family

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Abstract

Hepatocyte growth factor plays multiple roles in cancer, by acting as a motility and invasion stimulating factor, promoting metastasis and tumour growth. Furthermore, it acts as a powerful angiogenic factor. The pivotal role of this factor in cancer has indicated HGF as being a potential target in cancer therapies. The past few years have seen rapid progress in developing tools in targeting HGF, in the context of cancer therapies, including development of antagonists, small compounds, antibodies and genetic approaches. The current article discusses the potential value of HGF and its receptor as targets in cancer therapies, the current development in anti-HGF research, and the clinical value of HGF in prognosis and treatment.

Keywords: Hepatocyte growth factor; HGF; cMET; Cancer metastasis; Angiogenesis; Signal transduction; Cancer therapies