Inhibition of Cell Motility, Angiogenesis and Metastasis

Published date: Feb. 1, 2012

Technology description

Summary

The present invention relates to potent, highly selective antagonists of Grb2 Src homology-2 (SH2) domain binding. Grb2, through its SH2 domain, mediates growth factor driven cell motility in vitro and angiogenesis in vivo . These synthetic, small molecule antagonists have been shown to block cell motility stimulated by hepatocyte growth factor (HGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), and vascular endothelial cell growth factor (VEGF). They also potently inhibit HGF- and VEGF-stimulated morphogenesis and angiogenesis, respectively, in several model systems. HGF stimulates mitogenesis, motogenesis and morphogenesis in a wide range of cellular targets during development and adulthood, and its signaling pathway is frequently over-activated in human cancers, including colon, gastric, breast, lung, thyroid and renal carcinomas, melanoma, several sarcomas as well as glioblastoma. The ability of HGF to initiate a program of cell dissociation and increased cell motility coupled with increased protease production promotes aggressive cellular invasion and is frequently linked to tumor metastasis.
Metastasis, the primary cause of death in most forms of cancer, is a multistep process whereby cells from the primary tumor spread systemically and colonize distant new sites. Blocking critical steps in this process could potentially inhibit tumor metastasis and dramatically improve cancer survival rates. The small, synthetic Grb2 SH2 domain antagonists described in this invention have been shown to inhibit the induced and spontaneous metastasis of melanoma- and prostate cancer-derived tumor cells in mice. These results establish a critical role for Grb2 SH2 domain-mediated interactions in the metastatic process and support the potential efficacy of this class of compound in reducing the metastatic spread of primary solid tumors in humans.
Market:
An estimated 1,444,920 new cancer cases were diagnosed in the U.S. in 2007600,000 deaths caused by cancer in the U.S. in 2006
Cancer is the second leading cause of death in the U.S.
The cancer drug market will likely double to $50 billion in 2010 from $25 billion in 2006

Application area

Inhibition of cell motility-dependent processes, including angiogenesis and metastasis, in several types of cancer such as prostate, colon, gastric, breast, lung, thyroid and renal carcinomas, melanoma and various sarcomas.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com