

## PubMed

U.S. National Library of Medicine  
National Institutes of Health

Display Settings: Abstract

[Anticancer Agents Med Chem.](#) 2009 Dec 16. [Epub ahead of print]

### **An Orally Bioavailable c-Met Kinase Inhibitor Potently Inhibits Brain Tumor Malignancy and Growth.**

Guessous F, Zhang Y, Dipierro C, Marcinkiewicz L, Sarkaria J, Schiff D, Buchanan S, Abounader R.

Departments of Microbiology, University of Virginia, Charlottesville, VA, USA. ra6u@virginia.edu.

The receptor tyrosine kinase, c-Met and its ligand hepatocyte growth factor (HGF) are important regulators of malignancy in human cancer including brain tumors. c-Met is frequently activated in brain tumors and has emerged as a promising target for molecular therapies. Recently, an orally bioavailable small molecule kinase inhibitor of c-Met (SGX523) was developed by SGX Pharmaceuticals. We tested the effects of this inhibitor on c-Met brain tumor cell activation, c-Met-dependent malignancy, and in vivo glioma xenograft growth. SGX523 potently inhibited c-Met activation and c-Met-dependent signaling at nanomolar concentrations in glioma cells, primary gliomas, glioma stem cells and medulloblastoma cells. SGX523 treatment inhibited c-Met-dependent brain tumor cell proliferation and G1/S cell cycle progression. SGX523 also inhibited brain tumor cell migration and invasion. Furthermore, systemic delivery of SGX523 via oral gavage to mice bearing orthotopic human glioblastoma xenografts led to a significant decrease of in vivo tumor growth. These studies show that c-Met activation and c-Met-dependent brain tumor cell and stem cell malignancy can be inhibited by small molecules. The study also shows for the first time that oral delivery of a small molecule kinase inhibitor of c-Met inhibits intracranial tumor growth. These findings suggest that targeting c-Met with small molecule kinase inhibitors is a promising approach for brain tumor therapy.

PMID: 20015006 [PubMed - as supplied by publisher]

[LinkOut - more resources](#)