



A service of the [U.S. National Library of Medicine](#)
and the [National Institutes of Health](#)

Select 19706788

1: [Am J Physiol Endocrinol Metab.](#) 2009 Aug 25. [Epub ahead of print]



DIFFERENTIAL EFFICACY OF SSTR1, 2 AND 5 AGONISTS IN THE INHIBITION OF C6 GLIOMA GROWTH IN NUDE MICE.

[Barbieri F](#), [Pattarozzi A](#), [Gatti M](#), [Aiello C](#), [Quintero A](#), [Lunardi G](#), [Bajetto A](#), [Ferrari A](#), [Culler MD](#), [Florio T](#).

University of Genova.

Somatostatin receptors (SSTR1-5) mediate antiproliferative effects. In C6 rat glioma cells, somatostatin is cytostatic in vitro via phosphotyrosine phosphatase-dependent inhibition of ERK1/2 activity, mediated by SSTR1, 2 and 5. Here we analyzed the effects of SSTR activation on C6 glioma growth in vivo and the intracellular mechanisms involved, comparing somatostatin effects with selective agonists for SSTR1, 2 and 5 (BIM-23745, BIM-23120, BIM-23206) or receptor bi-selective compounds (SSTR1+2, BIM-23704 and SSTR2+5, BIM-23190). Nude mice subcutaneously xenografted with C6 cells were treated with somatostatin, SSTR agonists (50g, twice/day) or vehicle. Tumor growth was evaluated every 3 days for 19 days. The intracellular pathways responsible of SSTR effects in vivo were evaluated measuring Ki67, phospho-ERK1/2 and p27kip1 expression by immunohistochemistry in sections from explanted tumors. Somatostatin and SSTR1, 2 and 5 agonists strongly inhibited in vivo C6 tumor growth, intratumoral neo-vessel formation, Ki67 expression, ERK1/2 phosphorylation and induced up-regulation of p27Kip1, while only a modest activation of caspase-3 was observed. Somatostatin (acting on SSTR1, 2 and 5) displayed the highest efficacy; SSTR5 selective agonist showed a stronger effect than SSTR1 agonist and SSTR2 agonist was the less effective. On the other hand SSTR1 and 2 agonists maximally reduced tumor neovascularization. The combined activation of SSTR1 and 2 showed a synergistic activity reaching a higher efficacy than BIM-23206, while the simultaneous activation of SSTR2 and 5 resulted in a response resembling SSTR5 effects. Thus the simultaneous activation of different SSTRs inhibits glioma cell proliferation in vivo through both direct cytostatic and antiangiogenic effects. Key words: somatostatin, glioblastoma, antiproliferative activity, in vivo, ERK1/2.

PMID: 19706788 [PubMed - as supplied by publisher]
