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SOMATOSTATIN INHIBITS TUMOR ANGIOGENESIS AND GROWTH VIA SOMATOSTATIN RECEPTOR 3 (SSTR3) MEDIATED REGULATION OF ENDOTHELIAL NOS AND MAP KINASE ACTIVITIES

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Aim of investigation: Somatostatin (SST) inhibits Kaposi sarcoma (KS) development in nude mice. SST effects are purely antiangiogenic involving the modulation of both endothelial cell proliferation and invasion and monocyte activation. Here, we evaluate the SST receptor subtypes and the intracellular mechanisms involved in the SST effects, at endothelial cell level.
Methods: Angiogenesis was analyzed *in vivo* using the matrigel sponge test, cell proliferation using the [^{3}H]-thymidine uptake assay, eNOS and ERK1/2 activation by means of the Griess reaction and Western blot using phospho-specific antibody, respectively.
Results: SST inhibits *in vivo* neoangiogensis induced by both KS products and Tat-TNFα treatments, an effect reverted by the non-peptidic SSTR3 antagonist (BN81658). Using different endothelial cell lines (BAEC, EAhy926), we show that SST affects cell proliferation, through the inhibition of growth factor-stimulated ERK1/2 and eNOS activities. BN81658 reverts also SST inhibition of cell proliferation, NO production and ERK1/2 activation, suggesting that SSTR3 activation is required for the SST inhibition of endothelium proliferation, NO production and ERK1/2 activation. I*n vivo* experiments confirmed these data since in the presence of sodium nitroprusside, a NO donor, SST effects are abolished.
Conclusion: SST impairment of tumoral angiogenesis involves, at endothelial cell level, SSTR3-dependent inhibition of both eNOS and MAP kinase activities.

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