Dexamethasone reduced invasiveness of human malignant glioblastoma cells through a MAPK phosphatase-1 (MKP-1) dependent mechanism.

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Dexamethasone has been shown to inhibit tumor invasiveness. In the present study, the effects of dexamethasone on matrix metalloproteinases-2 (MMP-2) secretion, cell invasiveness, and intravasation in human U87MG glioma cells were examined. Dexamethasone decreased MMP-2 secretion and cell invasiveness in human glioma cells. Incubation of cells with dexamethasone increased mitogen activated protein kinase phosphatase-1 (MKP-1) expression. Ectopic expression of MKP-1 decreased cell invasiveness in vitro and intravasation in vivo. Because expression of inducible nitric oxide synthase (iNOS) has been implicated in the progression of malignant gliomas, we next investigated the possible roles of NO(-) in MMP-2 secretion and cell invasiveness in human U87MG glioma cells. Treatment of glioma cells with nitric oxide donor, sodium nitroprusside (SNP), increased MMP-2 secretion and the capacity of cell invasion in U87MG cells. Addition of dexamethasone or ectopic expression of wild-type MKP-1 suppressed the SNP-stimulated MMP-2 activation and glioma cell invasiveness in U87MG cells. Taken together, these results suggest that dexamethasone may suppress MMP-2 secretion and cell invasion through MKP-1 induction in human glioma cells.

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