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•	MKP-1 (II)
•	The Cytoprotective Effect of MKP-1 (II)
•	• NSC95-2320-B038-006
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•	9508 ~ 9607
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•	Lee, Horng-Mo
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•	MMP-2; ; Brain tumor; MKP-1; Dexamethasone
•	Dexamethasone glucocorticoids dexamethasone dexamethasone MMP-2 dexamethasone MKP-1 dexamethasone (adjuvanttherapy) iNOS NO (l-NAME) NOdonor(SNP) NO MMP-2 Dexamethasone rosiglitazone MKP-1 iNOS NO MMP-2 MKP-1 MAPK MMP-2
•	Dexamethasone is one of glucocorticoids has been shown to inhibit tumor invasiveness. However, the underneath mechanisms have not been elucidated. In the present study, we investigated the mechanism by which dexamethasone regulated the invasiveness in human malignant glioma cells. We demonstrated that dexamethasone decreased MMP-2 activity in malignant glioma cells. Incubation of glioma cells with dexamethasone increased a dose- and time-dependent induction of MAPK phosphatase-1 (MKP-1). Pretreatment of cells with RU486 (glucocorticoid receptor antagonist), actinomycin D or cyclohexamide before addition of dexamethasone decreased MKP-1 protein level, suggesting dexamethasone-induced MKP-1 expression required de novo protein

synthesis through glucocorticoid receptor. Treatment of cells with RU486 reversed the inhibition of MMP-2 activity and cell invasiveness by dexamethasone. Similarly, knockdown of MKP-1 by small interfering RNA or expression of dominant negative MKP-1 reversed the inhibition of MMP-2 activity by dexamethasone. These data suggest that dexamethasone-inhibited MMP-2 activity and cell invasiveness via MKP-1. On the other hand, we found that iNOS was constitutiely expressed in human malignant glioma cells. We found that NO- regulate MMP-2 expression in U87MG cells. Over-expression of wild type MKP-1 decreased iNOS expression but not in MKP-1 dominant negative. Taken together, our data revealed that dexamethasone might inhibit MMP-2 activity by suppressing iNOS induction through a MKP-1-dependent pathway. These results suggest that dexamethasone can be used as a potential therapeutic agent for treatment of metastasis of human gliomas.