Expression of matrix metalloproteinases MMP-1, MMP-11 and MMP-19 is correlated with the WHO-grading of human malignant gliomas

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Abstract

Glioblastomas (GBM) are the most prevalent type of malignant primary brain tumor in adults. They may manifest de novo or develop from low-grade astrocytomas (LGA) or anaplastic astrocytomas. They are characterized by an aggressive local growth pattern and a marked degree of invasiveness, resulting in poor prognosis. Tumor progression is facilitated by an increased activity of proteolytic enzymes such as matrix metalloproteinases (MMPs). Elevated levels of several MMPs were found in glioblastomas compared to LGA and normal brain (NB). However, data for some MMPs, like MMP-1, are controversially discussed and other MMPs like MMP-11 and MMP-19 have as yet not been analysed in detail. We examined the expression of MMP-1, MMP-9, MMP-11 and MMP-19 in NB, LGA and GBM by semiquantitative RT-PCR, Western blotting and immunohistochemistry and found an enhanced expression of these MMPs in GBM compared to LGA or NB in signal strength and in the percentage of tumors displaying MMP expression. The transition from LGA to GBM was characterized by a shift of pro-MMP-11 to expression of the active enzyme. Therefore, MMP-1, MMP-11 and MMP-19 might be of importance for the development of high-grade astrocytic tumors and may be promising targets for therapy.

Keywords: Matrix metalloproteinase; Glioma; Astrocytoma; Glioblastoma multiforme; Protein expression; Expression analysis

Abbreviations: DAB, diaminobenzidine; ECM, extracellular matrix; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; GBM, Glioblastoma multiforme; HRP, horseradish peroxidase; LGA, low-grade astrocytoma; MMPs, matrix metalloproteinases; NB, normal brain; PLB, protein loading buffer; TCEP, tris (2-carboxyethyl) phosphine hydrochloride; RT, reverse transcriptase; TBST, tris-buffered saline tween-20; U, unit

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