Osteopontin regulates human glioma cell invasiveness and tumor growth in mice

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摘要

Abstract

Human malignant glioma cells are characterized by local invasion. In the present study, we investigated the role of osteopontin (OPN) in the invasiveness of human glioma cells isolated from grade IV tumors. We found that the expression levels of OPN in these cell lines paralleled matrix metalloproteinase-2 (MMP-2) expression and cell invasiveness potential. When U87MG glioma cells (with a high-OPN expression level) were stably transformed with specific small hairpin RNA to knock down OPN expression, MMP-2 secretion, cell invasiveness, and tumor growth in implanted brains were dramatically reduced. Conversely, forced expression of OPN in GBM-SKH glioma cells (which expressed OPN at a low level) increased MMP-2 secretion, enhanced cell invasiveness, and increased tumor growth in a rodent xenograft model. Expression of OPN was associated with increased expression of vimentin and decreased expression of glial fibrillary acidic protein. Treatment of glioma cells with 5-aza-2'-deoxycytidine (5-aza-dC) suppressed OPN expression in a concentration-dependent manner. Suppression of OPN expression by 5-aza-dC was associated with reductions in MMP-2 secretion, vimentin expression, cell invasion, intravasation, and tumor growth. These data suggest that OPN may play important roles in regulating cell invasion in glioma cells and that 5-aza-dC may serve as a therapeutic agent for human gliomas.