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Genetically-engineered *Salmonella typhimurium* expressing TIMP-2 as a therapeutic intervention in an orthotopic glioma mouse model

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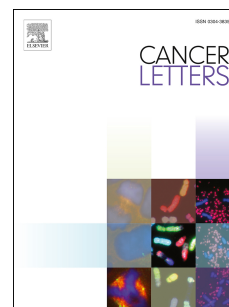
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ABSTRACT

Glioma is one of the most devastating and refractory cancers. The main factors underlying therapeutic failure include extremely invasive characteristics and lack of effective methods for drug delivery. Attenuated *Salmonella* strains presented a high concentration of tumor targets in various types of cancer models, suggesting a role as potential vectors for drug delivery. In this study, we genetically engineered an attenuated strain of *Salmonella* as an anti-invasive vector for the targeted delivery and expression of tissue inhibitor of metalloproteinases 2 (TIMP-2) in an orthotopic nude mouse model of glioma. The bioluminescence signals related to tumor size significantly declined in the TIMP-2-expressing *Salmonella* (SLpTIMP-2)-treated group compared with the control group. Compared with the control group with a survival rate of an average of 33 days, the SLpTIMP-2 group showed an extended survival rate by nearly 60% and lasted an average period of 53 days with TIMP-2 induction. These results indicated the promising therapeutic potential of *S. typhimurium* for targeted delivery and secretion of TIMP-2 in glioma.

Keywords: tissue inhibitor of matrix metalloproteinases 2 (TIMP-2), *Salmonella typhimurium*, glioma, matrix metalloproteinase 2 (MMP-2)

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