Tumor necrosis factor related apoptosis inducing ligand (TRAIL)

Because the tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) selectively kills tumor cells, it is one of the most promising candidates for cancer treatment.

TRAIL-secreting human mesenchymal stem cells (MSC-TRAIL) provide targeted and prolonged delivery of TRAIL in glioma therapy. However, acquired resistance to TRAIL of glioma cells is a major problem to be overcome.

A potential therapy that used MSC-TRAIL combined with the chemotherapeutic agent temozolomide (TMZ). The antitumor effects of the combination with MSC-TRAIL and TMZ on human glioma cells were determined by using an in vitro coculture system and an in vivo experimental xenografted mouse model. Intracellular signaling events that are responsible for the TMZ-mediated sensitization to TRAIL-induced apoptosis were also evaluated. Treatment of either TRAIL-sensitive or -resistant human glioma cells with TMZ and MSC-TRAIL resulted in a significant enhancement of apoptosis compared with the administration of each agent alone. We demonstrated that TMZ effectively increased the sensitivity to TRAIL-induced apoptosis via extracellular signal-regulated kinase-mediated upregulation of the death receptor 5 and downregulation of antiapoptotic proteins, such as X-linked inhibitor of apoptosis protein and cellular FLICE-inhibitory protein. Subsequently, this combined treatment resulted in a substantial increase in caspase activation. Furthermore, in vivo survival experiments and bioluminescence imaging analyses showed that treatment using MSC-TRAIL combined with TMZ had greater therapeutic efficacy than did single-agent treatments. These results suggest that the combination of clinically relevant TMZ and MSC-TRAIL is a potential therapeutic strategy for improving the treatment of malignant gliomas [1)].

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Kim SM, Woo JS, Jeong CH, Ryu CH, Jang JD, Jeun SS. Potential Application of Temozolomide in Mesenchymal Stem Cell-Based TRAIL Gene Therapy Against Malignant Glioma. Stem Cells Transl Med. 2014 Jan 16. [Epub ahead of print] PubMed PMID: 24436439.