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Multi-responsive nanofibers composite gel for local drug delivery to inhibit recurrence of glioma after operation

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Abstract

Background: The postoperative recurrence of malignant gliomas has presented a clinical conundrum currently. Worse, there is no standard treatment for these recurrent tumours. Therefore, novel promising methods of clinical treatment are urgently needed.

Methods: In this study, we synthesized reactive oxygen species (ROS)-triggered poly(propylene sulfide)60 (PPS60) mixed with matrix metalloproteinases (MMPs)-responsive triglycerol monostearate (T) lipids and TMZ. The mixed solution could self-assemble at 50 ℃ to generate hydrogels with MMPs- and ROS-responsiveness. We explored whether the T/PPS + TMZ hydrogel could achieve the MMP- and ROS-responsive delivery of TMZ and exert anti-glioma regrowth effects in vitro and in vivo. These results demonstrated that the T/PPS + TMZ hydrogel significantly improved the curative effect of TMZ to inhibit postsurgical recurrent glioma.

Results: The results confirmed the responsive release of TMZ encapsulated in the T/PPS + TMZ hydrogel, and the hydrogel showed excellent performance against glioma in an incomplete glioma operation model, which indicated that the T/PPS + TMZ hydrogel effectively inhibited the growth of recurrent glioma.

Conclusion: In summary, we successfully developed injectable MMPs- and ROS-responsive hydrogels that could achieve the sustained release of TMZ in the surgical cavity to inhibit local recurrent glioma after surgery.

Keywords: Local drug delivery, Glioma, Hydrogel, Operation, Recurrence

Background

Glioma is the most common type of primary tumour in the brain and is derived from the nerve epithelium [1, 2]. Although therapies against malignant gliomas, including surgery, radiotherapy and chemotherapy, have been widely used, the therapeutic effect remains poor [3–6]. The median survival of malignant glioma patients is less than 14.6 months [7, 8]. The hardest problem in treating glioma is postoperative recurrence. Complete resection is deemed impossible in high-grade gliomas, and residual glioma cells contribute to postoperative glioma recurrence [9]. Clinical studies found that 80–90% of recurrent gliomas occur within 2 cm of the original region [8, 10, 11]. Decreasing glioma recurrence caused by residual tumour cells has become an important topic in clinical research and practice.

Currently, there are no specific cures for recurrent gliomas. TMZ is still a first-line chemotherapeutic for the clinical treatment of recurrent gliomas [12–14]. However, the therapeutic efficacy of TMZ is often limited by several factors, including its short half-life in vivo, rapid

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