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ABSTRACT

Preventing the Progression and Recurrence of Glioblastoma Via Postoperative Injection of Targeted Drug-Loaded Hydrogel

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Despite aggressive treatments including surgery, chemotherapy, and radiotherapy, the prognosis of glioblastoma (GBM) remains dismal, and tumor recurrence is unavoidable. Although many targeted therapeutics showed excellent anti-glioma effects, their brain delivery is significantly restricted by the blood-brain barrier. Therefore, we aim to find an effective strategy efficiently deliver promising targeted agent(s) to GBM.

Recently, hydrogel-based drug delivery systems have demonstrated their potential advantages in injectability, sustained drug retention and bio-compatibility for cancer treatment. It is particularly suitable for GBM treatment, as the cavity left by surgical resection (required for most cases) of GBM provides room for drug-loaded hydrogel. Importantly, the postoperative in situ injection of hydrogel bypasses the blood-brain barrier and avoids several disadvantages of systemic administration: short (drug) half-life, rapid brain clearance, inadequate drug delivery and unwanted side effects.

To further enhance the anti-glioma efficacy of targeted therapy, we integrated the Fe3+/Cu2+ into the hydrogel to trigger the Fenton/Fenton-like reaction. It leads to accumulation of ROS, and subsequently cause cellular senescence, apoptosis or ferroptosis, depending on the exact targeted agent being loaded into hydrogel. Ultimately, the combination of Fenton/Fenton-like reaction and targeted therapy exhibited synergistic effect in inhibiting GBM progression/recurrence and prolonged the overall survival of treated mice. Together, our pre-clinical evidence proves the usefulness of hydrogel-based drug delivery system and provides a novel paradigm for the postoperative treatment of GBM and other brain malignancies.