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Research Paper

Engineered apoptotic bodies hitchhiking across the blood-brain barrier achieved a combined photothermal-chemotherapeutic effect against glioma

Yu Liu[1,2,4#], Dehong Hu[1#], Duyang Gao[1✉], Ping Gong[3], Hairong Zheng[1], Minjie Sun[2✉], Zonghai Sheng[1✉]

1. Paul C. Lauterbur Research Center for Biomedical Imaging, Institute of Biomedical and Health Engineering, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, 518055, P.R. China.
2. State Key Laboratory of Natural Medicines, Department of Pharmaceutics, China Pharmaceutical University, Nanjing, 210009, P. R. China.
3. Guangdong Key Laboratory of Nanomedicine, CAS Key Laboratory of Health Informatics, Shenzhen Bioactive Materials Engineering Lab for Medicine, Institute of Biomedicine and Biotechnology, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, 518055, P. R. China.
4. Cancer Centre, Institute of Translational Medicine, Faculty of Health Sciences, University of Macau, Taipa, Macau SAR, 999078, P. R. China.

[#] These authors contributed equally to this work.

✉ Corresponding authors: Email address: dy.gao@siat.ac.cn (D. Gao); msun@cpu.edu.cn (M. Sun); zh.sheng@siat.ac.cn (Z. Sheng).

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Abstract

Background: Glioma as a highly lethal tumor is difficult to treat since the blood-brain barrier (BBB) restricts drug delivery into the brain. It remains a huge need for developing strategies allowing drug passage across the BBB with high efficacy.

Methods: Herein, we engineered drug-loaded apoptotic bodies (Abs) loaded with doxorubicin (Dox) and indocyanine green (ICG) to cross the BBB for the treatment of glioma. The confocal laser scanning microscopy was used to characterize the structure and evaluate the hitchhiking effect of the Abs. The *in vivo* BBB-crossing ability and photothermal-chemotherapeutic effect of the drug-loaded Abs were investigated in mice orthotopic glioma model.

Results: Engineered Abs loaded with Dox and ICG were successfully prepared. The Abs were phagocytized by macrophages, actively penetrate the BBB *in vitro* and *in vivo* utilizing the hitchhiking effect. The whole *in vivo* process was visualized by near-infrared fluorescence signal with a signal-to-background ratio of 7 in a mouse model of orthotopic glioma. The engineered Abs achieved a combined photothermal-chemotherapeutic effect, leading to a median survival time of 33 days in glioma-bearing mice compared to 22 days in the control group.

Conclusions: This study presents engineered drug carriers with the ability to hitchhike across the BBB, providing new opportunities for the treatment of glioma.

Keywords: Apoptotic bodies, Blood-brain barrier, Drug delivery, Glioma, Photothermal therapy

Introduction

Glioma is a highly lethal tumor that starts in the glial cells of the brain or the spinal cord [1-3]. Surgical resection is the most effective intervention, but glioma is difficult to treat due to its rapid progression and blurred tumor margins [4, 5]. Other interventions, such as chemotherapy [6-8] and phototherapy [9, 10] are used to enhance the therapeutic efficacy. The blood-brain barrier (BBB) limits the passage of chemotherapeutic drugs or photosensitizers into the brain, reducing their potential benefits [11-13]. There is a current need for developing more efficient drug delivery strategies allowing drug passage across the BBB [14, 15].

Novel procedures have been implemented to deliver drugs into the brain, such as surface modification [16, 17], bionic [18-21] and cell-based drug delivery systems (DDSs) [22-24]. Cell-based DDSs combine the physiological properties (e.g., the