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iNanoGUN

Reactivation of antitumor immune responses in gliomas using nanotechnology based targeted delivery

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Glioblastomas are among the most aggressive and difficult-to-treat cancers. Besides advances in treatment, most of the tumors relapse and become refractory to treatment, leading to a 2-year-survival rate as low as 10-15 %.

Glioblastoma (GBM) is the most common and aggressive brain cancer for which the current therapy is ineffective. Immunotherapy is a new curative approach to trigger the immune system to fight cancer cells and completely eradicate cancer, while keeping healthy cells intact. However, many cancers (including GBM) respond poorly to immunotherapies because host immune built-in defenses are suppressed and their antitumor activity is actively blocked by cancer cells. In GBM, the most abundant immune cells, namely TAMs (tumor-associated macrophages), are re-programmed and support tumor invasion. At the same time they form the immunosuppressive microenvironment, in which the antitumor function of T cytotoxic lymphocytes and natural killer (NK) cells is impeded. In order to sensitize GBM to immunotherapies, we propose to reactivate immune responses in a cancer milieu by re-educating TAMs and NK cells. We will develop smart nanocarrier systems (targeted to the brain and passing through blood brain barrier) to deliver small interfering RNA (siRNA) to those immune cells, re-educate them and revive their antitumor activities. This project will validate the strategy of therapeutic modulation of immune cells in the tumor microenvironment to improve immunotherapy and provide a smart immunomodulatory nanosystem for future clinical applications.