

Triacetin Treatment for Brain Cancer Cells

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Overview

Gliomas are tumors that originate in the glial cells of the brain. Unlike tumors that spread from other organs to the brain, gliomas are highly malignant. Glioblastomas are the most aggressive glioma type and account for 80% of all gliomas (Goodenberger ML, 2012). Patients with glioblastoma have poor prognoses with a median survival of 14 months (Stupp R, 2005).

Due to the delicacy of the brain, surgery may not be an option. Even with surgery, radiation, and chemotherapy, glioma tumors return due, in part, to radiation and chemotherapy resistant glioma stem cells that rapidly reform tumors. Thus, novel therapies that target the glioma stem cells and can be taken long-term without the severe side effects of radiation and chemotherapy are in great demand.

Cancer cells exhibit genetic (DNA mutations), epigenetic (reversible changes to DNA or proteins associated with DNA) and metabolic changes from normal cells, with decreased acetate being one characteristic feature. Since acetate is needed for multiple biological processes, acetate supplementation may be an effective therapy.

Invention

This invention involves the novel use of an FDA approved food additive as an acetate delivery vehicle to increase chemotherapy efficacy.

Because free acetate is not readily taken up by cells, different acetate sources were tested. Treatment of glioma stem cells with N-acetyl-aspartate, the primary storage form of acetate in the brain, increased glioma stem cell growth (Long, 2013). However, Triacetin (glyceryl triacetate, GTA), a small, simple fat that can pass through the blood-brain barrier to deliver acetate, slows the growth of glioma stem cells in culture, but does not affect normal glial cells or neural stem cells (Tsen A, 2013). Thus, GTA would have minimal effects on normal brain cells or neural function (Arun P, 2010).

Most importantly, in pre-clinical studies, when GTA is administered prior to chemotherapy it functions as a powerful adjuvant, increasing chemotherapy effectiveness, to reduce tumor growth and increase survival more than chemotherapy alone. Moreover, GTA increases brain acetate without increasing NAA levels (Mathew R, 2005). Thus, GTA is a safe acetate delivery vehicle for the treatment of glioma.

Advantages

- Low risk of side effects
- Minimal toxicity to non-cancerous cells
- Orally administered and easily absorbed by the stomach and gastrointestinal tract
- Already chronically used for therapy of another disease with no adverse effects

Applications

- Chemotherapy adjuvant for treating gliomas in the central nervous system
- May be effective in treating a wide range of cancers as a chemotherapeutic adjuvant to any alkylating agent used to treat tumors

Patent Status

Patent Application Filed
Worldwide Rights Available

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