Sonodynamic therapy

- Fluorescence-Guided Surgery for Gliomas: Past, Present, and Future
- Focused ultrasound in pediatric neurosurgery: a scoping review of opportunities and challenges
- Carbon Dot-Based Nanoparticles: A Promising Therapeutic Approach for Glioblastoma
- Sonodynamic Therapy Using 5-Aminolevulinic Acid for Malignant Gliomas: A Review
- Overcoming the Blood-Brain Barrier: Focused Ultrasound in Glioblastoma Treatment
- Ruthenium Single-Atom Nanozyme Driven Sonosensitizer with Oxygen Vacancies Enhances Electron-Hole Separation Efficacy and Remodels Tumor Microenvironment for Sonodynamic-Amplified Ferroptosis
- Immunotherapy yields breed-specific worst survival outcomes among three investigated therapies in French bulldogs with high-grade glioma
- Sonodynamic therapy with a single neoadjuvant, diffuse delivery of low-intensity ultrasound with 5-ALA in treatment naive glioblastoma results in tumor-specific cytotoxic edema and increased apoptosis

Sonodynamic therapy is a type of cancer treatment that combines ultrasound waves with special compounds called sonosensitizers. These sonosensitizers accumulate more in tumor cells than in normal cells. When exposed to ultrasound, they produce reactive oxygen species (ROS) that can kill cancer cells, similar to how photodynamic therapy works with light instead of sound.

In short, sonodynamic therapy uses ultrasound plus a chemical agent to selectively destroy cancer cells.

Effectiveness

The effectiveness of traditional inorganic semiconductor sonosensitizers is hindered by rapid electron (e-) and hole (h+) recombination under ultrasonic (US) stimulation, as well as the hypoxic and reductive conditions of tumor microenvironment (TME), which limit the generation of reactive oxygen species (ROS). Herein, a ruthenium (Ru) single-atom nanozyme-driven superimposition-enhanced titanium dioxide-based sonosensitizer (Ru/TiO2-x SAE) is presented that features sufficient oxygen vacancies and high e-/h+ separation efficiency. Through synchrotron radiation-based X-ray absorption spectroscopy and extended X-ray absorption fine structure analysis, it is confirmed that oxygen vacancies in TiO2-x nanoparticles promote the immobilization of single-atomic Ru, forming Ru-O_4 active sites. Density functional theory calculations demonstrate that oxygen vacancies alter the electronic structure of the nanosensitizer, enhance e-/h+ separation, increase oxygen adsorption, and accelerate reaction kinetics under US stimulation, ultimately improving ROS production. Moreover, Ru/TiO2-x SAE boosts sonodynamic efficacy by mitigating the hypoxic and reductive TME. This is attributed to its catalase- and glutathione peroxidase 4-like activities, which facilitate the generation of ROS and trigger lipid peroxidation-mediated ferroptosis. These findings highlight the innovative role of single-atom Ru in optimizing sonosensitizers for SDT-induced ferroptosis, demonstrating its potential for advancing cancer therapy [1)].

Tserkovsky et al. is the first report to demonstrate the benefits of sono-photodynamic therapy (SPDT) consisting of low-power density ultrasound and PDT for the treatment of malignant glioma models [2].

Suehiro et al., from Matsuyama investigated the antitumor activity of sonodynamic therapy (SDT) combined with a sonosensitizer, 5-aminolevulinic acid (5-ALA), on malignant gliomas to explore the possibility for clinical use of 5-ALA-mediated SDT (5-ALA-SDT).

In vitro cytotoxicity of 5-ALA-SDT was evaluated in U87 and U251 glioma cells and in U251Oct-3/4 glioma stemlike cells. Treatment-related apoptosis was analyzed using flow cytometry and TUNEL staining. Intracellular reactive oxygen species (ROS) were measured and the role of ROS in treatment-related cytotoxicity was examined by analysis of the effect of pretreatment with the radical scavenger edaravone. Effects of 5-ALA-SDT with high intensity focused ultrasound (HIFU) on tumor growth, survival of glioma-transplanted mice, and histological features of the mouse brains were investigated.

The 5-ALA-SDT inhibited cell growth and changed cell morphology, inducing cell shrinkage, vacuolization, and swelling. Flow cytometric analysis and TUNEL staining indicated that 5-ALA-SDT induced apoptotic cell death in all gliomas. The 5-ALA-SDT generated significantly higher ROS than in the control group, and inhibition of ROS generation by edaravone completely eliminated the cytotoxic effects of 5-ALA-SDT. In the in vivo study, 5-ALA-SDT with HIFU greatly prolonged survival of the tumor-bearing mice compared with that of the control group ($p < 0.05$). Histologically, 5-ALA-SDT produced mainly necrosis of the tumor tissue in the focus area and induced apoptosis of the tumor cells in the perifocus area around the target of the HIFU-irradiated field. The proliferative activity of the entire tumor was markedly decreased. Normal brain tissues around the ultrasonic irradiation field of HIFU remained intact.

The 5-ALA-SDT was cytotoxic toward malignant gliomas. Generation of ROS by the SDT was thought to promote apoptosis of glioma cells. The 5-ALA-SDT with HIFU induced tumor necrosis in the focus area and apoptosis in the perifocus area of the HIFU-irradiated field, whereas the surrounding brain tissue remained normal, resulting in longer survival of the HIFU-treated mice compared with that of untreated mice. These results suggest that 5-ALA-SDT with HIFU may present a less invasive and tumor-specific therapy, not only for a tumor mass but also for infiltrating tumor cells in malignant gliomas [3].

2015

Endo et al. investigated the efficacy of sonodynamic therapy of glioma cells in vitro using porphyrin derivatives, including 5-aminolevulinic acid, protoporphyrin IX and talaporfin sodium, as sonosensitizers. These substances have been known to accumulate in glioma cells and are expected to have cytotoxic effects on sonication. The study found that the cytotoxicity of sonication of glioma cells is enhanced by each sonosensitizer and that the efficacy of sonodynamic therapy may depend on the degree of intracellular accumulation of sonosensitizer. Also, the study suggests that induction of apoptosis is a major mechanism underlying cell death. Though further investigations are necessary, the preliminary result indicates a potential for sonodynamic therapy with sonosensitizers in glioma treatment [4].

2014

A study with a rat C6 glioma experimental model showed that SDT can potentially be useful in the treatment of deep-seated malignant gliomas [5].

In vitro stimulation of calcium overload and apoptosis by sonodynamic therapy combined with hematoporphyrin monomethyl ether in C6 glioma cells[6]

Calcium overload and in vitro apoptosis of the C6 glioma cells mediated by sonodynamic therapy (hematoporphyrin monomethyl ether and ultrasound) [7].

2008

The data indicated that SDT could kill C6 glioma cells in vitro and possibility through induction of apoptosis and necrosis. Singlet oxygen [8].

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