Thermotherapy of Experimental Glioblastoma with Laponite-Embedded Magnetic Iron-Oxide Nanoparticles

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Learning Objectives

1. Thermotherapy of GBM by magnetic nanoparticles
2. Hyperthermia comparison of laponite-embedded IONPs to standard IONPs
3. Toxicity of laponite-embedded IONPs with no applied magnetic fields.
4. Antitumor effect of hyperthermia generation of laponite-embedded IONPs with applied magnetic fields.

Laponite-Embedded IONPs

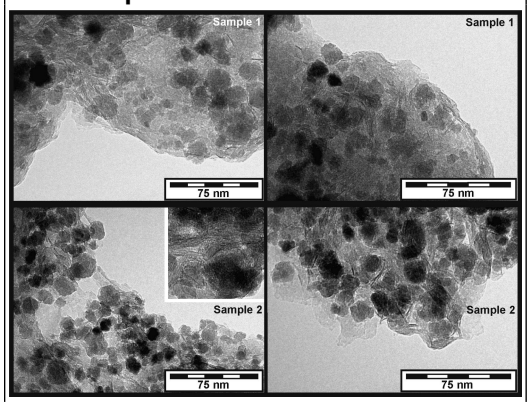

Figure 1. Maghemite IONPs (13 nm) immobilized on laponite nanodiscs and formation of composite materials.

Introduction

Local hyperthermia generated by magnetic nanoparticles (MNPs) has recently been described in patients for the thermotherapy of recurrent glioblastoma (GBM) after intratumoral implantation in high concentration. Here we describe the use of novel magnetic iron-oxide nanoparticles (IONPs) embedded on a synthetic clay matrix (laponite) for thermotherapy of experimental GBM that acheive high temperatures at low concentrations with safe applied magnetic fields (AMF).

Methods

A comparison of temperature elevation was made with standard IONPs (6 mg/ml; mean diameter of 15 nm) and laponite-embedded IONPs (3 mg/ml; mean diameter of 13 nm) after application of an AMF (288 kHz) for 10 min. Therapy-resistant human GBM cells (U87wtEGFR and U87EGFRvIII) that overexpress the wild-type (wt) EGFR or the deletion mutant EGFRvIII, were treated with laponite-embedded IONPs (3 mg/ml) or control (medium). After 24 h of incubation with the laponite-embedded IONPs, GBM cells were treated with an AMF (288 kHz) for 10 min. Cell survival and proliferation were assessed. Toxicity studies were performed with human GBM cells (U87EGFRvIII) and human foreskin fibroblasts (HFF) after treatment with laponite-embedded IONPs (12, 24, and 48 h) or control (medium) and no application of AMF.

Results

A greater than thirteen-fold elevation in temperature was achieved after application of an AMF with laponite-embedded IONPs (68 °C) in comparison to standard IONPs (5 °C) double in concentration. A large drop in GBM cell survival and proliferation was found in all therapy-resistant cell lines after application of an AMF and thermotherapy. Minimal to no toxicity was found in GBM or HFF cells at 12, 24, and 48 h of treatment with laponite-embedded IONPs in comparison to control treatment of cells.

IONP Hyperthermia Comparison

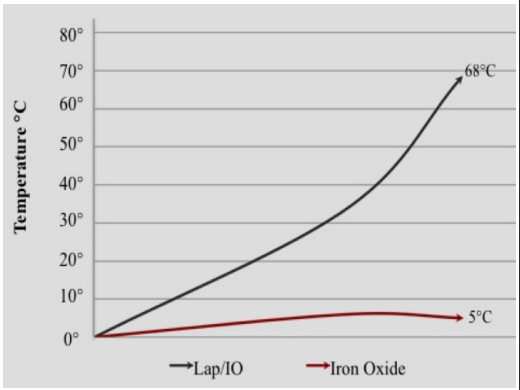

Figure 2. Greater hyperthermia effect was achieved with laponite-embedded IONPs after AMF application in comparison to polymer-coated IONPs.

Laponite-Embedded IONP Hyperthermia Generation and GBM Antitumor Effect

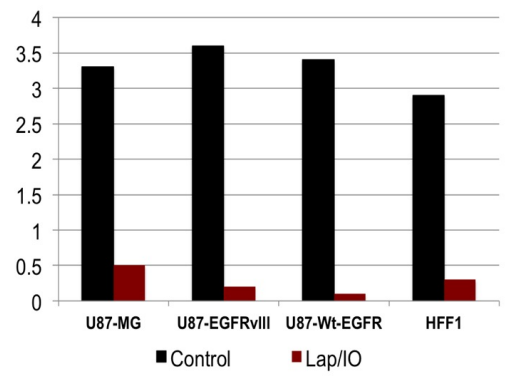

Figure 3. A large drop in GBM cell survival and proliferation was found in all therapy-resistant cell lines after application of AMFs and thermotherapy.

Cell Toxicity Without Hyperthermia

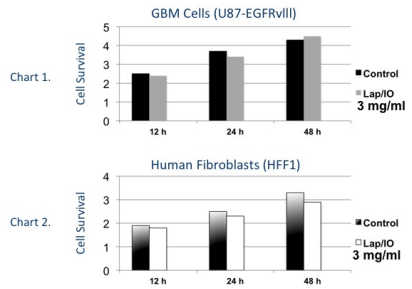

Figure 4. Minimal to no toxicity was found in GBM or HFF cells at 12, 24, and 48 h of treatment with laponite-embedded IONPs in comparison to control treatment of cells.

References

Maier-Hauff K, Ulrich F, Nestler D et al. Efficacy and safety of intratumoral thermotherapy using magnetic iron-oxide nanoparticles combined with external beam radiotherapy on patients with recurrent glioblastoma multiforme. J Neurooncol 2010.

Tzitzios V, Basina G, Bakandritsos A et al. Immobilization of magnetic iron oxide nanoparticles on laponite discs - an easy way to biocompatible ferrofluids and ferrogels. J Mater Chem 2010; 20: 5418-5428.

Conclusions

Laponite-embedded IONPs represent an ideal magnetic nanoparticle composite material for the thermotherapy of experimental GBM at low concentration when exposed to safe AMF.