Application of Graphene Oxide as Drug Delivery System for Combined Chemo-Hyperthermia Therapy in Resistant Cancer Cells

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Purpose
Drug resistance remains a major challenge for anticancer treatment, thus, requires combined treatment strategies to overcome drug resistance and enhance the therapeutics effect. The aim of this study is to investigate the achievement of multiple therapies by developing a dual-in-dual nanocarrier, as delivery system for DOX and IRI, for a synergistic effect.

Methods
Therapeutics agents were loaded into graphene oxide (GO) nanoparticles using poloxamer 188 as the stabilizer. The in vitro drugs release from GO were evaluated in acidic and physiological conditions. The application ability of this nanocarrier in chemo-hyperthermia treatment of cancer was determined by measuring intracellular uptake, cytotoxicity studies, and in vitro tumor ablation under NIR 808nm laser irradiation.

Results
GO loaded DOX and IRI nanoparticles are stable, have small size, narrow distribution and enable to induce heat which leads to cell death. In combination with NIR 808nm laser irradiation, GO loaded DOX and IRI showed higher cytotoxicity in all three cells compared with the treatment of free DOX and/or IRI, and blank GO. This effect was significantly observed in MDA-MB-231 resistant breast cancer cells. GO loaded DOX and IRI combined NIR treatment activated the intrinsic apoptosis pathway, which was confirmed by the overexpression of apoptosis-related proteins.

Conclusion
In comparison to single therapy, better synergistic effect observed in combined multiple drugs and thermotherapy treatments suggests higher therapeutic efficacy to overcome intrinsic resistance to chemotherapeutics.