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Image-guided synergistic photothermal therapy using photoresponsive imaging agent-loaded graphene-based nanosheets

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Abstract
We report the image-guided synergistic photothermal antitumor effects of photoresponsive near-infrared (NIR) imaging agent, indocyanine green (ICG), by loading onto hyaluronic acid-anchored, reduced graphene oxide (HArGO) nanosheets. Loading of ICG onto either rGO (ICG/rGO) or HArGO (ICG/HArGO) substantially improved the photostability of photoresponsive ICG upon NIR irradiation. After 1 min of irradiation, the NIR absorption peak of ICG almost disappeared whereas the peak of ICG on rGO or HArGO was retained even after 5 min of irradiation. Compared with plain rGO, HArGO provided greater cellular delivery of ICG and photothermal tumor cell-killing effects upon laser irradiation in CD44-positive KB cells. The temperature of cell suspensions treated with ICG/HArGO was 2.4-fold higher than that of cells treated with free ICG. Molecular imaging revealed that intravenously administered ICG/HArGO accumulated in KB tumor tissues higher than ICG/rGO or free ICG. Local temperatures in tumor tissues of laser-irradiated KB cell-bearing nude mice were highest in those intravenously administered ICG/HArGO, and were sufficient to trigger thermal-induced complete tumor ablation. Immunohistologically stained tumors also showed the highest percentages of apoptotic cells in the group treated with ICG/HArGO. These results suggest that photoresponsive ICG-loaded HArGO nanosheets could serve as a potential theranostic nano-platform for image-guided and synergistic photothermal antitumor therapy.

Graphical abstract

Keywords: image-guided photothermal therapy, photoresponsive imaging agent, indocyanine green, reduced graphene oxide nanosheets, theranostics.

1. Introduction.

Photothermal therapy (PTT) utilizes photoresponsive agents taken up by cells and the conversion of absorbed light into local heating to destroy malignant tissue [1]. PTT is considered a minimally invasive cancer treatment approach that is advantageous compared with conventional chemotherapy because its spatial and temporal controllability[2,3] limit side effects that commonly occur in chemotherapy owing to nonspecific drug delivery to all