INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

BMJ Journals

EP927 Ex-vivo antitumor efficacy of PEGylated-targeted nanodiamonds for docetaxel delivery in ovarian cancer

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Abstract

Introduction/Background The use of nanomaterial-based therapeutic systems is rapidly growing and covering several biomedical applications such as detection, diagnosis and treatment. Recently, nanodiamonds (NDs) have been demonstrated to have great potential as a multimodal imaging/therapy platform. NDs are attractive for use in drug delivery because of their rich surface chemistry. NDs enhance the ability of the drug to cross the cell membrane, increase intracellular drug delivery to the cancer cells, improve treatment efficacy, and decrease toxicity to normal cells or tissues. Docetaxel (DTX) 'a chemotherapeutic agent' has very low neurotoxic effect to the cancer patients. Therefore, we hypothesized that targeting HER-3 positive ovarian cancer (OC) *ex-vivo* explants by loading NDs with DTX would improve drug targeting and delivery. Thus, we aimed to investigate the efficacy of ND-conjugated DTX on OC *ex-vivo* explants.

Methodology Bare, uncoated NDs were PEGylated and functionalized with DTX (NDs/DTX) and conjugated with anti- HER-3 antibody. Dynamic Light Scattering (DLS) was used to measure the hydrodynamic diameter of individual NDs dispersed in solutions (NDs,ND/DTX/HER-3). *Ex-vivo* explants from OC patients were exposed to various concentrations of ND/DTX, ND/DTX/HER-3 and DTX for over 24 hour's incubation.

Cytotoxicity was examined by measuring cell viability changes, caspase 3 and caspase 8 activation and the molecular cell stress variation was investigated by examining the activation of transcription factor-2 (ATF-2).

Results Significant alterations of the examined biological markers were detected in OC *ex-vivo* explants. As expected no nuclear translocation of ATF-2 was observed in the nuclei of untreated explants. Interestingly, the *ex-vivo* explants showed greater responses to NDs/DTX/HER-3 versus ND/DTX and DTX alone.

Conclusion Our study demonstrates that NDs loaded with DTX exert significant inhibitory activities on OC explants. Thus, the proposed drug delivery system of ND-conjugated chemotherapy represents a promising, biocompatible strategy for targeting and enhancing chemotherapy efficacy and safety.

Disclosure Nothing to disclose.

http://dx.doi.org/10.1136/ijgc-2019-ESGO.973

Publication history

- First published November 1, 2019. Online issue publication November 01, 2019