LIPUS Activation of Gold Nanoparticle Anticancer Drug Carriers for Cancer Treatment

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With more than 10 million new cases of cancer predicted every year, there is significant motivation for the development of more efficient and accurate anticancer conventional druas [1]. When usina anticancer drugs healthy cells are often killed along with tumour cells, causing toxicity to the patient. Ultimately, this can limit the achievable dose to tumour cells, as well as patient outcome [1]. To overcome this limitation a number of anticancer drug delivery systems have been proposed, with one attractive method being that of nanoparticle drug delivery. Nanoparticle drua carriers can offer a number of including: advantages, the efficient delivery of lipophilic drugs, protection from aggressive environments, targeted and controlled drug delivery [2]. In this work the advantages of nanoparticle drug carriers and natural anticancer drugs, such as curcumin [3], were combined in a drug delivery system. Furthermore, active targeting was achieved by inducing anticancer drug release noninvasively via therapeutic low-intensity pulsed ultrasound (LIPUS) activation: either mechanical stimulation or bulk heating of a region of interest such as a tumour. Gold nanoparticles (GNPs) were selected as anticancer drug carriers due to their inertness and high surface to volume ratio. Additionally, gold compounds have been shown to inhibit proliferation and cause cell cycle arrest in tumour cells [4]. GNPs in particular have also been shown to play a role in mediating anti-cancer activity, and improving uptake of chemotherapeutic drugs into tumour cells [5]. In order to

model anticancer drug release, numerical COMSOL® based model of LIPUS activated anticancer drug release from GNP drug carriers was developed. Through simulating drug release for a variety of LIPUS and GNP parameters, the mechanisms of action behind ultrasound-nanoparticle interactions can be studied, and an optimized set of LIPUS exposure and GNP parameters can be determined. These parameters can then be applied experimentally to achieve efficient LIPUS induced targeted anticancer drug release from GNP drug carriers in ex vivo and in vivo tissue models.

References

[1] A. Dadwal *et al.*, Artificial Cells, Nanomedicine, and Biotechnology, 46 (2018) 295-305.

[2] N. Bruni et al., Molecules, 23(10) (2018) 2478.

[3] M. Yallapu et al., Drug Discovery Today, 17 (2012) 71-80.

[4] Chien et al. Molecules, 23(6) (2018)

[5] I. Mármol et al. Cancers, 11(6) (2019) 780.

Figures

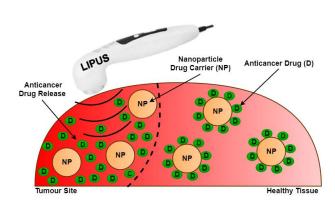


Figure 1: LIPUS activated targeted anticancer drug release from GNP drug carriers. Here anticancer drug release can be achieved at the tumour site, while sparing healthy tissue.