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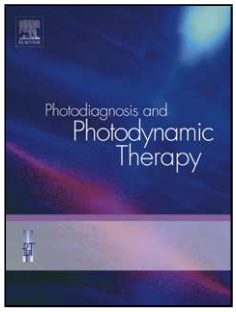

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Title: The current status of phototherapy in multimodal anti-cancer nanomedicines

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Highlights

- Nanomedicines can improve the precise delivery of therapeutics
- PDT and PTT can be efficiently delivered through nanomedicines
- Further investigation is crucial for clinical translation

Dear Editor,

We have read with great interest, the recently published article by Vivek *et al.* (2018), describing the authors' research on the therapeutic applications of a multifunctional

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nanomedicine [1]. This paper discusses the combined efficacy of photodynamic therapy (PDT), photothermal therapy (PTT) and carboplatin (CBP) chemotherapy, using CBP and indocyanine green (ICG) loaded nanoparticles (NPs), functionalised with polyethylene glycol and folic acid. Significant uptake and retention of NPs *in vitro*, was observed in the folate receptor-overexpressing breast cancer cell line, MCF7. The intracellular acidic pH environment of cancer cells induced the release of therapeutic agents into the cytoplasm. Upon near-infrared light irradiation, the increase in intracellular temperature and simultaneous increasing production of reactive oxygen species, was attributed to the photothermal conversion and photodynamic properties of ICG respectively [2]. The dual synergistic effect of PDT and PTT resulted in an apoptotic cell death. Furthermore, significant regression in tumour growth with no noticeable adverse effects, was observed in animal models treated with NPs and near-infrared light irradiation.

This study is a good example of the rapid growing interest in multifunctional anti-cancer nanomedicines, combining PDT, PTT and conventional chemotherapy. We recently reviewed the scope of photothermal therapy-based nanomedicines, in colorectal cancers and highlight the diverse combinations of phototherapeutic, chemotherapeutic, optical imaging and cancer-targeting nanomedicines that have been investigated in the past decade [3]. These nanomedicines have shown to significantly improve the management of solid colorectal cancers, by efficiently packaging different treatment methods into a single entity.

Unlike the study by Vivek *et al.* (2018) which demonstrated both PTT and PDT through ICG [1]. Seo et al. (2014) synthesised and evaluated PTT and PDT using NPs comprised of gold nanorods (to induce PTT) and methylene blue (to induce PDT) [4]. The authors successfully show synergy between PDT and PTT, in comparison to PDT

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or PTT alone. The aforementioned studies, demonstrate the flexibility in customising PTT and PDT inducing NPs, using different types of photosensitising agents.

Thus far, many novel multimodal PDT and/or PTT nanomedicines have been the subject of 'proof-of-principle' pre-clinical studies, showing potential clinical applications. Currently, PDT and PTT (through thermal ablation) are utilised in clinics to treat cancers and both techniques have independently proven to be successful as stand-alone methods and in combination with more conventional means of treatment [5,6]. However, due to the apparent lack of controlled and randomised clinical trials investigating phototherapy nanomedicines, it is difficult to design appropriate clinical protocols and identify key candidates for further evaluation and clinical translation. Nevertheless, the remarkable progression in this field with a focus on precision medicine means that the clinical application of phototherapy nanomedicines is feasible in the near future.

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Conflicts of interest

None

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