Augmenting the effect of sonodynamic therapy against pancreatic cancer using hematoporphyrin-carrying nanoparticles

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Introduction

Sonodynamic therapy (SDT) is an emerging, minimally invasive therapeutic approach with the potential to treat a variety of recalcitrant cancers, including pancreatic cancer. The treatment involves the use low intensity ultrasound in combination with non-toxic agents, known as sonosensitizers, for the site-specific ablation of tumours. After systemic administration of the sensitizing agent, the application of ultrasound can be performed extracorporeally, endoscopically or intraoperatively. This study evaluates the effectiveness of SDT using a new nanoparticulate formulation carrying hematoporphyrin in the in vitro treatment of human pancreatic cancer cells.

Materials and Methods

The human BxPC-3 cell line was used as an in vitro model for pancreatic adenocarcinoma. The target cells were incubated with free hematoporphyrin (free HP) and hematoporphyrin-containing nanoparticles (HPNP) that were formed by self-assembly with a polyglutamate-tyrosine co-polymer, in order to determine the cytotoxicity in the absence of ultrasound. Cells were treated with HPNP combined with ultrasound irradiation for determining the effect of SDT. These effects were examined at normoxic and hypoxic conditions, at pH 6.4 and pH 7.4.

Results and Discussion

The HPNP nanoparticles showed increased toxicity against the target cell line, when compared with free HP. The HPNP toxicity was further enhanced at acidic conditions and this is particularly important for confining the ablation effect within the acidic pancreatic tumour mass. Utilising the nanoparticle carrier, cellular uptake of hematoporphyrin was significantly increased compared to the free HP ($p<0.0001$), at both acidic and physiological pH. SDT, at varying ultrasound treatment conditions and at both normoxic and hypoxic environment, demonstrated a clear cytotoxic effect against the BxPC-3 cell line (<0.001), while toxicity of ultrasound alone or the nanoparticles alone was minimal.

Conclusion

BxPC-3 cells have significant positive response to treatment with SDT. Further preclinical experimentation is currently being carried out in experimental animals to evaluate the effect of SDT

in vivo for supporting the clinical translation of this promising therapeutic modality in the treatment of pancreatic cancer.