Thermally Triggered Theranostics for Pancreatic Cancer

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Background

Pancreatic cancer is the 4th most aggressive cancer in the western world with less than 34% of patients surviving past 5 years. Lack of specific symptoms results in delayed diagnosis. Theranostics are new platforms, which offer simultaneous diagnosis and therapy resulting in a decrease in treatment time. Here treatments are conjugated onto diagnostics by stimuli responsive binding allowing for controlled drug release resulting in a rapid and localised clinical effect. Hybrid nanoparticles are composed of an iron oxide core surrounded by a rigid gold shell. These particles undergo manipulation due to inherent magnetism of the core whilst laser irradiation of their gold shell results in localised heating due to surface plasmon resonance. Hence, they can be utlilised as diagnostics using MRI and laser irradiation can be used as a trigger for drug release.

Methods

Proof of concept studies have been carried out using a novel bisnaphthalamido (BNIP) based drug series. BNIPs are a series of novel compounds, which have exhibited exciting potential as chemotherapy agents. HNPs were fabricated and characterised using PCS, TEM, MRI, SQUID and zeta potential measurement. Drug conjugation and release was quantified using reverse phase HPLC. Cellular response and cytotoxicity assays were carried out using trypan blue exclusion, MTT assay and atomic force microscopy.

Results and Discussion

In our studies, we designed hybrid nanoparticles (50 nm) capable of drug loading onto their surface (3:1:0.25, Drug:Fe:Au). By exploiting the gold surface-to-drug interaction of a range of novel Bisnaphtalamido based agents a system with heat triggered drug release was produced. *In vitro* studies of these formulations showed the novel formulations possess a 10-fold lower IC_{50} value when compared with the free drug after only 24 h. These cytotoxicity studies combined with cellular uptake studies showed the formulations to be significantly more effective compared with gemcitabine. *In vivo* trials have commenced to further elucidate their viability for use as theranostics.

Conclusion

These data highlight the potential of HNPs as dual imaging agents and contrast agents for pancreatic cancer therapy.