Safety Optimisation of a hybrid nanoparticle based on thermo-responsive delivery system for pancreatic cancer treatment.

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Background:

Pancreatic cancer is the 4th most aggressive cancer in the western world. In the United States, it is the third leading cause of cancer-related deaths. The overall 5-year rate of survival for this type of cancer is 9%; very low in comparison to other cancers [1]. The lack of symptoms results in a delayed diagnosis and therefore, a delay in treatment of the cancer. Current therapies for pancreatic cancer include fluorouracil, gemcitabine and nab-paclitaxel. Nanotechnology offers the benefit of enhancing drug delivery to the targeted tissue because of increased drug permeability. This also reduces side effects and sustains drug release over a long period of time [2]. Thermo-responsive hybrid nanoparticles exhibit the potential for use as drug delivery systems for controlled drug release and have shown promise *in vivo* in pancreatic models, however further work is needed to get them ready for clinical trial.

[1] Campbell, D., Isch, E., Kozak, G. and Yeo, C., 2021. Journal of Pancreatic Cancer, 7(1), pp.1-7.

[2] Kadam, R., Bourne, D. and Kompella, U., 2012. Drug Metabolism and Disposition, 40(7), pp.1380-1388.

Methods:

Hybrid particles will be surface engineered to protect the drug molecules from metabolism until they are heated and drug release occurs, and their surface protection via different polymers determined. The particles will be fully characterised and their *in vitro* effects on cell response monitored in a number of assays including cytotoxicity, cell membrane integrity and production of reactive oxygen species in pancreatic cancer cell lines.

Results:

Hybrid nanoparticles composed of gold and iron oxide have been synthesized and characterized using transmission electron microscopy and dynamic light scattering. The particle size was determined to be around 100 nm, with a gold: iron ratio of 3:1. The particles have been incubated with BxPC-3 cells and preliminary data suggests that addition of a poly (ethylene glycol) long chain linker, further protects the cells from any associated stress or toxicity from the hybrid surface.

Conclusions:

This is a revolutionary area for nanotechnology therapies to be applied in the treatment of cancers particularly pancreatic cancer. Thermo-responsive drug delivery also offers a new approach to nanotechnology and will ensure controlled drug release. More work is needed in order to fully evaluate these systems and is ongoing in the lab.