Title

Evaluation of in vitro release kinetics of a chemotherapeutic drug in a 3D environment

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Background

ChemoGell™ is a patented hydrogel formulation with shear thinning and thermoresponsive gelation properties. It has been developed for injection and delivery of chemotherapeutics directly into solid tumours. Determining the *in vitro* release kinetics of drugs from ChemoGel in a 3D environment is important to help inform *in vivo* PK/PD studies and clinical translation, however standard approaches to release are not representative. Here we aim to evaluate sustained release and diffusion of gemcitabine from ChemoGell™ using a novel approach in a 3D *in vitro* model.

Methods

Gelma (methacrylated gelatin) forms three-dimensional structures suitable for cell growth and differentiation. Stiffness of the gel can be tuned via changes in polymer concentration, cross linking agent and UV irradiation and therefore can be used to represent tumours of varying stiffness.

Moulds for casting the gel were prepared using a custom designed 3D printed design. Gelma at a conc. of 5% was added to the plate and cross-linked with UV for 90 sec at 405nm wavelength which gave a stiffness of 4k Pa (representative of tumour stiffness). ChemoGell™ containing Gemcitabine was then applied to a section of the mould, after 24 h the gel was divided into slices of defined size and analysed for the presence of gemcitabine via HPLC.

Spheroids was cultured by loaded with $1x10^5$ BxPC3 cells in Gelma which over 7 days formed spheroids. Spheroid morphology and viability was determined via microscopy and confocol.

Results

Results showed that Gemcitabine diffused across the gel within 24 h and the concentration showed a gradient trend, illustrating the usability of this model and spheroids can be clearly observed both visually and through confocal. Future work will focus on culturing BxPC3 spheroids in Gelma to evaluate release kinetics on cell viability.