2013 NCRI Cancer Conference

3 - 6 November 2013

The BT Convention Centre Liverpool UK

conference.ncri.org.uk

B30

Superparamagnetic iron oxide nanoparticles (spions) for the hyperthermic treatment of malignant melanoma

Thomas Oxenham[1], Paul Southern[2], Dana Breisemeister[1], Jenny Yeung[1], Alex Freeman[3], Quentin Pankhurst[2], Karl Peggs[1,2], Sergio Quezada[1], Kerry Chester[1]

[1]University College Lonon Cancer Institute, London, UK, [2]Davy Faraday Research Laboratory, Royal Insitution of Great Britain, London, UK, [3]University College London Hospital, London, UK

Background

Despite several breakthroughs in the management of melanoma, detection and treatment of metastatic disease remains a significant clinical problem.

Hyperthermia is a promising treatment modality, where tissue is exposed to elevated temperatures to induce cell stress, apoptosis and/or necrosis. Whilst traditional hyperthermia treatments cause non-specific tissue damage, we hypothesise that SPIONs provide a novel solution. When placed into an alternating magnetic field (AMF), SPION generate heat in a localised fashion. This process is known as magnetic alternating current hyperthermia (MACH).

Method

Ferucarbotran, a SPION previously used for clinical imaging was obtained from Meito Sangyo (Japan). AMF conditions were established in vitro using Ferucarbotran concentrations of 1.75-56mg/ml and a bespoke MACH system delivering a range of AMF strengths at 6kA/m.

In vivo heating was tested in an inducible transgenic Tyr::CreERxBrafxPten murine model that developed tumours following topical application of 4-hydroxytamoxifen. Intradermal injection of the tumours with 56mg/ml Ferucarbotran was followed by AMF of ~4kA/m . Tumours were subsequently analysed using histological techniques. Particle biodistribution was visualised using Prussian Blue staining and electron microscopy.

Results

Temperature rises of 14-135°C were obtained in vitro. This data was used to determine optimum conditions in vivo taking into account the heat conductivity of tissue.

Thermal imaging technology showed that tumours could be heated in vivo in a highly localised manner. Tumours reached 46°C within 5 minutes of application of AMF, which was maintained for 30 minutes. Such conditions are known to induce cell death and facilitate immune recognition.

We also showed that SPIONs were taken up by the draining lymph basin within 5 minutes of tumour injection, and using electron microscopy, that metastatic lymphatic tumour deposits showed evidence of intracellular particle uptake.

Conclusion

These proof-of-concept studies indicate that SPIONs may have several translatable applications, as novel therapeutics and for sentinel lymph node detection.

Acknowledgements

This project was supported by Cancer Research UK (CRUK), the Experimental Cancer Medicine Centre (ECMC) and EU FP7 (DARTRIX project grant agreement No 278580).