CRT Licensing Opportunity

Novel Photosensitiser-Nanoparticle Conjugates

- Novel conjugates for use in photodynamic therapy (PDT)
- Enhanced *in vivo* efficacy in animal models
- Improved toxicity profile
- Strong intellectual property position

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Opportunity

Novel nanoparticle-based conjugates have been synthesised and are being tested *in vivo* for use in photodynamic therapy.

Background

Photodynamic therapy (PDT) combines the use of a photosensitiser agent with light to cause selective damage to target tissues, via the production of cytotoxic singlet oxygen. PDT is characterised by a series of advantages as compared with other therapeutic modalities for cancer including minimally invasive and targeted treatments, limited toxicities permitting repeat dosing and improved patient quality of life. PDT agents have received regulatory approval for numerous oncology indications, including lung, head and neck, gastric, bladder and cervical cancers.

Novel Photosensitiser-Nanoparticle Conjugates

Nanoparticle-based vehicles for the delivery of hydrophobic photosensitisers for the treatment of cancer indications using PDT have been developed. The basic formulation is based on gold nanoparticles that have been stabilised with a photosensitiser and a phase transfer reagent. The tri-component system (photosensitiser/nanoparticle/phase transfer reagent) produces cytotoxic oxygen species with 50% greater efficiency compared to free photosensitiser. A second formulation has recently been developed which includes modifications to render the conjugates water soluble.

Initial *in vitro* studies demonstrated that the photosensitiser-nanoparticle conjugates are endocytosed by HeLa cells, leading to increased cell mortality following irradiation with red light compared to free photosensitiser alone.

In vivo work has been performed using C57 mice bearing a transplanted amelanotic melanoma and has included comparative efficacy studies with approved photosensitisers (Figure 1).

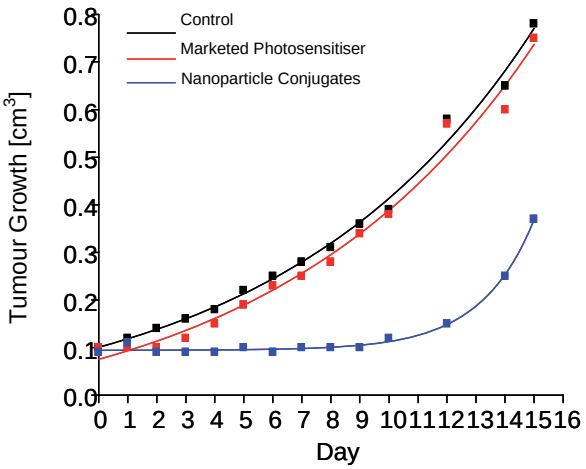

Figure 1: Growth of subcutaneously implanted amelanotic melanoma following a single photodynamic therapy treatment. A currently marketed photosensitiser exhibits limited action on the tumour. However, the phthalocyanine-nanoparticle conjugates clearly prevent tumour growth for up to 10 days following PDT.

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Recent work has successfully addressed issues surrounding the bulk production of photosensitiser-nanoparticle conjugates. In addition, pharmacokinetic studies have defined the biodistribution of the nanoparticle conjugates in a tumour bearing animal model. Emphasis has also been placed on determination of the skin phototoxicity of the new formulations.

Validation Milestones

The following validation milestones have been addressed:

1. Stable photosensitiser-nanoparticle conjugates have been formulated and used in *in vivo* studies of photodynamic therapy of implanted tumour models.

2. Optimised conditions for photodynamic therapy of subcutaneously implanted amelanotic melanoma models have been established.

3. Comparison of the PDT efficacy of nanoparticle conjugates, free photosensitiser and approved photosensitisers have been undertaken. The PDT efficacy of the nanoparticle conjugates was greater than that of the free photosensitiser or approved photosensitisers. A significant reduction in the rate of tumour growth is observed post irradiation, up to and including 15 days after treatment.

4. Full pharmacokinetic measurements have defined the biodistribution and excretory pathway of the nanoparticle conjugates in tumour-bearing animal models. No significant toxicity was observed

5. Positive skin phototoxicity data have been generated. The nanoparticle conjugates exhibit very limited phototoxicity with enhanced tumour to skin concentration in comparison to free photosensitiser.

Commercial Opportunity

CRT seeks a commercial partner for collaborative research and/or exclusive licensing related to the applications of this technology in oncology.

Intellectual Property

CRT holds the rights to an established patent portfolio in major territories worldwide, including granted claims in Europe (EP1455828B1). These rights are available for licensing together with associated data.

Patent pending for second, water soluble, formulation.

Originating Institute

Cancer Research UK and CRT are sponsoring the development of this programme. Work is being led by Professor David A. Russell at the University of East Anglia and by Professor Giulio Jori in Padova, Italy.

Reference

Wieder M.E., Hone D.C., Cook M.J., Handsley M.M., Gavrilovic J. and Russell D.A.. Intracellular photodynamic therapy with photosensitizer-nanoparticle conjugates: cancer therapy using a 'Trojan horse'. Photochem. Photobiol. Sci. 2006. **5**(8):727-34

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