Location! Location! Location! – PhotoBiotics' Key to Successful PDT

London; 31st July 2010: PhotoBiotics Ltd, a leading targeted therapeutics company, and Imperial College London are together unravelling key factors that affect the efficiency of photodynamic therapy (PDT) of tumours. Writing in the Royal Society of Chemistry (RSC) journal *Photochemical and PhotoBiological Sciences,* the team reports that how PDT damages or kills tumours and by what mechanism, depends on where inside a tumour cell the PDT drug localises.[1]

"Ultimately, this helps us design more potent and specifically targeted PDT agents", says Imperial College's Emeritus Professor David Phillips OBE, recipient of the prestigious 2010 Porter Medal for services to photochemistry, President of the RSC, one of the paper's principal authors, and a founder of PhotoBiotics.

In PDT, irradiation of photosensitisers (PS) with visible laser light leads to the conversion of molecular oxygen into highly reactive oxygen species which irreversibly damage cells' vital components, resulting in tumour cell death. Though PDT has many advantages over conventional cancer treatments, currently available PSs can be difficult to deliver, clear slowly from the blood, and are not selective, all of which can leave patients photosensitive long after treatment. Although 'second generation' PDT PSs are being developed with much improved photophysical properties and singlet oxygen production, none is truly targeted to the tumour.

The Imperial/PhotoBiotics team performed novel chemical modifications to a common second generation PS derived from chlorophyll called PPa. They produced two new PSs which significantly improve on PPa's water solubility, photophysical properties and singlet oxygen generation, while reducing unwanted interactions. However, the two new PSs had strikingly different phototoxicities to ovarian cancer cells *in vitro,* compared to PPa: the first was 13 times more phototoxic, the second, 18 times *less*.

Using confocal microscopy, the team tracked the localisation of the two new PSs in cancer cells, and found they differed: the first localised to lipid-rich vital membrane compartments such as the mitochondrion (cellular 'power station') where PDT damage was extensive; the second located to more hydrophilic environments, e.g., endosomes, where damage to the cell was less.

"To ensure PSs locate specifically to tumour cells, we are now concentrating on so-called third generation PDT involving the specific targeting of PhotoBiotics' novel PSs to lipid-rich organelles in tumours, via PhotoBiotics' unique ***Optilink*** conjugation technology, utilising single-chain antibody fragments," says Professor Phillips.[3, 4]

Notes for Editors:

1. 'Novel photosensitisers derived from pyropheophorbide-a: uptake by cells and photodynamic efficiency in vitro.' *Photochem Photobiol Sci* 2010; **9**: 1033-1041.

2. '*The Colours of Life: an introduction to the chemistry of porphyrins and related compounds*.' Oxford University Press, Oxford, 1997.

3. 'Targeted photodynamic therapy with multiply loaded recombinant antibody fragments.' *International Journal of Cancer* 2008; **122**: 1155-1163.

4. 'Fluorescence characterisation of multiply-loaded anti-HER2 single-chain Fv-photosensitiser conjugates suitable for photodynamic therapy'. *Photochemical and Photobiological. Sc*iences. 2007; **6**: 933-939.

About PhotoBiotics (see www.photobiotics.com)

PhotoBiotics Ltd was spun out from Imperial College London because of a recognised need to improve on the current light-activated cancer treatment, known as photodynamic therapy or PDT. PhotoBiotics brought together the disciplines of chemistry, photophysics and biochemistry to find a unique way to target PDT to the tumour, thus enhancing the efficacy of this cancer treatment and also reducing systemic ambient light sensitivity post-treatment (i.e. painful sunburn-like symptoms). PhotoBiotics' R&D team has succeeded in its primary objective of developing a technology platform to address the needs of PDT, and is now exemplifying how this platform, denoted ***OptiLink***, has utility across a wide range of other applications, in particular, MRI contrast agents and imaging and others. ***OptiLink*** is a unique and simple conjugation platform which enables multiple attachment of drugs to antibody fragments. Counter-intuitively, ***OptiLink*** allows far higher drug loadings on scFvs than has ever been achieved with whole monoclonal antibodies.

About PDT

Conventional PDT has an established niche in the treatment of certain cancers and in age related macular degeneration (AMD), with product sales in excess of $500m annually. However, conventional PDT's clinical development and use have been slow to evolve owing mainly to the novelty of the treatment regimen and to post-treatment systemic photosensitivity. The photosensitising agent remains in the system for up to six weeks post treatment in some cases, and when it reaches the skin, patients can become exquisitely photosensitive to ambient light even on cloudy days, leading to symptoms akin to acute sunburn in uncovered parts of the body. Photobiotics uniquely targeted approach to PDT overcomes the issue of photosensitivity without compromising efficacy, thus greatly extending the potential of this otherwise superior treatment modality.

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