Peptide-Targeted Photosensitisers: Synthesis and Applications in Photobiology

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The conjugation of porphyrin derivatives to peptide ligands is a valuable strategy for enhancing their aqueous solubility and tissue selectivity in the photodynamic therapy (PDT) of cancer. To this end, bioorthogonal ligation ("click") chemistries provide an efficient way to link porphyrins and other tetrapyrrole systems with complementary multifunctional peptides. We will describe some of our work in this area towards the generation of specific targeted conjugates between porphyrin and chlorin derivatives and tumour-homing or cell-penetrating peptide carriers [1, 2]. Linking otherwise hydrophobic photosensitisers to cationic cell-penetrating peptides (e.g. HIV Tat 48-57) provides amphiphilic derivatives with improved water solubility plus enhanced cellular uptake and predictable sub-cellular localisation. Such molecules are very suitable for use in the light-triggered delivery of macromolecular therapeutics by photochemical internalisation (PCI), which will be illustrated for the targeted delivery of the protein toxin, saporin [3].

Peptide targeting strategies are also valuable for PDT with 5-aminolevulinic acid (ALA) [4]. In ALA-PDT, administered ALA is converted within cells via the heme biosynthetic pathway to protoporphyrin IX which may then be exploited as a photosensitiser. In this context, we will present some recent chemical and biological data on the application of peptide targeting for the enhanced delivery of multiple ALA units to specific cell types [5].

References

[1] R. Dondi, E. Yaghini, K. M. Tewari, L. Wang, F. Giuntini, M. Loizidou, A. J. MacRobert, I. M. Eggleston, Org. Biomol. Chem. 14 (2016) 11488.

[2] E. Yaghini, R. Dondi, K. M. Tewari, M. Loizidou, I. M. Eggleston, A. J. MacRobert, Sci. Rep. 7 (2017) 6059.

[3] E. Yaghini, R. Dondi, K. J. Edler, M. Loizidou, A. J. MacRobert, I. M. Eggleston, Nanoscale 10 (2018) 20366.

[4] K. M. Tewari, I. M. Eggleston, Photochem. Photobiol. Sci. 17 (2018) 1553.

[5] K. M. Tewari, R. Dondi, E. Yaghini, C. Pourzand, A. J. MacRobert, I. M. Eggleston, Bioorg. Chem. 109 (2021) 104667.