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Editorial — Introduction to the Special Issue on Photodynamic Therapy

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Photodynamic therapy (PDT) is a minimally invasive treatment for malignant and nonmalignant diseases that uses light-activated photosensitizers to destroy or modify cells or tissues. It has been approved by health agencies in several countries for cancers of different sites and stages, and for treatment of age-related macular degeneration, various benign skin conditions and localized bacterial infections. PDT research has led to significant advances in the technologies (both light and drug) and to understanding of the basic mechanisms of action, as well as extending the range of clinical applications. The themes covered in the papers of this special issue include newly developed photosensitizers (PS) and delivery systems, optical technologies for monitoring PDT dose, and preclinical and clinical applications, together with new fundamental studies of phototoxicity.

The Chen group in Shanghai, China report two novel chlorin-based PS, namely 5, 10, 15, 20-tetrakis ((5-dipropylamino) pentyl)-chlorin[1] and meso-tetra (3-pyrrolidinomethyl- 4-methoxyphenyl) chlorin.[2] Both have a characteristic absorption peak at about 650 nm and were found to be effective both *in vitro* and *in vivo*. Complementing this research paper, a review article is contributed by Li *et al.* to introduce the photophysics, photochemistry, photobiology, and chemical and biological syntheses of perylenequinonoid pigment Elsinochrome A and the future prospects for EA are also briefly discussed.[3] As a promising PS for PDT, Deng *et al.* summarize the available drug delivery systems for hypocrellins A and B and discuss how the environment-sensitive fluorescence of this class of PS can be used for the recognition of various biomolecules in photodynamic diagnosis.[4]

In a study of PDT dosimetry, the Guest Editors and their colleagues report on the correlation between *in vivo* tumor response and near-infrared luminescence measurements of singlet oxygen ($^1O_2$) generated during meso-tetrahydroxyphenylchlorin (mTHPC)-mediated PDT in an animal model comprising luciferase- and green fluorescent protein-transduced gliosarcoma grown in a dorsal window chamber. The results clearly show the correlation between the bioluminescence-based PDT response and the volume-averaged $^1O_2$ tissue concentration, demonstrating the validity of $^1O_2$ luminescence as a PDT dose metric in tumor *in vivo*.[5]

Since PDT is inevitably subject to intrinsic cancer resistance at the cellular and molecular levels via drug efflux, hypoxia, levels of pigmentation and repair mechanisms, Huang *et al.* in Fuzhou, China review the recent progress in understanding the interaction between multidrug resistance (MDR) transporters and PS uptake.[6] In addition, emerging strategies are discussed to overcome such resistance, including the use of MDR transport inhibitors, anti-vascular PDT, photochemical internalization, intratumoral injection of PS, multifunctional PS nanocarriers and enhancing the antitumor immunity. These strategies aim to make anticancer PDT more effective in the clinic and so gain greater acceptance into mainstream medicine.

Fisher and Lilge in Toronto, Canada summarize the outcome of past clinical trials for PDT in the treatment of malignant brain tumors, particularly gliomas, and highlight the trends in PDT approaches to this very challenging clinical problem.[7] They also examine the current approaches for interstitial PDT and potential ways to increase the efficacy of PDT in glioma through exploiting both physical and biological approaches to maximize PDT selectivity and therapeutic index, particularly in brain adjacent to tumor.

In the clinical domain Wang and colleagues in Shanghai, China show that topical 5-aminolevulinic acid (ALA)-mediated PDT may be an effective alternative for treating cutaneous lichen planus without causing major side effects and recurrence. Their preliminary results are very encouraging and should lead to further trials.[8] In another clinical study, Prasanna *et al.* proposed methylene blue (MB)-mediated PDT as a possible modality for the treatment of oral lichen planus (OLP) and oral leukoplakia (OL).[9] They showed that MB-PDT is an effective modality in management of OLP and OL, but that OLP lesions appear to respond much better than OL.

In order to optimize the parameters of low-level near-infrared laser therapy for human brain, the effects of wavelength, beam type and size on the treatment efficiency were quantitatively evaluated by Li *et al.* in Chengdu, China. They suggest that the most suitable wavelength for light-based treatment for brain is 810 nm as compared to 660 and 980 nm, while the selection of light beam type and size is strongly dependent on the size of brain lesion.[10]

Finally, we would like to thank all the authors for their excellent contributions, and hope that this special issue will be informative and stimulating both for scientists currently active in PDT research and for those outside the field who may bring new methodologies and insights to further the development and applications of this emerging modality.

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