BODIPY-Based Photothermal Agents for Cancer Treatment

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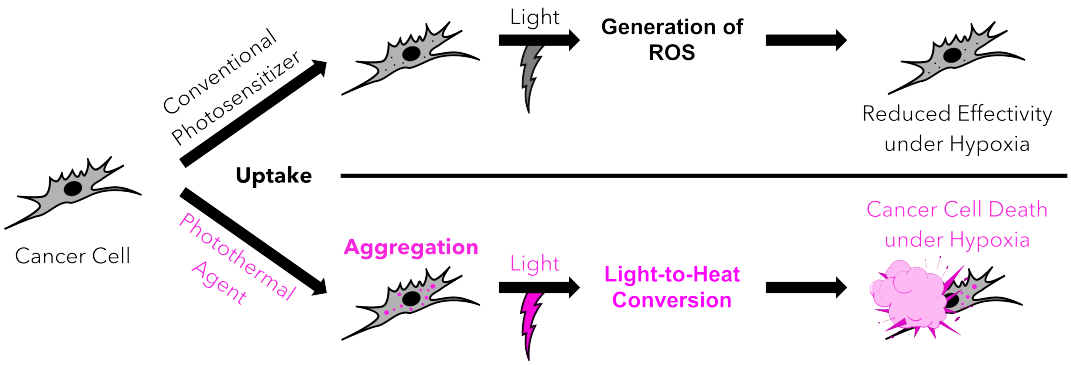
Photodynamic therapy (PDT) has become a widely used therapeutic approach for treating a variety of premalignant and malignant diseases. PDT typically involves the application of a photosensitizer (PS), which is activated by light within the tissue. The mechanism of action (MOA) relies on PS-mediated generation of reactive oxygen species (ROS).[1] However, despite the many advantages of PDT, a major drawback is the often insufficient oxygenation of tissue in solid tumours. In response, alternative phototherapeutic approaches, such as photothermal therapy (PTT), have emerged. PTT uses functional bioactive nanomaterials activated by near-infrared (NIR) light to eliminate tumour cells by generating heat upon irradiation. While PTT offers several benefits, concerns remain regarding the biocompatibility, biodegradation, long-term toxicity, and environmental impact of these nanomaterials.



Novel easily accessible BODIPY-based agents for cancer treatment will be presented. In contrast to established PSs for PDT, these agents exhibit photothermal activity, and their cytotoxicity is independent of ROS.[2] The compounds demonstrate high toxicity upon irradiation with light and low dark toxicity in various cancer cell lines, both in 2D culture and in 3D multicellular tumour spheroids (MCTSs). The dark-to-light toxicity ratio (phototoxic index, PI[3]) reaches values exceeding 830'000 after irradiation with energetically low doses of light at 630 nm. Under hypoxic conditions (0.2% O_2), a remarkable PI of 360'000 was observed, indicating a photothermal MOA. Both PI values represent the highest reported. The oxygen-dependent MOA of established PSs hampers effective clinical deployment. We anticipate that small molecule-based agents with a photothermal MOA, such as the BODIPY-based compounds presented here, may overcome this limitation and offer a promising new avenue for cancer therapy.

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