New photosensitizing drugs for photodynamic therapy of resistant cancers and microbes

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The major challenges in modern medicine encompass drug-resistance associated with advanced stage diseases that cannot be completely cured. Emerging evidence suggests that the unique mechanisms of photodynamic therapy (PDT) could be utilized to overcome drug resistance and even to re-sensitize resistant cells to standard therapies. Moreover, with the development of nanotechnology, light activation may be used not only to damage biological targets but also to enable controlled drug release to inhibit escape pathways that may lead to resistance or cell proliferation. The purpose of our studies is to determine and compare properties of structurally related but with various polarity bacteriochlorins in the context of their biomedical applications. The in vitro biological activity has been investigated against A549, B16F10 and CT26 cancer cells. The optimal formulation for photosensitizers and their time-dependent cellular uptake were described and characterized by fluorescence microscopy, dynamic light scattering (DLS) and transmission electron microscopy (TEM). We have demonstrated that Pluronic P123 efficiently loads hydrophobic and amphiphilic photosensitizers, increases their stability, improves cellular uptake, biodistribution, pharmacokinetics and enables the efficient generation of hydroxyl radicals resulting in efficient PDT of various types of cancers including melanoma.3 Designed by us photosensitizers with pH-sensitive block copolymers overcome the resistance of melanoma to PDT due to increased selectivity towards tumor and combine effect of oxidative stress in target tissue with a systemic immune response triggered by acute, local inflammation. Moreover, our most recent studies on strategies with multiple mechanisms of action based on light-activated hybrid materials, to overcome the pathogen's resistance will be discussed. The antimicrobial activity of these new entities in combination with light was tested against gram-positive, gram-negative bacteria and fungi. The unique structural and spectroscopic properties as well as redox or photochemical reactivity makes these materials appropriate to provide innovative antimicrobial platforms with simultaneous prevention of resistance development.

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