In Vitro Cellular Uptake and Dimerization of Signal Transducer and Activator of Transcription-3 (STAT3) Identify the Photosensitizing and Imaging-Potential of Isomeric Photosensitizers Derived from Chlorophyll-a and Bacteriochlorophyll-a

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Abstract

ABSTRACT: Among the photosensitizers investigated, both ring-D and ring-B reduced chlorins containing the *m*-iodobenzyloxyethyl group at position-3 and a carboxylic acid functionality at position-17[2] showed the highest uptake by tumor cells and light-dependent photoreaction that correlated with maximal tumor-imaging [positron emission tomography (PET) and fluorescence] and long-term photodynamic therapy (PDT) efficacy in BALB/c mice bearing Colon26 tumors. However, among the ring-D reduced compounds, the isomer containing the 1′-*m*-iobenzyloxyethyl group at position-3 was more effective than the corresponding 8-(1′-*m*-iodobenzyloxyethyl) derivative. All photosensitizers showed maximum uptake by tumor tissue 24 h after injection, and the tumors exposed with light at low fluence and fluence rates (128 J/cm^2, 14 mW/cm^2) produced significantly enhanced tumor eradication than those exposed at higher fluence and fluence rate (135 J/cm^2, 75 mW/cm^2). Interestingly, dose-dependent cellular uptake of the compounds and light-dependent STAT3 dimerization have emerged as sensitive rapid indicators for PDT efficacy in vitro and in vivo and could be used as *in vitro/in vivo* biomarkers for evaluating and optimizing the in vivo treatment parameters of the existing and new PDT candidates.