Synthesis of the pH-Responsive P(V)porphyrin Photosensitizer Based on Intramolecular Electron Transfer

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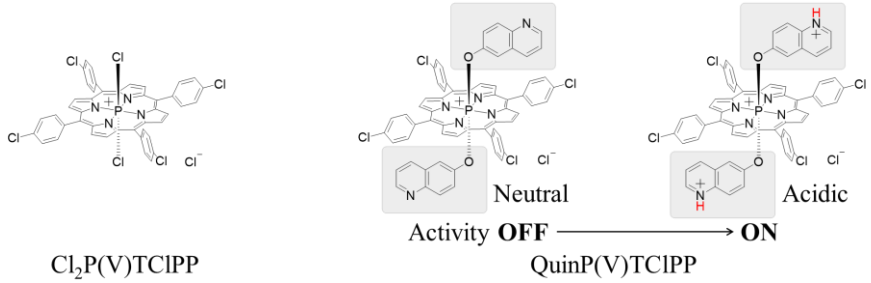
Photodynamic therapy (PDT) is a less invasive cancer treatment, and porphyrin derivatives are the important photosensitizers for PDT. Biomolecule oxidation through the formation of reactive oxygen species, such as singlet oxygen ($^1O_2$), is the important mechanism of PDT by porphyrins, however, hypoxic condition of tumors suppresses the PDT effect. To solve this problem, we have studied the porphyrin P(V) complexes, which can oxidize biomacromolecules through electron transfer.[1,2] In this study, we synthesized dichloroP(V)tetrakis(4-chlorophenyl)porphyrin (Cl_2P(V)TClPP) by focusing on the electron transfer mechanism. By introducing chlorine groups to the *meso*-phenyl groups of porphyrin ring, the redox potential (one electron reduction) of Cl_2P(V)TClPP was significantly lower than other similar P(V)porphyrin derivatives.

Furthermore, focusing on the fact that tumor tissues are slightly acidic than normal tissues, the quinoline-connecting P(V)porphyrin (QuinP(V)TClPP) was synthesized to control the photosensitizing activity of P(V)porphyrin by pH, as previous report.[1] Singlet excited state of QuinP(V)TClPP was effectively quenched under neutral condition and recovered under acidic condition. The pK_a of protonated QuinP(V)TClPP, which was analyzed from the absorption spectral change, was 4.6. The protein photodamaging effect was evaluated by light irradiation (585 nm, 2 mW/cm^2) with a light-emitting diode, as previous report using human serum albumin.[2] QuinP(V)TClPP photosensitized protein oxidation and the damaging quantum yield was increased under an acidic condition. These findings suggest that PDT activity of QuinP(V)TClPP can be switched in acidic cancer cells.



Cl_2P(V)TClPP QuinP(V)TClPP

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