DOCTORAL THESIS

Synthesis, characterization, photophysics and bioactivity studies of porphyrinoid and porphyrinate lanthanide based materials

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Synthesis, Characterization, Photophysics and Bioactivity Studies of Porphyrinoid and Porphyrinate Lanthanide Based Materials

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Abstract

A series of free base porphyrins and porphyrinate lanthanide complexes were designed, synthesized and characterized. Their photophysical properties and bioactivities were investigated in detail.

A series of amphiphilic porphyrin derivatives bearing different numbers of triphenylphosphonium cations and alkoxyl chains at different position were synthesized. The photophysical properties (UV absorption, emission spectra, singlet oxygen generation) were recorded and compared with typical porphyrin properties of tetraphenylporphyrin (H_2TPP). The in-vitro performance of these complexes, such as cell permeability and imaging, were monitored by confocal microscopy. Furthermore, two amphiphilic boron-dipyrromethene (BODIPY) porphyrin conjugates were synthesized. These two compounds exhibit large two-photon absorption cross-section values (1725 GM and 1407 GM, respectively) determined by the open-aperture Z-Scan method and show the potential as a new generation of photodynamic therapy agent via two photon excitation.

A series of lanthanide porphyrinate dimers (Ln = Yb^{III}, Er^{III}) were designed and obtained. The luminescent properties of these complexes were examined. The

complexes exhibit properties typical of lanthanide porphyrinate complexes and even have better performance than their monomers with enhanced NIR ytterbium emission at 1030 nm and 1555 nm for Yb^{III} and Er^{III} respectively. Moreover, a series of Yb^{III} lanthanide BODIPY conjugates based on the donor-acceptor framework were designed and synthesized. Photophysical studies show that the donor moiety (BODIPY) can absorb the light and transfer its energy to the Ln^{III} porphyrinate counterpart through the Förster energy transfer process, significantly enhancing the Yb^{III} NIR emission with good nonlinear properties.

On the basis of the above research, another series of amphiphilic lanthanide (Ln = Yb^{III}, Er^{III}) porphyrinate were subsequently prepared and fully characterized. Among these complexes, the ytterbium complex Yb-Rh was found to show not only impressive NIR emission with linear and nonlinear excitations in water but also mitochondria specific in HeLa cells confirmed by linear and multi-photon confocal laser scanning microscopy. Apart from this, it was found that an ytterbium complex (Yb-N) can recognize in-vitro anionic phospholipids and demonstrate visible to NIR emission. Anionic phospholipids are largely absent from the external leaflet of the plasma membrane of mammalian cells under normal conditions. Exposure of phosphatidylserine on the cell surface occurs

during apoptosis, necrosis, cell injury, cell activation, and malignant transformation. Our complex had been examined in five cancer cell lines (HeLa, A549, HK-1, HONE-1 and SK-N-SH) and three normal cell lines (QSG-7701, MRC-5 and WPMY-1) via confocal microscope and flow cytometry. The results of isothermal titration calorimetry have shown a strong binding between our complex (Yb-N) and phosphatidylserine (PS). In addition, a motif compound, metal free ligand Lig-N, was synthesized in conjunction with Yb-Rh acting as the negative control. Anionic phospholipids on tumor vessels could potentially provide markers for tumor cell targeting and imaging, and also serve as the drug delivery radar.

Lastly, a highly sensitive and selective ytterbium porphyrinate complex was synthesized to detect Hg^{2+} ion with responsive emission in the visible and near infra-red ($^2F_{5/2} \rightarrow {}^2F_{7/2}$) region in aqueous condition.

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