Efficient water-soluble, membrane-permeable and durable rotaxane-type porphyrin dyes used as photosensitizers for photodynamic therapy

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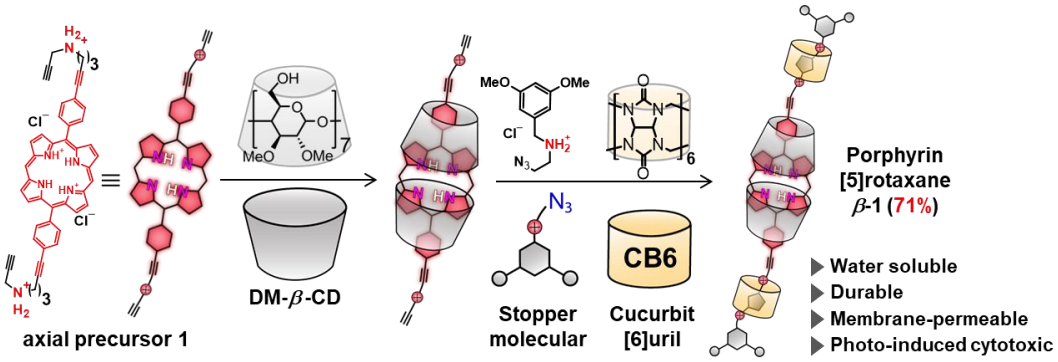
Photodynamic therapy (PDT) is an effective cancer treatment method that utilizes the generation of reactive oxygen species through light irradiation to photosensitizers. Porphyrin dyes are representative photosensitizers, and some of them are already clinically used for PDT. However, there are few reports of porphyrin derivatives having water-solubility, membrane-permeability, and photo-durability all in one for high therapeutic efficacy. We have developed water-soluble, rotaxane-type fluorescent dyes consisting of fluorescent molecules encapsulated within cyclodextrin derivatives (CDs)[1]. The outer CDs solubilized rotaxanes in water and improved their photo-durability due to the encapsulation of the inner fluorescent molecule for reactive oxygen species generated.

In this study, we planned to adapt the rotaxane strategy to porphyrin derivatives [2]. We synthesized [5]rotaxane ***β*-1** in a high yield by forming the complex of axial precursor **1** and dimethyl-*β*-CD (DM-*β*-CD) in H_2O and then adding stopper molecules and cucurbit[6]uril (CB6). Although the axial precursor **1** was insoluble in water, ***β*-1** was soluble, demonstrating the role of the outer CD. In addition, ***β*-1** showed higher photo-durability, cell membrane-permeability, and photo-induced cytotoxic ability than talaporfin sodium, presently used as a clinical photosensitizer. These results show that the rotaxane-type porphyrins might have potential for being ideal PDT drugs.



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