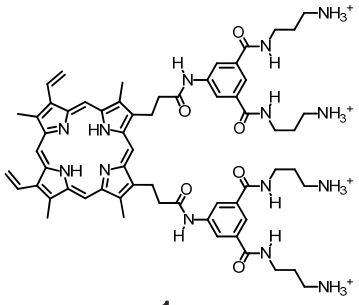
ポリアミン修飾によりミトコンドリアを標的する光線力学的療法用剤の開発

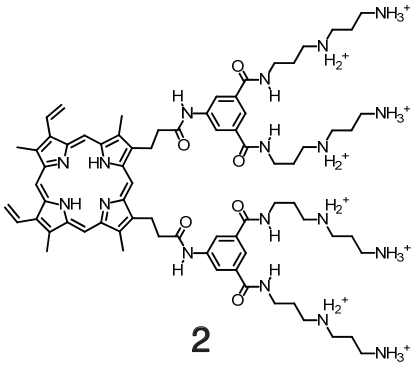
プロジェクト責任者	北海道大学大学院地球環境科学研究院
	教授　小野田 晃

プロジェクト概要

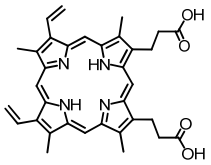
光線力学的療法（Photodynamic Therapy：PDT）は、腫瘍親和性のある光感受性物質である薬剤を投与した後、腫瘍組織にレーザ光を照射することにより光化学反応を引き起こし、腫瘍組織を変性壊死させる選択的治療法である。より低濃度で高い抗腫瘍効果を示す薬剤として、ポリアミン修飾によりミトコンドリアを標的する光線力学的療法用剤を開発した。本技術で調製した光線力学的療法用剤は抗腫瘍効果が約10倍に向上することをin vitroの細胞実験にて実証しており、in vivoでの利用を研究している。



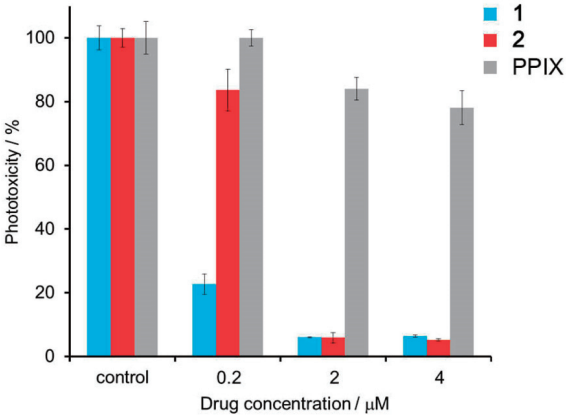
1



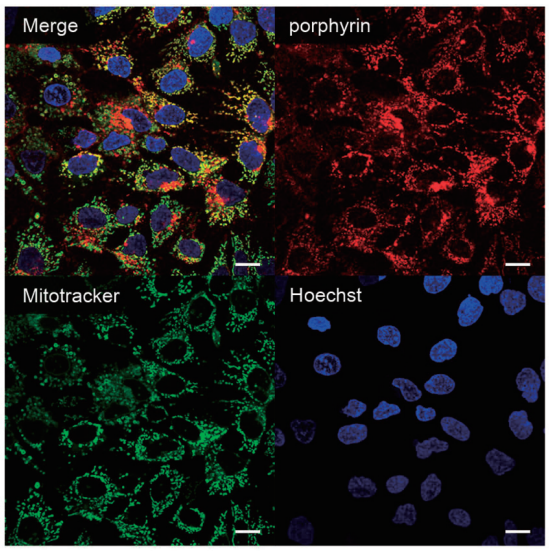
2



PPIX



Light toxicity of compounds **1** (blue), **2** (red), and PPIX (gray) in HT29; 660 nm light, 48 mW•cm^{-2}, 6 min irradiation.



Fluorescence and optical images of HEP3B cells after 12 h incubation with (a) **1** and (b) **2** (1 μM). The nuclei were stained with Hoechst for 4 h, and the mitochondria were stained with Mitotracker green for 2 h. Red emission channel showing the fluorescence of the compound. Green channel with mitochondria tracker green. Blue emission channel with the Hoechst stain. The scale bars represent 20 μm.

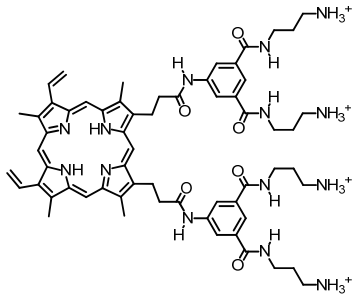
対象疾患：肺癌、悪性脳腫瘍、**技術の特徴**：ミトコンドリアへのターゲッティングによる光細胞毒性の向上

Photodynamic Therapy Reagents Targeting Mitochondria Using Polyamine Tethers

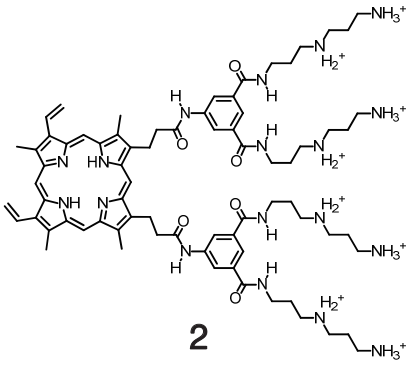
Principal Investigator	Faculty of Environmental Earth Science, Hokkaido University
	Professor Akira ONODA

Project Outline

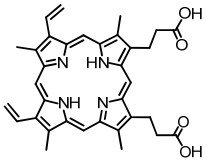
Photodynamic therapy (PDT) is a therapy inducing a photochemical reaction by irradiating tumor tissue with a laser beam after the administration of a photosensitizer, thereby tumor cells within the irradiated region. A photodynamic therapeutic agent targeting mitochondria by polyamine modification was developed as a drug that exhibits a high antitumor effect at a lower concentration. The photodynamic therapy agent prepared by this technology has been demonstrated by in vitro cell experiments that the antitumor effect is improved about 10 times. The application in vivo is currently underway.



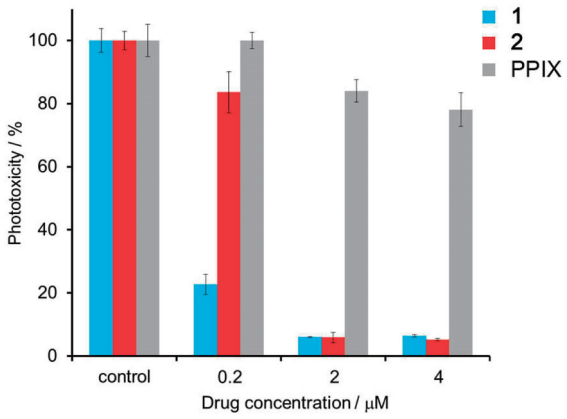
1



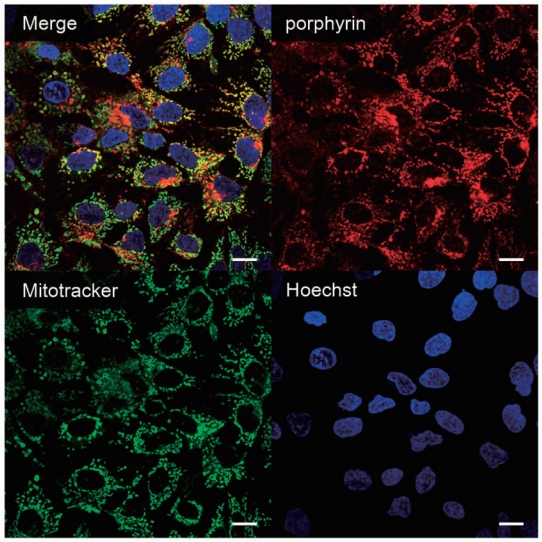
2



PPIX



Light toxicity of compounds 1 (blue), 2 (red), and PPIX (gray) in HT29; 660 nm light, 48 mW•cm^{-2}, 6 min irradiation.



Fluorescence and optical images of HEP3B cells after 12 h incubation with (a) 1 and (b) 2 (1 μM). The nuclei were stained with Hoechst for 4 h, and the mitochondria were stained with Mitotracker green for 2 h. Red emission channel showing the fluorescence of the compound. Green channel with mitochondria tracker green. Blue emission channel with the Hoechst stain. The scale bars represent 20 μm.

Target disease: Lung cancer, malignant brain tumor. Technology features: High phototoxicity enabled by targeting mitochondria via polyamine tethers