

## 論文の内容の要旨

論文題目 Development of novel fluorescent probes based on rhodol scaffolds for live cell/tissue imaging (新規ロドール型蛍光プローブの開発と細胞・組織のライブ蛍光可視化への応用)

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Fluorescence imaging in combination with fluorescent probes has been widely used to visualize specific biological phenomena and to understand physio-pathological conditions in real time. In this study, we designed and developed two types of novel fluorescent probes. The first one is photoactivatable fluorophores with improved intracellular retention, and the second one is new activatable yellow-emitting fluorescence probe for  $\beta$ -galactosidase based on new carborhodol scaffold.

Photoactivatable fluorophores are photofunctional small molecules that are weakly fluorescent before light irradiation but recover their original fluorescence after light irradiation. However, most of the existing small-molecular photoactivatable fluorophores lack of sufficient cell membrane permeability and intracellular retention. In this study, we have designed and developed non-fluorescent, cell-permeable photoactivatable fluorophores, photoactivatable SPiDERs (paSPiDERs), which exhibit fluorescence activation upon light irradiation, accompanied by the generation of a quinone methide intermediate that binds covalently to intracellular proteins. The fluorescence signal is durable for 24 hours, resistant to fixation and compatible with immunostaining, and selective cell labeling can be achieved at single-cell resolution.

Activatable fluorescent probes targeting enzymes upregulated in cancer has been developed for cancer-specific fluorescence imaging. Here, we developed yellow-emitting fluorescent probes that can potentially be used in combination with green-emitting and red-emitting fluorescent probes in order to detect cancer sites with improved sensitivity and specificity. By means of a synthetic approach to find a suitable scaffold dye for activatable probe of our purpose, we developed new series of yellow-emitting carborhodol dyes and found a promising scaffold. Based on the scaffold, we developed highly activatable fluorescence probe for  $\beta$ -galactosidase and successfully achieved fluorescence imaging of the enzyme-expressing cells.

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