水溶性 pH シアニン色素の応答型自己集合を利用する迅速かつ選択的な腫瘍検出

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Fast and selective tumor detection by water-soluble cyanine dye based on its pH-responsive aggregation (*[1] Graduate School of Engineering, Kyoto University, [2]Radiation Biology Center, Kyoto University*) ○Shuai Shao,[1] Huiying Mu,[1] Koji Miki,[1] Hiroshi Harada,[2] Kouichi Ohe[1]

We have developed a series of indocyanine green derivatives **CypHs** that exhibit pH-responsiveness due to the equilibrium between ring-opening and ring-closing of the 1,3-thiazinane incorporated in their structure. [1,2] Moreover, we found that the closed-ring form of **CypHs** is harder to aggregate than the open-ring form, probably because of its non-planar structure. Given this, we developed **CypH2S** as a contrast agent through the pH-responsive aggregation by introducing two sulfonate groups to the cyanine dye scaffol. It has been clearly confirmed that **CypH2S** with improved water-solubility exhibits good pH responsiveness in buffer solutions and the pH-responsive aggregation of **CypH2S** was characterized by dynamic light scattering and transmission electron microscopy. **CypH2S** facilitates fast and selective tumor visualization through its good fluorescent activation and pH-responsive aggregation in xenografted mice.

Keywords : pH-responsive, cyanine dye, aggregation, fluorescence imaging, tumor detection

当研究室では、構造中に含まれる 1, 3-チアジナン環の開環−閉環に基づく pH 応答型イドシアニングリーン誘導体 **CypHs** を開発している[1, 2]。また、閉環型 **CypHs** は開環型より凝集しにくいことを明らかにしている。これは開環型分子が非平面型構造であるためと考えられている。本研究ではシアニン色素の骨格に 2 つのスルホナト基を導入することで、pH に応じて自己集合できる蛍光プローブ **CypH2S** を開発した。高い水溶性を示す **CypH2S** が緩衝液中においてよい pH 応答性を示すことが確認された。また、動的光散乱測定と透過型電子顕微鏡観察により、**CypH2S** は自己集合体のサイズが pH に依存し変化することを見出した。さらに、**CypH2S** が迅速かつ選択的に担癌マウスの腫瘍の検出に利用できることも確認した。

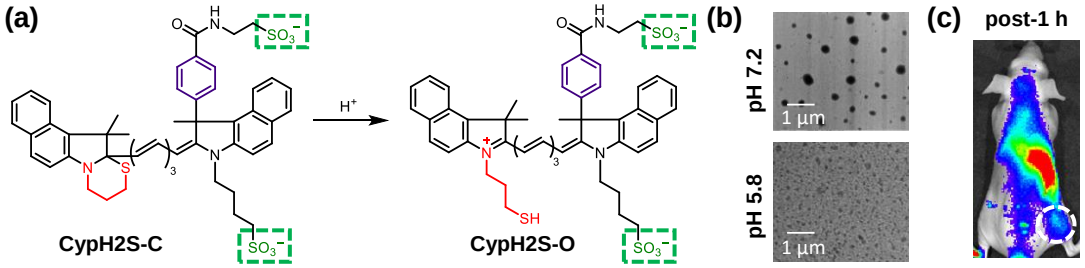

Figure 1. (a) pH-Responsive probe **CypH2S** in an equilibrium between **CypH2S-C** (closed-ring form) and **CypH2S-O** (open-ring form). (b) TEM image of self-assemblies of **CypH2S** (c) In vivo fluorescence imaging of tumor-bearing mice administrated with **CypH2S** (100 μM in 200 μL saline).

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