Development of a novel fluorescent probe for detection of extracellular sulfatase

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Sulfatases cleave sulfate esters in biological systems and play a key role in regulating the sulfation states of many physiological molecules.[1] Among human sulfatases, sulfatase-1 and sulfatase-2 have been implicated in the modification of sulfate moieties on glycosaminoglycans such as heparan sulfates and been reported to be secreted into the extracellular matrix.[2] Extracellular sulfatases are of great interest as they are upregulated in many cancer cells.[3] Previously, several probes having blue or green fluorescence emission have been developed to detect steroid sulfatases, which are located in the ER.[4] However, no probe has been developed yet for the detection of extracellular sulfatases. Thus, developing a fluorescent probe for detecting extracellular sulfatase activity is highly in demand, and the probe could be a valuable tool for the detection of cancer cells.

In this study, we aimed to develop a plasma membrane-targeting probe that can detect extracellular sulfatase secreted by cancer cells. Nile red fluorophore was chosen to be localized in the plasma membrane due to its lipophilic properties. To confirm the reactivity of the probe towards a sulfatase, the hydrolysis of the probe by a bacterial sulfatase was examined both *in vitro* and in cellular experiment. In fluorescence spectrometry studies, when the probe was hydrolyzed, it showed a 20-nm blue-shift of the emission spectrum in lipid environment. Similarly, the cellular experiment indicated a rapid and dramatic change in the probe localization from the plasma membrane to intracellular regions, suggesting that our probe has potential to specifically detect cancer cells based on localization change.

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