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Visualizing Matrix Metalloproteinase-2 Activity Using Extracellular Matrix-Immobilized Fluorescence Resonance Energy Transfer Bioprobe in Cancer Cells

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Abstract : Visualizing matrix metalloproteinases (MMPs) activity is necessary for understanding cancer metastasis because they are implicated in cell migration and invasion by degrading the extracellular matrix (ECM). While much effort has been made to sense the MMP activity, but extracellularly long-term monitoring of MMP activity still remains challenging. Here, we report a collagen-bound fluorescent bioprobe for the detection of MMP-2 activity in the extracellular environment. This bioprobe consists of ECM-immobilized part (including collagen-bound protein) and MMP-sensing part (including peptide substrate linked with fluorescence resonance energy transfer (FRET) coupler between donor green fluorescent protein (GFP) and acceptor TAMRA dye), which was constructed through intein-mediated self-splicing conjugation. Upon being immobilized on the collagen-coated surface, this bioprobe enabled efficient long-lasting observation of MMP-2 activity in the cultured cells without affecting cell growth and viability. As a result, the FRET ratio (acceptor/donor) decreased as the MMP2 activity increased in cultured cancer cells. Furthermore, unlike wild-type MMP-2, mutated MMP-2 expression (Y580A in the hemopexin region) gave rise to lowering the secretion of MMP-2 in HeLa. Conclusively, our method is anticipated to find applications for tracing and visualizing enzyme activity.

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