Development of photoswitchable protein that inhibits actin filament polymerization by near-infrared light irradiation

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Actin filaments in cells are essential for many cell functions such as cell migration, proliferation, and contraction. We wondered if we could regulate actin polymerization non-invasively, we could manipulate the mechanical force required for cell growth, motility, and cytoskeletal rearrangements. To this end, we noted the Rap1GAP protein. The Rap1GAP is known as GTPase-activating protein specific for Raps that are small monomeric GTP-binding proteins. The purpose of this study was to develop the genetically-encoded photoswitchable protein, which inhibited actin polymerization.

We used the near-infrared-responsive BphP1-QPAS1 optogenetic pair (1). The BphP1 was combined with plasma membrane translocating peptide, and the enzymatic domain of Rap1GAP was fused to QPAS1 and fluorescent protein (Rap1GAP-QPAS1). Then they were co-transfected to the HeLa cells. Firstly, the Rap1GAP-QPAS1 was localized at cytoplasm, whereas irradiation of 740 nm allowed Rap1GAP-QPAS1 to translocate to the plasma membrane. Moreover, the area of cells was becoming smaller than that of before irradiation. These results indicated that the enzymatic domain of Rap1GAP is translocated to the plasma membrane by irradiation of infrared, and inhibited the actin polymerization by suppressing the Rap1.

(1) Redchuk TA et al., Nat. Chem. Biol. 13, 633-639 (2017)