Core Alkynylated FLIPPER for Fluorescence Membrane Tension Probes

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The plasma membrane is a key interface that mediates cell mechanobiological responses to external mechanical stimuli. For example, a high stiffness environment induced the metastatic phenotype of integrin that is related to cancer.[1] To understand the mechanobiological response of the cell, a number of techniques focusing on the plasma membrane tension have been introduced**.** The most common methods are micropipette aspiration and atomic force microscope cantilevers. These methods can provide quantitative measurements but are considered invasive to the plasma membrane.

Fluorescence bioimaging allows researchers to monitor biomolecular processes in living cells using a noninvasive optical method. Recently, our group introduced a small organic molecule based on the dithienothiophene skeleton (FLIPPER) for a fluorescence membrane tension probe.[2] The working principle of FLIPPER probes is based on the twisted conformation of electron donor-acceptor dithienothiophene dimers. Planarization upon mechanical stimuli shifts excitation to the red along with the increase in fluorescence intensity. Therefore, the modification around the mechanosensitive bond greatly influences the performance of the probe in membranes.[3]

Organic compounds with aromatic groups that are conjugated through triple bond linkages show efficient electronic communication along their conjugated structures. This effect can be attributed to the cylindrical symmetry of the triple bond which is able to maintain conjugation between adjacent phenyl groups regardless of the relative orientation of the aromatic planes.[4] Herein, we report a series of novel FLIPPER probes having mono- and double-alkyne bonds at the central mechanosensitive bond between dithienothiophene dimers. The different dihedral angles between two dithienothiophene dimers could be due to several possibilities of p-orbital overlap, which can lead to a difference in photophysical properties upon planarization in different environments. The findings demonstrated the mechanosensitivity properties of the novel FLIPPER probes. Additionally, an examination of their characteristics in vesicles and cells as well as an analysis of their structural details are disclosed.

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