Endoplasmic Reticulum-Targeted Polarity-Sensitive Fluorescent Probes for Live Cell Imaging

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Résumé

The Endoplasmic Reticulum (ER) is an essential and dynamic organelle involved in protein synthesis, lipid metabolism and calcium regulation. ER dysfunction is associated with numerous diseases, including neurodegenerative diseases, inflammation, and cancer1, creating a strong need for tools able to image and monitor its structure in living cells. In this regards, small-molecule fluorescent probes are particularly attractive for live cell imaging. Among them, environment-sensitive fluorophores such as solvatochromic dyes are valuable for sensing local polarity and lipid organization of biomembranes through changes in their fluorescence properties, enabling ratiometric fluorescence imaging and quantitative analysis of membrane properties2. Most reported ER probes are based on fluorophores such as BODIPY, Nile Red, naphthalimides, coumarins, or rhodamines, but often suffer from poor aqueous solubility, limited sensitivity to the environment polarity and photostability, small Stokes shifts, or demanding syntheses. In contrast, fluorene-based push–pull dyes offer attractive photophysical properties including outstanding solvatochromism, high extinction coefficients and fluorescence quantum yield, red-shifted emission, and high photostability3. Here, we present fluorene-based fluorescent probes functionalized with specific ER-targeting units such as propyl chloride, phenylsulfonamide, or glibenclamide enabling selective localization. The obtained fluorene-based probes display significant solvatochromism in organic solvents and in models of lipid membranes. Moreover, ratiometric fluorescence microscopy techniques were used to prove sensitivity of synthesized probes to polarity and lipid order of ER membranes of live cells.

Mots-Clés: Endoplasmic reticulum, fluorescent molecular probes, cellular imaging

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