Single-molecule optical study of cholesterol-mediated dimerization process of EGFRs in different cell lines

CHIEN YU LIN, JUNG Y. HUANG, Department of Photonics, Chiao Tung University, LEU-WEI LO, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes — A growing body of data reveals that the membrane cholesterol molecules can alter the signaling pathways of living cells. However, the understanding about how membrane cholesterol modulates receptor proteins remains lacking. In this study we applies single-molecule optical tracking on ligand-induced dimerization process of EGFRs in the plasma membranes of several cancer and normal cell lines. We tracked individual EGFR and dual correlated receptors in the plasma membranes of live cells. We developed an energetic model based on the generalized Langevin equation and the Cahn-Hilliard equation to help extracting information from single-molecule trajectories. From the study, we discovered that ligand-bound EGFRs move from non-raft areas into lipid raft domains. This ligand-induced motion is a common behavior for all cell lines under study. By manipulating the total amount of cholesterol with methyl-β-cyclodextrin and the local concentration of cholesterol with nystatin, we found that the amount of cholesterol can affect the stability of EGFR dimers. The EGFR dimers in the plasma membrane of normal cells are more sensitive to the local concentration changes of cholesterol than EGFR dimers in the cancer cells.

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