

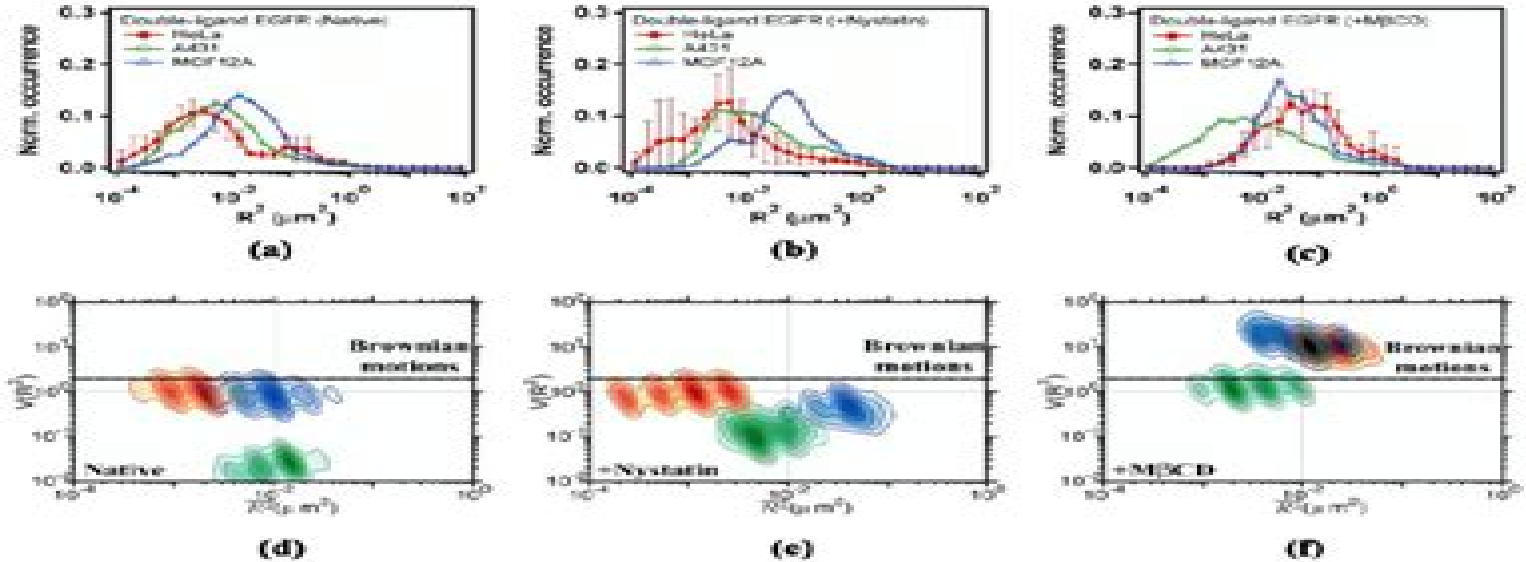


Figure 6. a, b, c Histograms of MSDs and (d, e, f) $V(\overline{R_r^2}) - \overline{R_r^2}$ plots of correlated Qdot585-EGF-EGFRs diffusing in the plasma membrane of (a, d) native cells, (b, e) nystatin-pretreated cells, and (c, f) M/PCD-pretreated cells. Trajectory segments with a degree of correlation exceeding 0.8 were analyzed. Trajectories were sampled with a frame period of $\tau=25$ ms. Data are shown in red for HeLa cells, green for A431 cells, and blue for MCF12A cells.

receptor to lipid domains. Based on the $V(\overline{R_r^2}) - \overline{R_r^2}$ analysis of single-molecule EGFR trajectories in live cells, we proposed a simple molecular-level model. Ligand binding to an EGFR can induce a conformational change of EGFR that may expose some residues with high cholesterol affinity. Thereby, liganded EGFRs may provoke an aggregate of their neighboring raft lipids (such as GM1) to form a cholesterol-rich lipid domain. Figure 7f presents a schematic representation (center) of correlated EGFRs (green) in a cholesterol-rich (yellow) lipid domain. Without membrane cholesterol (right schematic of Figure 7f), a deterministic dimerization interaction dominates, which causes the $V(\overline{R_r^2})$ value to be increased to higher than 10 as shown in Figure 6f. Liganded EGFR can also be attracted to an existing lipid domain. As pointed out above that coupling between inner and outer leaves of an asymmetric lipid bilayer could produce inhomogeneities of lipid phases with a nonzero curvature [37]. Such membrane deformations could affect the movements of liganded receptors with the deformed lipids. Because the three cell lines used for this study are quite diverse, our results may be useful to shed light on the mechanism of cholesterol-mediated interaction between activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells activated receptors in live cells.

5. CONCLUSIONS

In summary, we studied single-molecule optical trajectories of EGFRs moving in the plasma membranes of two cancerous cell lines (A431 and HeLa) and one normal epithelial cell line (MCF-12A). A stochastic

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