#### 2 Exploring in vivo cholesterol-mediated.

three cell lines used for this study are quite diverse, our results may be useful to shed light on the mechanism of cholesterolmediated interaction between activated receptors in live cells. content uscel in this document ES. only for view purpose. The original open access article Can be found http://doi.org/10.1186/s13628-016-0030-5 at

Keywords: Autotroph, Cytokinesis, Heterozygous., Unicellular microorganism, A coordinating organ of human body, Juicy fluid within flowers

## 1 Background

Receptor proteins are ubiquitous in the plasma membrane of mammalian cells, which transduce information about cellular environment to intracellular signaling networks Vaquerizas et al (2009); Yosef et al (2009); Purvis and Lahav (2013). There are approximately 1352 receptor proteins coded by human genome Almén et al (2009). The flow of information through those receptors is critically shaped by receptor interactions. The diverse cellular processes regulated by such receptor proteins include cell growth and division, differentiation, migration, and apoptosis Schlessinger (2000). Receptor signaling dysregulation is attributed to the pathogenesis of several diseases Gschwind et al (2004); Mendelsohn and Baselga (2000). Therefore, understanding the interactions, molecular processes and relevant structures of such signaling receptors is imperative.

Human receptor proteins, including the epidermal growth factor receptor (EGFR), share a common molecular architecture, consisting of an extracellular binding domain, a single transmembrane helix, a flexible juxtamembrane segment, and an intracellular tyrosine kinase domain Citri and Yarden (2006). Ligand binding to the extracellular domains induces conformational reorganization that promotes receptor dimerization, leading to the activation of the intracellular tyrosine kinase domain. However, conclusions about the mechanism of ligand-induced dynamic recruitment and dimerization of membrane-associated receptors remains controversial Kusumi et al (2012). Conventional steady-state ensemble approaches cannot be used to address the stochastic nature of activated receptors that encounter each other in a highly heterogeneous and fluidic plasma membrane. Recent advancements in singlemolecule fluorescent imaging and tracking have provided further insights into the behavior of EGFR in vivo Teramura et al (2006); Chung et al (2010); Hiroshimaa et al (2012). For example, Lidke et al. devised a two-color quantumdot tracking method to visualize the state-dependent dimerization processes of human EGFR in living cells Low-Nam et al (2011). A hidden Markov model was used to extract the kinetic parameters of the underlying free, co-confined, and dimerized states.

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