Asymmetric quantum dots (QD) provide non-blinking imaging probes yielding orientation-dependent optical signals from individual cell surface proteins. The Invitrogen QD655 measures 12.8 x 5.8 nm and exhibits an initial fluorescence anisotropy of about 0.1. Calculated rotational correlation times for rotation in water about the particle short and long axes, 0.27 µs and 0.18 µs respectively, suggest that the nanoparticle can probe molecular rotation down to the µs timescale. We have used QD655 conjugated to A2 DNP-specific IgE to explore slow rotation of the Type I Fc rotation down to the

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a Wednesday, February 29, 2012

Inhee Chung

The Nature of Constitutive Activation of HER2 at the Single Molecule Level

Inhee Chung, Robert Akita, Lily Shao, Gabriele Schaefer, Mark Sliwowski, Ira Mellman.

Genentech, Inc., South San Francisco, CA, USA.

HER2 is a highly active kinase that is distinguished from the other HER family members in that no ligand has been identified to directly bind the receptor. HER2 can be trans-activated by forming complexes with other receptors, but it also exhibits constitutive activation when it is over-expressed. In fact, this ligand-independent activation plays an important role in driving the growth of HER2 amplified tumors. To gain further mechanistic understanding of the constitutive HER2 activation, we performed single molecule tracking studies of HER2 and its mutants on the living cell membrane and developed new analysis tools. From these studies, we found that activation of HER2 is less regulated by the structural features of its ectodomain than that of EGFR as we previously demonstrated. Rather, HER2 activation may be largely related to its interaction with membrane subdomains, which in turn modulates its local density. Indeed, we found that cholesterol content and distribution pattern on the membrane altered the diffusion dynamics of HER2 and its phosphorylation status. The modulation of HER2 activation by cholesterol may have relation to tumor cell response to trastuzumab.

Auditory Systems

3321-Pos Board B182

An Active Mechanism for Signal Detection in the Mammalian Ear

Daiibhid O. Mooloeligh, A.J. Hudspeth.

Howard Hughes Medical Institute and Laboratory of Sensory Neuroscience, The Rockefeller University, New York, NY, USA.

The ear’s exquisite sensitivity, sharp frequency tuning, and broad dynamical range result from an active process known as the cochlear amplifier. Although outer hair cells play a central role in cochlear amplification, their mechanism of action remains uncertain. In non-mammalian ears hair bundles, the sensory orga-

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