A symbiosis: tracking cell signaling with expression probes, quantum dots and a programmable array microscope (PAM)

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Keywords: single-molecule imaging, EGF receptor, dendritic cells

Quantum dots (QDs) are colloidal inorganic semiconductor nanocrystals composed typically of a CdSe, CdS or CdTe core and a ZnS shell. There are many advantages in the use of QDs as fluorophores: they can be excited over a broad spectral range and they have narrow emission bands that can be tuned from ultraviolet to infrared by adjusting size and composition. Their bright emission fluorescence and resistance to photobleaching make QDs ideal for single-particle detection and permit imaging over prolonged time periods. Because of these advantages, QDs are finding increasing use in *in vivo* and *in vitro* studies [1].

Activation of the erbB receptor tyrosine kinases (erbB1, 2, 3 & 4) induced by the extracellular binding of peptide ligands triggers signaling cascades responsible for cellular motility, cell division, and differentiation. We have genetically tagged the ErbB proteins with fluorescent proteins and/or the acyl carrier protein (ACP) sequence [2]. QDs have been targeted to receptors on the external cell surface through the growth factor receptor, EGF, or by covalently linking to the ACP tag allowing the visualization in living cells of individual receptors, the diffusion of which has been determined on different cell types. We have also used them to detect dimerization and activation of the transmembrane erbB proteins upon ligand binding. These reagents have revealed a new mode of retrograde transport of the activated receptor from filopodia to the surface of the cell [3,4]. The process is linked to treadmilling of actin filaments. This phenomenon acts as a biosensor, in that receptors are transferred from remote sites of detection/activation to the transduction mechanisms in the cell body.

Results from basic research studies of erbB tyrosine kinase receptors have led to the application of QD probes in delineating glioblastoma tumors in normal brain in collaboration with neurosurgeons. The objective of these studies is to facilitate the localization of tumor margins during surgery, thereby facilitating the accurate resection of the tumor with minimal loss of normal brain tissue.

A. Aretz, B. Hermanns-Sachweh, J. Mayer (Eds.): EMC 2008, Vol. 3: Life Science, pp. 335–336,
DOI: 10.1007/978-3-540-85228-5_168,