Nanoparticle Probe Design Principles for Single-Molecule Analysis of Cells and Tissues

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Numerous analytical tool have recently been developed to detect, count, and image individual molecules within cells and tissues. Nanomaterials are playing an important role in these ongoing efforts by providing tunable probes and substrates that amplify tiny signals into detectable optical signatures that are measurable as discrete events in microscopes and devices. This talk will describe recent results from the Smith Lab at the University of Illinois to engineer semiconductor nanocrystals as light-emitting probes to count and track nucleic acids and proteins within cells and tissues. Early variants of semiconductor nanocrystals exhibited limitations in stability, physical dimensions, and optical tunability that hindered widespread adoption and standardized use. These challenges have largely been overcome through rigorous studies of probe design principles in single-molecule applications. New technologies include photophysical engineering processes to precisely control light emission flux independently from wavelength,[1] new polymer coatings to shrink the hydrodynamic size from 30 to 7 nanometers while maintaining year-long stability and precise bioconjugation,[2] and image analysis tools to quantify absolute molecular stoichiometries in living cells.[3] We are using these new nanomaterials to observe accurate single molecule processes in the neuronal synapse,[4] to count nucleic acids in single cells,[5] and to quantitatively analyze signal transduction processes at the single-cell level.[6] This talk will further describe future developments needed to overcome barriers to widespread adoption and commercialization.

References

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