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Novel Fluorescent and Raman-Active Noble Metal Quantum Dots as a New Class of Biolabels

Few-atom silver nanoclusters created in dendritic, oligonucleotide, and peptide matrices exhibit size-tunable, discrete, highly polarizable electronic transitions with emission that is up to two orders of magnitude stronger than that from organic dyes. These new fluorophores are being developed through a modular approach enabling parallel optimization while separately optimizing membrane transport and in vivo conjugation chemistries. Significant progress on each of these points has been made, and a trifunctional linker with three orthogonal chemistries has been synthesized. This linker will facilitate the combination of all functionalities into a single multifunctional macromolecule. Separate tests of each component can be made while fluorophore creation studies progress in parallel. Our ultimate goal is the creation of small Ag nanocluster-based fluorophores that show strong fluorescence and/or Raman of the encapsulating scaffold. We have pursued several fronts, identifying peptide sequences that strongly bind Ag nanoclusters and showing they can pass through the plasma membrane through non-endocytotic pathways. These are being optimized for brightness and stability. We have also created high concentrations of Ag nanoclusters (Ag_{2-7}) in ss-DNA with excellent photostability, high detected single-molecule emission rates (ranging from 10,000 cps to 250,000 cps), and nearly no blinking. These oligonucleotide-encapsulated nanoclusters already offer ~10-fold improvement in brightness and photostability over existing fluorophores, while maintaining small size and having essentially no blinking on experimentally relevant timescales. Initial attempts at conjugation to proteins and cellular imaging will be reported. Synthesizing new mono or bifunctional dendritic scaffolds with $\text{C}\equiv\text{C}$ and $\text{C}-\text{D}$ bonds as Raman tags incorporated in the cores has enabled new, ultra narrow features to be observed as a shift from the laser excitation wavelength. Orthogonal functional groups for monovalent or divalent labeling and incorporation of coupling chemistries have now been added to the dendritic scaffolds. Separately, schemes for in vivo labeling of proteins and screening of peptide libraries are being performed to assay for the most effective labeling scheme. While many challenges remain, results from the second year of this Center's effort clearly demonstrate the advantages that our unique ultra bright materials offer for next generation cellular imaging studies.

Publications

Ritchie, C.M., Johnsen, K.R., Kiser, J.R., Antoku, Y., Dickson, R.M., Petty, J.T. 2007. Ag nanocluster formation using a cytosine oligonucleotide template. *J. Phys. Chem. C*, **111**: 175.

Yu, J., Patel, S.A., Dickson, R.M. 2007. *In vitro* and intracellular production of peptide-encapsulated fluorescent silver nanoclusters. *Angew. Chem. Int. Ed.*, **46**: 2028.

Zheng, Z., Nicovich, P.R., Dickson, R.M. 2007. Highly fluorescent noble metal quantum dots. 2007. *Ann. Rev. Phys. Chem.*, **58**: 409.