

New and Notable

Fluorescent Dendritic Nanoprobes: A New Class of Fluorescent Probes for Biological Applications

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The microscopist's utopia is filled with small, bright, photostable fluorescent probes. The contemporary toolbox of fluorescent probes—organic dyes, fluorescent proteins, and quantum dots—provides a range of sizes and photophysical properties, but we still await the perfect fluorescent probe.

In a recent *Biophysical Journal*, Kim et al. (1) at the University of Illinois at Urbana-Champaign describe the synthesis, photophysical characterization, and use of a new class of fluorescent probes that they have named fluorescent dendritic nanoprobes (FDNs). FDNs consist of generation-5 and generation-6 polyaminoamine (PAMAM) dendrimers, with diameters of ~5 nm, used as scaffolds for the conjugation of multiple Cy5 or Cy3 fluorophores as well as functional groups such as biotin and dibenzocyclooctyne.

The size of the FDNs places them on the same scale as fluorescent proteins: larger than single fluorescent dyes and smaller than quantum dots (2). The conjugation of multiple Cy5 fluorophores to the PAMAM dendrimers provides FDNs with a 6–10×

increase in photostability. Kim et al. (1) show that the photobleaching half-lives of the FDNs are ~140 s compared to 15 s for a single Cy5. The biological applications of the FDNs are illustrated with a single-molecule protein pull-down assay and an immunofluorescence experiment. Using a Cy5-FDN-secondary antibody to image microtubules in human kidney cells allows exposure times of 120 s compared to just a few seconds for single Cy5-labeled secondary antibodies. High-resolution fluorescence microscopy methods based on localization of fluorescent probes also benefit from the use of FDNs. As expected for the greater number of photons emitted from the FDNs, the position of a single FDN can be localized with greater precision than an individual Cy5 molecule: a 12-nm full width at half-maximum compared to a 23-nm full width at half-maximum.

Dendrimers have been used previously as scaffolds for fluorophores and functional groups for bioconjugation (3–6). These include polyphenylene dendrimers developed by Minard-Basquin et al. (3) and Oesterling and Mullen (4), and PAMAM dendrimers from Fei et al. (5). Although these systems are conceptually similar to the FDNs developed by Kim et al. (1), the FDNs benefit from being truly optimized for the single molecule and cellular imaging communities with a focus on water-solubility, brightness, and bioconjugation.

What remains to be seen is whether the FDNs will find widespread use in the biophysical community. The conjugation of fluorophores and functional groups to the PAMAM dendrimer is based on use of N-hydroxysuccinimide ester linkages, standard chemistry for fluorescent labeling. This makes it likely that other researchers will synthesize their own FDNs. While no fluorescent probe will be suitable for all applications, the FDNs are an exciting addition to the fluorescent probe toolbox as medium-sized, bright, photostable fluorescent probes with multiple options for bioconjugation.

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