Citations

Shift into high gear

Researchers needing a high-performance method to quantify subtle differences in DNA amount may want to consider shifting their attention to gel shifts. So argue Zhang et al., who introduce “QEMSA” (quantum dot electrophoretic mobility shift assay) in *ACS Nano*. The method capitalizes upon differences in the electrophoretic mobility of quantum dots (QDs) and DNA. QDs excel at producing bright, stable fluorescence, but languish at the back of the pack when electrophoresed in a standard agarose slab gel. But that’s a useful property, because when QDs are coated with streptavidin and incubated with biotinylated DNA to form a QD-DNA nanocomplex, the surface DNA conjugation increases the electrophoretic mobility of the assembly and accelerates migration. In QEMSA, it is greater band migration, not intensity, that heralds higher DNA concentrations. Preparing a standard curve of migration distance against DNA/QD ratio sets up straightforward determination of DNA amount from distance traveled. Strikingly, Zhang et al. show that QEMSA can distinguish 1.1-fold differences in DNA concentration; this is significant because quantitative PCR is considered to run into difficulty discriminating between DNA concentrations when the amounts vary by less than two-fold. The authors suggest that QEMSA’s sensitivity could be put to

good use in assaying copy number variations, some of which are believed to have physiological consequences even when differences are very small (eg, 4 vs 5 copies). In proof-of-principle detection of copy number difference, Zhang et al. used QEMSA to detect oncogene amplification in an ovarian cancer line compared with normal cells, at the same time confirming that there was no distinction between the samples in copy number of a reference sequence. As an example of another application in which small differences can be difficult to pick up reliably by quantitative PCR, the authors assessed DNA methylation by measuring the product obtained from methylation-specific PCR. Here QEMSA reliably teased apart 1.25-fold differences in methylation. This novel take on gel shift may represent a paradigm shift in the effort to accurately quantify DNA in genetic and epigenetic studies examining subtle but important variations.

Zhang et al. Mapping DNA quantity into electrophoretic mobility through quantum dot nanotethers for high-resolution genetic and epigenetic analysis. *ACS Nano*. [Epub ahead of print, December 7, 2011; doi:10.1021/nn204377k].

Learning by immersion

The fastest way to find out about a new environment is to jump into the thick of things. That’s a lesson not lost upon Yan et al., who describe a nanowire “endoscope” for peeking into cells in *Nature Nanotechnology*. The authors literally glue a tin oxide nanowire to the tapered tip of an optical fiber, which optically couples the 100-nm diameter nanowire to an excitation laser for delivering waveguided light or a spectrometer for detecting optical signals from the endoscope’s local environment. Unlike fluorescence imaging using a tapered optical fiber tip, the nanowire is small enough to slip through a cell membrane without rupturing the cell or noticeably affecting its health. Like previously described nanotube delivery systems, the new endoscope can deliver payloads into cells. However, instead of relying on the cell’s reducing environment to cleave disulfide bonds that tether the cargo to the nanotube, which can take up to half an hour, Yan et al. attach their payloads with a photocleavable linker. In this way, payload delivery can be controlled by brief ultraviolet illumination, a premise confirmed by fluorescence imaging of delivery and release of nanoprobe-inserted

Selective illumination of an adjacent quantum dot (QD) by a nanowire endoscope. Source: Nature Nanotechnology

quantum dots (QDs). Once delivered, the QDs can be lit up by nanoprobe-emitted illumination; because of the high directionality of the laser light, the endoscope could selectively trigger fluorescence of just one of a pair of QD clusters separated by only 2 μm . Focused illumination also enables high spatial resolution imaging of organic dyes; for instance, in a cell stained with a mitochondrial marker, an observer can focus exclusively on a picoliter region of that organelle. This specificity is not at the cost of temporal resolution, meaning the endoscope can also claim subcellular fluorescence tracking as an application. To establish the ability of the nanowire endoscope to collect (not trigger)

fluorescent signals, the authors preloaded a QD into the cytoplasm, illuminated the region from above, and imaged the QD through the nanoprobe. As expected, the signal fades sharply as the distance between the endoscope and QD grows, a property useful for high-resolution mapping. Other applications are sure to follow given the versatility of the nanowire endoscope, and should encourage cell biologists to dip into a whole new way of viewing their subject matter.

Yan et al. Nanowire-based single-cell endoscopy. *Nature Nanotechnol.* [Epub ahead of print, December 18, 2011; doi:10.1038/nnano.2011.226].

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