Monitoring Cancer Cell Changes With Quantum Dots

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One of the earliest events that changes a normal cell into a malignant one is known as deoxyribonucleic acid (DNA) hypermethylation, a biochemical alteration that inactivates critical tumor-suppressor genes. A team of investigators at Johns Hopkins University has developed a quantum dot-based method that can quantify DNA methylation in premalignant cells harvested from human patients.

Jeff Tza-Huei Wang, Ph.D., and Hetty E. Carraway, M.D., led the team of researchers that developed the method they call methylation-specific quantitative fluorescence resonance energy transfer (MS-qFRET). The details of their work appear in the journal *Genome Research*.

The MS-qFRET process starts by treating sample DNA with sodium bisulfite, which converts all unmethylated cytosines (one of the four nucleic acid components of DNA) into uracil, leaving any methylated cytosines unchanged. The treated DNA then is amplified using a modified polymerase chain reaction procedure that differentiates between methylated and unmethylated DNA. This procedure also introduces fluorescent markers and biotin molecules on each piece of methylated DNA. Finally, streptavidin-coated quantum dots are added to the amplified DNA, binding tightly to the biotin-linked DNA molecules.

Quantification of methylated DNA occurs by the FRET process, in which energy transfers between the fluorescent molecule and the nearby quantum dot. The amount of fluorescence quenching, measured using confocal microscopy, provides a sensitive and accurate measure of DNA

methylation. The technique is sensitive enough to enable the investigators to monitor methylation changes after premalignant cells are treated with drugs known to alter methylation patterns. The researchers also note that this technique is amenable to multiplexing, which affords the opportunity to compare multiple samples from the same patient.

This work, which was supported in part by the National Cancer Institute, is detailed in the paper “MS-qFRET: A quantum dot-based method for analysis of DNA methylation.” An investigator from the Lovelace Respiratory Research Institute in Albuquerque also participated in this study. An abstract of the paper is available at the journal's Web site.

Source: National Cancer Institute (news : web)